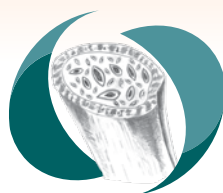




Congress Program



BMJD

6TH WORLD CONGRESS
on Controversies, Debates & Consensus
in Bone, Muscle & Joint Diseases

Bangkok, Thailand
November 8-10, 2018



Endorsed by



bmjd-congress.org

Timetable

Thursday, November 8, 2018	
	Hall A
15:15-15:45	Opening Session
15:45-16:10	Break
16:10-17:00	Asia Pacific League of Associations for Rheumatology (APLAR) Symposium: Recent progress on genetic and cellular rheumatology in APLAR
17:00-17:10	Break
17:10-18:00	Industry Symposium: Understanding patient needs in the treatment of symptomatic osteoarthritis Supported by Mylan
18:00	Networking Reception
Friday, November 9, 2018	
	Hall A
08:00-08:50	Session: JAK inhibitors should be first line before biologic agents Supported by Pfizer
08:50-08:55	Break
08:55-09:45	Industry Symposium: Management strategies for rheumatoid arthritis in 2018 Supported by Eli Lilly
09:45-10:00	Break
10:00-10:50	Session: How to deal with vaccination of patients with inflammatory arthritis
10:50-10:55	Break
10:55-11:45	Meet the Experts: Inflammation in osteoarthritis as a therapeutic target
11:45-11:55	Break
11:55-12:45	Industry Lunch Symposium: New perspectives with Diacerein Supported by TRB
12:45-12:55	Break
12:55-13:45	Meet the Experts: How to best manage osteoporosis in patients with arthritis
13:45-14:00	Break
14:00-14:50	Session: Osteoarthritis, a disease of the bone/subchondral bone? Implication for treatment Supported by Samumed
14:50-14:55	Break
14:55-15:45	Session: Biosimilars: Are rheumatologists and patients ready for transitioning patients from an originator to a biosimilar?
15:45-16:00	Break
16:00-16:50	Industry Symposium: Biosimilar infliximab: Switching from an originator to a biosimilar Supported by Celltrion
16:50-16:55	Break
16:55-17:55	Guided Poster Tour Supported by Samumed
Saturday, November 10, 2018	
	Hall A
08:00-08:50	Session: Management of challenging osteoarthritis cases in daily practice: Well-kept secrets
08:50-08:55	Break
08:55-09:45	Session: When is biologic monotherapy the treatment of choice?
09:45-10:00	Break
10:00-10:50	Session: Novel therapeutic targets and cellular therapies for osteoarthritis Supported by ORLIFE Pharmaceuticals - a MEDIPOST Company
10:50-10:55	Break
10:55-11:45	Session: Psoriatic arthritis: How to balance management of the skin and the joints
11:45-13:00	Lunch Break and Poster Viewing
13:00-13:50	Meet the Experts: Non-radiographic spondyloarthropathy: If you were paying for it, would you commence biologic therapy?
13:50-13:55	Break
13:55-14:50	Session: Intraarticular therapy for arthritis: Interesting new findings for patients Supported by Sanofi
14:50-15:00	Break
15:00-15:50	Meet the Experts: Lupus and pregnancy: Good news for the doctor and the mother
15:50-15:55	Break
15:55-16:25	Oral Abstracts and Award Presentations

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Welcome Letter

Dear Friends,

We would like to personally welcome you to the 6th World Congress on Controversies, Debates & Consensus in Bone, Muscle & Joint Diseases (BMJD), taking place November 8-10, 2018 in Bangkok, Thailand.

BMJD has enhanced the format of its congress program for 2018 offering participants a novel approach to yet more productive interactions and discussions between experts and participants through debates of controversial issues, and clinically relevant updates, that can be used in the day to day practice of physicians in the field.

Expert debates of the many advancements in the clinical and basic science fields of bone, muscle and joint diseases will focus on providing practical management solutions to a number of challenging and clinically relevant issues encountered in daily practice.

We thank you for your participation and contribution to the BMJD Congress and welcome you to Bangkok.

Sincerely,

BMJD Chairpersons



Johanne Martel-Pelletier

Canada



Jean-Pierre Pelletier

Canada



Boulos Haraoui

Canada

COMMITTEES

Congress Chairpersons

Mohit Kapoor, *Canada*

Tore K. Kvien, *Norway*

Kevin Pile, *Australia*

Scientific Program Committee

Laniyati Hamijoyo, *Indonesia*

Rohini Handa, *India*

Syed Atiqul Haq, *Bangladesh*

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Tsutomu Takeuchi, *Japan*

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Devendra K. Taneja, *India*

Wen-Chan Tsai, *Taiwan*

Huji Xu, *China*

Kazuhiko Yamamoto, *Japan*

Swan Sim Yeap, *Malaysia*

General Information

Congress Venue

Hilton Millennium
123 Charoennakorn Road
Klongsan
Bangkok 10600
Thailand

Language

The official language of the Congress is English.

Registration Desk

The registration desk will be open during the following hours:

Thursday, November 8, 2018	12:00 – 18:30
Friday, November 9, 2018	07:00 – 18:00
Saturday, November 10, 2018	07:30 – 17:30

Name badge

All participants are kindly requested to wear their name badges throughout the Congress in order to be admitted to the lecture halls and scheduled activities.

Certificate of attendance (non CME/CPD)

Certificates of attendance will be available for all participants on Saturday, November 10, 2018.

Exhibition

Exhibition will be open during session hours.

Clothing

Business casual for all occasions.

Smoking policy

This is a non-smoking event.

Refreshments

A Networking Reception will be held on Thursday, November 8, 2018 at 18:00.
Lunch and coffee will be served during the breaks.

Speakers' Preview Room

Invited speakers and oral presenters are invited to visit the Speakers' Preview Room to upload their presentations.

Poster Display

Please check the Scientific Program for the board number on which you should display your poster(s). Posters should be mounted between 07:30-08:30 on Friday, November 9, 2018 and removed by the end of the sessions on Saturday, November 10, 2018.

Photography

It is forbidden to take photographs, film or make recordings during the scientific program (sessions and posters).

Safety and Security

Please do not leave any bags or suitcases unattended at any time, whether inside or outside session halls.

Social Media

Follow BMJD on social media for the latest updates, key date reminders, and discussions with colleagues and experts from around the world.

Facebook - @BMJDCongress

LinkedIn - Controversies in Bone, Muscles & Joint Diseases (BMJD)

Twitter: @BoneAndMuscle

YouTube: BMJDCongress

We also invite you to tweet your comments live on-site from the congress.

Liability

The Congress Secretariat and Organizers cannot accept liability for personal accidents or loss or damage to private property of participants either during or directly arising from the 6th World Congress on Controversies, Debates & Consensus in Bone, Muscle & Joint Diseases (BMJD). Participants should make their own arrangements with respect to health and travel insurance.

Congress Organizer



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Scientific Program





The essential journal for timely clinical research

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Rheumatology

Thursday, November 8, 2018

15:15-15:45	Opening Session	Hall A
Chairperson:	Jean-Pierre Pelletier , Canada	
15:15-15:45	General Welcome Jean-Pierre Pelletier , Canada Johanne Martel-Pelletier , Canada Boulos Haraoui , Canada	
15:45-16:10	Break	
16:10-17:00	Asia Pacific League of Associations for Rheumatology (APLAR) Symposium: Recent progress on genetic and cellular rheumatology in APLAR	Hall A
Chairperson:	Wen Chan Tsai , Taiwan	
16:10	What do we learn from cross ethnic genetic studies in rheumatic diseases? Huji Xu , China	
16:30	Discussion	
16:35	Genetics and functional genetics of rheumatoid arthritis Kazuhiko Yamamoto , Japan	
16:55	Discussion	
17:00-17:10	Break	
17:10-18:00	Industry Symposium: Understanding patient needs in the treatment of symptomatic osteoarthritis <i>Supported by Mylan</i>	Hall A
Chairperson:	Worawit Louthrenoo , Thailand	
17:10	Treatment approach for osteoarthritis: Placing patient well-being at centre stage Jean-Pierre Pelletier , Canada	
17:30	Evidence from clinical trials in osteoarthritis: Selecting what matters for patient care Lucio Rovati , Italy	
17:50	Q&A/Discussion	
18:00	Networking Reception	

Friday, November 9, 2018

08:00-08:50

Session:
JAK inhibitors should be first line before biologic agents
Supported by Pfizer

Hall A

Chairperson:

Boulos Haraoui, Canada

08:00

How to start and how to taper JAK inhibitors
Tsutomo Takeuchi, Japan

08:20

Pros and cons of JAK inhibitors over biologic DMARDs
Mark C. Genovese, USA

08:40

Discussion

08:50-08:55

Break

08:55-09:45

Industry Symposium:
Management strategies for rheumatoid arthritis in 2018
Supported by Eli Lilly

Hall A

Chairperson:

Worawit Louthrenoo, Thailand

08:55

Welcome and introduction
Worawit Louthrenoo, Thailand

09:00

Management strategies for rheumatoid arthritis in 2018
Tore K. Kvien, Norway

09:30

Q&A

09:40

Closing remarks

09:45-10:00

Break

10:00-10:50

Session:
How to deal with vaccination of patients with inflammatory arthritis

Hall A

Chairperson:

Monika Østensen, Norway

10:00

Practical application of an immunization program in patients with inflammatory arthritis
Boulos Haraoui, Canada

10:20

Vaccination in patients with inflammatory arthritis - are they really safe?
Worawit Louthrenoo, Thailand

10:40

Discussion

10:50-10:55

Break

10:55-11:45	Meet the Experts: Inflammation in osteoarthritis as a therapeutic target	Hall A
Chairperson:	Ying Ying Katy Leung , Singapore	
10:55	Inflammation in osteoarthritis. Local, systemic or both: Therapeutic implications Johanne Martel-Pelletier , Canada	
11:15	The role of matrix degradation product in the inflammation and pain in OA Hyun Ah Kim , Korea	
11:35	Discussion	
11:45-11:55	Break	
11:55-12:45	Industry Lunch Symposium: New perspectives with Diacerein <i>Supported by TRB</i>	Hall A
Chairperson:	Pongsak Yuktanandana , Thailand	
11:55	Preclinical evidence supporting the therapeutic effect of Diacerein in osteoarthritis Johanne Martel-Pelletier , Canada	
12:05	An international, multicentre, double-blind, randomised study of the effect of Diacerein vs. Celecoxib in symptomatic knee osteoarthritis patients (DISSCO study) Jean-Pierre Pelletier , Canada	
12:20	Diacerein as an adjunct to Methotrexate in the treatment of rheumatoid arthritis: Results of a multicentre, double-blind, randomized, placebo-controlled trial Worawit Louthrenoo , Thailand	
12:35	Q&A/Discussion	
12:45-12:55	Break	
12:55-13:45	Meet the Experts: How to best manage osteoporosis in patients with arthritis	Hall A
Chairperson:	Yeong-Wook Song , Korea	
12:55	Risk factors for osteoporosis in patients with arthritis Swan Sim Yeap , Malaysia	
13:15	Treatment of glucocorticoid-induced osteoporosis Graeme Jones , Australia	
13:35	Discussion	
13:45-14:00	Break	

14:00-14:50	Session: Osteoarthritis, a disease of the bone/subchondral bone? Implication for treatment <i>Supported by Samumed</i>	Hall A
Chairperson:	Graeme Jones , Australia	
14:00	How to demonstrate structural modification in osteoarthritis: A clinical and regulatory struggle Lee S. Simon , USA	
14:20	Bisphosphonates in OA: What is the evidence? Rohini Handa , India	
14:40	Discussion	
14:50-14:55	Break	
14:55-15:45	Session: Biosimilars: Are rheumatologists and patients ready for transitioning patients from an originator to a biosimilar?	Hall A
Chairperson:	Mark C. Genovese , USA	
14:55	European experience with switching from originator to biosimilar products in rheumatology Tore K. Kvien , Norway	
15:15	The impact of biosimilars in the treatment of rheumatoid arthritis: Similarities and differences of biosimilars compared to original biologics Yeong-Wook Song , Korea	
15:35	Discussion	
15:45-16:00	Break	
16:00-16:50	Industry Symposium: Biosimilar infliximab: Switching from an originator to a biosimilar <i>Supported by Celltrion</i>	Hall A
Chairperson:	Boulos Haraoui , Canada	
16:00	Welcome and introduction: Biosimilar Boulos Haraoui , Canada	
16:05	Switching from an originator to a biosimilar: Key clinical trials and real world data of biosimilar infliximab Tore K. Kvien , Norway	
16:25	Expanding access to treatment: Pharmacoeconomic of biosimilar infliximab Michael L. Tee , Philippines	
16:40	Q&A, Open discussion	
16:50-16:55	Break	
16:55-17:55	Guided Poster Tour <i>Supported by Samumed</i>	
Chairpersons:	Mohit Kapoor , Canada Chak-Sing Lau , Hong Kong	

Saturday, November 10, 2018

08:00-08:50

Session:
Management of challenging osteoarthritis cases in daily practice:
Well-kept secrets

Hall A

Chairperson:

Hyun Ah Kim, Korea

08:00

What to do when nothing really works? A Canadian approach
Jean-Pierre Raynauld, Canada

08:20

Treatment of osteoarthritis: An Australian perspective
Graeme Jones, Australia

08:40

Discussion

08:50-08:55

Break

08:55-09:45

Session:
When is biologic monotherapy the treatment of choice?

Hall A

Chairperson:

Lee S. Simon, USA

08:55

Biologic monotherapy is rarely the treatment of choice
Kevin Pile, Australia

09:15

The benefit and timing of biologic monotherapy
Tsutomu Takeuchi, Japan

09:35

Discussion

09:45-10:00

Break

10:00-10:50

Session:
Novel therapeutic targets and cellular therapies for osteoarthritis
Supported by ORLIFE Pharmaceuticals - a MEDIPOST Company

Hall A

Chairperson:

Flavia Cicuttini, Canada

10:00

Emerging therapeutic avenues in osteoarthritis
Mohit Kapoor, Canada

10:20

Allogeneic cord blood-derived mesenchymal stem cells for cartilage regeneration in OA patients
Kwan-Hong Do, Korea

10:40

Discussion

10:50-10:55

Break

10:55-11:45 **Session:**
Psoriatic arthritis: How to balance management of the skin and the joints

Hall A

Chairperson: **Kevin Pile**, Australia

10:55 Diagnosis and management of psoriatic disease: A domain-based approach
Christopher T. Ritchlin, USA

11:15 Evolving therapies of psoriasis
Paulo Lorenzo, Philippines

11:35 Discussion

11:45-13:00 **Lunch Break and Poster Viewing**

13:00-13:50 **Meet the Experts:**
Non-radiographic spondyloarthropathy: If you were paying for it, would you commence biologic therapy?

Hall A

Chairperson: **Christopher T. Ritchlin**, USA

13:00 Non-radiographic axial SpA: The concept, disease burden and principles of treatment
Nigil Haroon, Canada

13:20 The purpose of treating non-radiographic spondyloarthropathy, structure preservation or function restoration? Is it cost-effective when using biologic therapy?
Wen Chan Tsai, Taiwan

13:40 Discussion

13:50-13:55 **Break**

13:55-14:50 **Session:**
Intraarticular therapy for arthritis: Interesting new findings for patients
Supported by Sanofi

Hall A

Chairperson: **Jean-Pierre Pelletier**, Canada

13:55 Introduction
Flavia Cicuttini, Australia

14:00 Viscosupplementation: What have we learned from 25 years of experience?
Jean-Pierre Raynauld, Canada

14:20 Intraarticular corticosteroid and newbies
Ying Ying Katy Leung, Singapore

14:40 Discussion

14:50-15:00 **Break**

15:00-15:50 **Meet the Experts:**
Lupus and pregnancy: Good news for the doctor and the mother

Hall A

Chairperson: **Swan Sim Yeap**, Malaysia

15:00 Treatment challenges in lupus pregnancy
Monika Østensen, Norway

15:20 Improving outcomes of lupus related recurrent abortion
Chak-Sing Lau, Hong Kong

15:40 Discussion

15:50-15:55 **Break**

15:55-16:25 **Oral Abstracts and Award Presentations**

Hall A

Chairpersons: **Johanne Martel-Pelletier**, Canada
Boulos Haraoui, Canada

15:55 Presentation to Abstract Awardees

16:00 **OA Best Abstract:**
Controversy over the association between vitamin D and osteoarthritis: A meta-analysis
Guntur Darmawan, Indonesia

16:10 **IA Best Abstract:**
Sustained remission of rheumatoid arthritis and its predictive factors in unselected Chinese population:
A retrospective study (2009-2018)
Wenhui Xie, China

16:20 Questions

Poster Presentations

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- P01 BODY MASS INDEX; IMPORTANT BUT FORGOTTEN. THE MOST INFLUENTIAL RISK FACTOR OF SUBCLINICAL ATHEROSCLEROSIS IN LUPUS ERYTHEMATOSUS SYSTEMIC POPULATION
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- P02 OSTEOARTHRITIS AND GLUCOSAMINE USE: A SURVEY-BASED STUDY FROM MALAYSIA
Hairul Hadi Ariff, Malaysia
- P03 SAFETY PROFILE OF BARICITINIB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS UP TO 5.5 YEARS: AN UPDATED INTEGRATED SAFETY ANALYSIS
Subhashini Arthanari, India
- P04 EFFICACY AND SAFETY OF IXEKIZUMAB AT WEEK 24 IN BIOLOGIC EXPERIENCED PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS SUMMARY RESULTS
Subhashini Arthanari, India
- P05 EFFICACY AND SAFETY OF IXEKIZUMAB AT WEEK 52 IN BIOLOGIC NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS (SPIRIT-P1)
Subhashini Arthanari, India
- P06 ULTRASONOGRAPHY PROFILES OF ASYMPTOMATIC HYPERURICEMIC PATIENTS
Awalia Awalia, Indonesia
- P07 RENAL DYSFUNCTION EVALUATION SHOULD BE WARRANTED IN AGED PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING METHOTREXATE AND NON-STEROIDAL ANTI-INFLAMMATORY DRUG
Han Joo Baek, South Korea
- P08 JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT
Charlie Chan, Philippines
- P09 COMPARING THE EFFECTIVENESS OF INTRAVENOUS PATIENT-CONTROLLED ANALGESIA (IVPCA) VERSUS PERIOPERATIVE ANALGESIA (POA) TO RELIEVE POSTOPERATIVE PAIN AFTER TOTAL KNEE REPLACEMENT SURGERY: A RETROSPECTIVE STUDY
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- P10 MITOCHONDRIAL DYSFUNCTION-MEDIATED SARCOPENIA IS ASSOCIATED WITH OSTEOPOROSIS BY MYOTOKINE
Hyo Kyun Chung, South Korea
- P11 PREDICTIVE ROLE OF BIOMARKERS REGARDING RESPONSE TO ETANERCEPT THERAPY IN RHEUMATOID ARTHRITIS
Claudia Ciofu, Romania
- P12 GENISTEIN EFFECTS ON BONE METABOLISM IN POSTMENOPAUSAL WOMEN: A META-ANALYSIS
Guntur Darmawan, Indonesia
- P13 EFFECTIVENESS OF PREGABALIN FOR FIBROMYALGIA PAIN: A META-ANALYSIS
Guntur Darmawan, Indonesia
- P14 TRANSVERSE MYELITIS IN AN INDONESIAN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENT
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Ana Monica Estrella, Philippines

- P16 PREDICTORS FOR THE RESPONSE TO ANTI-TNF THERAPY IN RHEUMATOID ARTHRITIS: WHERE OLD AND NEW BIOMARKERS STAND?
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Byeongzu Ghang, South Korea
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Oliver Malle, Austria
- P27 MIND THE GAP: PREVALENCE OF OSTEOPOROSIS TREATMENT AFTER AN OSTEOPOROTIC FRACTURE – RESULTS OF THE AUSTRIAN BRANCH OF THE INTERNATIONAL COSTS AND UTILITIES RELATED TO OSTEOPOROTIC FRACTURES STUDY (ICUROS)
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- P29 MACHINE LEARNING BASED PATIENT-SPECIFIC PREDICTION MODELS FOR KNEE OSTEOARTHRITIS
Johanne Martel-Pelletier, Canada
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Maniventhan Nachimuthu, Malaysia

- P31 STORY OF A PAIR: A CASE REPORT
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- P32 EFFICACY AND SAFETY OF INTRA-ARTICULAR CROSS-LINKED HYALURONIC ACID IN COMBINATION WITH TRIACINOLONE HEXACETONIDE (TH) FOR MODERATE TO SEVERE OSTEOARTHRITIS: A REPORT IN 32 ASIAN PATIENTS
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- P35 METABOLIC SYNDROME AND TRAJECTORIES OF PAIN SEVERITY AND NUMBER OF PAINFUL SITES IN KNEE OSTEOARTHRITIS: DATA FROM A 10.7-YEAR PROSPECTIVE STUDY
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- P36 IMPACT OF ORAL OSTEOARTHRITIS THERAPEUTICS USAGE AMONG OTHER RISK FACTORS ON KNEE REPLACEMENT: A NESTED CASE-CONTROL STUDY USING THE OSTEOARTHRITIS INITIATIVE COHORT
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- P39 SERONEGATIVE RHEUMATOID ARTHRITIS WITH OVERHANGING EDGES: A REPORT OF TWO CASES
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- P43 BONE MINERAL DENSITY PROFILE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AT RHEUMATOLOGY CLINIC DR. HASAN SADIKIN GENERAL HOSPITAL BANDUNG INDONESIA
Herlina Yani, Indonesia
- P44 OSTEOPOROSIS IN AN ELDERLY PATIENT WITH OSTEOARTHRITIS OF THE KNEE JOINT
Hiroshi Yonezu, Japan
- P45 MICRORNA-1915-3P IN SERUM EXOSOME IS ASSOCIATED WITH DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS IN KOREA
Jihyung Yoo, South Korea
- P46 A RANDOMIZED CONTROL CLINICAL STUDY ON SMALL-NEEDLE-KNIFE THERAPY COMBINED WITH EXERCISE THERAPY FOR KNEE OSTEOARTHRITIS: 3-MONTH FOLLOW-UP VISIT
Yuehong Bai, China
- P47 THE EFFECT OF BPA ON BONE MINERAL DENSITY (BMD) IN RATS
Hong Je Kang, South Korea

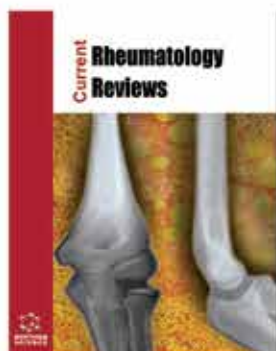


Abstracts



BMJD

JOURNALS FROM BENTHAM SCIENCE

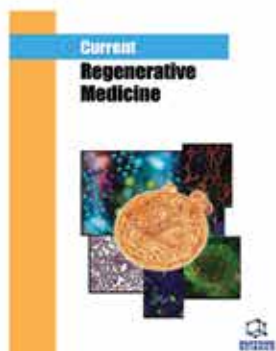


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PROS AND CONS OF JAK INHIBITORS OVER BIOLOGIC DMARDS

Mark C. Genovese, USA

Improved understanding of the immunopathogenesis of Rheumatoid Arthritis (RA) has paved the way for new specific immune interventions for this inflammatory disease. Over the past two decades we have seen the advent of new biologic and small molecule approaches to the treatment of patients with active RA. Despite these advances we lack specific biomarkers or surrogates to predict which patient will respond to an individual agent or combination of agents. The goal of any therapy initiated in RA (including the patient with difficult disease) is to provide meaningful benefit in a safe, convenient, and economically sustainable fashion. Currently existing conventional synthetic DMARDs (csDMARD) and new targeted synthetic DMARDs should help us achieve this goal. Current guidelines from EULAR and the ACR provide guidance to both practitioners and payers regarding general approaches. The growing body of literature, based on trials and real world data, supports the utility of Janus kinase inhibition given efficacy equal or greater than that of existing csDMARD+ biologic as standard of care. The challenges moving forward will be to understand which individuals or patient populations will be best served by each class of therapy and basing therapeutic decisions on a comprehensive understanding of the potential safety concerns and economic hurdles for individual patients and regions of the world.

OSTEOARTHRITIS, A DISEASE OF THE BONE/SUBCHONDRAL BONE? IMPLICATION FOR TREATMENT BISPHOSPHONATES IN OA - WHAT IS THE EVIDENCE?

Rohini Handa

Indraprastha Apollo Hospitals, New Delhi, India

Emerging evidence shows that Osteoarthritis (OA) affects the entire joint and not merely the cartilage. Apart from cartilage degradation, subchondral bone remodelling and synovial inflammation play a role in the pathobiology of OA. Subchondral bone sclerosis is characterized by trabecular thickening increased osteoid volume, and decreased calcium binding to collagen fibers. Despite an increase in bone volume fraction, subchondral bone is hypomineralized due to abnormal bone remodelling. Other changes in the subchondral bone include microdamage, bone marrow edema (BME) and bone cysts. Bisphosphonates have been shown to reduce the size of BME lesions in OA and associated knee pain. What might be, and whether this will translate into, long-term benefits is still not clear? A recent metaanalysis that included 3566 patients in 15 randomized controlled trials where bisphosphonate therapy was compared with a placebo or a conventional medication showed that bisphosphonate treatment improved pain, stiffness and function significantly in OA as assessed by the Western Ontario and McMaster Universities Arthritis Index scale. Osteophyte score was also reduced significantly. However, this meta-analysis reported no significant differences in need for joint replacement. The data interpretation was hampered by the heterogeneity in type and dose of bisphosphonate used, duration of use, and the lack of long-term data on OA joint structure modification. Interestingly, a recent population-based study of older women with incident knee OA in UK showed that those with incident bisphosphonate use had lower risk of knee replacement surgery as compared to non-users of bisphosphonates. Similar results were reported from Taiwan. The question of how early to introduce bisphosphonates in the treatment of OA is also to be resolved. Given the immense societal burden of this disease coupled with paucity of effective treatments, large, long term randomised controlled trials are in order to determine the exact place and role of bisphosphonates in the treatment of OA.

PRACTICAL APPLICATION OF AN IMMUNIZATION PROGRAM IN PATIENTS WITH INFLAMMATORY ARTHRITIS

Boulos Haraoui, Canada

The most frequent comorbidities associated with inflammatory arthritis or their treatment are infectious episodes. They could be benign but recurrent or serious and even life threatening. The risk factors are multi-factorial and include: Disease severity and disease activity; other co-morbid conditions such as diabetes or COPD; older age and several therapies used to treat arthritis such as corticosteroids, methotrexate and the bDMARDs as well as the tsDMARDs (JAK inhibitors). The most common infections involve the upper and/or the lower respiratory tract, the skin the urinary tract and may also include viral infections such as herpes zoster and several other opportunistic infections. Several strategies have been developed to minimize the risk based on a better patient education, better disease control, better management of co-morbid conditions and avoiding certain medications such as corticosteroids. One other preventive measure is a program of active immunization. We have been applying at our center a pro-active approach to all patients diagnosed with inflammatory arthritis which include all recall antigens, pneumococcal vaccine, haemophilus influenzae vaccine, yearly influenza, hepatitis A and B in at risk groups, HPV vaccine in young women. This approach is also supported by the Public Health authorities and is easily applicable with a good acceptance by patients.

NON-RADIOGRAPHIC AXIAL SPA: THE CONCEPT, DISEASE BURDEN AND PRINCIPLES OF TREATMENT

Nigil Haroon, Canada

The term 'Axial Spondyloarthritis' (AxSpA) refers to inflammatory arthritis predominantly affecting the spine. The spectrum of AxSpA includes ankylosing spondylitis (AS), the classification of which requires radiographic changes in the Sacro-Iliac joints (SIJs). However, in some patients, despite the presence of supportive clinical features, radiographic sacroiliitis is not seen. These patients are considered to have non radiographic AxSpA (nrAxSpA) and they may have evidence of inflammation in the SIJs in MRI images and may have the susceptibility gene HLA-B27. Although nrAxSpA patients have no X-ray changes, their disease burden is similar to AS patients. AxSpA patients are known to have activation of several cellular systems with the final cascade of cytokines including TNF and IL-17. The biologic basis of treatment will be discussed and this lecture will be followed by a lecture by Professor WC Tsai on the treatment of nrAxSpA.

TREATMENT OF GLUCOCORTICOID-INDUCED OSTEOPOROSIS

Graeme Jones, Australia

It is clear glucocorticoids increase the risk of all fractures especially vertebral and rib and this effect is most marked in postmenopausal women. This effect appears rapidly reversible if glucocorticoids are reduced below 3mg/day prednisone equivalent or stopped, so this should be the chief aim if one wants to reduce fracture risk. Where this is not an option, there is weak data suggesting calcium and vitamin D supplementation may be modestly effective. There is now considerable data from studies of pharmacologic agents using intermediate outcomes such as bone density. These studies would suggest that parathyroid hormone, zoledronic acid and denosumab have the greatest increments in bone density when compared to alendronate or risendronate which, in turn, are superior to placebo. This appears the case whether therapy is used in a preventive sense or in a treatment sense. This is similar to the primary osteoporosis literature although it should be noted that these studies have generally not been large enough to document if these changes lead to greater reductions in fracture risk. There is also some combination data especially with parathyroid hormone and zoledronic acid suggesting a greater benefit. In Australia, few of these options are reimbursed meaning the clinician has to be creative in how they are used and strong consideration should be given to using them when corticosteroids are initiated.

TREATMENT OF OSTEOARTHRITIS: AN AUSTRALIAN PERSPECTIVE

Graeme Jones, Australia

Australia is struggling under the twin burden of an ageing population that is also becoming increasingly overweight. Joint replacement rates have been rapidly increasing and passed 100,000 per annum in 2016. This is causing substantial cost to the Australian health system. Despite this, there is no concerted effort to standardize therapy and many patients go straight to joint replacement without considering conservative therapy. There are also many patients on opioids despite the evidence that they are at best of modest benefit and lead to increased mortality in Australia. At a minimum, all patients should get a trial of weight loss (especially if overweight), physical therapy, paracetamol and NSAIDs (esp topical). At a specialist level, other options become more often utilized. I use corticosteroid injections when there is an effusion, night pain and/or morning stiffness. I often use alternative medicine as there is quite an evidence base for some of these agents (curcumin, Rose hip, avocado-soybean, krill oil, SAME, ginger extract and 4 jointz) and controversial evidence for others (glucosamine and chondroitin). I occasionally use rheumatoid arthritis DMARDs but note that the evidence base for the non effectiveness of these agents is becoming clear with the potential exception of methotrexate and IL-1 inhibition. In those with bone driven disease, I have tended to use antiresorptive therapy and the evidence underlying this will be discussed.

EMERGING THERAPEUTIC AVENUES IN OSTEOARTHRITIS

Mohit Kapoor

Arthritis Program Krembil Research Institute, University Health Network, Toronto, Ontario, Canada

Osteoarthritis (OA) is among the most prevalent chronic human health disorders and the most common form of arthritis. It is among the leading causes of disability worldwide, and with an increasing life expectancy, OA is a major socioeconomic and clinical concern. In OA, cartilage is destroyed and synovium gets inflamed causing joint stiffness, pain and disability. The disease progresses relatively unnoticed; by the time it is diagnosed, the damage is often so severe that treatments are no longer effective. Specific mechanisms associated with a joint destruction during OA are largely unknown. Due to the lack of specific biomarkers, it is impossible to identify patients exhibiting early stages of OA, leading to severe joint destruction. Furthermore, due to poor understanding of the underlying disease mechanisms, no disease-modifying therapies to treat OA exist. Recent studies have identified promising therapeutic targets and strategies for future drug development in the field of OA. This talk will provide an overview of emerging therapeutic targets and strategies to counteract joint destruction during OA. Specifically, key preclinical and clinical studies on the new disease modifying therapies will be discussed focusing on antisense therapy (using oligonucleotides to target microRNAs), small molecule inhibitors such as those targeting Wnt pathway, as well as recent clinical trials involving cell therapy for OA treatment.

THE ROLE OF MATRIX DEGRADATION PRODUCT IN THE INFLAMMATION AND PAIN IN OA

Hyun Ah Kim

Hallym University College of Medicine, Korea

Osteoarthritis (OA) is the most prevalent joint disease in older people and is characterized by the progressive destruction of articular cartilage, synovial inflammation, changes in subchondral bone and peri-articular muscle, and pain. Because our understanding of the etiopathogenesis of OA remains incomplete, no cure for OA yet exists. Traditionally, OA has been considered non-inflammatory arthritis which is in contrast with autoimmune/autoinflammatory arthritides such as rheumatoid arthritis. As technology in molecular biology advances, however, the alteration of pro-inflammatory vs anti-inflammatory balance gained much interest in the understanding of joint degeneration in OA. In addition to pro-inflammatory

cytokines and chemokines, there is also the possibility that matrix damage induces inflammation in the OA joint. The innate immunity is a host defense system against invading pathogens that can be activated immediately once a pathogen enters an organism. Pattern recognition receptors (PRRs), including toll-like receptors (TLRs) and nucleotide-binding and oligomerization domain (NOD), recognize pathogen-associated molecular patterns (PAMPs), including bacterial peptidoglycan (PGN) and lipopolysaccharide (LPS). PRR responds not only to pathogen but also to molecules generated after tissue injury, which are termed damage-associated molecular patterns (DAMPs). TLR-2, TLR-3, TLR-4, and TLR-5 are overexpressed in OA cartilage compared with normal cartilage, and chondrocytes responds to TLR2 or 4 ligands. Fibronectin fragments (FN-fs) are increased in the joint fluid of OA patients and have a potent chondrolytic effect. For example, 29-kDa FN-f upregulates matrix metalloproteinase (MMP)-1, MMP-3, and MMP-13 expression via TLR-2/MyD88 signaling pathway. In addition, in 29-kDa FN-f-treated cells, expression of xylosyltransferase-1 (XT-1), an essential enzyme that catalyzes the initial and rate-determining step in glycosaminoglycan chain synthesis, is significantly suppressed through modulating the activity of the transcription factors specificity protein 1 (Sp1), Sp3, and activator protein 1 (AP-1). In addition to the catabolic signaling leading to matrix degradation, recent studies show that matrix degradation product may aggravate pain of OA. A 32-amino-acid aggrecan fragment (32-mer), a degradation product of aggrecan with a disintegrin and metalloproteinase with thrombospondin motif 4 (ADAMTS-4) or ADAMTS-5 and MMPs was found to excite dorsal root ganglion nociceptive neurons. In addition, intra-articular injection of the 32-mer fragment provoked knee hyperalgesia in WT but not Tlr2-null mice, and blocking the production or action of the 32-mer in transgenic mice prevented the development of knee hyperalgesia in a murine model of OA. These findings suggest that matrix degradation product and inflammation may form a vicious cycle, with the progression of one having detrimental effects on the other. Therapeutic strategy targeting matrix degradation product, thus, holds promise for both protection of cartilage degradation and alleviation of pain in OA.

IMPROVING OUTCOMES OF LUPUS RELATED RECURRENT ABORTION

Chak-Sing Lau

Daniel CK Yu and Chair Professor of Rheumatology and Clinical Immunology, Department of Medicine, The University of Hong Kong, Hong Kong

Systemic lupus erythematosus (SLE) primarily affects women of reproductive age and rheumatologists often have to manage patients during pregnancy, as well as complications that may arise as a result of pregnancy. Regular counselling, close monitoring of underlying lupus disease activity, judicious use of steroids and immunosuppressive agents, and control of comorbid conditions, particularly hypertension, are keys to successful outcomes of pregnancy in lupus. Recurrent abortion is one of the most important complications of lupus pregnancy and is commonly associated with the presence of antiphospholipid antibodies (APLs) including the anticardiolipin antibodies, anti- β_2 glycoprotein I antibodies and lupus anticoagulant. APLs precipitate pregnancy loss primarily through induction of thrombosis in the placenta. Aspirin and heparin have therefore been the main stay of treatment of APL associated pregnancy loss with approximately 70% of women achieving a successful pregnancy outcome. Treatment failure in the 20-30% of patients highlight other pathogenic mechanisms are likely to be in play. These include APLs binding directly to the trophoblast, inducing secretion of hormones and cytokines, and inducing cellular apoptosis. Other treatment options are therefore needed and are currently being explored. For example, retrospective studies have shown the use of pravastatin may be beneficial in preventing APL related pre-eclampsia and that the immunomodulatory agent hydroxychloroquine has general beneficial effects in the prevention of APL related pregnancy complications.

INTRAARTICULAR CORTICOSTEROID AND NEWBIES

Katy, Ying Ying Leung

Senior Consultant, Department of Rheumatology & Immunology, Singapore General Hospital, Associate professor, Duke-NUS Medical School

Intra-articular corticosteroid (IACS) has been used in the management of knee osteoarthritis for decades. It has been widely used for short term relief of pain and restoring function in times of flares. Despite its perceived effectiveness and safety records, there are ongoing debates. Meta-analysis generally revealed moderate benefit in relieving pain, but the responses were short lasting. Results from studies that evaluate predictors of patient-, treatment-, disease- and drug-related factors that may predict the response to IACS have been conflicting. There are some new studies that give insight into new formulations that may be more efficacious. However, discrepancies between efficacies derived from scientific evidence and clinical experience still exist. This efficacy paradox will be explained and how to deal with it will be discussed.

PSORIATIC ARTHRITIS: HOW TO BALANCE MANAGEMENT OF THE SKIN AND JOINTS

Jose Paulo Lorenzo, Philippines

Psoriatic disease is a common inflammatory condition seen worldwide with a prevalence ranging from 0.1% to 3%. It is characterized primarily by involvement of the skin typified by erythematous scaly papules and plaques and the musculoskeletal system. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) in its 2015 treatment recommendations for psoriasis is guided by 5 domains of this disease with many manifestations. These domains include the skin and nails, peripheral arthritis, spondylitis, enthesitis and dactylitis. These domains may also be used for standardizing diagnostic tools, disease activity measures, treatment strategies, response to treatment and research. This talk will focus on the skin and nails in psoriatic disease. A brief discussion on the pathophysiology of skin disease will include three main components. The first comprises the genes identified with this domain, such as the MHC Class 1 gene HLA-Cw02 with its prognostic implications. The second, the environmental triggers of disease such as infections, trauma, stress and medications; and third, the inflammatory response in the skin, new blood vessel formation and the different cells of the innate (dendritic cells and macrophages) and acquired immune systems (T-lymphocytes) that participate and have been identified in psoriasis inflammation. The T-cell responses (TH1, TH17), the cytokines such as IL-12-23 and IL-17 and the signalling pathways such as the PDE-4 pathways that are contributing to the new targeted treatments to control skin disease will also be explained. The diagnosis of skin psoriasis and the different phenotypes of the disease (Plaque, Guttate, Inverse, Pustular and Erythrodermic) will be highlighted with more emphasis on the more common Plaque type. This will be followed by a discussion on the grading tools of disease severity (mild, moderate or severe) that are being used. There has been no consensus among dermatologists on the preferred standard of grading skin involvement and severity. The use of the Body Surface Area (BSA), Psoriasis Area and Severity Index (PASI) and subjective quality of life measures are all used in grading skin disease. The latter part of the talk will focus on the treatment of disease wherein the desired treatment target is to achieve remission and control skin flares. These will include the use of topical ointments, photo UV therapy, laser treatments and the conventional oral synthetic and biological treatments. Most patients with mild disease receive topical treatments such as topical steroids, vitamin D analogs or combinations of these. Phototherapy with PUVA or UVB combined with topical treatments are used for those with moderate to severe disease occasionally in combination with oral systemic therapies methotrexate, vitamin A derivatives Acitretin and calcineurin inhibitors. Biologic treatments with anti-TNF, anti-IL-12 and anti-IL17A have proven effective for skin and nail psoriasis. Updates on the indications, safety signals and therapeutic benefits will be discussed. Finally, a brief discussion of the unmet needs of skin psoriasis such as biomarkers for diagnosis, response to treatment, monitoring of treatment and treatment modalities present research opportunities for this disease. This will be followed

by a talk on the management of psoriatic arthritis and an open forum on the management of both the skin and joints.

PRECLINICAL EVIDENCE SUPPORTING THE THERAPEUTIC EFFECT OF DIACEREIN IN OSTEOARTHRITIS

Johanne Martel-Pelletier

Professor of Medicine, University of Montreal; Director, Osteoarthritis Research Unit, University of Montreal Hospital Research Centre, Montréal, Canada

Osteoarthritis (OA) involves a complex series of interactive degradative and repair processes that occur in all tissues of the joint, causing adjunct symptoms. The current pharmacological management of OA, including nonsteroidal anti-inflammatory drugs (NSAIDs), anti-cyclooxygenase-2 (anti-COX-2) and analgesics, although effective on the disease symptoms, are palliative and do not stop the disease progression. There are, however, compounds such as diacerein that have been shown to reduce the symptoms as well as the severity of this disease process. This lecture will focus on bringing a better understanding of the factors that are involved in the complex interaction between the OA tissues, leading to the progression of joint structural changes in this disease. Diacerein, an antirheumatic drug from the anthraquinone chemical class, has proven beneficial in treating OA symptoms in patients, and has also been found to have disease modifying properties in vitro in human articular cells/tissues and in experimental models of OA. This drug appears to act, at least in part, through its impact on the IL-1 system. These basic science data provide a coherent body of evidence of this drug's positive effect in clinical studies. Hence, diacerein treatment has a direct beneficial role on the abnormal metabolic activities of OA articular cells of the cartilage, synovial membrane and subchondral bone. In brief, it reduces the altered catabolic activities responsible for the structural changes occurring during the course of OA.

INFLAMMATION IN OSTEOARTHRITIS. LOCAL, SYSTEMIC OR BOTH: THERAPEUTIC IMPLICATIONS

Johanne Martel-Pelletier

Professor of Medicine, University of Montreal; Director, Osteoarthritis Research Unit, University of Montreal Hospital Research Centre, Montréal, Canada

Osteoarthritis represents the failure of the joint as an organ. A role of inflammation as well as its deleterious effects in osteoarthritis is well established. However, do we know which type of inflammation to target for therapeutic strategies: local, systemic, or both? During this lecture, three questions will be addressed and discussed. i) What is the evidence that inflammation plays a role in the progression of this disease and, if so, at what stage? ii) What are the inflammatory factors involved? I will also review the clinical trials targeting a specific cytokine: were they successful and, if not, why? iii) In osteoarthritis, is inflammation only local or could it also be systemic? A major change in our understanding of the pathophysiology of this disease has come with the realization that osteoarthritis is a systemic disease with inflammation having a critical role in the interplay between the joint tissues. Such metabolic disturbances could start at joint sites, but induce systemic chronic inflammation, exacerbating osteoarthritis. An array of proinflammatory cytokines secreted by multiple cell types have been shown to govern this disease pathogenesis. Data also revealed that, at least, local (synovial membrane and fluid) inflammatory factors are found in higher amounts in early compared to late stages of osteoarthritis. These data in addition to those from failed clinical trials using anti-inflammatory therapies suggest that, to obtain therapeutic efficacy at reducing articular structure damage, such an agent should be broad enough to be effective, but selective enough to avoid deleterious off-target effects, as well as administered at an earlier stage of the disease. However, an effective treatment might require a combination of approaches.

TREATMENT CHALLENGES IN LUPUS PREGNANCY

Monika Østensen

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Pregnant women with SLE present an increased risk for maternal complications, pregnancy loss and adverse child outcomes. Active disease, organ manifestations and comorbidities contribute to maternal and fetal risks. Unplanned pregnancy in women with active disease may end in adverse maternal and fetal outcomes. Planning of pregnancy in a period of remission and while on stable therapy is therefore necessary. The medical regimen should be optimized before conception to sustain remission or low disease activity. Continuation of hydroxychloroquine in addition to other immunosuppression reduces the risk of lupus flares. Fetotoxic agents like cyclophosphamide and mycophenolate derivatives must be discontinued before conception and the patient switched to pregnancy compatible drugs. Azathioprine, cyclosporine and tacrolimus are medications that can be continued in pregnancy and lactation. A lupus flare during pregnancy may require methylprednisolone pulses for disease control. Careful monitoring is needed to avoid side effects of corticoids. Intravenous immunoglobulins or cyclophosphamide in the 2nd or third trimester may be considered in patients suffering severe organ flares refractory to standard therapy. In such cases, treatment with rituximab or belimumab can also be discussed though experience on the safety of these biologics is limited. Low-dose aspirin should be considered for prevention of preeclampsia and intrauterine growth restriction in all lupus pregnancies. Lupus patients positive for phospholipid antibodies or with the antiphospholipid syndrome require anticoagulants to prevent obstetric or thrombotic complications. Thromboprophylaxis must be continued during the first six weeks postpartum even in patients without previous thrombotic events. Maintaining adequate control of disease activity and treating flares in pregnancy quickly and effectively should be a central goal during prenatal care.

TREATMENT APPROACH FOR OSTEOARTHRITIS: PLACING PATIENT WELL-BEING AT CENTRE STAGE

Jean-Pierre Pelletier

Professor of Medicine, University of Montreal; Director, Osteoarthritis Research Unit, University of Montreal Hospital Research Centre, Montreal, Canada

Osteoarthritis (OA), the most common form of arthritis, causes joint pain, impairment of quality of life and will be the fourth leading cause of disability by 2020. Standard pharmacological treatment focuses on symptom relief with analgesics and non-steroidal anti-inflammatory drugs (NSAIDs), which can cause serious adverse effects. Therefore, the need for treatment with an improved balance between the benefits and risks for patients is becoming a priority. In high quality trials, pharmacological grade symptomatic slow acting drugs for OA (SYSADOAs), such as glucosamine and chondroitin sulfate, have been shown to provide a positive benefit-to-risk ratio in the treatment of knee and hip OA. Physicians like to rely on an orderly and rational approach to pharmacological treatment of medical conditions such as OA. Experience has proven that a comprehensive therapeutic algorithm with a stepwise approach to treatment would improve disease management and benefit the quality of life of the vast majority of OA patients. Most practice guidelines for OA analyse the evidence behind each proposed treatment; however, they do not prioritize the interventions in a given sequence. A treatment algorithm that is easy to interpret based on the available evidence and easily applicable in daily practice is therefore highly useful. The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) has established an easy-to-follow treatment algorithm for the management of knee OA, which provides practical guidance for the prioritization of interventions. It allows for an easy-to-follow treatment flow in clinical practice, in support of the clinicians' individualized assessment of the patient. The algorithm proposes a first line background maintenance therapy with SYSADOAs, with prescription formulations of pharmacological grade crystalline glucosamine sulfate and chondroitin sulfate. Paracetamol

may be added as rescue analgesia only, due to limited efficacy and increasing safety signals. Topical NSAIDs may provide additional symptomatic treatment for the advanced management of persistent symptoms, with cycles of oral NSAIDs as a second step. A careful patient stratification and treatment selection is advocated to maximize the benefit-to-risk ratio in patients receiving oral NSAIDs. Intra-articular therapies with steroids or hyaluronic acid as a next step can also provide clinical benefit with long lasting symptom relief. As a last step before surgery, a weak opioid could be used with extreme caution, particularly in older patients, due to significant side effects with morbidity. Pharmacological treatment strategies for OA need to be comprehensive and understandable by physicians and patients. The use of prescription grade SYSADOAs, such as glucosamine and chondroitin sulfate, is of the utmost importance in the first line management of symptomatic knee OA. The benefit of such therapy lies not only in the proven effectiveness on OA symptoms but also the improved benefit-to-risk ratio of the disease management by reducing the need for treatment by drugs that can be associated with significant morbidity, such as NSAIDs and opioids.

AN INTERNATIONAL, MULTICENTRE, DOUBLE-BLIND, RANDOMISED STUDY OF THE EFFECT OF DIACEREIN VS. CELECOXIB IN SYMPTOMATIC KNEE OSTEOARTHRITIS PATIENTS (DISSCO STUDY)

Jean-Pierre Pelletier

Professor of Medicine, University of Montreal; Director, Osteoarthritis Research Unit, University of Montreal Hospital Research Centre, Montreal, Canada, on behalf of the DISSCO study group

Objectives: The primary outcome of this study is to show that diacerein is non-inferior to celecoxib in terms of pain reduction (WOMAC A pain subscale) after 6 months of treatment in moderate-to-severe symptomatic knee osteoarthritis (OA) patients. **Methods:** A randomised double-blind multicentre trial conducted in four European countries (Spain, Belgium, Austria, Czech Republic) and in Canada evaluating treatment with diacerein (Artrodar®, Verboril®) versus celecoxib in patients with Kellgren-Lawrence grades 2-3 knee OA and moderate-to-severe pain (VAS pain score [0-100 mm] while walking on a flat surface ≥ 40 mm). Patients diagnosed according to American College of Rheumatology criteria were randomised to receive 50 mg diacerein twice a day or 200 mg celecoxib every day for 6 months. The primary outcome is the change from baseline in WOMAC pain subscale after 6 months of treatment. Secondary outcomes include WOMAC function and stiffness, VAS pain, presence of joint swelling/effusion, rescue medication consumption, percentage of Osteoarthritis Research Society International (OARSI) responders, and SF-36. **Results:** The last patient completed the study in June 2018. A total of 380 patients were randomised in the study. The per protocol (PP), intention-to-treat (ITT), and safety populations will be analysed. The primary outcome assessment on the PP population will be followed by sensitivity analysis on the ITT population. Exploratory statistical analysis on other efficacy criteria and safety will also be performed. All data will be presented. **Conclusion:** This 6-month clinical study will enable a comparison of the efficacy of diacerein to celecoxib in reducing pain and stiffness and improving function, as well as an evaluation of the clinical relevance of diacerein in patients with painful knee OA. It will also provide new and most useful information on the safety profile of diacerein.

BIOLOGIC MONOTHERAPY IS RARELY THE TREATMENT OF CHOICE

Kevin Pile, Australia

The EULAR and ACR recommendations for RA management begin with methotrexate (MTX) monotherapy and in the presence of ongoing disease activity combine additional csDMARDs such that lack of efficacy and/or toxicity brings us to the addition of a bDMARD or JAK inhibitor. The combination of the old and the new are generally more effective than biological monotherapy, although the addition of a bDMARD to an obviously failing or toxic may have little rationale to a patient. It also has to be recognised that up to a third of patients are non-adherent with the co-prescribed csDMARD because of pill burden, concerns about adverse effects, fear of toxicity, or restriction

on alcohol consumption. Most trials add bDMARD or tsDMARD to ongoing MTX, with a small percentage continuing alternative csDMARDs. The combination of MTX and b/tsDMARD is more effective clinically and radiographically for anti-TNF therapies and often but not always in abatacept and anti-IL-6 studies. Registry data suggest lesser advantage of combination therapy over biologic monotherapy which may reflect differences from the RCT cohorts in duration or disease activity, but may also be to the lower csDMARD adherence in the real world. However, persistence of bDMARD therapy is greater amongst those continuing MTX/csDMARD therapy. That these csDMARD/bDMARD combinations are particularly effective is reinforced by trials showing that the removal of the MTX/csDMARD associates with loss of response in the majority of subjects. The potential exception again being anti-IL-6 therapy, and JAK inhibition with tofacitinib. Continuing a csDMARD when starting a bDMARD is no more toxic, has less immunogenicity, has better persistence of the bDMARD, and greater clinical and radiographic efficacy. Clinicians should convey this message to assist adherence and achieve even better outcomes.

VISCOSUPPLEMENTATION: WHAT HAVE WE LEARNED FROM 25 YEARS OF EXPERIENCE?

Jean-Pierre Raynaud

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Osteoarthritis (OA) is a chronic condition characterized by a loss of joint cartilage and is a major cause of disability. Knee OA leads to persistent pain and loss of function, and treatment goals primarily focus on symptom relief and retention of function. Injecting supplemental intra-articular hyaluronic acid (IAHA) into the joint capsule, a procedure also named viscosupplementation, has been demonstrated to provide therapeutic benefits. This short review will summarize findings up to the present at addressing controversies surrounding IAHA therapy for mild to moderate knee OA. Our review showed consistent and statistically significant improvements in pain, function and stiffness up to 26 weeks with IAHA therapy compared to IA placebo or controls, regardless of study size or trial quality. Many studies also report improved outcomes with higher compared to lower molecular weight HA compounds. In addition, several modes of action have been proposed to explain the long-term efficacy of IAHA, most of them converging on the role of the synovial macrophage and its key surface receptor CD44. Concepts of Minimal Clinically Important Differences (MCID) favoring IAHA over most other OA treatments will also be presented. The full therapeutic effect of IAHA therapy is of considerable clinical importance, consisting of the combined IA placebo and HA therapeutic effects. Available evidence also strongly suggests that HA therapy is safe with no increased risk of serious adverse events compared to placebo. IAHA therapy is a safe and effective option for patients with mild to moderate knee OA failing first-line pharmacological therapy. These findings are based on strong basic science studies and clinical trials.

WHAT TO DO WHEN NOTHING REALLY WORKS? A CANADIAN APPROACH

Jean-Pierre Raynaud

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Osteoarthritis (OA) is a common condition. Symptomatic treatments for OA are widely used in the treatment of OA of the knee, yet the best available evidence does not undoubtedly demonstrate a consistent clinical benefit for all patients individually. This is possibly related to the heterogeneity of the disease. The overall efficacy of OA treatments was evaluated through review of recent literature and data obtained from published double-blind clinical trials. Beyond non-pharmacological modalities such as education, self-management, exercise, and weight reduction, the ACR guidelines¹ recommend, based on extensive literature review, systemic (NSAIDs, paracetamol, co-analgesia, etc.) and local therapies such as topical NSAIDs and intra-articular injections of steroids or hyaluronate for the management of patients with knee and possibly hip OA. Intra-

articular injections of steroids are often effective but such efficacy is often short-lived. Still, this approach has been regularly used repetitively for decades and results from the few trials evaluating the long-term safety of such injections, except for a few, are reassuring. The pros and cons of such approach will be briefly presented. Intra-articular hyaluronate (IAHA) injection trials generally report positive effects on pain and function scores compared to placebo, but the evidence on clinical benefit is uncertain due to variable trial quality, differences in the hyaluronate compounds and preparations, potential publication bias, and unclear clinical significance of the changes reported. Recent published data from the basic science domain may explain the mode of action of long-term IAHA and will be presented. Other approaches such as platelet enriched plasma (PRP) injections, stem cell injections, autologous chondrocyte transplants, hydroxychloroquine, anti-nerve growth factor (NGF) and diacerein will also be briefly described. Several therapeutic options exist for symptomatic OA. Systemic treatments are generally used by primary care physicians, chiefly for ease of prescription and oral administration. However, local treatments, by virtue of their excellent efficacy/safety profiles should be favored for localized OA pain management, hence satisfying the paradigm: “a local treatment for a local disease.”

¹Hochberg MC, Altman RD, April KT, et al. Arthritis Care Res. 2012;64(4):465-74.

HOW TO DEMONSTRATE STRUCTURAL MODIFICATION IN OSTEOARTHRITIS: A CLINICAL AND REGULATORY STRUGGLE

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Around the world typically drugs are approved for osteoarthritis (OA) based upon evidence from adequate and well-controlled trials demonstrating the clinical benefit of how a patient feels, functions or survives while identifying potential harms of the therapy. In the context of OA, the clinical benefit is represented by “signs and symptoms” which typically include measurements of change from baseline in patient reports of pain and physical function measured by the WOMAC or the KOOS along with a patient global response. It was suggested that these necessary standard measured benefits might not be achieved concomitantly with demonstrated improvements in structural characteristics due to problems with both the timing of these measurements as well as powering of trials for various complicated outcomes. In 1992, in the US, FDA instituted the **accelerated approval** regulations that allowed approval of drugs for serious conditions that filled an unmet medical need on the basis of a surrogate endpoint which might be some biomarker, either soluble or imaging which would be reasonably likely to predict a clinical outcome. Previously, the Osteoarthritis Research Society International (OARSI) submitted a white paper to FDA which demonstrated that OA in some patients is a serious disease. It is hoped that the use of imaging and/or biochemical markers during DMOAD trials could provide early indications of a potential treatment related effect on structure. Initial approval on the basis of a surrogate could allow for marketing of a product and the acquisition of revenue to facilitate funding of the necessary post-marketing confirmation trials with acceptable clinically relevant endpoints and/or joint survival assessments to verify and describe its clinical benefit, required under FDA’s accelerated approval regulations (21 CFR 314.510). When there is uncertainty as to the relation of the measured surrogate endpoint to clinical benefit, it is critical to validate either the patient reported outcomes or the characteristics of the joint survival. Exactly what trials are necessary to do this remains controversial. Structural modification therapies in OA must not only consider alterations of cartilage but also subchondral bone and soft tissues. Thus, the develop of disease modifying therapy in OA remains a struggle.

THE IMPACT OF BIOSIMILAR IN RA TREATMENT: SIMILARITY AND DIFFERENCE OF BIOSIMILAR COMPARED TO ORIGINAL BIOLOGICS

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Biosimilar is biological product which is highly similar to the reference product not withstanding minor differences in clinical inactive components and there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. Generic drug is a copy of a small-molecule (chemical) drug, which can be fully defined structurally and reproduced with an identical chemical structure. However biosimilars can never be identical to reference product due to complex manufacturing process of biologic agents. For the biosimilar, a greater emphasis is on nonclinical (physicochemical, biologic, and animal) development compared with originator emphasis on clinical trials. A comparative clinical study for a biosimilar development program should be designed to investigate whether there are clinically meaningful differences between the proposed product and the reference product. Extrapolation of clinical trial results between disease states, such as rheumatic disease and gastrointestinal diseases should proceed with caution, since safety and immunogenicity issues may arise. To date, safety profiles of the biosimilars have been consistent with those of the originator biologics. But anti-drug antibody response to biosimilars may lead to a number of deleterious consequences, such as loss of efficacy, altered pharmacokinetics, cross-reactivity to endogenous protein and adverse events. Because of high cost biologics, biosimilar therapy could reduce the pressure on healthcare budgets. It increases patients' access to biologics and further to new regimens and new drugs. It reduces cost of expensive biologic medicinal products and contribute to reduce the price of reference biologics. Therefore regulatory bodies need to ensure that appropriate analytical, preclinical and clinical studies are done to ensure comparable safety and efficacy between biosimilar and bio-originator. Switching between a bio-originator and a biosimilar appears not to compromise efficacy and safety. However multiple switching, between biosimilar and biosimilar, remains an unknown. More studies, and more real-world data will be needed to ensure that safety is maintained. For the approved biosimilars for infliximab, etanercept, adalimumab and rituximab, the similarity in efficacy, safety and immunogenicity was demonstrated. But in some points, no clinically significant differences were noted (eg., injection site reaction and immunogenicity).

THE PURPOSE OF TREATING NON-RADIOGRAPHIC SPONDYLOARTHROPATHY, STRUCTURE PRESERVATION OR FUNCTION RESTORATION? IS IT COST-EFFECTIVE WHEN USING BIOLOGIC THERAPY?

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Axial spondyloarthritis (SpA) is an umbrella term that comprises ankylosing spondylitis (AS) and non-radiographic SpA (nr-axSpA). It has long been reported, besides some demographic difference, two diseases have same burden physically and functionally. Strong argument to strengthen the validity of the concept of axSpA as a single disease with different stages is the progression from nr-axSpA to AS. In fact, cohort studies indicated that some population of nr-axSpA did progress to AS after short period of follow up. Broad consensus about the management of nraxSpA is emerging among clinicians, but the evidence base remains to be established more firmly. Several studies have demonstrated that TNFi are efficient in nr-axSpA both objectively measured by inflammation markers, composite scores and subjectively by patient report outcomes. Furthermore, after biologic treatment, there are no markedly difference in terms of efficacy and safety in patients with both entities of axial SpA. In some countries, biologics are now indicated and reimbursed for the treatment of nr-axSpA based on this clinical finding. Unfortunately, for most countries, biologics are not reimbursed for nr-axSpA. Further long-term studies are expected to watch whether the use of biologics can stop the radiographic

progression from na-axSpA to AS. If it were the case, the use of biologics in treating patients with nr-axSpA will be the milestone in the history of rheumatology paving the road for preventing the development of an old disease.

GENETIC AND FUNCTIONAL GENETICS OF RHEUMATOID ARTHRITIS AND OTHER AUTOIMMUNE DISEASES

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The majority of autoimmune disease are multifactorial diseases that develop by the interaction of several factors such as genetic factors and environmental factors. A limited numbers of disease susceptibility genes, including major histocompatibility complexes, were reported for several decades. Genome-wide association studies (GWAS) have then been used for more than 10 years to identify susceptibility genes of representative autoimmune diseases. These findings have contributed to enhance our idea of the pathogenesis. As the analysis of susceptibility genes has been progressed, it has become obvious that many disease susceptibility polymorphisms are involved in the expression level of genes. Furthermore, expression of genes related to the pathogenesis turns out to be often cell-specific, and epigenetics is closely involved in this process. Genetic information exists before the onset of the disease, and thus has a clear causal relation to the disease. Therefore, with regard to the understanding of pathological mechanisms using these pieces of information and its application to drug discovery, the involvement of analyses on genomic function is essential. On the other hand, we also believe that the analyses of lymphocyte subset-specific transcriptome would be another approach. For example, regarding systemic lupus erythematosus (SLE), as many as 19 immune cell subsets in peripheral blood mononuclear cells (PBMCs) were identified, sorted and processed for RNA-Seq. Upregulation of Interferon (IFN) signature was detected in all subsets from SLE patients. Further, the numbers of differentially expressed genes (DEGs) remarkably increased in memory B cells. Pathway analysis revealed the enrichment of mitochondrial dysfunction as well as oxidative phosphorylation (OXPHOS) especially in memory B cells. Expression of mitochondrial electron transport chain were significantly higher in memory B cells. Transmission electron microscopy revealed mitochondrial enlargement in memory B cells but not in naïve B cells from SLE patients. Weighted gene co-expression network analysis (WGCNA) in memory B cells confirmed a correlation between mitochondria-related modules and autoantibody production in SLE. GWAS of SLE identified risk variants related to mitochondria. Our analyses suggest that several such variants have eQTL effects of genes related to mitochondrial function, conferring the pathological significance of memory B cells in SLE.

RISK FACTORS FOR OSTEOPOROSIS IN PATIENTS WITH ARTHRITIS

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Osteoporosis (OP) is defined as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture. Osteoporotic fractures are the end result of compromised bone strength/low bone density and typically occur at the hip, spine and wrist (Colles' fracture). In the arthritides, OP is a recognised extra-articular complication of both rheumatoid arthritis (RA) and ankylosing spondylitis (AS). Patients with RA have an increased risk of hip and vertebral fractures, independent of glucocorticoid usage. Low bone mineral density (BMD) has been found both at the spine and hip in patients with active AS, with an increased risk of vertebral fractures. Bone loss is due to and can be exacerbated by disease-related factors. The cytokine-mediated inflammation in active disease will increase bone resorption, decrease bone formation but most commonly affects both of these processes resulting in an uncoupling of bone formation from

resorption in favour of excess resorption. Arthritis associated disability can cause bone loss from immobilization. The use of glucocorticoids leads to an inhibition of bone formation. However, there is conflicting data on whether low-dose Prednisolone (<7.5 mg daily) is deleterious for bone. Nonetheless, it is possible that, if low dose glucocorticoid therapy leads to better disease control and thus greater mobility and exercise tolerance, the increase in bone loss from the therapy would be offset by an increase in new bone formation associated with the increase in weight-bearing from better mobility. In addition, many RA patients are vitamin D deficient/insufficient which may adversely affect BMD. Prevention of OP in patients with inflammatory arthritis includes having an adequate calcium and vitamin D intake, encouraging weight-bearing exercise/improving mobility and aiming for good control of disease activity.

ORAL ABSTRACTS

OR01

CONTROVERSY OVER THE ASSOCIATION BETWEEN VITAMIN D AND OSTEOARTHRITIS: A META-ANALYSIS

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Problem statement: Osteoarthritis (OA) is a worldwide public health issue related with morbidity, costs, and disability. Since vitamin D deficiency and OA are frequently found to be coexisted, there has been high interest in the association between vitamin D deficiency and OA. Vitamin D has been proposed to play promising role in OA. However, numerous literatures evaluating the link between vitamin D and OA show inconsistent results. We investigated the controversy over the relationship between vitamin D and OA in several approaches, including OA pain and vitamin D supplementation. **Methods:** We conducted the study according to the meta-analysis PRISMA guideline. Relevant studies were identified from a search of PubMed, Cochrane, and EBSCO databases. Quality of selected studies was evaluated using STROBE for observational studies and Jadad score for randomized placebo-controlled trials (RCT). For observational studies, we used fully adjusted pooled odds ratio (OR) with 95% confidence interval (CI). For RCT, we used pooled standardized mean difference (SMD) with 95% CI. Statistical analysis was performed using Review Manager 5.3. **Results:** Fourteen of 185 initial observational studies and 3 of 8 initial RCTs met inclusion criteria. Due to various study designs and outcome approaches, we grouped the studies based on prevalence, incidence progression, OA site, and outcome approach. There was a tendency favoring positive association between lower serum vitamin D and knee OA prevalence with no statistical significant. There was a significant association between serum vitamin D and OA pain (OR: 1.19; 95% CI: 1.08-1.31; p 0.0003). In the RCT, the only significant association was demonstrated in WOMAC function (SMD: -0.47; 95%CI: -0.83 to -0.10; p 0.01). In contrary, there were no statistical significant changes in WOMAC pain, WOMAC stiffness, VAS pain, and tibial cartilage volume although the result showed a benefit in favor of vitamin D supplementation. **Conclusion:** Our study showed no association between serum vitamin D and OA. Further longitudinal studies are needed to confirm the association between serum vitamin D and OA pain. There is insufficient evidence to support the benefit of vitamin D supplementation in knee OA progression. All authors declare no conflict of interest

OR02

SUSTAINED REMISSION OF RHEUMATOID ARTHRITIS AND ITS PREDICTIVE FACTORS IN UNSELECTED CHINESE POPULATION: A RETROSPECTIVE STUDY (2009-2018)

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Problem statement: Sustained remission is more desirable treatment target for the management of rheumatoid arthritis (RA) in clinical practice. Notwithstanding, there are a number of cohort studies reported the prevalence of sustained remission in different countries, no study so far has demonstrated the issue in Chinese population. Moreover, further investigative studies need to be performed due to limited and conflicting predictors of sustained remission in previous studies. **Methods:** All the medical records of RA patients from 2009 to 2018 were retrospectively reviewed. Remission was defined according to DAS28-ESR, CDAI, SDAI, and Boolean criteria. Remission of no less than 6 months duration was regarded as sustained remission. Kaplan-Meier estimator was applied to plot cumulative possibility of sustained remission and calculate the median time to sustained remission. Cox regression analyses were performed to identify predictors of sustained remission. **Results:** In total, 779 patients contributing 7,958 clinic visits were included. During the follow-up period, nearly half of patients achieved sustained remission according to DAS28-ESR (51.6%), CDAI (45.6%), SDAI (44.0%), as well as Boolean definitions (42.4%). Median times to sustained remission were respectively 20.5, 28.7, 30.6, and 32.9 months based on above criteria. Specifically, the 1-year cumulative probabilities of sustained remission defined by above-mentioned criteria ranged from 29.4% to 41.2%. Additionally, the median time of remission persistence in cohort period was roughly 1.8 years. Furthermore, multivariate Cox-regression indicated Increasing age, long disease duration, higher baseline disease activity scores were independently correlated with reduced chance of sustained remission, as measured by nearly all four definitions. Conversely, male, early RA, DMARD-naïve and lower disease activity scores in remission assessed by corresponding criteria positively contributed to sustained remission. Importantly, the T2T adherence therapy and shorter time-to-remission were identified as stable determinants of sustained remission across all definitions. **Conclusion:** Sustained remission was not uncommon in daily practice. Male, early RA, treatment-naïve, T2T application, shorter time-to-remission, as well as lower disease activity scores in remission, increased the occurrence of sustained remission, while advanced age, long disease duration, high baseline disease activity scores reduced the chance of sustainability.

POSTER ABSTRACTS

P01

BODY MASS INDEX; IMPORTANT BUT FORGOTTEN. THE MOST INFLUENTIAL RISK FACTOR OF SUBCLINICAL ATHEROSCLEROSIS IN LUPUS ERYTHEMATOSUS SYSTEMIC POPULATION

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Problem statement: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease, and coronary artery disease is one of the major cause of its morbidity and mortality. Traditional risk factors cannot explain the accelerated atherosclerosis phenomenon of the SLE patients. Whereas, non-traditional risk factors such as disease duration, disease activity, organ damage, inflammatory markers and exposure to therapy are counted to have more significant impact. This study is aimed to compare the influences of traditional and non-traditional risk factors on subclinical atherosclerosis of SLE population of Indonesia, West Java to specified. **Methods:** This is a cross sectional study conducted at Dr. Hasan Sadikin Hospital Bandung, from August to September 2017. The inclusion criteria were women, SLE patients age 18 s/d 65 years old and the exclusion criteria were: smoker, poor echocardiographic window, significant symptom of coronary artery disease, type 2 diabetes mellitus, and SLICC score more than 0 with cardiovascular involvement. The analysis began with bivariate analysis to determine the relationship of each independent variables (non-traditional risk factor and traditional risk factor) with the outcome variable: carotid Intima-media thickness (CIMT). The analytical process was followed by multiple linear regression. **Results:** Total of 70 women patients with SLE, a median age of 34 years and median disease duration of 4 years were analyzed. The result of multiple linear regression analysis showed the coefficient of determination (R²) of the traditional risk factor group was 0,301 or 30,1%, while the non-traditional risk factor group was 0,024 or 2,4%. Individual test was done with t test showed that only Body Mass Index (BMI) gave a significant effect on CIMT with the parameter estimation value (b) BMI ≥ 25 kg/m² after adjusting to other variables was 0.521 (p=0.009). It means each increased BMI of 5 kg/m² in patient with SLE who has BMI ≥ 25 kg/m², at risk to develop thickening of intima media tunica of carotid artery as much as 0.1 mm. **Conclusions:** Traditional risk factors have more significant effect towards CIMT than non-traditional risk factors in SLE patients, and the most influential factor is body mass index.

P02

OSTEOARTHRITIS AND GLUCOSAMINE USE – A SURVEY-BASED STUDY FROM MALAYSIA

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Objectives: The objectives of the study were to explore the factors associated with having self-reported osteoarthritis (OA) and to assess glucosamine use among participants with self-reported OA. **Methods:** A cross-sectional survey study with a 96-item questionnaire was conducted. We recruited participants from a pool of patients and relatives above the age of 40 years attending medical outpatient clinics in University of Malaya Medical Centre. Data pertaining to demographic characteristics, health status, OA symptoms, and glucosamine use were collected. Logistic regression modelling, that included demographic and health status characteristics, was conducted using a backward stepwise method. **Results:** Osteoarthritis was more common in

women (OR 1.47), 50-59 years age group (OR 3.09), ex-smokers (OR 1.72), divorcees (OR 3.33), those with monthly household income RM 3000-RM 4999 (OR 2.13) and those with overall poor quality-of-health (OR 1.58). The odds of having OA along with osteoporosis, back pain, depression, hypertension, hypercholesterolemia, anxiety, and overweight were 9.10, 2.44, 1.85, 1.57, 1.61, 1.45, and 1.37, respectively. The odds of glucosamine use were increased in ex-smokers (OR 5.00), those perceived financially secured (OR 2.53), and osteoporosis (OR 2.33). The OA patients who had poor quality-of-health (OR 2.38) were more likely to use glucosamine, as were those with very good (OR 4.00) or good (OR 5.00) quality-of-life. **Conclusion:** This study highlighted the factors associated with OA and glucosamine use in Malaysia. The data may have implication in public health and future health promotion. **Keyword:** Osteoarthritis, glucosamine, complementary medicine

P03

SAFETY PROFILE OF BARICITINIB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS UP TO 5.5 YEARS: AN UPDATED INTEGRATED SAFETY ANALYSIS

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Problem statement: Baricitinib (bari), an oral, selective JAK 1 and JAK 2 inhibitor is approved in the EU for the treatment of moderate to severely active RA in adults. We further describe the drug's safety profile with updated data from an on-going long-term extension (LTE) study. **Methods:** Long-term safety of once-daily bari was evaluated in "all-bari-RA" dataset [all active RA patients on bari from 8 randomized trials (4 Ph3, 3 Ph2, 1 Ph1b) and 1 LTE study (data up to 01-Sept-2016)]. PBO comparisons were evaluated up to Wk 24 in "PBO-4mg" dataset from 6 Ph2/3 trials, in which patients were randomized to bari 4mg, censoring at rescue or treatment switch. Dose responses were evaluated from 4 Ph2/3 trials, in which patients were randomized to 2 or 4mg and includes data from LTE ("2mg-4mg-extended" dataset) censoring at rescue or dose change (as-treated analysis). Because of latent period for malignancy, 2mg-4mg-extended was analyzed without censoring for rescue or dose change. Incidence rates (IR) per 100 patient-years (PY) were calculated. **Results:** 3492 patients received bari for 6637 total PY of exposure (2400 PY increase from previous analysis); maximum exposure was 5.5 yrs. No differences were seen for bari 4mg vs PBO in AEs leading to permanent discontinuation, death, malignancy, serious infection, or MACE. Herpes zoster IR was significantly higher for bari 4mg vs PBO (IR 1.0 vs 4.3). Malignancy (excluding non-melanoma skin cancer) IR were 0.5 and 1.3 for 2mg and 4mg (as-treated analysis) and 0.7 and 0.9 (as-randomized analysis). IRs for aforementioned events and lymphoma (0.09), gastrointestinal perforation (0.05), and tuberculosis (0.15, all in endemic areas) in the current all-bari-RA were similar to previous reports. Less than 1% of patients discontinued due to abnormal lab results. **Conclusion:** Baricitinib maintained a safety profile similar to previous reports¹ and acceptable in the context of demonstrated efficacy.^{2,3} **References:** • Smolen JS et al. Ann Rheum Dis 2016;75(Suppl 2):243-4. • Taylor PC et al. NEJM 2017;376:652-62. • Genovese Mc et al. NEJM 2016;374:1243-52. •

ultrasonography examination. **Methods:** Fifteen AHU patients (90 joints) were obtained. Six patients (40%) were male. Average age was 49.27 ± 12.35 (with range 32-69 years old). Average serum uric acid level was 7.91 ± 1.51 (with range 7.0 – 12.9 mg/dL). Joints examined were metacarpophalanges digiti I (MCP), metatarsophalanges digiti I (MTP), and trochlear knees. Ultrasound machine was Hitachi HI-VISION Avius (linear transducer 5-10 MHz). **Results:** From ultrasonography of MCP digiti I we found joint effusion in 11 patients (73%), double contour in 10 patient (66%), tophus in 1 patient (6%), snow storm appearance in 1 patient, hypervascularization in 1 patient, and synovitis in 3 patients (20%). No bone erosion was found. Four patients (26%) showed normal features. MTP digiti I joints showed 13 joint effusions (86%), double contour in 13 patient (86%), 1 bone erosion (6%), 3 tophi (20%), and 2 synovitis (13%). There was no hypervascularization nor snow storm appearance found. Two patients (13%) showed normal USG. From trochlear knees we found 1 joint effusion (6%), 1 double contour (6%), and 14 patients (93%) were normal. **Conclusions:** Even in AHU patients we found 87% had abnormal USG. The most frequent joint affected was MTP digiti I. Whether abnormal USG will influence our decision of when to initiate urate-lowering therapy and chronic anti-inflammatory treatment is still to be determined.

P07

RENAL DYSFUNCTION EVALUATION SHOULD BE WARRANTED IN AGED PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING METHOTREXATE AND NON-STEROIDAL ANTI-INFLAMMATORY DRUG

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Problem statement: Methotrexate (MTX) and non-steroidal anti-inflammatory drugs (NSAIDs) are potentially nephrotoxic drugs. However, renal dysfunction is underestimated in the patients with rheumatoid arthritis (RA) who are taking these medicines. **Methods:** This study enrolled the patients with RA who had been treated with the regimen including weekly MTX and daily NSAID. They visited the rheumatology clinic in our hospital between April and June 2018. We collected the clinical and laboratory data of the patients including demographic factors, body weight, height and serum creatinine levels. We calculated estimated glomerular filtration rate (eGFR) using CKD-EPI creatinine equation and MDRD study equation with or without body surface adjustment (BSA). **Results:** Fifty-seven patients were enrolled. Female to male ratio was 4.7: 1.0. Their age was 57 ± 11 (mean \pm SD) years. Almost all (98%) had serum creatinine level below 1.0 mg/dL. By CKD-EPI creatinine equation, moderate decrease in eGFR (30-59 ml/min) was observed in 3 patients (5%) with BSA and 4 patients (7%) without BSA. Sixteen patients (28%) showed mild eGFR reduction (60-90 ml/min) with BSA; 23 patients (40%) without BSA. In particular, decrease in eGFR was predominant in the aged patients. Forty-one percent of those aged over 50 years (N=27) had decreased eGFR with BSA; 100% without BSA. The results were similar by MDRD study equation. **Conclusions:** In the patients with RA treated with MTX & NSAID, prevalent renal dysfunction is evident by eGFR, especially in aged patients over 50 years, at the normal range of serum creatinine. Thus further evaluation for kidney damage and renal toxicity monitoring are essential in these patients.

P08

JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT

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Problem statement: Systemic lupus erythematosus (SLE) is an autoimmune multisystem disease associated with various clinical manifestations. Juvenile-onset SLE is extremely rare and comprises only 15-20% of SLE cases. The prevalence of SLE in this age group is 6.3-19.3 per 100,000 in Asia. The ratio of female to male is 4.7-6.2:1. The mean age at diagnosis of pediatric-onset SLE is 8.6-13.5 years. Due to its rare occurrence in the pediatric age group and

uncommon sexual predilection in males, we now report a case of a 15-year-old male patient diagnosed with SLE. **Methods/ Results:** A 15-year old male initially presented with 1-year generalized joint pains accompanied by frequent episodes of frothy urine. Persistence of joint pains prompted consult, with subsequent determination of anemia and a positive Antinuclear Antibody (ANA). Further confirmatory tests for SLE were done. Presence of significant proteinuria led to kidney biopsy and showed Class III Lupus Nephritis. Patient was subsequently treated with immunosuppressant. **Conclusion:** Childhood SLE is a challenge on both diagnosis and treatment. The greater awareness of SLE as a potential diagnosis, particularly in fertile females, may lead to bias and eventual delay in diagnosis and treatment in males with similar symptoms. The consequence would be a risk for greater burden of inflammation and subsequent damage over time. This case emphasizes that although males with SLE represent the minority of cases, these cases should not be subordinated to females with SLE in terms of health-related issues. The clinicians should be aware of the greater risk of systemic complications in children with SLE. Henceforth, pediatric SLE patients should be continually followed up and appropriate therapy should be initiated depending on the disease activity to reduce morbidity and mortality. Rheumatologists caring for children with SLE must be aware of the greater risk of major hematological and renal involvement as well as long-term morbidity.

P09

COMPARING THE EFFECTIVENESS OF INTRAVENOUS PATIENT-CONTROLLED ANALGESIA (IVPCA) VERSUS PERIOPERATIVE ANALGESIA (POA) TO RELIEVE POSTOPERATIVE PAIN AFTER TOTAL KNEE REPLACEMENT SURGERY: A RETROSPECTIVE STUDY

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Problem statement: Suboptimal pain management may have jeopardized the rehabilitation progress and imposed negative impacts on osteoarthritis patients undergone total knee replacement (TKR). The conventional modalities intravenous patient-controlled analgesia (IVPCA) with morphine and tramadol for this group of patients might seem inadequate to relieve their pain and opioids could induce adverse effects. A new perioperative analgesia (POA) approach of using etoricoxib and oxycontin may be an effective alternative. **Methods:** This retrospective study analyzed data from patients undergone TKR surgery to determine the effectiveness of IVPCA versus POA on postoperative pain relief and any opioid-related side effects. Among a total of 102 patients, 53 received both IVPCA and regular oral analgesic from September 2016 to February 2017, while 49 patients were given preemptive oral etoricoxib before surgery and duly together with oxycontin after surgery from September 2017 to February 2018 as the mainstay analgesics. Pain scores as the primary outcome were measured by Numeric Rating Scale (0-10) at rest (NRS-R) and on movement (NRS-M). It was analyzed by one-way ANCOVA (analysis of covariance), and side effects (such as nausea) were analyzed by fisher's exact test as secondary outcome. **Results:** Demographic data of both groups were comparable. NRS-R of POA was significantly lower [mean (M) = .37, standard error (SE) = .16] when compared with the IVPCA group (M = .87, SE = .16) with a mean difference of .50, 95 CI [.049, .944], $p = .030$, while NRS-M was also found significantly lower (M = 2.96, SE = .31) in POA group than the IVPCA group (M = 4.26, SE = .29) with a mean difference of 1.29, 95 CI [.46, 2.13], $p = .003$. A higher proportion of patients in the IVPCA group experienced at least one adverse effect than in the POA group (45% vs. 18%, fisher's exact $p = .006$). **Conclusion:** The POA approach provided better postoperative pain relief and reduced opioid-related side effects than conventional IVPCA treatment to enhance patients' rehabilitation. We also found that oxycontin may be an effective analgesic for pain management of TKR patients. Prospective studies are suggested to evaluate and compare the costs and effectiveness between IVPCA and this POA regimen.

P10 MITOCHONDRIAL DYSFUNCTION-MEDIATED SARCOPENIA IS ASSOCIATED WITH OSTEOPOROSIS BY MYOTOKINE

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Objective: Emerging evidence has shown that sarcopenia, an aging-induced loss of skeletal muscle mass, is an important risk factor for osteoporotic fractures. However, sarcopenia-induced factors for the development of osteoporosis have not been elucidated. **Methods:** We used a mouse model of skeletal muscle-specific deficiency of Crif1 (MKO), an integral protein in the large subunit (39S) of the mitoribosome, to identify the factors associated with osteoporosis. **Results:** MKO mice exhibited reduced muscle mass and lower grip strength compared to WT mice, suggesting the development of sarcopenia induced by mitochondrial dysfunction in muscle of MKO mice. To assess trabecular and cortical bone morphology, ex vivo micro-CT analyses of the tibia was performed in MKO and WT mice. MKO mice showed significantly reduced levels in bone mineral density, bone volume/tissue volume, trabecular number, trabecular thickness, and cortical thickness compared to WT mice. Moreover, serum P1NP was decreased and serum CTX was increased in MKO mice. Additionally, a transcriptomic analysis was conducted using a RNA seq to identify the secretory factors from skeletal muscle of MKO mice. In the qRT-PCR analysis, the expression of fgf21, gdf15, and ostn was significantly enhanced in skeletal muscle of MKO mice. Furthermore, the levels of serum FGF21 and GDF15 were significantly increased in MKO mice compared to WT mice. Therefore, we treated recombinant GDF15 in BMMs, there was significant stimulated RANKL-mediated osteoclast differentiation. **Conclusion:** Muscle specific mitochondrial dysfunction induced loss of skeletal muscle mass and reduced bone mineral density in mice. Moreover, mitochondrial dysfunction in muscle enhanced the expression of Fgf21 and Gdf15, which might be involved in the development of osteoporosis in mice. We are going to show in the near future that mitochondrial dysfunction-mediated sarcopenia contribute to the increase in the expression of Gdf15, which may promote osteoporosis in mice.

P11 PREDICTIVE ROLE OF BIOMARKERS REGARDING RESPONSE TO ETANERCEPT THERAPY IN RHEUMATOID ARTHRITIS

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Problem statement: 20-40% of the patients with rheumatoid arthritis are declared nonresponders to at least one of the anti-TNF therapies. **Objectives:** evaluating the predictive role for the response to Etanercept therapy of RF IgM, IgA, anti-CCP, anti-MCV, 14-3-3 eta protein and COMP. We also assessed the status pretreatment of these biomarkers and the response to treatment. **Methods:** prospective, observational study including 16 patients followed 12 months with active RA, uncontrolled by conventional synthetic DMARDs. Clinical assessment was performed at 0,6 and 12 months according to ACR criteria approved by OMERACT and evaluation of treatment response according to EULAR criteria (good/moderate/nonresponder). **Results:** of the 16 patients included in the study, 13 (81.3%) were women and 3 (18.7%) men, the average age of the entire group was 58.56 ± 8.52 years. At 6 months, 3 patients were declared nonresponders, 9 achieved moderate response and 4 good response. Following baseline immunological parameters titres and the response at 6 months, general tests have identified significant differences between groups only for one of the six biomarkers studied. Lower baseline titres of 14-3-3 eta protein (0.25±0.380 ng/ml, p=0.004) had predictive value for achieving a good response at 6 months. Grouping patients in 2 categories (responders/nonresponders), 14-3-3 eta protein maintained predictive value

for the response at 6 months (p=0.0005). After 12 months 3 patients achieved moderate response and 10 good response. At this evaluation we didn't find significant differences between baseline immunological parameters titres and the EULAR response (moderate/good response RF type Ig M 218.67±71.287/133.21±138.976 U/ml, p=0.3458, RF type Ig A 142.57±139.556/13.70±14.295 U/ml, p=0.0898, anti-CCP 91.80±50.331/75.09±51.751 ng/ml, p=0.6317, anti-MCV 164.68±263.570/166.84±231.329 ng/ml, p=0.9892, 14-3-3 eta protein 0.00±0.000/0.32±0.404 ng/ml, p=0.1483, COMP 1055.9±130.509/895.1±209.980 ng/ml, p= 0.2429. Following the status pretreatment of biomarkers and EULAR response to Etanercept therapy, we identified differences almost significant for 14-3-3 eta protein at 6 months, all 3 patients declared nonresponders were 14-3-3 eta positive, and only 3/9 (33.3%) from those with moderate response and 1/4 (25%) of good responders were tested positive (p=0.0504). **Conclusions:** 14-3-3 eta protein could be one of the biomarkers for identifying pretreatment the patients who will respond to biologic therapy in Rheumatoid Arthritis.

P12 GENISTEIN EFFECTS ON BONE METABOLISM IN POSTMENOPAUSAL WOMEN: A META-ANALYSIS

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Problem statement: Estrogen deficiency is a major cause of osteoporosis worldwide. Considering the risk of hormone replacement therapy, there is mounting interest in phytoestrogen as potential natural treatment option. Genistein, an isoflavone phytoestrogen, has been proposed to play role in postmenopausal bone metabolism. Our study aimed to evaluate the effects of genistein on bone metabolism in postmenopausal women. **Methods:** We conducted the study according to the meta-analysis PRISMA guideline. Relevant studies were identified from a search of PubMed, Cochrane, and EBSCO databases. Studies using combination of genistein and other phytoestrogens were excluded. Quality of each selected randomized placebo-controlled trials (RCTs) was evaluated using Jadad score. We pooled mean difference (MD) with 95% confidence interval (CI) of bone mineral density (BMD) and bone-specific alkaline phosphatase (B-ALP). Statistical analysis was performed using Review Manager 5.3. **Results:** Three high quality RCTs involving 570 postmenopausal women were included in this study. Subjects analyzed in the studies were healthy women in the first study, osteopenic women in the second study, and osteoporosis women in the third study. One study had one year treatment duration and 2 studies had 2 years treatment duration. All 3 studies used the same dose of genistein (54 mg/day). Genistein had tendency in improving lumbar BMD although statistically was not significant. Genistein significantly increased BMD in the femoral neck after 1 year treatment (MD 0.04, 95% CI 0.03-0.06; p 0.00001), and the effect was greater after 2 years treatment (MD 0.09, 95% CI 0.05-0.14; p 0.0001). Likewise, genistein markedly increased serum B-ALP, with higher result seen after 2 years treatment (MD 4.39, 95% CI 3.44-5.33; p 0.0001) rather than 1 year treatment (MD 3.64, 95% CI 3.08-4.2; p 0.0001). **Conclusion:** Our study demonstrated genistein has time-dependent effects on femoral bone density and bone turn-over. It showed benefit in bone metabolism over healthy, osteopenic, or osteoporosis postmenopausal women. More studies with larger sample size and longer duration of treatment are warranted.

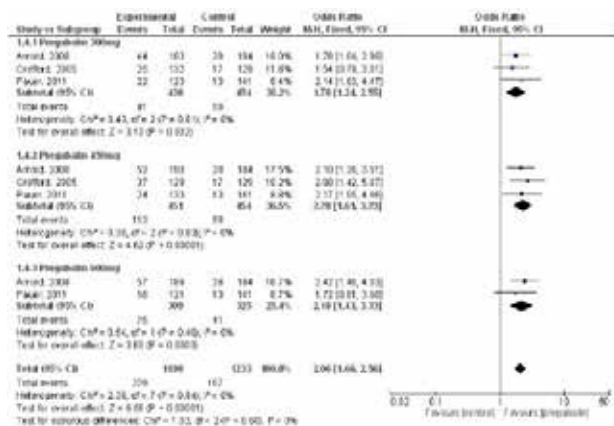


All authors declare no conflict of interest

P13 EFFECTIVENESS OF PREGABALIN FOR FIBROMYALGIA PAIN: A META-ANALYSIS

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Problem statement: Fibromyalgia is a difficult-to-treat chronic musculoskeletal pain and tenderness syndrome. It is considered due to augmented pain processing in central nervous system. Interest in antiepileptic drugs, included pregabalin, for treatment of fibromyalgia is currently growing. This study aimed to investigate the effectiveness of pregabalin for fibromyalgia. **Methods:** We conducted the study according to the meta-analysis PRISMA guideline. Relevant randomized controlled trials (RCTs) were identified from a search of PubMed, Cochrane, and EBSCO databases. Quality of selected studies was assessed using Jadad score for randomized placebo-controlled trials (RCT). Primary outcome was pain score reduction (30% and 50% reduction) and secondary outcome was patient global impression of change. Statistical analysis was performed using Review Manager 5.3. **Results:** Six international, multicenter, high-quality RCTs with 8-15 weeks duration of treatment met inclusion criteria. Four studies used different fixed dose (300 mg/d, 450 mg/d, 600mg/d) and 2 studies used titrated dose in evaluating the efficacy of pregabalin. There was statistically significant benefit of pregabalin over placebo in mean pain score reduction [odds ratio (OR) 1.81, 95% confidence interval (CI) 1.56-2.10 p 0.00001 in fixed dose pregabalin 30% pain reduction; OR 2.06 95% CI 1.66-2.56 p 0.00001 in fixed dose pregabalin 50% pain reduction; OR 1.53 95% CI 1.10-2.13 p 0.01 in titrated dose pregabalin 30% pain reduction; OR 1.80 95% CI 1.12-2.88 p 0.01 in titrated dose pregabalin 50% pain reduction]. Pregabalin also demonstrated significantly better patient global impression of change than placebo. No heterogeneity was seen in most groups. No publication bias was observed. **Conclusion:** Our study showed pregabalin monotherapy was effective for pain treatment associated with fibromyalgia. Further studies with longer treatment duration are needed to confirm the long term effectiveness of pregabalin for fibromyalgia treatment. All authors declare no conflict of interest



P14 TRANSVERSE MYELITIS IN AN INDONESIAN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENT

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Background: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease characterized by the formation of various autoantibodies and multiple organ involvement. Transverse myelitis is one of various manifestations of neuropsychiatric lupus (NPSLE) with clinical manifestations of motoric, sensoric, and autonomic dysfunctions. Its annual incidence is

1.34:1.000.000 and occurs in 1-2% SLE patients. It is one of the more debilitating manifestations of NPSLE. However, only few studies reported transverse myelitis in Indonesian SLE patients. **Case:** A 36-years old Japanese female came into emergency department with muscle weakness in upper and lower extremities for 21 days. Muscle weakness was described as progressive, involved distal area of both extremities, and debilitating. She also complained of teary eyes, blurred vision, pain and swelling in both eyes. History of past illness, she had fever, anemia, arthritis and muscle weakness 3 years ago. By her previous attending physician she was considered to have an autoimmune disease and she was given methylprednisolone, the symptom became better. On physical examination, she was found to have muscle weakness on flexor and extensor both extremities, hypesthesia as high as thoracic VII segment, hyporeflexia in both extremities, visus oculi dextra (VOD) 2/60, visus oculi sinistris (VOS) 1/300. She also had fever, rashes on both legs and oral ulcer. Laboratory examinations revealed anemia, hypocomplementemia (C3 56 mg/dL, C4 <6.0 mg/dL), positive ANA test 377,79 with nucleosome pattern. CT scan examination revealed lacunar infarction in internal capsule and intraluminal lesion in the level of right M1 with high consideration of stenosis. Electromyography examination revealed the presence of axonal sensory motor polyradiculoneuropathy with muscle denervation. She was diagnosed as SLE with transverse myelitis and papilitis oculi on both eyes and she was given pulse dose methylprednisolone (500 mg/day) for 3 consecutive days and cyclophosphamide. Methylprednisolone was continued 1 mg/kgBW/day and the dose was tapered off after one month administration. Routine physical rehabilitation therapy was performed. After the third cycle of cyclophosphamide administration, her clinical condition improved. **Conclusion:** Transverse myelitis as well as papilitis is a rare form of neuropsychiatric lupus which can be debilitating and impair patient's quality of life. Combination of medication and physiotherapy can improve patient's condition. **Keyword:** Systemic Lupus Erythematosus, transverse myelitis, neuropsychiatric lupus, muscle weakness

P15 CASE SERIES THERAPY FOR ANCA ASSOCIATED VASCULITIS: PHILIPPINES BASED EXPERIENCE

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Introduction: ANCA associated vasculitis (AAV) is a group of chronic, relapsing, primary systemic vasculitis affecting small to medium sized vessels. It is relatively an uncommon disease with prevalence rates ranging from 10 to 22 per million. Combination of glucocorticoids and cyclophosphamide has been the standard therapy for remission of disease activity. Recommendations (EULAR/ERA-EDTA) have also stated the use of alternative therapies depending on the classification of disease involvement. Due to the rarity of disease, there has been limited published data involving management of this subset of patients. We present two cases of Granulomatosis with Polyangiitis (GPA), an ANCA associated vasculitis, representing different treatment strategies. Therapies given were guided by clinical status and published recommendations. **Case 1:** A 72 year old female diagnosed GPA who presented with biopsy proven necrotizing glomerulonephritis. Initially given combination glucocorticoids and cyclophosphamide, however, the patient developed painless hematuria after first dose. She was given alternative rituximab therapy (375 mg/m²) weekly for four weeks. After which, the patient was further maintained on a low dose steroid. Seven months after and on tapering steroid dose, the patient showed progressive clinical improvement with no signs of relapse of disease. **Case 2:** A 55 year old female who had transient vision loss and chronic draining sinus over zygomatic area. Biopsy of the ethmoid tissue showed GPA with background of chronic inflammation, granulation, necrosis and fibrosis. She initially underwent combination glucocorticoid and cyclophosphamide pulse therapy. But due to the patient's preference to oral non-cyclophosphamide therapy, azathioprine was subsequently given. While on azathioprine therapy, there was recurrence of headache, facial fullness and re-appearance of the draining sinus.

Intensification of azathioprine and steroid doses was done but the patient was eventually shifted to mycophenolate mofetil due to persistence of symptoms. Two months after switching therapy, patient was noted to have improved clinical status with no recurrence of the draining sinus. **Conclusion:** The cases presented reinforce that clinical patient status as well as guidelines should be considered for ideal management of AAVs.

P16
PREDICTORS FOR THE RESPONSE TO ANTI-TNF THERAPY IN RHEUMATOID ARTHRITIS-WHERE OLD AND NEW BIOMARKERS STAND?

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Problem statement: identifying pretreatment patients who will/not respond to biologic therapy is necessary for reducing the possible side effects of the treatments and reducing the costs for treating patients. The aims of the study were to test the possible predictive role of RF type IgM and Ig A, anti-CCP, anti-MCV, 14-3-3 eta protein 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 conventional synthetic DMARDs. 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, anti-CCP, 14-3-3 eta protein and COMP 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 maintained their predictive value for the response at 6 months (Table 1).

	Nonresponders	Moderate responders	Good responders	p-value	Nonresponders	Moderate responders	Good responders	p-value
RF type IgM	93.93 \pm 99.402	91.73 \pm 111.47	93.34 \pm 91.918	0.43479	93.316	93.91 \pm 99.907	93.316	0.31048
RF type IgA	93.93 \pm 99.402	93.93 \pm 99.402	93.93 \pm 99.402	0.99999	93.93 \pm 99.402	93.93 \pm 99.402	93.93 \pm 99.402	0.99999
Anti-CCP	93.93 \pm 99.402	93.93 \pm 99.402	93.93 \pm 99.402	0.99999	93.93 \pm 99.402	93.93 \pm 99.402	93.93 \pm 99.402	0.99999
Anti-MCV	93.93 \pm 99.402	93.93 \pm 99.402	93.93 \pm 99.402	0.99999	93.93 \pm 99.402	93.93 \pm 99.402	93.93 \pm 99.402	0.99999
14-3-3 eta protein	93.93 \pm 99.402	93.93 \pm 99.402	93.93 \pm 99.402	0.00001	93.93 \pm 99.402	93.93 \pm 99.402	93.93 \pm 99.402	0.00001
COMP	93.93 \pm 99.402	93.93 \pm 99.402	93.93 \pm 99.402	0.00001	93.93 \pm 99.402	93.93 \pm 99.402	93.93 \pm 99.402	0.00001

Table 1. Baseline titres and EULAR/2 groups response to anti-TNF therapy at 6 months

After 12 months, 1 patient was declared nonresponder, 11 achieved moderate response and 44 good response. For this visit, lower baseline titres for RF type Ig M (92.93 ± 120.22 U/ml, $p=0.01032$) and Ig A (49.96 ± 98.08 U/ml, $p=0.00247$) had predictive value for achieving a good response at 12 months. We didn't obtain other information grouping patients in 2 categories. The status pretreatment influenced the good response for COMP at 6 months ($p=0.0001$) and RF IgA at 12 months ($p=0.0041$). 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 $\lambda^2 = 5.795$, $p = 0.670 \geq 0.05$ 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.

P17
RISK FACTORS FOR RELAPSE IN INFLAMMATORY MYOPATHY
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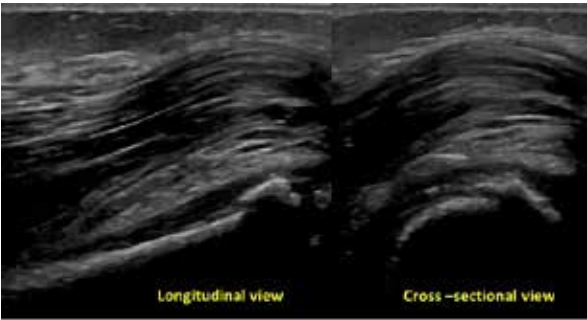
Problem statement: Many inflammatory myositis patients experience relapse (relapse rate: 48~65%). Risk factors for relapse in inflammatory myositis remain uncertain. We investigate the relapse and related factors in patients with inflammatory myopathy. **Methods:** Retrospectively, the patients who met the Bohan and Peter criteria for the diagnosis of dermatomyositis and polymyositis were collected in a tertiary hospital between Jan. 2005 to Dec. 2016. The relapse was defined as resuming glucocorticoid or dose up of glucocorticoid more than 50% due to myositis or skin aggravation after improvement of inflammatory myositis by initial treatment. We investigated factors associated with the relapse using Multivariate Cox proportional hazards models with backward elimination. **Results:** We identified 138 patients (61 dermatomyositis, 3 inclusion body myositis, and 74 polymyositis), and high dose (1mg/kg) of glucocorticoid (median, 60mg [50.0-60.0], prednisolone equivalent) was given as an initial treatment for inflammatory myopathy. Glucocorticoid dose has been reduced less than 15 mg (prednisolone equivalent) until 5 months (median, [4-7]) after initial treatment. However, during glucocorticoid tapering, relapse occurred in 86 patients (62%) after 12 months (median, [7-25]) of initial treatment. Independent risk factors for relapse on multivariable analysis in the overall inflammatory myopathy patients included anti-Ro antibody positivity (adjusted HR 1.84, $p=0.028$), elevated level of creatine kinase at 1 month after initial glucocorticoid treatment (adjusted HR 2.10, $p=0.007$), administration of immunomodulators for maintenance (methotrexate, azathioprine, or cyclosporine; adjusted HR 0.41, $p=0.003$). **Conclusion:** Administration of immunomodulator for maintenance may help to reduce the risk of relapse in inflammatory myopathy.

P18
CASE REPORT: FIVE YEARS OLD BOY WITH A PHYSEAL FRACTURE, DIAGNOSED BY MUSCULOSKELETAL ULTRASOUND

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Image: An ultrasound image showed a bony fragment of physal plate on patient femur; left: longitudinal view; right: cross-sectional view.



A case of five years old boy presented with severe knee pain after sport injury. The plain radiograph was normal. But musculoskeletal (MSK) ultrasound of the knee demonstrated a type II physal fracture according to the Salter and Harris

classification. Physeal fracture was occur 30% of the fracture in children. Magnetic resonance and computer tomography were used to determine the type of physeal fractures and the prognosis. Using MSK ultrasound to evaluate knee injuries could be done at bed - side and could done without contrast – media exposure or sedation. It is a reliable investigation to diagnose physeal injuries in small children.

P19
RADIOLOGY PROFILE OF ANKYLOSING SPONDYLITIS IN DR. SOETOMO GENERAL HOSPITAL SURABAYA

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Problem statement: Ankylosing Spondylitis (AS) is a common cause of back pain in Indonesia populations. The incidence of new case AS was 18% in all rheumatology outpatient department during 2017. Despite the role of HLA-B27, previous study revealed that the low prevalence of HLA-B27 in native and Chinese Indonesian populations (8% and 62.2%). Therefore, diagnosis of AS relies on radiology examination. Despite the extensive use of radiology examination, there are limited studies which explores the radiological manifestations in Indonesian patients. **Methods:** Observation analytic study with cross sectional design was conducted in February - May 2018. 33 AS patients who visited rheumatology outpatient clinic was included in this study. There were no history of malignancy or recent hospitalization in all patients. Lumbosacral and cervical radiology examination were performed in all patients. Radiological severity was measured using mSASSS. Disease activity was observed using BASDAI, BASFI, and ASDAS-ESR. **Results:** There were 10 (30.3%) males (group 1) and 23 (69.7%) females (group 2). The average of mSASSS score was 24.36±9.28 (interobserver variance K=0.93, p=0.00). There were no mean differences of mSASSS between male and female (26.9±15.1 vs 23.3±5.3 p=0.005). Radiology manifestations observed ranging from squaring of vertebrae which was observed in all patients to complete bridging which was observed in 4 (12.1%) patients. Positive correlation was observed between mSASSS with disease duration (r:0.36, p=0.04) and age (r:0.47, p:0.00). However, there were no correlation observed between mSASSS with other disease indices such as BASDAI, BASFI, and ASDAS-ESR (r:0.13, p=0.54; r:0.11, p=0.59; r:-0.03, p=0.88). **Conclusion:** Squaring of vertebrae is the most common radiology manifestations in AS patients and the severity of radiological damage correlates with duration of disease. Therefore, routine radiology evaluation for detecting long term complication of AS is recommended.

P20
PHYSIOTHERAPISTS COULD REPLACE PHYSICIANS AS PRIMARY ASSESSORS FOR PATIENTS WITH SUSPECTED KNEE OSTEOARTHRITIS—A RANDOMISED CONTROLLED STUDY

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Problem statement: Common osteoarthritis (OA) symptoms such as pain and physical disability directly affect patients' social interactions, mental functioning, and sleep quality. Patients with knee OA report among the lowest health-related quality of life (HrQoL) compared with other chronic diseases. It has been estimated that consultations to healthcare will probably increase with 30-50% among patients with OA over the next 20 years. Physiotherapists are primary assessors for patients with knee OA and provide recommended treatments. However, it is unclear if a physiotherapist could be the only primary assessor for this patient group. We hypothesise that all patients with suspected knee OA could be assessed by a physiotherapist first and be referred to physician only when it is acquired. The aim of this study was to explore differences in HrQoL, pain and physical function in patients with suspected knee OA after being assessed, diagnosed and treated by physiotherapist first

compared with being assessed by a physician first. **Methods:** Patients seeking primary care with suspected knee OA were randomised to either a physiotherapist or a physician for assessment, diagnose and treatment. HrQoL (Euroqol - EQ5D-3L index, EQ5D-3L VAS), pain intensity (visual analogue scale) and physical function (30 seconds chair stand test) were measured before randomisation, and at 3-, 6- and 12 months. Mann-Whitney's test and Chi² test for independence were used with a significance level of p0.05. **Results:** A total of 363 patients with knee pain were screened for OA, 69 patients with suspected knee OA were randomised to either a physiotherapist (n=35) or a physician (n=34). Both groups improved their HrQoL, pain and physical function at all follow ups. Patients rated significantly better HrQoL (EQ5D-3L VAS) one year after physiotherapy assessment (84 (SD 11); 74 (SD 15), p=0.018). **Conclusion:** These results showed that physiotherapy assessment could replace physician assessment without having impact on patient reported outcome after treatment for patients with suspected knee OA. We believe that this will play a role in managing the expected increase in OA consultation in primary care.

P21
ASSOCIATION OF SYNOVIAL URIC ACID WITH INFLAMMATORY OSTEOARTHRITIS: A REPORT OF 30 PATIENTS

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Problem statement: Osteoarthritis (OA) is not only a degenerative arthritis, but often then not inflammatory in nature. Synovial fluid uric acid has been suggested to be a biomarker of the severity of OA. We report a consecutive series of 30 Asian patients with inflammatory OA and their association with synovial fluid uric acid. **Methods:** All patients with knee OA seen in the clinic from January to June 2018 were reviewed. 30 patients with inflammatory OA on ultrasound and had synovial fluid analysis done were selected. The synovial fluid uric acid levels and the presence of uric acid crystals were reviewed and the results collated. The duration of follow-up was 1-4 months. **Results:** 7 male patients and 23 female patients were studied. Age range 48-77 years old, with 25 Chinese, 3 Malays and 2 Indians. All had inflammatory OA on ultrasound with effusion, synovitis, positive color doppler signals and osteophytes. OA Grades: I - 7; II - 16; III - 6 PATIENTS. 1 had Post Total Knee Replacement. 5 had concomitant Rheumatoid Arthritis. Duration of knee pain: 1 month to 5 years, mean of 9 months. Synovial fluid uric acid levels ranged from 2.2-11.1mg/dl (mean 5.2) Uric Acid Crystals - Few: 7 patients; 1+ : 20 patients; 2+ : 3 patients. 12 patients had repeated synovial fluid uric acid analysis. All patients had intraarticular steroid injections. 4 had intraarticular NSAIDs injections. 22 had intraarticular viscosupplementation. All except 2 patient had urate lowering therapy including 4 - ncariccin and 2 - febuxostat. 22 were on uric acid lowering supplements like bellerina terminalis. **Conclusions:** Inflammatory OA is associated with the presence of synovial fluid uric acid. Synovial fluid uric acid may serve as a biomarker of inflammatory OA and with recurrent synovitis. Uric acid crystals is known to be associated with IL-16 and IL-18 levels and trigger inflammasome reactions and hence contributing to flares of OA. Synovial fluid uric acid may represent a prognostic factor of more severe OA and also be a potential therapeutic target to ameliorate the progression of OA.

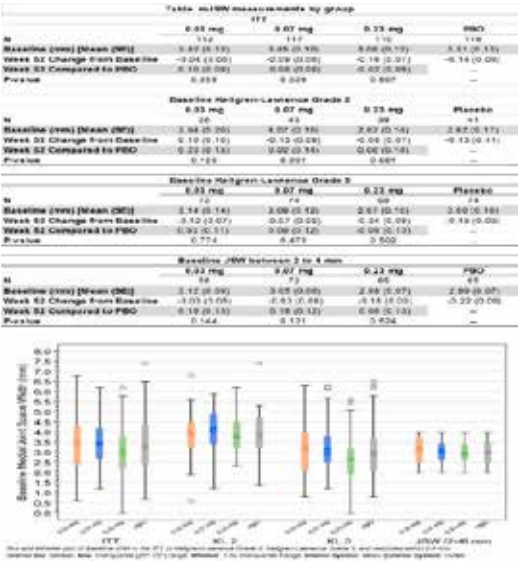
P22
EFFICACY OF COMBINATION URIC ACID LOWERING SUPPLEMENTS IN THE TREATMENT OF HYPERURICAEMIA IN GOUT PATIENTS: A PILOT STUDY OF 22 PATIENTS

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Problem statement: Hyperuricaemia and gout is commonly encountered in the community rheumatology clinic. While urate lowering therapy (ULT) like allopurinol, benzbromarone and febuxostat remain the mainstay of treatment but they are not without side effects. And despite these ULTs, some patients

fail to reach the target uric acid levels, There are also some patients who prefer natural supplements to synthetic medicines. Previous studies have shown the efficacy of Vitamin C, Tart Cherry extracts and Terminalia Bellerica extracts in lowering uric acid levels, including one done by the author. We explore the efficacy of combination supplements (Vitamin C + Tart Cherry extracts + Terminalia Bellerica extracts) in a pilot study in our patients with hyperuricaemia. **Methods:** 22 consecutive patients with hyperuricaemia and/or gout that were given the Gout Preventive Formula in our clinic from May 2017 to May 2018 were reviewed. Gout Prevention Formula consists of Terminal bellerica 500mg, Vitamin C 1000mg and Tart cherry powder 480mg, packed into a sachet of 3 capsules each. The patient consumes 1 sachet a day. The serum uric acid levels were measured before and after the supplements were started, and the results collated. The duration of follow-up was 1 month - 12 months. **Results:** 16 female and 6 male patients were studied, with 18 Chinese, 3 Malays and 1 Thai patient. The age range was from 31 to 83 years old. The response rate was positive in 16 patients (73%). The mean reduction in uric acid levels was 1.72 mg/dl (range 0,1 to 4.9mg/dl). 6 patients did not respond. Benzbromarone and febuxostat were added in these cases. All patients except 1 had no adverse effects to the Gout Prevention Formula. 1 patient had leg cramps after the supplements and discontinued. **Conclusion:** In our pilot study, "Gout Prevention Formula" was shown to be safe and had a modest effect in 73% of our patients with hyperuricaemia. Combination uric acid supplements is a useful adjunct therapy in those patients with mild hyperuricaemia as monotherapy, and can also be added to conventional therapy in those who fail to achieve target erum uric acid levels.

Infirist, Medivir, Merck Serono, Novartis, Ono Pharmaceutical Co., Samumed, LLC; M. Bowes and A. Brett: employees of Imorphics, subsidiary of Stryker; C. Latterman: consultant for Samumed, LLC, Vericel, and Cartiheal.



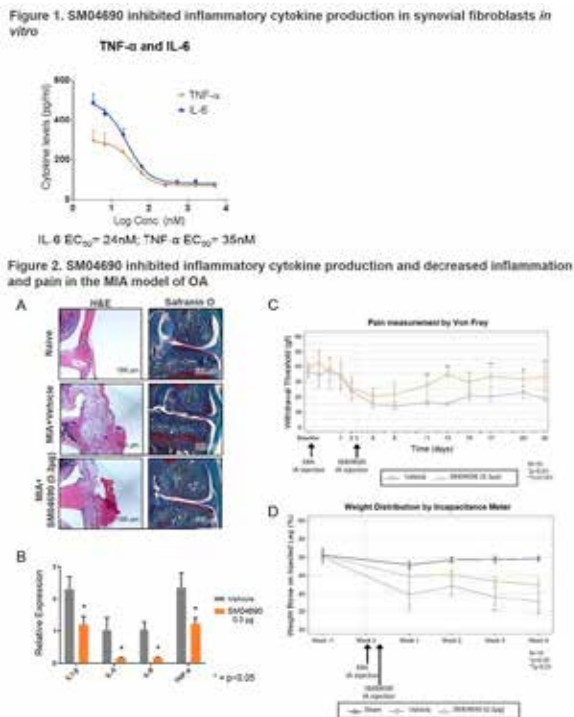
P23
JOINT SPACE WIDTH CRITERIA CAN REDUCE KNEE OSTEOARTHRITIS TRIAL HETEROGENEITY: PHASE 2 POST-HOC DATA FROM WNT PATHWAY INHIBITOR SM04690
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Problem statement: Limitations of Kellgren-Lawrence (KL) grading in osteoarthritis (OA) trials include inconsistent interpretation leading to study population heterogeneity. Knees with radiographic 2-4 mm medial joint space width (mJSW) showed improved responsiveness for OA biomarkers during a 12-month follow-up period. This criterion was applied post-hoc to data from a phase 2 trial of SM04690, a small molecule Wnt pathway inhibitor in development as a potential disease-modifying drug in knee OA (DMOAD). **Methods:** Knee OA subjects, KL grades 2-3 were randomized to receive a single 2 mL intra-articular injection of 0.03 mg, 0.07 mg, or 0.23 mg SM04690 or placebo (PBO) into the target (most painful) knee at Day 0. Radiographs (posteroanterior, weight-bearing, QuAP™ positioned), were taken at Weeks 0 and 52. Two blinded, centralized readers measured mJSWs, which were compared qualitatively, post-hoc, between groups (intent-to-treat [ITT], KL 2, KL 3, mJSW 2-4 mm). Heterogeneity was assessed with mJSW box-and-whisker plots. Finally, to assess effects of baseline heterogeneity, Week 52 in-group changes in mJSW were compared. **Results:** Of 453 subjects, 161 were graded as KL 2 and 290 as KL 3, and 258 had baseline mJSW 2-4 mm. Baseline heterogeneity was reduced in the 2-4 mm group compared with ITT, KL 2, and KL 3 groups (Figure). Observed mJSW changes at Week 52 compared with PBO were beyond measurement error (>0.13 mm; Dupuis et al., *Osteoarthritis and Cartilage* 2003) for 0.03 mg and 0.07 mg SM04690 doses in the 2-4 mm group, and 0.03 mg dose in the KL 2 group (Table). **Conclusion:** A less heterogenous baseline reduces measurement variability, which may reduce the required population size in a clinical trial while maintaining statistical power to detect change beyond radiographic measurement error. Specific mJSW inclusion criteria should be considered in knee DMOAD trials. **Disclosures of Interest:** J. Tambiah, C. Swearingen, and S. Kennedy are all shareholders and employees of Samumed, LLC; P. Conaghan: Consultant for Flexion Therapeutics, AbbVie,

P24
SM04690, A WNT PATHWAY INHIBITOR: ANTI-INFLAMMATORY AND CARTILAGE PROTECTIVE EFFECTS IN PRECLINICAL OA MODELS
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Problem statement: Osteoarthritis (OA) is characterized by pain, swelling, and reduced function in the knee joint. Upregulated Wnt signaling drives OA through synovial inflammation, increased subchondral bone, and thinning cartilage. SM04690, a small molecule Wnt pathway inhibitor that demonstrated chondrogenic and anti-inflammatory properties preclinically, was further evaluated to determine its potential to reduce inflammation, protect cartilage, improve joint health, and modify pain in OA. **Methods:** Cytokine secretion (IL-6 and TNF-α) from IL-1β-stimulated and SM04690-treated synovial fibroblasts was measured by ELISA. A single intra-articular injection of SM04690 or vehicle was evaluated in an in vivo rat knee monosodium iodoacetate (MIA) OA model. Joint inflammation was evaluated by H&E staining, inflammatory cytokines (IL-1α, IL-1β, IL-6, TNF-α and IFN-γ) by qPCR, and cartilage protection by qPCR for matrix metalloproteinases (MMPs). Histological evaluation of cartilage health was performed using OARSI score and thickness by Safranin-O staining. Pain was measured as paw withdrawal threshold using Von Frey apparatus and weight distribution using incapacitance meter and analyzed using generalized estimating equation regression. **Results:** SM04690 dose-dependently inhibited IL-1β-induced cytokine secretion in synovial fibroblasts (EC50 ~ 30nM; Fig. 1). In the rat MIA OA model, compared with vehicle, SM04690 injection reduced visible knee swelling, inflammatory cells, and proinflammatory cytokine and MMP production (p<0.05). SM04690 increased (p<0.01) paw withdrawal threshold from Day 6 and improved weight distribution to the affected limb in treated rats, at multiple timepoints, compared with vehicle (Fig. 2). SM04690 increased Safranin-O stained cartilage thickness and decreased OARSI score (p<0.05) compared with vehicle. **Conclusions:** In a rat MIA OA model, SM04690 injection reduced inflammation, protease production, and pain, with improved cartilage and joint health, compared with vehicle. Previously demonstrated regenerative effects in nonclinical studies, along with anti-

inflammatory properties, show SM04690 may improve symptoms and potentially provide disease modification in OA. Clinical studies are ongoing. Disclosures of interest: V. Deshmukh, T. Seo, C. Swearingen, and Y. Yazici are shareholders and employees of Samumed, LLC.



P25
VITAMIN D STATUS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENT AND ITS CORRELATION WITH DISEASE ACTIVITY AND ERYTHROCYTE SEDIMENTATION RATE AT SANGLAH GENERAL HOSPITAL DENPASAR
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Background: Vitamin D have a significant role in inflammation and immune abnormality in systemic lupus erythematosus (SLE) patient. Deficiency of vitamin D has been associated with disease activity of SLE. **Objective:** To identify serum 25 hydroxy (OH) vitamin D [25(OH)D] levels and its correlation with disease activity and erythrocyte sedimentation rate in SLE patient. **Problem statement:** Role of vitamin D on disease activity of SLE still controversies. **Methods:** A cross sectional study was conducted SLE patient at Sanglah General Hospital. Serum concentrations of 25(OH)D(3) were measured with electrochemiluminescence immunoassay (ECLIA). Disease activity was assessed by the MEX-SLEDAI. Pearson correlation test to determine correlation between vitamin D status and erythrocyte sedimentation rate. Nonparametric test were used to examine the association between level of vitamin D and disease activity. **Result:** The study included 68 female patients with SLE (30 active and 38 non active disease activity base on MEX SLEDAI), mean age 31,32±9,07. Mean serum concentration of 25(OH)D(3) was 13,65 ± 9,07 ng/ml, 25 % (17) deficiency, 70,6 % (48) insufficiency and only 4,4 % (3) normal range. Mean of erythrocyte sedimentation rate (ESR) 31,22± 26,85. Levels of 25(OH)D(3) correlated inversely with ESR (r=-0,27;p=0,02). Mean vitamin D level of active disease is not differ from nonactive disease (14,31 vs 13,13; p=0,20) **Conclusion:** There were low level of 25(OH)D(3)

serum in SLE patient. Vitamin D level has a correlation with marker of inflammation. Keyword: Vitamin D, systemic lupus erythematosus, disease activity, erythrocyte sedimentation rate

P26
USEFULNESS OF THE TRABECULAR BONE SCORE IN DIALYSIS PATIENTS
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Introduction: The number of patients on dialysis is steadily increasing. Associated comorbidities include cardiovascular diseases and an impaired mineral and bone metabolism leading to a higher fracture possibility, increased morbidity and mortality rate and decreased quality of life. Representing the structural condition of the bone microarchitecture dual-energy X-ray absorptiometry (DXA) is often used in combination with Trabecular Bone Score (TBS) to assess metabolic bone disorders. The aim of this study was to evaluate the clinical relevance of DXA and TBS with regard to fracture prediction in dialysis patients. **Methods:** 82 patients, who underwent dialysis at the university hospital of Graz, were included. All patients were interviewed for prevalent fractures and musculoskeletal pain. Statistical analysis was performed to correlate the results of DXA and TBS with musculoskeletal pain and fracture rate considering the kind and duration of dialysis as well as the number of kidney transplantations. **Results:** 36 out of 82 patients (43.9%) patients suffered from musculoskeletal pain and 32 out of 82 patients (39%) had a positive history of fracture. There was a significant linkage between dialysis duration and fracture rate (p<0.05) as well as musculoskeletal pain (p<0.01). No significant correlation between the DXA- and TBS-parameters and musculoskeletal pain could be established. DXA scores did not correlate with fracture history with the exception of DXA radius measurements. However, a high fracture rate in patients on dialysis significantly correlates with a low TBS (p < 0,001). **Conclusion:** DXA has a limited role in fracture prediction in patients on dialysis. However, the TBS seems to be a better predictor regarding the fracture risk in this patient population.

Osteodensitometry

	Patients with history of fracture (n=32)	Patients without history of fracture (n=50)	p-value
L1-L4			
BMD (g/cm ²)	0.877 ± 0.140	0.913 ± 0.176	p=0.69
T-score	-2.0 ± 1.49	-1.86 ± 1.47	p=0.8
Z-score	-1.36 ± 1.22	-1.16 ± 1.16	p=0.47
Femur neck			
BMD (g/cm ²)	0.791 ± 0.127	0.784 ± 0.156	p=0.85
T-score	-1.96 ± 1.12	-2.06 ± 1.14	p=0.67
Z-score	-1.13 ± 0.9	-1.32 ± 1.04	p=0.3
Femur total			
BMD (g/cm ²)	0.801 ± 0.115	0.809 ± 0.147	p=0.85
T-score	-1.85 ± 1.15	-2.03 ± 1.16	p=0.42

Z-score -1.77 ± 2.47 -1.37 ± 1.12 p=0.71

Radius ultradistal

BMD (g/cm²) 0.376 ± 0.096 0.402 ± 0.091 p=0.21

T-score -3.03 ± 1.81 -2.31 ± 1.74 p=0.08

Z-score -2.14 ± 2.03 1.61 ± -1.98 p=0.38

Radius 33%

BMD (g/cm²) 0.714 ± 0.141 0.781 ± 0.141 p=0.04

T-score -2.42 ± 1.3 -1.78 ± 1.28 p=0.04

Z-score -1.74 ± 1.11 -1.13 ± 1.31 p=0.05

Radius total

BMD (g/cm²) 0.537 ± 0.105 0.592 ± 0.117 p=0.04

T-score -2.82 ± 1.5 -2.05 ± 1.54 p=0.04

Z-score -2.06 ± 1.42 -1.42 ± 1.57 p=0.08

TBS 1.081 ± 0.088 1.174 ± 0.119 p<0.001

P27

MIND THE GAP: PREVALENCE OF OSTEOPOROSIS TREATMENT AFTER AN OSTEOPOROTIC FRACTURE – RESULTS OF THE AUSTRIAN BRANCH OF THE INTERNATIONAL COSTS AND UTILITIES RELATED TO OSTEOPOROTIC FRACTURES STUDY (ICUROS)

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Introduction: Despite availability of effective treatment options proven to prevent osteoporotic fractures, a huge gap in osteoporosis treatment exists. Reasons for this gap include underdiagnosis of osteoporosis, lack of adequate patient management, and concerns of adverse events. The aim of the present study was to evaluate the treatment rate after osteoporotic fracture in Austria, one of the 25 wealthiest countries worldwide by measure of gross domestic product at purchasing power parity (PPP) per capita. **Methods:** The ICUROS is a prospective observational study aimed to describe costs and Quality of Life (QoL) consequences of osteoporotic fractures. An amendment to the protocol of the Austrian arm of the ICUROS aimed at assessing the treatment rate after fracture without a concomitant awareness program, thus providing data from the “real world”. Patients who had sustained a major osteoporotic fracture were interviewed at the time of the index fracture, and 4, 12, and 18 months thereafter. **Results:** A total of 915 patients with a recent fracture were recruited at 8 different trauma centers throughout Austria. 78.3% of these patients were female. Mean age at the time of fracture was 75.5 ± 10.2 yrs. Female and male patients were stratified into 2 groups, depending on whether she or he received an osteoporosis treatment at the time of fracture or not. At the time of fracture, 25.2% of the patients were receiving osteoporosis treatment. In this group, follow-up analysis after 4, 12 and 18 months revealed a treatment rate of 65%, 54% and 60%, respectively, in female patients. Comparable results were detected in male patients. The treatment rate in the female group without osteoporosis medication at the time of fracture was 18%, 16%, and 15%, after 4, 12, and 18 months,

respectively, and the treatment rate in the respective male group was 8%, 12%, and 10%. **Discussion:** Only 1 in 10 men, and less than 2 in 10 women who do not receive an osteoporosis treatment at the time of fracture is prescribed an adequate osteoporosis treatment in Austria. Even worse, roughly every second patient who receives an osteoporosis treatment at the time of fracture will be deprived of his/her treatment after the fracture.

P28

HIGH IN VIVO LEVELS OF THE ADIPOKINE ADIPSIN LEAD TO INCREASED KNEE TISSUE DEGRADATION IN OSTEOARTHRITIS: DATA FROM HUMANS AND ANIMAL MODELS

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Problem statement: Adipokines have emerged as inflammatory/metabolic mediators that contribute to osteoarthritis. This study aimed to explore the role of the adipokine adipsin in knee osteoarthritis. **Methods:** Control and osteoarthritic articular tissues, cells, and serum were obtained from human individuals. Serum adipsin levels of human osteoarthritic individuals were compared with cartilage volume loss as assessed by magnetic resonance imaging at 48 months. Human adipsin expression was determined by PCR, its production in tissues by immunohistochemistry, and in synovial fluid and serum by a specific assay. Osteoarthritis was surgically induced in wild-type (Df+/+) and adipsin-deficient (Df-/-) mice, and synovial membrane and cartilage processed for histology and immunohistochemistry. **Results:** Adipsin levels were significantly increased in human osteoarthritic serum, synovial fluid, synovial membrane, and cartilage compared to controls, but the expression was similar in chondrocytes, synoviocytes, and osteoblasts. Multivariate analysis demonstrated that human serum adipsin levels were significantly associated (p=0.045) with cartilage volume loss in the lateral compartment of the knee. DMM-Df-/- mice showed a preservation of the osteoarthritic synovial membrane and cartilage lesions (p≤0.026), the latter corroborated by the decreased production of cartilage degradation products and proteases (p≤0.047). The adipsin effect is likely due to a deficient alternative complement pathway (p≤0.036). **Conclusion:** In human osteoarthritis, higher serum adipsin levels were associated with greater cartilage volume loss in the lateral compartment and adipsin deficiency led to a preservation of knee structure. Importantly, we documented an association between adipsin and osteoarthritic synovial membrane and cartilage degeneration through the activation of the complement pathway. This study highlights the clinical relevance of adipsin as a valuable biomarker and potential therapeutic target for osteoarthritis. Disclosure of Interest: JPP: shareholder in ArthroLab, JMP: shareholder in ArthroLab

P29

MACHINE LEARNING BASED PATIENT-SPECIFIC PREDICTION MODELS FOR KNEE OSTEOARTHRITIS

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Problem statement: Current guidelines are not well suited for diagnosing patients in the early stages of knee osteoarthritis, do not discriminate patients for whom the disease might progress rapidly, and have not truly helped in identifying and classifying patients who will benefit most from a treatment. Efforts are needed in patient subgrouping and developing comprehensive patient-specific risk prediction models to help knee osteoarthritis physicians make decisions within a short time. Conventional statistical modelling approaches exist; however, these models are limited in the amount of information they can adequately process. Approaches such as data mining and

machine learning should aid in the development of such patient-specific prediction models. **Methods:** Literature on the current prediction models for osteoarthritis using data mining and machine learning approaches combined with studies on knee osteoarthritis risk assessment were searched in the PubMed, Embase, NCBI, Google Scholar, ScienceDirect, and Osteoarthritis Initiative databases up to July 12, 2017. **Results:** Fourteen studies were eligible. Compared with other diseases, little progress has been achieved with respect to predictive modeling for knee osteoarthritis using machine learning methods (6 studies). Their major limitations include the validation approach, small populations studied, and most were based on a few well-known parameters (e.g. age, body mass index). **Conclusion:** To enhance the prediction accuracy, several other variables, risk factors, and imaging features (e.g. MRI) should be included in the models in addition to the common ones. Approaches should comprise machine learning algorithms, multivariate time-series data sets and non-linear feature selection methods. Data could be used to build a tool to guide clinical decision-making, and help to distinguish the responders from the non-responders to a given therapy. Although a challenging task, the technology and some osteoarthritis databases are now available.

P30

A BLACK BONE DILEMMA: A CASE REPORT

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Introduction: First identified by Dr Archibald Garrod in 1901 in London, Black bone disease also known as alkaptonuria is a rare autosomal recessive genetic disorder caused by deficiency of homogentisate 1.2 dioxygenase activity with a low prevalence 1:100,000-250,000^{1,2}. Joint replacements are often only textbook indications, but rarely seen or done in the field of Orthopedics. **Case report:** A 49 year old male presented to us with complains of bilateral knee pain for over 20 years, gradually worsening with continuous ambulation. Examination of bilateral knees revealed he had antalgic gait with mild varus deformity and palpable crepitus. Diagnosed as osteoarthritis of bilateral knees, he was then planned for left total knee replacement as his chief complaint was pain from the left side. It was during the preoperative investigation that it came to be known that he was diagnosed to have bilateral horse shoe kidney, and old records showed that he was diagnosed to have alkaptonuria! He had however defaulted his follow up and only sought for over the counter medications. He then underwent total knee replacement, with immediate exposure of the knee joint pre-implantation showing blackish-blue discolouration of his joints. Synovial biopsy was obtained, and results later showed features of inflammation with ochronosis.



Intraoperative left knee finding

Discussions: Accumulation of homogentisic acid (2,5-dihydroxyphenylacetic acid) and its oxidative products leads to excretion via urine and deposition to connective tissue. Deposition to joint cartilage causes loss of normal resiliency and become more brittle. Erosion of abnormal cartilage leads to progressive degenerative disease of the joint manifesting by the fourth decade of life.

Conclusion: Awareness of the existence of alkaptonuria among doctors of various disciplines including physicians and orthopaedic surgeons, even patients themselves is vital for the best treatment with best possible outcome.

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P31

STORY OF A PAIR: A CASE REPORT

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Introduction: The phrase tumoral calcinosis was originally described in 1943 by Inclan. The original condition was described in 1899, when Duret described the process in siblings with multiple calcifications in the hips and elbows¹. It is an uncommon lesion, composed of ectopic calcified tissue. Patients will often present with localized swelling and reduced mobility around the involved joints and may interfere with daily activities. **Case report:** A 58 years old lady post menopause 8 years ago with no known medical illness presented to our clinic with chief complaints of sudden pain over right hip since August 2017. She had underwent proximal femoral nailing for proximal femur fracture 9 years ago. She didn't seek any medical attention until she was referred by her community doctor for unresolving pain. Our assessment revealed palpable mass over her right iliac region, minimal pain upon palpation. Proceeding with pelvic X-ray, to our surprise there was presence of calcified mass was noted at bilateral iliac region.

Latest Pelvic X Ray of the patient



As patient was not keen for surgical intervention, she was regularly followed up. Fortunately subsequent follow up x rays did not show any increase in bilateral mass size. Patient's complaint of pain has also ceased as expressed during her latest follow up in March. **Discussion:** As originally described, tumoral calcinosis is a heredity condition or familial type. The term is now routinely and erroneously used to describe any soft-tissue periarticular calcification. Histologically, these lesions appear the same, which explains why periarticular calcifications are often called tumoral calcinosis, regardless of the aetiology. Fortunately, the treatment is the same for all conditions. Complete surgical clearance is required, with inadequate removal will inevitably cause recurrence. **Conclusion:** It is vital for early recognition of the signs for this condition, as otherwise differentials such as malignant variant of mass may be missed. Awareness of probable causes for both the treating medical personnel and the patient themselves is vital for the management for tumoral calcinosis. Reference: 1. Duret MH. Tumeurs multiples et singulieres des bourses seruses. *Bull. Soc. Anat. Paris.* 1899;74:725.

P32

EFFICACY AND SAFETY OF INTRA-ARTICULAR CROSS-LINKED HYALURONIC ACID IN COMBINATION WITH TRIACINOLONE HEXACETONIDE (TH) FOR MODERATE TO SEVERE OSTEOARTHRITIS: A REPORT IN 32 ASIAN PATIENTS

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Problem statement: Intra-articular injection with cross-linked hyaluronic acid viscosupplementation has been shown to be effective symptom and disease modifying osteoarthritis drug (DMOAD) for knee osteoarthritis as shown in recent Magnetic Resonance Imaging (MRI) studies. Since corticosteroid are not water soluble, steroid particles can be suspended in the Hyaluronic gel so both can reside separately and remain unchanged in formulation. Cingal is indicated as viscoelastic supplement or replacement of synovial fluid in human joints. **Methods:** 32 patients with moderate to severe knee osteoarthritis who had recurring knee pain with partial or failed response to previous Intra-articular steroid, IA non steroidal anti-inflammatory drugs (NSAIDs) and VS were recruited between Oct 2017 to Jan 2018. A single injection, cross-linked sodium HA 88mg combined with corticosteroid TH 18mg as 4ml unit dose in 5ml syringe. Cingal was administered into the affected knee. Patient was given a survey question on pre and post administration of injection using the "Western Ontario And McMaster Universities Osteoarthritis Index (WOMAC) Questionnaire and Visual Analogue Scale (VAS) pain score. **RESULT:** All patients had up to 3 months follow up. Average patients age ranges from 30-90 years old. 3 patients were male and 29 are female. All got similar results from ultrasound done showing synovitis in different percentage and had previous IA NSAIDs/steroids and VS. IA cross-linked HA + TH corticosteroid was administered without any adverse effects but some complained of post injection site pain and redness but were relieved by applying cold compress. 20 out of 32 patients completed the VAS pain score while the remaining 12 were incomplete but shows a lot of improvement except for 1 who had recurrent knee pain and went for total knee replacement. **CONCLUSIONS:** Intra-articular administration of combination of cross-linked HA + corticosteroid TH (Cingal) provides rapid action and longer duration pain relief in the Treatment of moderate to severe osteoarthritis knee with good safety profile. This innovation could be a new therapeutic alternative for those patients who failed or relapsed with the conventional VS.

P33

BONE TRABECULAR MORPHOLOGY CONTRIBUTES TO DIABETIC SKELETOPATHY IN THE ZUCKER DIABETIC SPRAGUE DAWLEY (ZSD) RAT: A THREE-DIMENSIONAL MICRO-FOCUS X-RAY COMPUTED TOMOGRAPHY STUDY

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Problem statement: Type 2 diabetes is increasingly becoming a health burden due to the resultant skeletopathy characterised by poor bone health, increased fractures and osteoporosis. We sought to investigate bone trabecular morphology to gain insight on how diabetes compromises skeletal integrity using a relatively new rat model of diabetes, the Zucker Diabetic Sprague Dawley (ZSD). **Methods:** Twelve, 15-week old, male ZSD rats were given a high fat diet for 13 weeks to induce diabetes mellitus. An equal number of normal Sprague Dawley rats were given normal rat chow and served as controls. Diabetes mellitus was determined by monitoring glucose handling through oral glucose tolerance tests, insulin levels, metabolic profiles (fasting glucose, triglycerides and cholesterol) and changes in body mass. An intraperitoneal lethal dose of sodium pentobarbital was used to terminate the animals. Bilateral humeri were then harvested, and then fixed in 10% buffered formalin before three-dimensional micro-focus x-ray computed tomography assessment of total volume to bone ratio (BV/TV), trabecular thickness (TbTh), trabecular number (TbN) and trabecular spacing (TSp). **Results:** The ZSD rats

exhibited significantly greater fasting glucose levels than controls. Additionally, the ZSD rats had impaired blood glucose regulation as indicated by elevated oral glucose tolerance tests. Progressive weight loss occurred in the ZSD rats from 22 weeks of age as well as hyperinsulinemia. The ZSD rats have a lower BV/TV, thicker trabecular (TbTh), trabecular number (TbN) and greater trabecular spacing (TSp). **Conclusion:** Our findings show that bone quality in diabetes is compromised through a disruption of the internal trabecular morphological characteristics.

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A CASE OF BONE MARROW PLASMACYTOSIS IN RHEUMATOID ARTHRITIS

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Problem statement: Rheumatoid arthritis is associated with development of lymphoproliferative disorder (namely malignant lymphoma), possibly attributable to chronic immunogenic hyperactivity. Yet, the risk of multiple myeloma is still uncertain though recent meta-analysis in 2014 reported no increased risk. Bone marrow plasmacytosis which could mimic multiple myeloma had been reported in rheumatoid arthritis cases in the 1950s. **Methods:** A 77 year-old lady presented with asymmetrical oligoarthritis for 6 months, associated with constitutional symptoms. She's close contact of an index case of pulmonary tuberculosis. Physical examination showed inflamed left wrist, right elbow and left knee joints. She had pallor but no jaundice. Lung examination was unremarkable. There were no lymphadenopathy and hepatosplenomegaly. **Results:** Laboratory investigations showed hyperglobulinaemia with reversed albumin/globulin ratio, elevated serum M protein (IgA: 7.4 g/L, IgG: 28.2 g/L), serum beta-2 microglobulin (4.14 mg/L) and erythrocyte sedimentation rate (101mm/hour). The urine Bence Jones protein was negative and light chains were not detected. She had hypochromic and microcytic anaemia which was due to iron deficiency. The serum calcium, urea and creatinine were within normal limits. Skeletal survey showed no osteolytic lesions. Both rheumatoid factor and anti-cyclic citrullinated peptide antibody were positive. MRI of left wrist showed evidence of synovitis with bony erosions. Synovial and marrow (lunate bone) histopathological examination displayed numerous polygonal plasma cells (positive for both Kappa and Lambda stains) with background admixture of acute and chronic inflammatory cells. Microbiological analysis of the synovial tissue was negative for Mycobacterium Tuberculosis Complex. A diagnosis of seropositive rheumatoid arthritis with reactive plasmacytosis was made and combination conventional Disease-Modifying Antirheumatic Drug therapy was initiated. She achieved disease remission within 6 months. The hyperglobulinaemia resolved and ESR normalised then. **Conclusion:** Hyperglobulinaemia and bone marrow plasmacytosis had been reported in rheumatoid arthritis cases, which were attributable to underlying inflammatory process. Yet it's important to distinguish this from multiple myeloma. As the risk of multiple myeloma in rheumatoid arthritis couldn't be completely excluded, surveillance is needed for all patients. Disclosure of Interest: None declared

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METABOLIC SYNDROME AND TRAJECTORIES OF PAIN SEVERITY AND NUMBER OF PAINFUL SITES IN KNEE OSTEOARTHRITIS: DATA FROM A 10.7-YEAR PROSPECTIVE STUDY

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Problem statement: Metabolic syndrome (MetS) has been suggested as having a role in osteoarthritis (OA) pathogenesis. No study has assessed whether MetS and its components are associated with pain severity and number of painful sites (NPS) and their courses over time. We aimed to examine the association of MetS and its components with trajectories of pain

severity and NPS in people with radiographic knee OA (ROA) over 10.7 years. **Methods:** 1,099 participants (mean age 63 years) had data on demographic, psychological, lifestyle and comorbidities, blood pressure, glucose, triglycerides, and high-density lipoprotein (HDL) cholesterol at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. MetS was defined using National Cholesterol Education Program-Adult Treatment Panel III criteria. ROA was assessed by X-ray. Pain severity and NPS were measured by questionnaires at each time-point. Group-based trajectory modelling was applied to identify pain trajectories. **Results:** 60% of participants had ROA and 32% had MetS at baseline. Three pain severity trajectories were identified: 'Marginal pain' (50%), 'Mild pain' (35%) and 'Moderate pain' (15%). Three NPS trajectories were identified: 'Low NPS' (10%), 'Medium NPS' (38%), and 'High NPS' (52%). In univariate analyses, MetS was associated with increased risk of both 'Mild pain' (Relative Risk: 1.47, 95%CI: 1.10–1.96) and 'Moderate pain' (2.22, 1.54–3.20) relative to 'Marginal pain'. It was also associated with increased risk of both 'Medium NPS' (2.25, 1.11–4.54) and 'High NPS' (3.36, 1.70–6.63) compared to 'Low NPS'. In multivariable analyses, abdominal obesity was associated with increased risk of both 'Mild pain' (1.70, 1.17–2.49) and 'Moderate pain' (2.75, 1.63–4.64), and MetS and low HDL were associated with 'Moderate pain'. Abdominal obesity was the only component associated with increased risk of both 'Medium NPS' (2.82, 1.39–5.70) and 'High NPS' (3.60, 1.79–7.24), and MetS was only associated with increased risk of 'High NPS'. However, these associations became non-significant after further adjustment for body mass index, but hypertension became protective with 'Mild pain'. **Conclusion:** MetS is predominantly associated with trajectories of pain severity and NPS through abdominal obesity, suggesting that weight management is the most important way of controlling OA pain.

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IMPACT OF ORAL OSTEOARTHRITIS THERAPEUTICS USAGE AMONG OTHER RISK FACTORS ON KNEE REPLACEMENT: A NESTED CASE-CONTROL STUDY USING THE OSTEOARTHRITIS INITIATIVE COHORT

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Problem statement: The aim of this study was to measure the association between exposure to commonly used oral osteoarthritis (OA) therapeutics and relevant confounding risk factors on the occurrence of knee replacement (KR), using the Osteoarthritis Initiative (OAI) database. **Methods:** In this nested case-control design study, participants who had a KR after cohort entry were defined as "cases" and were matched with up to four controls for age, gender, income, WOMAC pain, Kellgren-Lawrence grade, and duration of follow-up. Exposure to oral OA therapeutics (acetaminophen, non-steroidal anti-inflammatory drugs [NSAIDs], cyclooxygenase-2 [COX-2] inhibitors, narcotics, and glucosamine/chondroitin sulfate) was determined within the three years prior to the date of the KR. Conditional regression analyses were performed to estimate the association between KR and exposure to oral OA therapeutics as well as other potential confounding risk factors. **Results:** A total of 218 participants who underwent a KR (cases) were matched to 540 controls. The median time to KR was 4.3 years among cases. The majority in both groups were Caucasian with mean age of 69 years and 61% were female. Numerically, cases were more exposed to acetaminophen, NSAIDs, and COX-2 inhibitors. Exposure to narcotics and glucosamine/chondroitin sulfate was relatively similar between cases and controls. No significant association was found between the occurrence of KR and exposure to any of the oral OA therapeutics within the three years prior to KR. A significantly higher occurrence of KR was found for Caucasian subjects (OR 1.84; 95% CI, 1.13–2.99; p=0.015) and subjects with body mass index (BMI) ≥ 27 kg/m² (OR 1.65; 95% CI, 1.06–2.58; p=0.027). **Conclusion:** This study provides evidence that the main risk factors leading to KR are disease severity, symptoms and high BMI. Importantly, exposure to oral OA therapeutics was not associated with the occurrence of KR. Disclosure of Interest: MD: Consultant, ArthroLab, JMP: Consultant,

Bioibérica; Shareholder, ArthroLab, JPR: Consultant, ArthroLab, JPP: Consultant, Bioibérica; Shareholder, ArthroLab

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INTRAUTERINE ALCOHOL EXPOSURE AFFECTS BONE EPIPHYSEAL PLATE CHONDROCYTE PROLIFERATION BY INHIBITING TRANSFORMING GROWTH FACTOR BETA-1 (TGFB1) IN 3-WEEK-OLD RAT (SPRAGUE DAWLEY) HUMERUS

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Problem statement: Intrauterine alcohol exposure causes delayed bone growth and development as well as increased osteoporosis and fracture risk. Most studies emphasize the former, with a lack of literature on the implications on osseous tissue. This study aimed to investigate how prenatal alcohol consumption affects the proximal and distal end of the growth plate of the humerus in 3-week old rats. **Methods:** Time-mated (n=15) pregnant Sprague Dawley dams were assigned to either the ethanol (n=6), saline control (n=6) or untreated control (n=3) group. The former two groups were treated with 0.015ml/g of 25.2% ethanol and 0.9% saline for the first 19 days of gestation respectively. The untreated group received no treatment. Once born, the pups remained with their dams for 21 days before termination. Two pups from each dam were used so that the ethanol (n=12), saline control group had 12 pups each while the untreated control had 6 pups. From the pups, left humeri were processed for routine histology and serial sections cut with a microtome at 5µm thickness. These sections were stained with Haematoxylin and Eosin (H&E) for normal morphology and immunolabelled with anti-Ki-67 antibody for cell proliferation as well as immunolocalization of chondrocytes expressing transforming growth factor beta-1 (TGFB1). **Results:** Prenatal alcohol exposure resulted in adverse effects on the growth plate in respect of its general size, zone sizes and the number of cells in each zone. Fewer proliferative cells were found using the anti-Ki67 antibody including cells positive for TGFB1. **Conclusion:** These results indicate that gestational alcohol exposure may lower bone structural quality by inhibiting epiphyseal plate chondrocyte number and slowing cell proliferation by suppressing TGFB1 expression.

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PAGET'S DISEASE OF THE BONE

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Introduction: Initially described by Dr James Paget in a paper published in 1877, he told of five patients with "a rare disease of bones" which presented with slowly progressive bone deformities in the 4th and 5th decades of age. Commonly known as **Paget's disease** or historically, **osteitis deformans** is a condition involving cellular remodeling and deformity of one or more bones¹. **Case report:** A 70 years old lady with no known medical illness gave history of right leg deformity for the past 10 years. Noticing further deformity of her right leg, she sought medical attention after having minimal pain and sorting to use a walking stick. X ray done of her right leg revealed bowing of her right tibia with mixed osteolytic changes. MRI imaging done was suggestive of Paget's disease of tibia. She was decided for conservative management with regular bisphosphonate therapy.



X Ray image of the right tibia

Discussion: With the exact cause unknown, although leading theories indicate both genetic and acquired factors. Paget's disease may affect any one or multiple bones of the body (most commonly pelvis, femur, and lumbar vertebrae, and skull, but never the entire skeleton), and does not spread from bone to bone, in this case the right tibia. The disease is progressive and slowly worsens with time, although people may remain minimally symptomatic. Treatment is aimed at controlling symptoms, but there is no cure. Often treatments with bisphosphonates have shown improvements in patients bone density that is regularly monitored. **Conclusion:** Paget's disease of the bone is often diagnosed incidentally during medical evaluation for other problems. As such it is vital for all teams involved to be aware and to appropriately address all patients individually. **Reference** 1. Paul Tuck, Stephen; Layfield, Robert; Walker, Julie; Mekayil, Babitha; Francis, Roger (2017-12-01). Adult Paget's disease of bone: a review. *Rheumatology*. **56** (12): 2050–2059

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SERONEGATIVE RHEUMATOID ARTHRITIS WITH OVERHANGING EDGES: A REPORT OF TWO CASES

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Problem statement: Inflammatory arthritis may present forthright clinically with florid joint swelling and tenderness supported by elevated inflammatory markers, antibody levels and a strong clinical history. Conversely, in other circumstances, arthritis may progress into unusual clinical manifestations later showing radiographic findings consistent with other types of inflammatory arthritides. In these two cases, we are presented with patients with clinical symptoms of rheumatoid arthritis but with radiographic evidence of gout. The question is whether these two types of inflammatory arthritis may coexist in one patient. Their coexistence is a rarity and few case reports have been published. **Methods:** This is a report of two cases presenting with clinical signs and symptoms compatible with rheumatoid arthritis. However, upon further investigation, radiographic studies depicted findings consistent with gout. **Results:** The two patients were seen for multiple joint pains and upon physical examination had swan neck deformities, boutonniere's, ulnar deviation and Z-line deformity. They both tested negative for rheumatoid factor and anti-cyclic citrullinated peptide. The uric acid levels of both patients were highly elevated. Arthrocentesis and crystal analysis of synovial fluid were done, which revealed monosodium urate crystals. Radiographic studies done on both hands showed subluxation of metacarpophalangeal joints with joint space narrowing compatible with rheumatoid arthritis and punched out lesions with overhanging edges, albeit in different proximal and distal interphalangeal joints consistent with gout. **Conclusion:** Rheumatoid arthritis, albeit rare, may co-exist with gout. However, when the clinician considers the several factors that distinguish the two entities, this may direct you to the more likely diagnosis. In spite of the different pathophysiologic mechanisms of the two diseases, the damage due to inflammation may present similarly clinically in different chronological orders. A thorough history, physical examination and complete diagnostic studies may be necessary to prove their coexistence.

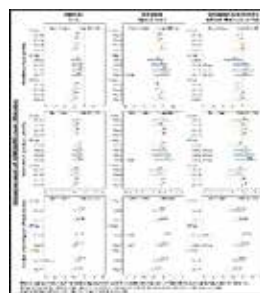
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RESULTS FROM A 52-WEEK RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY OF A NOVEL, WNT PATHWAY INHIBITOR (SM04690) FOR KNEE OSTEOARTHRITIS TREATMENT

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Problem statement: Wnt signaling is upregulated in osteoarthritis (OA) and is involved in cartilage degradation. SM04690, a small molecule Wnt pathway inhibitor, is in development as a potential disease-modifying OA drug (DMOAD) for knee OA. A phase 2, multicenter, 52-week, placebo (PBO)-controlled trial was conducted to identify a target population, determine optimal dose, and assess safety. **Methods:** Knee OA subjects, Kellgren-Lawrence (KL) grades 2-3, received a single 2-mL injection of SM04690 (0.03 mg, 0.07 mg, 0.23 mg) or PBO in their target (most painful) knee. WOMAC Pain and Function were assessed (Weeks 0, 4, 13, 26, 39, 52) and fixed flexion radiographs (QuAP™ positioned; Weeks 0, 26, 52) assessed medial joint space width (mJSW). Analysis of covariance adjusted for baseline with multiple imputation in the intent-to-treat (ITT) population and pre-specified subgroup analyses of subjects with unilateral symptoms with or without widespread pain (UNI and UNI WP-, respectively) were performed. **Results:** 455 subjects (mean age 60.3 [±8.7] years, BMI 29.9 [±4.6] kg/m², female 58.9%, KL grade 3 [64.4%], unilateral symptomatic OA [36.0%]) were enrolled. SM04690 appeared well-tolerated, and incidence of adverse events was similar in treatment and PBO groups. In ITT, minimum clinically important differences (10% full range) in WOMAC Pain and Function compared with baseline were seen in all groups at all timepoints. In 0.07 mg UNI, at 52 weeks, WOMAC Pain (4.4; *P*=0.049), and Function (17.5, *P*=0.035) were significantly improved compared with PBO. In 0.07 mg UNI WP-, at Weeks 26, 39, and 52, WOMAC Pain (4.6, *P*=0.039; 5.9, *P*=0.042; and 5.6, *P*=0.025, respectively) and Function (16.3, *P*=0.027; 19.7, *P*=0.035; and 22.8, *P*=0.017, respectively) were significantly improved compared with PBO (Figure). At 26 and 52 weeks, 0.07 mg UNI (0.5 mm, *P*=0.006 and 0.4 mm, *P*=0.021, respectively) and 0.07 mg UNI WP- (0.5 mm, *P*=0.016 and 0.4 mm, *P*=0.032, respectively) demonstrated significant increases from baseline in mJSW compared with PBO (Figure). **Conclusion:** A target subgroup of unilateral symptomatic knee OA subjects was identified. Findings support SM04690 as a potential DMOAD, especially at the 0.07 mg dose in unilateral symptomatic subjects without WP.



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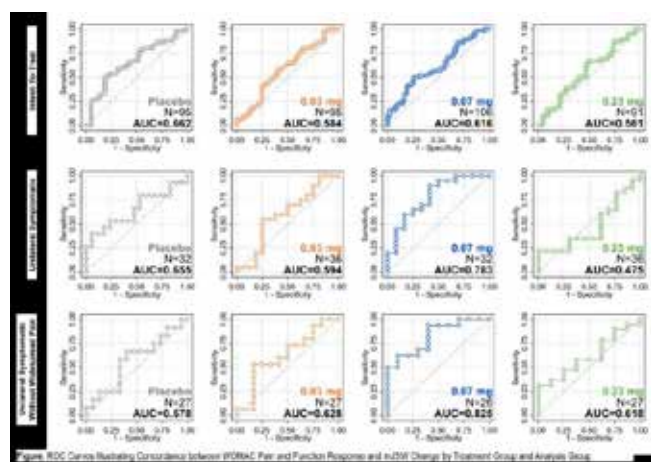
RADIOGRAPHIC OUTCOMES WERE CONCORDANT WITH PAIN AND FUNCTION RESPONSE: POST-HOC ANALYSIS FROM A PHASE 2 STUDY OF SM04690, A WNT PATHWAY INHIBITOR FOR KNEE OSTEOARTHRITIS TREATMENT

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Problem statement: SM04690, a Wnt pathway inhibitor, is a potential disease-modifying knee osteoarthritis (KOA) drug. A phase 2 study evaluated Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscore and medial joint space width (mJSW) changes. To test the hypothesis that mJSW changes are associated with WOMAC subscore improvements, post-hoc concordance analyses were performed. **Methods:** KOA subjects, Kellgren-Lawrence (KL) grades 2-3, received 2 mL intra-articular SM04690 (0.03, 0.07, 0.23 mg) or placebo (PBO) in the target (most painful) knee. WOMAC Pain [0-50], Function [0-170], and mJSW were assessed over 52 weeks. Logistic regression analyses generating receiver-operator characteristic (ROC) curves estimated concordance between mJSW change and subjects who achieved

WOMAC Pain and Function improvements $\geq 50\%$ and ≥ 20 [of 100] points response. ROC area under curve (AUC) 0.7 was 'acceptable' and 0.8 'excellent'. Intent-to-treat (ITT) and two subgroups were analyzed: 1) unilateral symptomatic (pre-specified: UNI) and 2) UNI without widespread pain or comorbid symptoms (Widespread Pain Index ≤ 4 and Symptom Severity ≤ 2 , post-hoc: UNI-WP). **Results:** 455 subjects were enrolled (age 60.3 years, BMI 29.9 kg/m², 268 [58.9%] female, 292 [64.2%] KL 3, 164 [36.0%] UNI KOA). At Week 52, response was achieved in ITT (53%), UNI (56% [0.03 mg], 63% [0.07 mg], 64% [0.23 mg], 47% [PBO]), and UNI-WP (56% [0.03 mg], 62% [0.07 mg], 70% [0.23 mg], 44% [PBO]). 0.03 mg (UNI, NS; UNI-WP, $P=0.047$) and 0.07 mg (UNI, $P=0.009$; UNI-WP, $P=0.013$) doses also demonstrated increased mJSW compared with PBO. In ITT, no group achieved acceptable concordance (Figure); in UNI only the 0.07 mg dose achieved acceptable concordance (AUC=0.783), and the UNI-WP 0.07 mg dose achieved excellent concordance (AUC=0.825). **Conclusion:** In UNI and UNI-WP KOA subjects treated with SM04690 0.07 mg in this study, concordance was demonstrated between structure (mJSW change) and clinical outcomes (WOMAC Pain and Function response). **Disclosures of interest:** J. Tambiah, C. Swearingen, and S. Kennedy are shareholders and employees of Samumed, LLC; M. Hochberg: consultant for Bioberica, EMD Serono, Novartis Pharma AG, Plexxikon, Pfizer, Proximagen, Regeneron, Samumed, LLC, and Theralogix, LLC.



P42 COMPARISON OF THE PATIENT REPORTED OUTCOME ACTIVITY INDEX (AI) WITH THE HAQ QUESTIONNAIRE: A VALIDATION STUDY WITH 100 RA PATIENTS IN CHINA

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Background: Rheumatoid arthritis (RA) is an autoimmune disease where the person's immune system attacks joint tissues for unknown reasons, thus causing inflammation. **Objectives:** The objective of this study was to compare the patient reported outcome "Activity Index" (AI) with the HAQ questionnaire in 100 RA patients with different stages of disabilities and activity limitations. **Methods:** To improve the communication between RA patients and physicians we have developed an easy-to-use patient reported outcome instrument "Activity Index" (AI: Scale of activity limitation) that extends the "Stanford Health Assessment Questionnaire" (HAQ: Disability Index) by 4 additional dimensions. In this study we aimed to validate the self assessment disability scale "AI" through a sample of 100 Chinese RA patients with different disease stages. Specifically, we were interested in the inter-relationship between the clinical disease activity and the radiologically joint damages (erosions and narrowing of joint space as measured by image analyses), and the quantitative scores on the AI and HAQ scales. Therefore, all patients were asked to fill out the AI and HAQ instruments twice within 2 weeks. **Results:** Patients generally

accepted the AI and HAQ as easy-to-use instruments. For the sample as a whole entity we found modest, yet statistically significant correlation ($p<0.05$) in terms of physical disabilities. The correlation between the objectively disease activity and the quantitative AI and HAQ scores were highly significant ($p<0.0001$) in the range of $0.468 \leq r \leq 0.482$. There was a strong concordance between AI (pain/impairment during the past 24 hours) and HAQ as reflected by the correlation coefficient of $r=0.703$. As expected, the supplementary AI dimensions "Satisfaction" and "General Health" were negatively correlated with joint damages. **Conclusions:** Having externally validated the AI instrument through "objective" data, the AI extends the well-established HAQ and provides additional information that can be expected to significantly improve the communication between RA patients and doctors and to monitor activity limitations in RA patients. The AI can be used as a telemedicine instrument to monitor disability of RA patients. Acknowledgements: This project was funded by the QUALITOUCH Foundation, Switzerland and the research fund of Prof ZG Li / China

P43 BONE MINERAL DENSITY PROFILE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AT RHEUMATOLOGY CLINIC DR. HASAN SADIKIN GENERAL HOSPITAL BANDUNG INDONESIA

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Problem statement: Systemic lupus erythematosus (SLE) is a chronic, autoimmune, multisystem disease of unknown etiology. Beside the disease itself and the use of steroid as treatment, the frequency of alterations in bone mineral density relative high, varies between 25% and 74%, although its diagnosis is not standardized. This study is aimed to describe the bone densitometry of SLE patients at Rheumatology Clinic, Dr. Hasan Sadikin General Hospital, Bandung Indonesia. **Methods:** Descriptive cross-sectional method was used to analyse secondary data driven outpatient medical records, from January 2016-December 2017 which met the inclusion criteria and exclusion criteria. All subjects underwent Bone Mineral Density (BMD) examination by dual-energy X-ray absorptiometry (DXA). BMD were defined according to World Health Organization criteria. **Result:** A total of 54 female patients with SLE were included. These SLE patients had the following characteristics: mean age was 44 ± 11 years; mean body mass index (BMI) was 22.9 ± 5.4 kg/m². Of the 33 subjects (61.1%) were premenopausal patients; in this group 8 (24.2%) were classified with below the expected range for age; there were 21 (38.9%) postmenopausal patients, in this group 3 subjects (14.3%) were diagnosed with osteoporosis and 16 (76.2%) with osteopenia. **Conclusion:** Osteopenia the most common bone densitometry results were found in patients with systemic lupus erythematosus.

P44 OSTEOPOROSIS IN AN ELDERLY PATIENT WITH OSTEOARTHRITIS OF THE KNEE JOINT

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Problem statement: The association between Osteoarthritis of the knee joint (knee OA) and osteoporosis is controversial, but the coexistence of these conditions increases in elderly individuals. In late years, elderly patients have higher late of total knee arthroplasty (TKA). The most common cause for revision TKA is aseptic loosening. One of the factors contributing to aseptic loosening is the bone quality of the patient. There are some reports on the bone density of patients with knee OA and osteoporosis. However, there are only a few reports on blood examinations such as those estimating the calcium (Ca), phosphorus (P), and parathyroid hormone (PTH) levels and renal function, of these patients. The purpose of this study was to investigate the

correlation between Ca, P, PTH levels and renal function in elderly patients with knee OA and osteoporosis. **Materials and Methods:** We evaluated 64 patients who had been treated for osteoporosis and knee OA (2men, 62 women; mean age 76.4 years). Blood examinations included measurement of Ca, P, bone-specific alkaline phosphatase (BAP; a marker of bone formation), tartrate-resistant acid phosphatase 5b (TRACP5b; a marker of bone resorption), and intact PTH levels, as well as estimated glomerular filtration rate (eGFR). Bone mineral density (BMD) was measured at the level of the lumbar spine and proximal femur using dual-energy X-ray absorptiometry. **Results:** The eGFR decreased with age, resulting in a negative correlation ($r=-0.230$, $p<0.01$). BAP and TRACP5b increased with age resulting in an equilateral correlation ($r=0.269$, p). **Conclusion:** It is necessary to consider the measurement of intact PTH levels to manage osteoporosis in patients with knee OA, even if the Ca and P levels are within the normal range. **Conflict of Interests:** There are no conflicts of interest for this study.

P45 MICRORNA-1915-3P IN SERUM EXOSOME IS ASSOCIATED WITH DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS IN KOREA

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Problem statement: Rheumatoid arthritis (RA) is a chronic inflammatory disease that is characterized by severe tissue damage and chronic synovial inflammation. Using analysis of gene polymorphism, biochemical assays, and proteomics approaches, several promising biomarkers for treatment response have been proposed, including red blood cell (RBC) MTX polyglutamate levels, as well as serum levels of proteins such as cytokines, growth factors, and autoantibodies. However, these markers need further development and refinement to attain sufficient sensitivity and specificity. We used a miRNAarray approach to identify new miRNA in exosome that are related to disease activity in patients with RA who showed inadequate response to treatment. We also examined the relationship between the levels of expression of the RNAs and various serologic parameters of the patients. **Methods:** Forty-two RA patients were included in the study. Disease activity was measured using the 28-joint disease activity score with ESR (DAS28-ESR). Patients with RA were stratified according to the following criteria: the clinical remission (CR) group ($n=22$), DAS28-ESR ≤ 2.6 ; and the non-CR group ($n=20$), DAS28-ESR > 2.6 . By exosome preparation, miRNA array, and Reverse Transcription-qPCR reactions, several miRNAs were as potent markers for disease activity. **Results:** After data processing for relative quantification of miRNA in exosome between the CR and non-CR groups, we identified 47 miRNAs with a relative fold change (non-CR/CR) ≥ 2 . The expression levels of 37 miRNAs were found decreased in non-CR group, while 10 miRNAs increased in non-CR group. To validate these results, five miRNAs were selected (hsa-miR-1915-3p, hsa-miR-4516, hsa-miR-6511b-5p, hsa-miR-3665, hsa-miR-3613) showing at least 2-fold change between the CR and non-CR groups. Both levels of hsa-miR-1915-3p and hsa-miR-6511b-5p were significantly increased in CR group; hsa-miR-1915-3p was 43.75 in the CR group and 24.68 in the non-CR group ($p=0.004$), and hsa-miR-6511b-5p was 3.02 in the CR group and 2.45 in the non-CR group ($p=0.03$). **Conclusion:** hsa-miR-1915-3p showed promise as additional markers for evaluating disease activity in patients with RA. Prospective investigation of hsa-miR-1915-3p may facilitate development of new diagnostic tools to assess disease activity and prognosis in RA and other autoimmune diseases.

P46 A RANDOMIZED CONTROL CLINICAL STUDY ON SMALL-NEEDLE-KNIFE THERAPY COMBINED WITH EXERCISE THERAPY FOR KNEE OSTEOARTHRITIS: 3-MONTH FOLLOW-UP VISIT

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Problem statement: Small-needle-knife therapy for knee osteoarthritis (KOA) has no uniform location, operation and mechanisms of action. Studies have proved that exercise therapy can enhance muscle strength, increase stability of the knee, improve joint range of motion, and effectively relieve pain. This study was to observe the clinical effect of small-needle-knife therapy combined with exercise therapy for treatment of KOA via a randomized controlled clinical trial. **Methods:** 122 patients were randomly divided into treatment group ($n=61$; small-needle-knife therapy combined with exercise therapy) and control group ($n=61$; low-frequency therapy combined with exercise therapy). Then, clinical efficacy in the two groups were assessed by statistical analysis of visual analog scale, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), swelling degree of the knee joint, quadriceps circumference, flexion and extension of the knee joint before and after treatment. Meanwhile, adverse reactions in patients were recorded for safety evaluation. **Results:** (1) The visual analog scale and WOMAC scores in the two groups were both significantly improved at 2 weeks after treatment ($P=0.05$). Moreover, these scores in the treatment group were significantly lower than those in the control group ($P=0.05$). (2) At 12 weeks after treatment, the WOMAC score in the treatment group was better than that in the control group ($P=0.05$), and the range of motion of the knee joint was also better in the treatment group than the control group ($P=0.05$). (3) According to the full analysis set and per protocol set, the total efficiency rates in the treatment group were both superior to those in the control group ($P=0.001$). **Conclusion:** Small-needle-knife therapy combined with exercise therapy is superior to physiotherapy combined with exercise therapy in the total efficiency. Follow-up results of 3 months have been confirmed, but long-term effects need further exploration. There are no conflicts of interest in the study.

P47 THE EFFECT OF BPA ON BONE MINERAL DENSITY(BMD) IN RATS

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INTRODUCTION: Bisphenol A (BPA), one of the environmental hormones, is plastic material that binds to the estrogen receptor in the body and acts like estrogen, which can cause endocrine and reproductive diseases. However, there are not many studies done regarding the effect of BPA on osteoporosis. In this study, we investigated the effect of BPA on bone mineral density (BMD) in rats. **MATERIALS AND METHODS:** Six to eight week-old rats were divided into three groups: male, female, and ovariectomized rat (OVX). Nine rats were assigned to each group. Again, according to the dose of BPA, we divided them into 3 groups: control group, low dose group, and high dose group, and each group was assigned 3 rats. They orally administered BPA for 12 weeks. At the time of 6 and 12 weeks after the start of the study, BMD of tibia was measured by q-CT. Percent bone volume, trabecular separation, trabecular thickness] were measured and the changes in BMD between the two groups were compared. In addition, BPA concentration and bone formation marker procollagen type 1 amino-terminal propeptide (PINP) and bone resorption marker C-telopeptide of type 1 collagen (CTX1) were measured in the rats' serum at the time of 12 weeks after the start of the study. **RESULTS:** In the female and ovariectomized rat (OVX) groups, 4 BMD values all showed increasing tendency according to the dose of BPA. On the contrary, there was no correlation between the two in the male group. Serum BPA levels were 0.112ng/ml, 0.4075ng/ml, and 1.1705ng/ml, respectively in the control, low dose, and high dose groups. On the other hand, CTX1 showed significant

decrease according to the dose of BPA, whose values were 11.210ng/ml, 8.524ng/ml, and 5.814ng/ml, respectively, in the three groups.

CONCLUSION: BPA in rats decreased bone resorption markers in serum and increased BMD in female, ovariectomized rat (OVX). However, there was no difference in bone markers and BMD in males. This is similar to the effect of selective estrogen receptor modulator (SERM), a medication for osteoporosis, and may be due to estrogen-like effects of BPA. As a result of this animal model, the effect of BPA in the human body has more variables and needs further studies.

INVITED SPEAKERS' ABSTRACTS (Late submission)

EUROPEAN EXPERIENCE WITH SWITCHING FROM ORIGINATOR TO BIOSIMILAR PRODUCTS IN RHEUMATOLOGY

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Biosimilars represent a new opportunity for lowering the cost of treatment with biological disease-modifying antirheumatic drugs (bDMARDs). Studies have demonstrated large inequities in the access to bDMARDs across countries and this inequity is related to economic parameters such as gross domestic product. Thus, reduced costs of bDMARDs should potentially lead to better treatment for more patients, especially in countries with low economy. The regulatory agencies in Europe and in US have set up strict guidelines for approval of biosimilars which include extensive pre-clinical examinations (structure and functional characteristics) but less clinical data than for an originator product. The clinical part of this comparability exercise focuses on efficacy, safety, pharmacokinetics as well as immunogenicity. An increasing number of biosimilars have been approved in Europe with marketing authorization. CT-P13 is a biosimilar infliximab which was approved in the fall 2013 (marketed in most EU countries from 2015 with the brand names Remsima® and Inflectra®). SB4 (biosimilar etanercept (Benepali®)) and SB2 (Biosimilar infliximab Flixabi®), but also others, were more

recently approved in Europe, and biosimilars to rituximab are also available. Some biosimilars to adalimumab have also been approved and the patent for Humira® expired in many countries in Europe October 2018. It is a growing acceptance about the use of these biosimilars, also in extrapolated indications when treatment are started or changed for medical reasons. Most rheumatologists will consider the biosimilars on the same level as originator products in these situations. However, replacing an originator product by a biosimilar for non-medical reasons (i.e. to reduce cost) is more controversial, but is important because of the large potential cost-savings. Switching evidence is available from four different types of studies which will be discussed: Extension of phase 3 RCTs, Switching within RCTs, Real life data (eg from DANBIO), Randomizing patients on stable long-term treatment. In the NOR-SWITCH trial - totally funded by the Norwegian government - 482 patients on stable treatment with Remicade® across 6 indications (RA, SpA, PsA, UC, CD, PsO) were randomized to continued treatment with the reference product or switch to CT-P13 (Remsima®) (Jørgensen KK et al. Lancet 2017;389:2304-2316). The primary endpoint was occurrence of disease worsening, defined by the disease-specific composite measures or clinically significant worsening leading to a major change in treatment. Overall, disease worsening occurred in 26.2% of patients who continued treatment with the originator infliximab and in 29.6% of patients who switched to CT-13. The adjusted treatment difference (95% CI) was -4.4% (-12.7 - 3.9) which was within the prespecified non-inferiority margin of -15%. The occurrence of adverse events, including infusion reactions, was similar across both groups. There were no differences between the two groups in secondary endpoints, including time to study drug discontinuation, remission rates, CRP levels, anti-drug antibody formation and drug trough levels. The extension study (not yet published) showed that switching from originator to biosimilar was not inferior to continued treatment with the biosimilar. In conclusion, the NOR-SWITCH study demonstrated that switching to CT-P13 was not inferior to continued treatment with originator infliximab, adding to the increasing real-world evidence that switching from originator to biosimilar bDMARD is safe and efficacious. The safety of non-medical switching has also been supported by real life data, e.g. from DANBIO.



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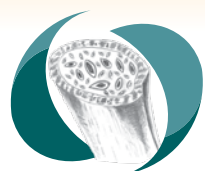
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