

# REUMATIZAM

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## CECR Central European Congress of Rheumatology

Zagreb, hotel Westin, 6.–8. december 2018.

**BOOK OF ABSTRACTS**



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# REUMATIZAM

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# CECR Central European Congress of Rheumatology 2018

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# CENTRAL EUROPEAN CONGRESS OF RHEUMATOLOGY 2018

**Under the high auspices of**

**Kolinda Grabar-Kitarović**  
President of the Republic of Croatia

**Under the auspices of**

**Croatian Medical Association**

**Organizer**

**Croatian Society for Rheumatology**

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cecr2018@globtour.hr

## VENUE

The Westin Zagreb Hotel  
Izidora Kršnjavog 1, Zagreb, Croatia

The Westin Zagreb Hotel is centrally located in the very heart of Zagreb. The hotel is situated in a leafy green area adjacent to the Mimara Museum and the world famous National Theatre and Opera House, and is within easy walking distance to the central square, markets, the many trendy cafés, restaurants, designer boutiques, rich cultural attractions and capital city business destinations. Recognised for offering discreet surroundings and professional, caring service, The Westin Zagreb is a regular host to high profile local, national and international events.

The tram stop is right in front of the Hotel and the tram present the main mean of public transport towards and from the city centre. Trams no. 12, 13, 14 and 17 will take you to the hotel. Get off at the Vodnikova ulica (Vodnikova Street) stop.

## REGISTRATION /INFORMATION DESK

The conference registration/information desk is located on the ground floor of the Westin Hotel. All participants should register at the Registration/Information Desk upon their first arrival to the conference venue.

Registration/Information Desk opening hours:  
Thursday, 6 December, 11:00 – 20:00  
Friday, 7 December, 07:30 – 20:00  
Saturday, 8 December, 08:00 – 20:00

## THE CONFERENCE FEE INCLUDES:

- Conference materials (bag, name tag, Final programme and Book of abstracts)
- Admission to all sessions of the scientific programme
- Admission to the Welcome Reception
- Coffee breaks and lunch boxes at the conference venue for the duration of the conference

## NAME TAGS

Name tags will be issued when registering at the conference. For security purposes, the conference name tag must be worn at all times during the conference and social functions.

## SOCIAL PROGRAMME

Welcome Reception: Thursday, 6 December starting at 19:15 at the Hotel Westin, Ground floor and exhibition area).

Zagreb Sightseeing Tour for accompanying persons: Friday, 7 December, at 12:00.

The meeting point – Westin Hotel main entrance.

Conference dinner: Friday, 7 December, starting at 20:00.

The conference dinner will take place in the Vinodol restaurant, Teslina 10.

Dress code for both programmes: Casual

Note: Congress dinner is not included in registration fee for congress.

Due to limited number of places please make your registration on time. Registrations are based on the „first come first served“ principle.

## PHOTOS AND RECORDINGS

Photos and videos will be taken during the CECR 2018.

## INTERNET / WiFi

Free WIFI is available throughout the congress centre and the hotel.

## SPEAKERS

A speaker preparation desk will be located at the REGISTRATION DESK.

Presentations can be submitted to a technician in pdf or powerpoint format. Speakers are required to provide the technician with their presentation as soon as possible and no later than half an hour before the start of the session.

## EXHIBITION

An exhibition will take place in the temporary structure at Hotel Westin parking.

## EXHIBITORS

Abbvie d.o.o.  
Amgen d.o.o.  
Berlin-Chemie Menarini Hrvatska d.o.o.  
Celgene d.o.o.  
Celltrion Healthcare  
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Pliva d.o.o.  
Roche d.o.o.  
Sandoz d.o.o.  
Sanofi-Aventis Croatia d.o.o.  
STADA



*Dear rheumatologists, dear colleagues and friends,*

*a very warm welcome to the Central European Congress of Rheumatology (CECR), a traditional meeting of rheumatologists. The Congress is organized every other year by seven central European countries (Austria, Czech Republic, Hungary, Poland, Slovakia, Slovenia and Croatia).*

*Since its introduction, CECR became the perfect place for exchange of scientific and clinical information. This time CECR 2018 is organized by the Croatian Society for Rheumatology in Zagreb (Croatia).*

*This meeting is a great opportunity to present your results and to share your experience. It is also a great opportunity to meet your colleagues and friends, renew old and make new friendships, start new collaborations and plan new projects. The scientific programme of CECR usually covers a wide range of topics on basic, translational and clinical science. Scientific and organizing committees of CECR 2018 decided to continue with good practice and each organizing country chose a scientific/clinical topic and organized one session.*

*There is going to be a separate session for young rheumatologists and poster session. Organizing committee is also planned after-congress workshop on scientific writing and publishing.*

*Beginning of December, during the Advent, is the perfect time to visit Zagreb, a beautiful central European town, capital of Croatia.*

*Welcome to CECR 2018, welcome to Zagreb!*

*Sincerely,  
Branimir Anić, PhD,  
President of the Croatian Society for Rheumatology*



## Thursday, 6<sup>th</sup> December 2018

- 11.00 – 20.00 Registration**
- 12.00 – 12.30 Pre-Congress refreshment**
- 12.30 – 13.30 Opening ceremony**
- 13.30 – 14.00 Invited plenary lecture**  
*Maurizio Cutolo (ITA). Influence of Mediterranean diet on incidence and course of inflammatory rheumatic diseases.*
- 14.00 – 15.30 Section I – host country Croatia**  
**Topic: Epidemiology of SLE in Central Europe**  
 Plenary lectures
- 14.00 – 14.20 *Ivan Padjen, Mislav Cerovec, Miroslav Mayer, Marko Barešić, Dubravka Bosnić, Mirna Sentić, Marijan Erceg, Ranko Stevanović, Branimir Anić. Causes of early and late death and survival of SLE patients over a 10-year period: analysis from a Croatian tertiary center.*
- 14.20 – 14.40 *Felina Anić, Srđan Novak. Disease activity and damage index in 110 SLE patients.*
- 14.40 – 15.00 *Ljiljana Smiljanić Tomičević, Darija Čubelić, Miroslav Mayer. Ultrasound evaluation of the ankle joints and tendons in systemic lupus erythematosus.*
- Selected oral communications
- 15.00 – 15.10 *Daniela Marasović Krstulović, Leona Žuvan, Dijana Perković, (HRV). The differences between clinical manifestations and comorbidities between women and men with SLE treated in University Hospital of Split from January 2007 to December 2017.*
- 15.10 – 15.20 *Nastasia Čekada, Mario Šestan, Emilija Hostička, Maja Novoselec, Mateja Batnožić Varga, Ivan Padjen, Marijan Frković, Domagoj Kifer, Branimir Anić, Drago Batinić, Kristina Potočki, Ivan Malčić, Marija Jelušić, (HRV). Childhood-onset systemic lupus erythematosus over the last 25 years: predicting organ damage.*
- 15.20 – 15.30 *Veronika Balajková, Radka Moravcová, Marta Olejárová, (CZE). Cognitive dysfunction in systemic lupus erythematosus is more associated with non-inflammatory mechanism than inflammation.*
- 15.30 – 15.45 Break**
- 15.45 – 17.15 Section II – host country Austria**  
**Topic: Rheumatoid arthritis – beyond the disease**  
 Plenary lectures
- 15.45 – 16.05 *Judith Sautner. Rheumatoid arthritis and female sexual dysfunction.*
- 16.05 – 16.25 *Rudolf Puchner. Rheumatoid arthritis – psyche and depression.*
- 16.25 – 16.45 *Helga Radner. Comorbidities in rheumatoid arthritis.*
- Selected oral communications
- 16.45 – 16.55 *Joško Mitrović, Katarina Borić, Simeon Grazio, Frane Grubišić, Željka Kardum, Tatjana Kehler, Nikolina Ljubičić Marković, Daniela Marasović-Krstulović, Ksenija Maštrović-Radončić, Sonja Milanović, Višnja Prus, Ivana Tomljanović Rudar, Jadranka Morović-Vergles, (HRV). Disease activity and treatment patterns in patients with rheumatoid arthritis in Croatia.*
- 16.55 – 17.05 *Krešimir Rukavina, Goran Šukara, Branimir Anić, (HRV). Difficult to treat – a patient with rheumatoid arthritis and T-cell large granular lymphocyte leukemia (T-LGLL).*
- 17.05 – 17.45 Break for refreshment**  
**Industry sponsored symposia**
- 17.45 – 18.45 Eli Lilly (Suisse) S.A.**
- 17.45 – 18.45 Sanofi – Aventis Hrvatska d.o.o.**
- 18.45 – 19.15 Break**
- 19.15 – 22.00 Welcome reception**

**Friday, 7<sup>th</sup> December 2018**

**07.30 – 20.00 Registration**

**07.45 – 09.15 Section III – host country Slovenia**

**Topic: Giant Cell Arteritis**

**Plenary lectures**

07.45 – 08.05 Alojzija Hočevar. *Giant cell arteritis – an overview.*

08.05 – 08.25 Iztok Holc, Metka Koren Krajnc, Artur Pahor. *Early diagnosis of giant cell arteritis – does it matter?*

08.25 – 08.45 Rok Ješe, Žiga Rotar, Matija Tomšič, Alojzija Hočevar. *Colour doppler sonography of facial and occipital arteries in patients with giant cell arteritis.*

**Selected oral communications**

08.45 – 08.55 Marcin Milchert, Marek Brzosko, (POL). *Giant cell arteritis in Poland. How to increase diagnostic rate?*

08.55 – 09.05 Ana Marija Lukinac, Željka Kardum, Ivana Kovačević, Jasminka Milas-Ahić, Višnja Prus, (HRV). *The occurrence of paraneoplastic syndromes in patients with polymyalgia rheumatica treated at the University Hospital Center Osijek.*

09.05 – 09.15 Eugene J. Kucharz (POL). *Diagnosis and management of patients with granulomatosis with polyangiitis.*

**09.15 – 09.30 Break**

**Industry sponsored symposia**

**09.30 – 10.30 Celgene d.o.o.**

**09.30 – 10.30 Merck Sharp & Dohme d.o.o.**

**10.30 – 11.00 Break for refreshment**

**11.00 – 12.30 Section IV – host country Hungary**

**Topic: Advances in inflammatory myopathies and systemic sclerosis**

**Plenary lectures**

11.00 – 11.10 Jiří Vencovský, Kateřina Kubínová, (CZE). *MRI in evaluation of inflammatory myopathy.*

11.10 – 11.20 Zoltan Griger. *Novel classification of inflammatory myopathies.*

11.20 – 11.30 Cecília Varjú, Katinka Gulyás, Tünde Minier, Tímea Berki, László Czirják, Endre Pál. *Survival and subset classification analysis of 82 patients with inflammatory myopathy.*

11.30 – 11.40 Attila Balog. *Biomarkers and activity markers in scleroderma.*

11.40 – 11.50 Szilvia Szamosi. *Osteoporosis in systematic sclerosis.*

11.50 – 12.00 Melinda Szabo. *Novel factors associated with cyclophosphamide efficacy in autoimmune diseases.*

**Selected oral communications**

12.00 – 12.10 Monika Chrzanowska, Magdalena Włoch-Targońska, Przemysław Kotyla, Eugeniusz Józef Kucharz, (POL). *Clinical course of systemic sclerosis patients.*

12.10 – 12.20 Hana Storkanova (CZE), Sabina Oreska (CZE), Maja Spiritovic (CZE), Barbora Hermankova (CZE), Karel Pavelka (CZE), Jiri Vencovsky (CZE), Joerg HW Distler (GER), Ladislav Senolt (CZE), Radim Becvar (CZE), Michal Tomcik, (CZE). *HSP90 plasma levels are increased in patients with systemic sclerosis especially with interstitial lung involvement and skin fibrosis.*

12.20 – 12.30 Barbora Heřmánková (CZE). *Impaired sexual functioning in women with systemic sclerosis.*

**12.30 – 14.00 Poster viewing and poster tours** (see list of posters at the end of programme)

**12.30 – 14.00 Boxed lunch**

**14.00 – 15.30 Section V – host country Poland****Topic: Specific aspects of SpA****Plenary lectures**

- 14.00 – 14.20 Mariusz Korkosz. *Innate immune system in the pathogenesis of spondyloarthritis – monocytes involvement.*
- 14.20 – 14.40 Hanna Przepiera-Bedzak, Marek Brzosko. *Risk factors for extra-articular signs in spondyloarthritis.*
- 14.40 – 15.00 Hanna Przepiera-Bedzak, Marek Brzosko. *SAPHO syndrome – clinical symptoms, imaging and treatment – based on a group of Polish patients.*

**Selected oral communications**

- 15.00 – 15.10 Alan Šučur, Zrinka Jajić, Marina Ikić Matijašević, Marinko Artuković, Darja Flegar, Tomislav Kelava, Nina Lukač, Antonio Markotić, Danka Grčević, (HRV). *Abberancies of specific peripheral blood T-cell and monocyte subpopulations in ankylosing spondylitis correlate with disease activity parameters.*
- 15.10 – 15.20 Hana Storkanova, Kristyna Bubova, Sabina Oreska, Maja Spiritovic, Barbora Hermankova, Monika Gregova, Katerina Zegzulkova, Jana Horinkova, Karel Pavelka, Jiri Vencovsky, Jiri Stolf, Marketa Husakova, Sarka Forejtova, Ladislav Senolt, Michal Tomcik, (CZE). *Plasma levels of HSP90 are increased in axial spondyloarthritis and psoriatic arthritis patients with structural changes.*
- 15.20 – 15.30 Frane Grubišić, Hana Skala Kavanagh, Ines Doko, Jure Aljinović, Tonko Vlask, Petra Kovačević, Simeon Grazio, (HRV). *Which demographic disease related variables may be predictors of quality of life in psoriatic arthritis patients?*

**15.30 – 15.45 Break for refreshment****Industry sponsored symposia**

- 15.45 – 16.45 Novartis Hrvatska d. o. o.
- 15.45 – 16.45 Pfizer Croatia d. o. o.

**16.45 – 17.00 Technical break****17.00 – 19.00 Young rheumatologists section**

- 17.00 – 17.20 Katja Perdan-Pirkmajer, Rok Ješe, Alojzija Hočevar, Žiga Rotar, Sanja Markez, Milena Pavić-Nikolić, Matija Tomšič (SVN). *The incidence rate and clinical characteristics of rheumatoid arthritis in Slovenia.*
- 17.20 – 17.40 Marija Bakula, Nada Čikeš, Branimir Anić (HRV). *Validation of SLICC-12 and ACR-97 classification criteria in a patient cohort with SLE treated in University Hospital Centre Zagreb.*
- 17.40 – 18.00 Paul Studenic (AUT), Simon R. Stones (UK), Alessia Alunno (ITA), Valentin Ritschl (AUT), Elena Nikiphorou (UK). *Social media use for health-related purposes by people with rheumatic and musculoskeletal diseases.*
- 18.00 – 18.20 Klára Prajzlerová, Olga Kryštůfková, Petra Hánová, Hana Hulejová, Monika Gregová, Karel Pavelka, Jiří Vencovský, Ladislav Šenolt, Maria Filkova (CZE). *Increase in non-classical subpopulations of monocytes and decrease in numbers of NK cells in the pre-clinical phase of rheumatoid arthritis.*
- 18.20 – 18.40 Magdalena Wloch-Targonska (POL). *Hemophagocytic lymphohistiocytosis.*
- 18.40 – 19.00 Veronika Lorand, Gabriella Nagy, Zsófia Bálint, Dalma Komjáti, Balázs Németh, Tünde Minier, Gábor Kumánovics, Nelli Farkas, László Czirják, Cecília Varjú (HUN). *Responsiveness of articular disease activity indices in patients with systemic sclerosis.*

**20.00 – 22.30 Gala dinner**

## Saturday, 8<sup>th</sup> December 2018

**08.00 – 20.00 Registration**

**08.00 – 09.30 Section VI – host country Slovakia**

**Topic: Imaging in Rheumatology**

Plenary lectures

08.00 – 08.20 Martin Zlňay. *Highlights and pitfalls of MRI imaging in axial spondyloarthritis patients.*

08.20 – 08.40 Zdenko Killinger. *Importance of trabecular bone score in fracture risk prediction in rheumatoid arthritis and ankylosing spondylitis.*

08.40 – 09.00 Tomáš Dallos, Juraj Lysý. *Temporomandibular joint arthritis and the role of imaging.*

Oral presentations

09.00 – 09.10 Mario Šestan, Natasia Čekada, Daniel Turudić, Mateja Batnožić Varga, Jagoda Stipić, Marko Barešić, Marijan Frković, Domagoj Kifer, Marija Jelušić, (HRV). *Comparison of computerized color telethermography and nailfold capillaroscopy in diagnostics of secondary Raynaud's phenomenon in children.*

09.10 – 09.20 Simeon Grazio, Frane Grubišić, Hana Skala Kavanagh, Ines Doko, Rudolf Vukojević, Lora Bolić, Luciana Mijačika, Marija Punda, (HRV). *Application of FRAX and trabecular bone score in patients with psoriatic arthritis.*

09.20 – 09.30 Olga Sleglova, Olga Ruzickova, Karel Pavelka, Ladislav Šenolt, (CZE). *Progression of pain, stiffness, function changes, and ultrasound detected synovitis and osteophyte formation in patients with hand osteoarthritis over three years.*

**09.30 – 09.45 Break for refreshment**

Industry sponsored symposia

09.45 – 10.45 Oktal Pharma d.o.o. Celltrion Healthcare

09.45 – 10.45 Mylan Hrvatska d.o.o.

**11.00 – 12.30 Section VII – host country Czech Republic**

**Topic: Biomarkers in Rheumatology**

Plenary lectures

11.00 – 11.20 Ladislav Šenolt. *Biomarkers in rheumatology, what do we really know?*

11.20 – 11.40 Kristyna Bubova, Ladislav Šenolt. *Biomarkers in axial spondyloarthritis.*

11.40 – 12.00 Maria Filkova. *MiRNAs as biomarkers in autoimmune rheumatic diseases.*

Selected oral communications

12.00 – 12.10 Klára Prajzlerová, Olga Kryštůfková, Petra Hánová, Hana Hulejová, Monika Gregová, Karel Pavelka, Jiří Vencovský, Ladislav Šenolt, Mária Filková, (CZE). *Expression of CXCL16 in peripheral blood of individuals in the pre-clinical phase of rheumatoid arthritis.*

12.10 – 12.20 Sara Sekelj (UK), Branimir Žarković (HRV), Miroslav Mayer (HRV), Renata Zadro (HRV), Marija Miloš, (HRV). *Investigating the potential of mean lymphocyte volume and mean monocyte volume as biochemical markers for diagnosis and follow up of rheumatoid arthritis and ankylosing spondylitis.*

12.20 – 12.30 Kristyna Bubova, Hana Storkanova, Sabina Oreska, Maja Spiritovic, Barbora Hermankova, Karel Pavelka, Jiri Vencovsky, Jindriska Gatterova, Ladislav Senolt, Michal Tomcik, (CZ). *Plasma levels of HSP90 are increased in rheumatoid arthritis and osteoarthritis patients.*

**12.30 – 13.00 Final remarks and closing of the Congress**

**13.00 – 14.00 Boxed lunch**



## Posters

- P1 Jozef Lukáč, Olga Lukáčová, (SVK). *Advances in management of systemic lupus erythematosus.*
- P2 Marta Skoczynska, Malgorzata Chowaniec, Agata Sebastian, Maria Misterska – Skora, Piotr Wiland, (POL). *When a rheumatologic disease gets a head start. A case report of seronegative antiphospholipid syndrome.*
- P3 Antica Pasarić, Branimir Anić, Ivan Marković, Ivan Padjen, Jadranka Morović-Vergles, (HRV). *Neutrophil to lymphocyte ratio (NLR) in patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).*
- P4 Zbynek Hrnčir, Doris Vokurkova, Marcela Drahosova, Tomas Soukup, (CZE). *Deficiency of marginal-zone-like B cell absolute values in peripheral blood in systemic lupus erythematosus – a twelve-month follow-up study.*
- P5 Frane Grubišić, Katarina Borić, Željka Kardum, Tatjana Kehler, Daniela Marasović Krstulović, Nikolina Ljubičić Marković, Sonja Milanović, Jadranka Morović Vergles, Joško Martinović, Višnja Prus, Ksenija Maštrović Radončić, Ivana Rudar Tomljanović, Simeon Grazio, (HRV). *Efficacy of biologic treatment on quality of life in rheumatoid arthritis patients in Croatia: results from a non-interventional, multicenter, cross-sectional study to estimate disease activity and treatment patterns in patients with rheumatoid arthritis.*
- P6 Ines Doko, Frane Grubišić, Hana Skala Kavanagh, Simeon Grazio, (HRV). *Association between ICF brief core set for hand conditions and grip strength in rheumatoid arthritis patients.*
- P7 Vera Milić, Milka Grk, Biljana Jekić, Nela Maksimović, Ivana Maksimović, Nemanja Damjanov, (SRB). *Association of rs17004921 ADORA2A gene polymorphism with efficacy of methotrexate in patients with rheumatoid arthritis.*
- P8 Ivana Ježić, Marko Barešić, Luka Simetić, Davorin Herceg, Branimir Anić, (HRV). *Treatment options in patient with rheumatoid arthritis and history of malignancy – intracranial chondrosarcoma /osteochondroma.*
- P9 Vibeke Strand (USA), Nemanja Damjanov (SRB), Craig Scoville (USA), Namita Tundia (USA), Heidi Camp (USA), Kun Chen (USA), Jessica L Suboticki (USA), Ronald F van Vollenhoven (NLD), Orsolya Nagy (non-author presenter). *The association between patient reported outcomes and clinical measures among rheumatoid arthritis patients: analyses using phase 3 clinical trials of upadacitinib.*
- P10 Ronald F van Vollenhoven (NLD), Tsutomu Takeuchi (JPN), Aileen L Pangan (USA), Mohamed-Elsam F Mohamed (USA), Su Chen (USA), Maureen Rischmueller (AUS), Ricardo Blanco (ESP), Alan Friedman (USA), Ricardo M Xavier (BRA), Vibeke Strand (USA), Orsolya Nagy (non-author presenter). *A phase 3, randomized controlled trial comparing upadacitinib monotherapy to MTX monotherapy in MTX-naïve patients with active rheumatoid arthritis.*
- P11 Roy Fleischmann (USA), Aileen L Pangan (USA), Eduardo Mysler (ARG), Louis Bessette (CAN), Charles Peterfy (USA), Patrick Durez (BEL), Andrew Ostor (AUS), Yihan Li (USA), Yijie Zhou (USA), Ahmed A Othman (USA), Ih-Ho Song (USA), Mark C Genovese (USA), Orsolya Nagy (non-author presenter). *A phase 3, randomized, double-blind study comparing upadacitinib to placebo and to adalimumab, in patients with active rheumatoid arthritis with inadequate response to methotrexate.*
- P12 Marija Ščepović Ljučević, Dubravka Bosnić, (HRV). *The efficacy of subcutaneous application of tocilizumab in a patient with long standing large vessel vasculitis relapse, a case report.*
- P13 Mateja Batnožić Varga, Natasia Čekada, Mario Šestan, Saša Sršen, Lucija Ružman, Maja Zaninović, Aleksandar Ovuka, Ivana Oždanovac, Marija Pečnjak, Domagoj Kifer, Marijan Frković, Alenka Gagro, Marija Jelušić, (HRV). *Childhood-onset of Henoch-Schönlein purpura nephritis in Croatia: a study conducted in five tertiary care centres over nine years.*
- P14 Radim Bečvář (CZE). *Potential markers of skin fibrosis in systemic sclerosis.*

- P15 Andrea Smržová, Pavel Horák, Anna Petráčková, Marketá Schubertová, Martina Skácelova, Tereza Dyšková, Regína Fillerová, Gabriela Gabčová, František Mrázek, Eva Kriegová (CZE). *Inflammation-related proteins as potential markers of disease activity in patients with systemic sclerosis.*
- P16 Dijana Perković, Marin Petrić, Ivona Božić, Daniela Marasović Krstulović, Katarina Borić, Dušanka Martinić Kaliterna, (HRV). *Systemic sclerosis and immunoglobulin therapy: our experience in the last 5 years.*
- P17 Maja Spiritovic, Hana Smucrova, Sabina Oreska, Hana Storkanova, Barbora Hermankova, Petr Cesak, Adela Rathouska, Olga Ruzickova, Karel Pavelka, Ladislav Senolt, Jiri Vencovsky, Radim Becvar, Michal Tomcik, (CZE). *Efficacy of an intensive 24-week physical-occupational therapy program with subsequent 24-week follow-up in patients with systemic sclerosis – preliminary data from a single-center controlled study.*
- P18 Sabina Oreska, Maja Spiritovic, Petr Cesak, Michal Cesak, Hana, Storkanova, Hana Smucrova, Barbora Hermankova, Barbora Sumova, Olga Ruzickova, Herman Mann, Karel Pavelka, Ladislav Senolt, Jiri Vencovsky, Radim Becvar, Michal Tomcik, (CZE). *Differences in body composition in scleroderma patients and healthy controls and association with disease activity, physical activity and serum levels of inflammatory cytokines.*
- P19 Barbora Heřmánková (CZE). *Impaired sexual functioning in women with idiopathic inflammatory myopathies.*
- P20 Sabina Oreska, Maja Spiritovic, Petr Cesak, Ondrej Marecek, Hana Storkanova, Hana Smucrova, Barbora Hermankova, Katerina Kubinova, Martin Klein, Lucie Vernerova, Olga Ruzickova, Karel Pavelka, Ladislav Senolt, Herman Mann, Jiri Vencovsky, Michal Tomcik, (CZE). *Negative changes of body composition in myositis patients compared to healthy controls and associations with myositis-related clinical manifestations.*
- P21 Maja Spiritovic, Sabina Oreska, Hana Storkanova, Barbora Hermankova, Petr Cesak, Adela Rathouska, Katerina Kubinova, Martin Klein, Lucia Vernerova, Olga Ruzickova, Herman Mann, Karel Pavelka, Ladislav Senolt, Jiri Vencovsky, Michal Tomcik, (CZE). *Efficacy of an intensive 24-week specialized ADL exercise program with subsequent 24-week follow-up in patients with idiopathic inflammatory myopathies – preliminary data from a single-center controlled study.*
- P22 Ana Gudelj Gračanin, Joško Pavan, Ana Marija Valetić, Jadranka Morović Vergles, (HRV). *Ocular manifestations in ankylosing spondylitis and rheumatoid arthritis.*
- P23 Mikel Jordhani, Dorina Ruci, (ALB). *The relationship between HLA-B27 and ocular involvement in male Albanian patients with ankylosing spondylitis.*
- P24 Mirjam Szabo (HUN). *Anti-JAK treatment and infection in a patient with spondyloarthritis.*
- P25 Lorena Petrač, Miroslav Mayer, (HRV). *Spontaneous biceps femoris rupture hematoma with secondary inflammation in a patient with psoriatic arthritis treated with secukinumab developing myelodysplastic syndrome (MDS) – case report.*
- P26 Marta Olejárová (CZE). *Inhibition of IL-17 by secukinumab lead to the remission of severe psoriatic arthritis and symptoms of pemphigus vulgaris in a patient coincidence of these conditions.*
- P27 Mislav Čaić, Miroslav Mayer, Ivana Knežević Štromar, (HRV). *Apremilast as a treatment of choice for psoriatic arthritis in a patient with difficult to treat autoimmune hepatitis.*
- P28 Pavel Horák (CZE). *Innate immunity gene expression signature in patients with autoimmune diseases in active disease stage: RA, SLE, SSc.*
- P29 Lucie Andrés Cerezo (CZE), Hana Hulejová (non-author presenter). *S100A11 (calgizzarin) induces inflammation via TLR-4 signalling and stimulates secretion of angiogenic factors IL-8 and VEGFs by mononuclear cells in rheumatoid arthritis.*
- P30 Jana Bohatá, Veronika Horváthová, Kateřina Pavelcová, Blanka Stibůrková, (CZE). *Interaction of p.Q141K variant in ABCG2 gene with clinical data and cytokines levels in primary hyperuricemia and gout.*



- P31 Felina Anić, Tatjana Kehler, Marija Rogoznica, Frane Grubišić, Simeon Grazio, Marta Žuvić, Srđan Novak, (HRV). *Real life experience with golimumab in Croatia.*
- P32 Simeon Grazio, Dijana Perković, Ana Gudelj Gračanin, Nadica Laktašić Žerjavić, Marija Glasnović, Frane Grubišić, Jadranka Morović-Vergles, Porin Perić, Iva Žagar, Helena Mitrović, Petra Šimac, Željka Kolak, Ines Doko, (HRV). *Efficacy and safety of switching from oral to subcutaneous methotrexate in everyday clinical practice: results of the six-month observational prospective study in Croatia.*
- P33 Kristina Kovač Durmiš, Mislav Pap, Duje Birkić, Nadica Laktašić Žerjavić, Iva Žagar, Porin Perić, (HRV). *Infections and malignancies in patients treated with biological disease modifying antirheumatic drugs- our experience.*
- P34 Tatjana Zekić, Ita Hadžisejdić, Srđan Novak, (HRV). *Clinical outcomes of macrophage activation syndrome in University Hospital Centre.*
- P35 Agnė Petrulionienė, Daiva Radzišauskienė, Arvydas Ambrozaitis, Saulius Čaplinskas, Algimantas Paulauskas, Algirdas Venalis, (LTU). *Lyme disease. Most frequent observed symptoms. Is arthralgia among them?*
- P36 Olga Lukáčová, Jozef Lukáč, (SVK). *TRAPS (Tumor necrosis factor receptor- associated periodic syndrome).*
- P37 Margarita Soloshenko, Ekaterina Alexeevna, Rina Denisovna, Tatyana Dvoryakovskaya, Ksenia Isaeva, Anna Mamutova, Nikolay Mayansky, Natalyaya Tkachenko, Irina Zubkova, Marina Fedoseenko, (RUS). *The relationship between the duration of methotrexate / etanercept therapy and serum anti-SPP IgG antibodies in patients with JIA without systemic manifestations.*
- P38 Karel Pavelka (CZE). *Structure modification in OA and present and future perspectives.*
- P39 Sonja Golubović (SRB). *Hypokalemic paralysis as a presenting manifestation of primary Sjögren's syndrome: case report.*
- P40 Marta Skoczynska, Beata Maciazek – Chyra, Malgorzata Chowaniec, Piotr Wiland, (POL). *A rheumatologic disease or a paraneoplastic syndrome with a rheumatic manifestation? Case report.*
- P41 Dubravka Bosnić, Hrvoje Barić, Mirna Reihl Crnogaj, Ivan Padjen, Savko Dobrota, Dražen Jelašić, Branimir Anić, (HRV). *Severe course of polyarteritis nodosa presenting with asynchronous spontaneous retroperitoneal hemorrhage and spontaneous hepatic rupture: case report and literature review.*
- P42 Lorena Petrač, Miroslav Mayer, (HRV). *Aseptic systemic abscesses syndrome – case report.*
- P43 Marina Barguil Macedo, Alexandre Lima Matos, Edgard Torres dos Reis Neto, (BRA). *Arthritis of the ankles as a major manifestation of Poncet's disease – case report.*
- P44 Željka Kardum, Marija Šola, Jasminka Milas Ahić, Marta Biljan, Ana Kovač, Ana Marija Lukinac, Ivana Kovačević, Kristina Stranski Kovačević, Višnja Prus, (HRV). *Generalized telangiectasia misinterpreted as vasculitis – case report.*
- P45 Anna Kotulska-Kucharz (POL). *Educational expectations of the Polish patients with rheumatic disorders treated with biopharmaceuticals.*



## INVITED PLENARY LECTURE / UVODNO PREDAVANJE

### INFLUENCE OF MEDITERRANEAN DIET ON INCIDENCE AND COURSE OF INFLAMMATORY RHEUMATIC DISEASES

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The Greek “Father of Medicine” and physician Hippocrates, said around 400 B.C. “Let thy food be thy medicine and thy medicine be thy food” (Nikiphorou et al. 2018)

Therefore, over the last decades we become increasingly aware and concerned about how nutrition affects our health and the field of nutrition have meet unprecedented interest and expansion.

On the other hands, a number of dietary factors might act as environmental triggers in rheumatic and muskulo-skeletal diseases (RMDs) development. Overall, a ‘Western’ type diet rich in energy intake, total and saturated fat, an unbalanced ratio of n-3 to n-6 fatty acids, high in sugar and low in fiber and antioxidants might increase the risk of RMDs both directly through increasing inflammation (Minihane et al. 2015) and indirectly through increasing insulin resistance, obesity and associated co-morbidities, with obesity being a known risk factor for RMDs (Qin et al. 2015).

In detail, high consumption of foods characteristic of the ‘Western-type’ diet such as red meat, meat and meat products combined, or total protein have been shown to increase the risk of inflammatory polyarthritis suggesting a role of advanced glycation end products (AGEs) (Pattison et al. 2004).

This is supported by findings of regular consumption of sugar-sweetened soda, but not diet soda, being associated with an increased risk of seropositive rheumatoid arthritis (RA) in women (Hu et al. 2014), and of high-fructose corn-syrup sweetened soft drinks, fruit drinks and apple juice being associated with arthritis in young US adults (DeChristopher et al. 2016).

It is hypothesized that regular consumption of excess free fructose and HFCS contributes to fructose reactivity in the gastrointestinal tract and intestinal in situ formation of enFruAGEs, which once absorbed, travel beyond the intestinal boundaries to other tissues and promote inflammation (DeChristopher et al. 2016). Individual biomarkers of antioxidant intake have also been previously investigated in relation to RA with some evidence that low serum levels of selenium and alpha tocopherol (Knekt et al. 2000) and beta carotene (Comstock et al. 1997) are associated with an increased disease risk.

Interestingly, a meta-analysis also suggests that coffee consumption of  $\geq$  four cups per day is associated with an elevated risk of seropositive RA but not seronegative RA (Lee et al. 2014). However, the results should be interpreted with caution due to other potential confounders. The same meta-analysis found no association between tea consumption and risk of RA (Lee et al. 2014).

On the contrary, consumption of long-chain omega-3 polyunsaturated fatty acids, derived from fish and fish oil, is associated with a reduced risk of inflammatory RMD like RA (Di et al. 2014) probably due to their anti-inflammatory properties.

The Mediterranean diet (MD), rich in plant-based foods such as wholegrains, legumes, fruit, vegetables, extra-virgin olive oil and low in red meat consumption, might have the potential to reduce the risk of RA. It has been shown that greater adherence to the MD is associated with lower concentrations of inflammatory biomarkers (Fung et al. 2005), while daily consumption of monounsaturated fatty acids from olive oil is thought to be the key factor in suppressing RA disease activity (Matsumoto et al. 2017).

Other nutritional approaches like vegan, elemental or elimination diets did not showed any superiority to the MD (Ciccia et al 2018, Philipou et al. 2018) regarding the interference on RMDs.

In addition, recent evidences suggest the diet pattern, by modifying the composition of intestinal microbiome, might influence the activation of innate immune pathways such as inflammasome and autophagy directly involved in the production of pro-inflammatory cytokines such as IL-1b and IL-18 with effects on RMDs

Based on current research evidence, it is concluded that adherence to the MD with an increased consumption of fatty fish, reduced consumption of sugar-sweetened drinks and maintenance of a normal body weight, contributes to reducing the risk of RA.

Interestingly, looking at the “chrononutrition” following the body circadian rhythms (Nobel Prize for Medicine 2017) it has been assessed that circadian misalignment, behavioral processes such as food intake or sleep occurring at inappropriate endogenous circadian times, commonly occurs during shift work (i.e. night shift workers) are associated with serious health problems over the time including RMDs (Cutolo 2018). In conclusion, both correct quality and timing in nutrition, are essential in prevention and/or co-management of RMDs.

**Disclosure:** None

## ORAL COMMUNICATIONS – PLENARY LECTURES / ORALNA PRIOPĆENJA – PLENARNA PREDAVANJA

### CAUSES OF EARLY AND LATE DEATH AND SURVIVAL OF SLE PATIENTS OVER A 10-YEAR PERIOD: ANALYSIS FROM A CROATIAN TERTIARY CENTER

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**Background:** Causes of death (CODs) and survival serve as indicators of overall care of SLE patients. While most of the available data on CODs and survival originate from highly developed healthcare settings and dedicated lupus cohorts, data from Croatia and neighboring countries are still lacking.

**Objectives:** Retrospective analysis of disease features and CODs of SLE patients deceased from 2002 to 2011; assessment of survival of patients diagnosed over the same period.

**Methods:** We analyzed features of 90 patients followed-up at our center, who deceased over the 2002–2011 period. Early death (ED) was defined as death occurring within 5 (10) years following diagnosis, while late death (LD) was defined as death occurring thereafter. An extensive set of variables was compared between the ED and LD groups: demographics, ACR classification criteria, damage and causes of death. We also analyzed survival in a retrospective cohort of 213 patients.

**Results:** Among 90 deceased patients (68 females), mean age at death was 58±15 years. The most frequent classification criteria were antinuclear antibodies (96%), immunological (92%) and hematological disorder (83%), with no difference between the ED and LD groups. 85/90 (94%) patients accrued organ damage, most frequently in the musculoskeletal (59%), cardiovascular (51%) and neuropsychiatric (NP) (48%) domains. The most frequent CODs were cardiovascular diseases (40%), followed by infections (33%), active SLE (29%) and malignancies (17%). There was no difference between the frequencies of CODs, except for stroke, which caused death exclusively ≥10 years after diagnosis. SLE was recorded in death certificates of 41/90 patients. Five- and ten-year survival in the retrospective cohort (185 non-deceased, 28 deceased patients) was 91% and 80.5%, respectively. NP and renal disorder, serositis and later-onset disease were identified as predictors of death.

**Conclusions:** Five-year survival >90% is in line with survival rates observed in developed countries, while ten-year survival is lower. The contribution of SLE to death seems to be underrecognized in SLE patients' death certificates.

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### DISEASE ACTIVITY AND DAMAGE INDEX IN 110 SLE PATIENTS

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**Background:** Assessment of disease activity and accumulated damage in systemic lupus erythematosus (SLE) patients is important for the successful treatment management. In 1996 Systemic Lupus International Collaborating Clinics (SLICC)/ American College of Rheumatology (ACR) damage indeks (SDI) has been developed to

assess irreversible damage in SLE patients, independently of its cause. The maximum possible score is 47. The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is one of the standard scales used to assess the activity of the disease. The maximum possible score of SLENA / SLEDAI index is 105. The first classification criteria for SLE were developed in 1971, revised in 1982, and adopted by ACR in 1997. They were revised and validated by SLICC group in 2012. SLICC classification criteria improved the clinical relevance of the ACR criteria.

**Objectives:** 1) to determine SLICC/ACR damage index score in all patients, 2) to determine the prevalence and the correlation between both classification criteria and activity of disease and 3) to determine the correlation between activity and damage index with duration of disease.

**Methods:** We performed a cross-sectional analysis of 110 consecutive patients with SLE who were examined by physicians at our hospital center during the period of 3 months. SLEDAI index, SDI and the total number of ACR and SLICC classification criteria were determined.

**Results:** Median SLICC/ACR damage index score of all SLE patients was 2 (IQR 0-3). The most frequently observed organ systems were musculoskeletal, then neuropsychiatric, ocular, pulmonary, cardiovascular, renal and malignancy. The most frequently observed components of SLICC/ACR damage index were osteoporosis with fracture or vertebral collapse and cranial or peripheral neuropathy. The number of SLICC classification criteria met per patient was significantly higher than the number of ACR criteria (7[IQR 6-8] vs 5[IQR 4-6],  $P < 0.001$ ). Moderate correlation were detected between the number of SLICC classification criteria and disease activity index, both in case of active ( $r = 0.48$ ,  $P = 0.003$ ) and inactive disease ( $r = 0.43$ ,  $P < 0.001$ ). There was a good correlation between SLICC/ACR damage index and disease duration ( $r = 0.63$ ,  $P < 0.001$ ).

**Conclusions:** Patients with longer duration of disease had a larger damage index score. SLICC classification criteria correlate with disease activity because they capture more manifestations also included in the SLEDAI index.

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## ULTRASOUND EVALUATION OF THE ANKLE JOINTS AND TENDONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with musculoskeletal involvement as one of the most common and earliest clinical manifestations which occur in 95% of patients. High-resolution ultrasound (US) already proved to be a useful diagnostic tool for the evaluation of pathological changes of the joints and tendons in the majority of inflammatory rheumatic diseases. There are no studies that evaluate the frequency of involvement of ankle joints in adult patients with SLE.

**Objectives:** The aim of this study is to assess the frequency of ankle joints and tendons involvement in SLE patients using US and correlate the findings with physical examination, laboratory tests, and disease activity scores. Here we will show preliminary results of the survey in the first 10 out of 60 included patients.

**Methods:** Ten consecutive SLE patients were enrolled in the study and underwent clinical evaluation, laboratory tests and bilateral high-resolution US on the same day. Gray-scale and power Doppler (PD) US were performed for imaging the talocrural (TC), subtalar joints (ST) and ankle tendons, then second and third MCP joints, second and third PIP joints, wrists and second and third MTP joints. Ankle inflammatory US score and global inflammatory US score were calculated.

**Results:** Preliminary results in 10 patients show the US detected inflammatory joint abnormalities in 7/10 (70%) patients and tendon involvement in 1/10 (10%). A total of 180 joints and 200 tendons were examined. Both of MTP and TC joints were affected in 60% patients, MCP joints in 50%, ST in 40%, wrists in 30% and PIP joints in 10% of patients. The most prevalent pathological US finding was joint effusion, less frequently synovial hypertrophy while positive PD signal was rarely presented. Only one patient had bony erosion detected. Effusion in TC



joints was present in 60% patients, synovial hypertrophy in 40% and positive PD in 10%. As many as 62,5% of patients without inflammatory joint symptoms had pathological US findings in ankle joints. The global US inflammatory score had a mean value of 5,6, and ankle US inflammatory mean value score 2,9.

**Conclusions:** Results of the preliminary study show a high prevalence of US verified inflammatory joint changes in SLE patients. Surprisingly, the foot and ankle joints were most commonly affected and a great number of asymptomatic patients had pathological US findings in ankle joints.

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**Disclosure:** None

## **RHEUMATOID ARTHRITIS AND FEMALE SEXUAL DYSFUNCTION**

Judith Sautner

(Abstract not received)

## **RHEUMATOID ARTHRITIS – PSYCHE AND DEPRESSION**

Rudolf Puchner

(Abstract not received)

## **COMORBIDITIES IN RHEUMATOID ARTHRITIS**

Helga Radner

(Abstract not received)

## **GIANT CELL ARTERITIS – AN OVERVIEW**

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Giant cell arteritis (GCA) is the most common systemic vasculitis in adults over age of 50 years in Western countries, affecting aorta and its primary branches (1). Though detailed etiopathogenesis of GCA is not completely understood, studies point to the breakage of immune privilege of vessel wall, resulting in predominantly TH1 and TH17 mediated vascular inflammation and damage (2). Symptoms and signs of GCA are heterogeneous and reflect tissue and organ ischemia due to vessel wall inflammation, stenosis and/or occlusion (eg. headache, jaw claudication, vision disturbances, arm claudication, etc.), and systemic inflammation (constitutional symptoms, increased inflammatory parameters, polymyalgia rheumatica, ect.) (3). Based on the location of inflamed arteries, GCA could be divided into “cranial limited” and “extracranial large vessel” GCA. Due to severe ischemic manifestations (such as an irreversible vision loss or stroke), GCA represents a medical emergency. Major improvements in the diagnostic approach were reached in the last years, with the implementation of fast track clinics and imaging (mainly ultrasonography) into daily practice (4). Besides, European League Against Rheumatism recently published recommendations on imaging in large vessel vasculitides, acknowledging imaging result in clinically suspected GCA as sufficient for diagnosing GCA and thus equivalent to the position of histology (i.e. temporal

artery biopsy) (5). Furthermore, advances in the treatment of GCA have been made. The treatment goals are the prevention of ischemic complications and the achievement of sustained remission, with the minimum treatment related adverse events. Glucocorticoids have been for decades the standard therapy in GCA. As prolonged glucocorticoid therapy could be associated with significant adverse events, different medications have been evaluated for the steroid sparing effect (6). Methotrexate was the most common conventional immunosuppressive drug used until very recently, when tocilizumab was approved for the GCA treatment, based on GiACTA trial (7). But therapeutic armamentarium is rapidly evolving and new medications (i.e. biologic and conventional targeted) for GCA are expected in the future.

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**Disclosure:** None

## EARLY DIAGNOSIS OF GIANT CELL ARTERITIS – DOES IT MATTER?

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**Purpose:** If untreated, giant cell arteritis can lead to blindness and stroke. The study objectives were to assess diagnostic procedures and treatment in early interventional clinic in University Clinical Centre Maribor in patients with temporal arteritis.

**Methods:** Retrospective study (from 2012 to 2017) of patients diagnosed with temporal arteritis. We assessed epidemiological data, delay of diagnosis, and diagnostic procedures. Results were assessed with statistical methods (SPSS 22.0).

The main goal was to determinate the delay in days between symptom onset and admission to the interventional rheumatology clinic and to assess the causes of delay.

**Results:** Fifty-three GCA (66 % female) patients with mean age 76.25 (from 63 – 89 years) years were included. Mean time duration of symptoms before admission to our early interventional clinic was 33.74 (0–180) days. The diagnostic procedure was completed in mean time of 2.04 days from the presentation at our interventional rheumatology clinic. The median time to the temporal artery biopsy (TAB) performed in 52 /53 patients was 2 days, with the median 2 days to the preliminary histological results from admission. TAB was positive in 43 (81.1%) of cases. The median time from admittance to colour Doppler sonography (CDS) of aortic arch branches was 2 days and it was positive in all 19 (35.8%) performed cases. 16 (30.2%) patients had polymyalgia rheumatica, 35 (66%) patients had visual disturbances, permanent one eye blindness occurred in 12 (22.64%) patients, and 2 (2.8%) patients experienced permanent blindness on both eyes.

Seventeen patients (32.1%) were initially treated with intravenous methylprednisolone pulse. The mean initial dose of oral methylprednisolone was 45.55 (+/- 15.54) mg. All patients received low dose Aspirin.

**Conclusions:** Early diagnosis and treatment of giant cell arteritis are very important as miss- or non-diagnosed GCA can lead to permanent blindness of the patient.

With better education and public awareness, better access and better professional education of primary care physicians, and early admission to secondary interventional clinics we might spare these patients from the devastating consequences of the GCA.

**Key words:** giant cell arteritis, delayed admission, interventional clinic

**Disclosure:** None



## COLOUR DOPPLER SONOGRAPHY OF FACIAL AND OCCIPITAL ARTERIES IN PATIENTS WITH GIANT CELL ARTERITIS

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**Background:** Giant cell arteritis (GCA) is the most common systemic large and medium size artery vasculitis in Western countries. Colour Doppler Sonography (CDS) allows the study of involvement of cranial arteries other than the temporal arteries, which are inconvenient to biopsy, such as the facial (FaA), and occipital (OcA) arteries.

**Objectives:** We aimed to estimate the frequency of the FaA, and OcA involvement in GCA; and to explore the clinical characteristics of these subgroups of patients.

**Methods:** From 1 January 2014 to 31 December 2016, we prospectively performed a CDS of the FaA, and OcA in addition to the temporal (TA), and the extracranial supra-aortic arteries in all newly diagnosed patients suspected of having GCA. We used a Philips IU22 with a 5–17.5 MHz multi-frequency linear probe from January 2014 to August 2016 and a Philips Epiq 7 with a 5–18 MHz multi-frequency linear probe from September 2016 to December 2016. All the arteries were evaluated in two planes for the highly specific halo-sign.

**Results:** During the 36-month observation period we performed a CDS of the cranial and extra-cranial arteries in 93 GCA (66.7% female) patients. The patients' median (IQR) age was 73.7 (66.1–79.1) years, and they had a median (IQR) symptom duration of 30 (21–90) days. We observed the halo-sign on the FaA, and OcA in 38 (40.9%), and 29 (31.2%) cases, respectively. The FaA, and OcA were simultaneously affected in 18/93 (19.4%) cases. Either FaA, or OcA were affected in 4/22 (18.2%) patients with a negative TA CDS. FaA involvement significantly correlated with jaw claudication and with severe visual manifestations, including permanent visual loss. Patients with OcA involvement least commonly had extracranial large vessel disease.

**Conclusions:** A fifth of patients with a negative CDS of the TAs had signs of vasculitis on the CDS of the FaA, or OcA. The addition of FaA and OcA CDS to the routine CDS of the TAs could identify 4.3% more patients and thus further improve the sensitivity of the CDS in the suspected GCA.

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## MRI IN EVALUATION OF INFLAMMATORY MYOPATHY

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**Background:** MRI of skeletal muscles has been widely used to assess several types of myopathies, including inherited and acquired muscle diseases.

**Objectives:** To describe current possibilities in use of MRI in diagnostics and assessment of idiopathic inflammatory myopathies (IIMs).

**Methods:** T2 weighted images with fat suppression (T2W/FS) or short tau inversion recovery (STIR) sequence with long time to echo (TE) and T1 weighted images were used to evaluate inflammatory changes (STIR) and muscle atrophy or fat substitution (T1). Simple scoring system was used for correlative studies with histopathological changes. New and more elaborate system for scoring of MR scans was developed and used to evaluate longitudinal images during the therapeutic study.

**Results:** Muscle biopsy guided by positive MRI finding contains significantly more inflammatory cells than the biopsy taken from MRI identified non-affected sites. However, even in parts of muscles, which look unaffected on MR scan, important numbers of the inflammatory cells can be found. It is mainly the signal intensity in MR scan, which is associated with disease activity in the acute presentation of IIMs. Longitudinal follow-up of patients with IIMs showed significant reduction of signal intensity in number of muscles when using new detailed scoring method.

**Conclusions:** Muscle MRI is a useful method to guide the biopsy site in IIMs. Scoring system that uses semiquantitative assessment of individual muscles is sensitive for evaluation of improvement during the treatment. No universal scoring method has been validated and accepted so far for evaluation of inflammation and atrophic

changes during IIMs. Developmnet of standard recommendations for muscle MRI assessment in IIMs is very much needed.

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## NOVEL CLASSIFICATION OF INFLAMMATORY MYOPATHIES

Zoltan Griger

(Abstracts not received)

## SURVIVAL AND SUBSET CLASSIFICATION ANALYSIS OF 82 PATIENTS WITH INFLAMMATORY MYOPATHY.

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**Background:** Idiopathic inflammatory myopathies (IIM) are characterised by chronic muscle inflammation, various organ involvements and the presence of certain specific autoantibodies.

**Objectives:** We assessed survival and characterized subsets based on muscle biopsy and myositis specific autoantibodies (MSAs).

**Methods:** Eighty-two patients with muscle biopsy proven IIM were included in the study. All cases had MSA and myositis associated antibody (MAA) tests (Jo-1, PL-7, PL-12, Mi-2, SRP, Pm-Scl, Ku, ribosomal, AMA-M2) using Western-blot kits. Survival analysis was performed by Kaplan Meier test.

**Results:** Fifty-nine women and 23 men with a mean age of  $49.3 \pm 14.6$  years and with  $7.5 \pm 4.5$  years of mean follow-up time were included. Interstitial lung disease (ILD) (51.2%), arthritis (51.2%), Raynaud's phenomenon (42.7%), skin symptoms (45.1%), dysphagia (24.4%) and significant cardiac involvement (15.9%) were the most prevalent disease-manifestations. 15 cases were associated with malignancies.

Myositis subsets were as follow: 26.8% (n=22) polymyositis /PM/, 30.5% (n=25) dermatomyositis/DM/, 1.2% (n=1) juvenile PM/DM, 8.5% (n=7) inclusion body myositis /IBM/, 22% (n=18) overlap myositis /OM/, and 11% (n=9) immune mediated necrotizing myopathy /IMNM/.

Malignancy was most frequently associated with IMNM (7 out of 9 patients).

Altogether 18 patients died from which 15 deaths can be connected to myositis related events. Eight patients died of malignancies, 5 patients due to cardiac events (heart failure, arrhythmia), 2 due to lung fibrosis and 3 by unknown causes. The worst prognosis with a 10-year survival of 31 % was in the IMNM subgroup ( $p < 0.01$ ), followed by patients with PM (68%), IBM (84%) OM (85.1%) and DM (85.3%). Mi-2 positive patients had a favourable prognosis with a 10-year survival of 100%. Patients with IMNM had the worst prognosis (10-year survival of 31.1%), followed by PM (76%), DM and IBM (85.7% each). Patients with antisynthetase antibody-positivity had worse prognosis compared to patients with other antibodies or no identifiable antibodies (10-year survival of 55%,  $n=16$ ) ( $p < 0.05$ ).

**Conclusions:** The worst survivals were seen in the IMNM and PM groups, due to the high frequency of the underlying malignancies and cardiac manifestations. Although ILD was the most frequent involvement, it was not the main cause of death.

**Disclosure:** None

## BIOMARKERS AND ACTIVITY MARKERS IN SCLERODERMA

Attila Balog

(Abstract not received)

## OSTEOPOROSIS IN SYSTEMATIC SCLEROSIS

Szilvia Szamosi

(Abstract not received)

## NOVEL FACTORS ASSOCIATED WITH CYCLOPHOSPHAMIDE EFFICACY IN AUTOIMMUNE DISEASES

Melinda Szabo

(Abstract not received)

## INNATE IMMUNE SYSTEM IN THE PATHOGENESIS OF SPONDYLOARTHRITIS – MONOCYTES INVOLVEMENT

Marius Korkosz

(Abstract not received)

## RISK FACTORS FOR EXTRA-ARTICULAR SIGNS IN SPONDYLOARTHRITIS

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**Background:** There are data that development of different extra-articular symptoms in seronegative spondyloarthropathies (SpA) is connected with elevated levels of different markers of inflammatory process

**Objectives:** The aim the study was to assess risk factors of different extra-articular symptoms in SpA.

**Methods:** We studied 287 SpA patients: 131 had AS, 110 had PsA, and 46 had SAPHO. We assessed extra-articular symptoms in all cases. In 191 SpA patients, we measured serum interleukin-6 (IL-6), interleukin-18 (IL-18), interleukin-23 (IL-23), endothelin-1 (ET-1)

**Results:** In SpA patients as compared to healthy controls:

1. Increased serum levels of IL-6 (P=0.02), IL-23 (P=0.03), and IL-18 (P=0.0006) were associated with increased risk of acute anterior uveitis (AAU).
2. Increased serum levels IL-18 (P=0.03) were associated with an increased risk of inflammatory bowel disease (IBD).
3. Increased serum levels of IL-18 (P=0.0002) and decreased serum levels of ET-1 (P=0.006) were associated with increased risk of skin psoriasis.
4. Increased serum levels of IL-18 (P=0.0002) and decreased serum levels of ET-1 (P=0.008) were associated with increased risk of psoriatic onychopathy.
5. Increased serum levels of IL-18 (P=0.01) was associated with increased risk of palmo-plantar pustulosis. SpA patients with AAU (P=0.0008) and IBD (P=0.03) had higher VAS. SpA patients with skin psoriasis (P=0.001) and psoriatic onychopathy (P=0.006) had lower VAS.

**Conclusions:** In SpA patients, increased serum IL-18 and decreased serum ET-1 were associated with an increased risk of extra-articular symptoms. Increased VAS was connected with AAU and IBD, decreased VAS – with skin psoriasis and psoriatic onychopathy.

## SAPHO SYNDROME – CLINICAL SYMPTOMS, IMAGING AND TREATMENT – BASED ON A GROUP OF POLISH PATIENTS.

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**Background:** Synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO) syndrome is a very rare disease presenting as a constellation of skin and osteoarticular symptoms.

**Objectives:** We studied clinical symptoms, imaging and treatment in 52 Polish SAPHO patients.

**Methods:** The following data were recorded: age, sex, disease duration, type of joint involvement, type of skin changes, bone scintigraphy results, HLA-B27, rheumatoid factor (RF), comorbidities and treatment. The patient's pain due to the disease was assessed using a visual analogue scale (VAS). We also assessed the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).

**Results:** SAPHO syndrome was more common in women with the mean age at diagnosis 50.0 years. All patients had a negative RF. 25% of 23 assessed patients had a positive HLA B-27 antigen. 88.5% of patients had palmo-plantar pustulosis.

Swelling and pain of sternoclavicular joints were the most common joint symptoms (present in 96.1 % of patients). Two patients (3.8%) had mandible involvement.

Despite hypertension, the most prevalent comorbidities were hypothyroidism (9.8%), diabetes (9.8%) and depression (5.9%).

DMARDs and antibiotics were useful in treatment.

**Conclusions:** Mandible involvement is a rare manifestation of SAPHO syndrome. Increased incidence of autoimmune diseases and depression was observed. DMARDs and antibiotics were useful in treatment.

## HIGHLIGHTS AND PITFALLS OF MRI IMAGING IN AXIAL SPONDYLOARTHRITIS PATIENTS

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Conventional radiography is still a cornerstone of diagnosis and classification in ankylosing spondylitis (AS). However, it has limitations in early stages of the disease, because it can only visualize the consequences of inflammation. Magnetic resonance imaging (MRI) is superior to conventional radiography in early stages because of its ability to visualize active inflammatory changes in sacroiliac joints when the pelvic radiographs are normal or equivocal. MRI of sacroiliac joints is also included in the Assessment of Axial Spondyloarthritis (ASAS) classification criteria for axial spondyloarthritis (SpA). For classification purposes a positive definition of MRI sacroiliitis was proposed as a clear presence of subchondral bone marrow edema (osteitis), which does not cross anatomical borders and is usually present on more consecutive slides. Besides quantitative definition of positive MRI signal (2 lesions on one slide or 1 lesion on two and more consecutive slides), the quality of MRI signal is maybe more important. There are many lesions that can mimic inflammation in the sacroiliac joints and the spine as well. The more intense the signal is on fluid sensitive MRI sequences, the better it reflects active inflammation, because small focal bone marrow edema lesions may also occur in patients with mechanical back pain, as well as in healthy individuals. The presence of structural lesions such erosions and fatty metaplasia can enhance diagnostic utility of MRI in cases of not highly suggestive appearance of osteitis. When MRI findings are not clear, an additional MRI of the spine can be performed, especially of the area with the most pronounced complaints. Evidence of bone marrow edema in three or more vertebral edges is considered as highly suggestive of axial SpA, especially in patients of younger age, when degenerative changes are expected to play minor role for differential diagnosis. The author will present examples of MRI lesions typical for SpA, and especially the lesions that can mimic SpA, not sufficient for making the diagnosis of axial SpA that we are dealing with in every day practice.

**Disclosure:** None

## IMPORTANCE OF TRABECULAR BONE SCORE IN FRACTURE RISK PREDICTION IN RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS.

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One of the most deleterious effects induced by the chronic inflammation is bone loss.

Fracture is one of the most common comorbidities in rheumatoid arthritis (RA) patients, especially patients using glucocorticoids. Bone mineral density (BMD) by dual-energy x-ray absorptiometry (DXA) is the gold standard of diagnosing and monitoring osteoporosis but does not entirely explain the fracture risk in patients suffering from systemic inflammatory diseases. A number of fractures are observed in patients with T-scores, which are not in the osteoporotic range. This discrepancy may be related to alterations of bone quality and measurements of bone mineral density are overestimated.

A challenge in clinical practice is to detect patients with a risk of having fractures although their BMD is in osteopenia.

The trabecular bone score (TBS), novel texture parameter reflects degradation of trabecular bone and therefore could be used as another bone measure to predict the risk of fragility fracture.

Little is known about the importance of TBS in fracture risk prediction in systemic inflammatory disease and about the influence of biologic treatment on TBS changes.

Because the same cytokines are involved in local and systemic bone loss, it is rational to assume that biologics may influence bone turnover and systemic bone loss. Several new studies showed that therapies targeting specific cytokines and its signaling pathways with biologic

DMARDs may protect the skeleton but outcomes in these clinical studies were based mostly on bone turnover markers and BMD changes.

We compared the effects of biological disease-modifying antirheumatic drugs (bDMARDs) and conventional synthetic (cs) DMARDs (methotrexate) on BMD, bone turnover markers (BTM) and trabecular bone score (TBS) in patients suffering from active RA.

**Methods:** A 12-month prospective trial in 105 active RA patients.

**Results:** Treatment with bDMARDs led to increase of 1.7 % ( $p < 0.05$ ) in TBS but not on BMD. The greatest TBS increase (2.7%,  $p < 0.05$ ) was observed in premenopausal females treated with bDMARDs. No effect of csDMARDs on measured parameters was observed. Based on our observation and literature data TBS could contribute to fracture risk prediction especially in RA patients with osteopenia. Although several studies reported favorable actions of biologic therapies on bone protection, there are still unmet needs for studies regarding their actions on the risk of bone fractures.

**Disclosure:** None

## TEMPOROMANDIBULAR JOINT ARTHRITIS AND THE ROLE OF IMAGING

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Temporomandibular joints (TMJs) are complex ginglymoarthrodial articulations. TMJs comprise synovium and can be affected by chronic synovitis. TMJ involvement occurs in up to 50% of children with juvenile idiopathic arthritis (JIA) and can occur in rheumatoid arthritis (RA), too. TMJ arthritis and its sequelae have significant impact on the function of TMJs and affect quality of life profoundly. In children, early onset TMJ arthritis causes growth disturbances of the mandible with severe cosmetic, dental and functional sequelae. Early diagnosis and treatment are thus essential to prevent permanent damage.

Subjective complaints (pain, stiffness, crepitation) have low sensitivity (26%) and even may not be reported by patients with TMJ arthritis. Objective findings (tenderness, crepitation, limited mouth opening or deviation of the mandible) have a somewhat higher sensitivity (26–64%), but are not specific for TMJ arthritis. In children, sequential measurement of the inter-incisor distance and its assessment with age-specific reference values can be helpful. Ultrasound, despite its many advantages, has low sensitivity, but may be a useful screening method. X-rays and X-ray based assessments visualize mainly sequelae of arthritis (erosions, growth abnormalities).



Among these, cone-beam CT provides the highest accuracy with a low exposure to radiation. Contrast enhanced MRI can visualize active synovitis in TMJs, differentiate active disease from its sequelae and thus determine the need for therapy, as well as its effectiveness.

In summary, TMJ arthritis is frequent, has the potential to cause permanent damage and is difficult to diagnose clinically. Imaging techniques improve diagnostic accuracy, among these contrast-enhanced MRI a cone-beam CT are most helpful for identification of active synovitis and its sequelae, respectively.

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**Disclosure:** None

## BIOMARKERS IN RHEUMATOLOGY, WHAT DO WE REALLY KNOW?

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The diagnosis of rheumatic diseases is made mostly on the basis of clinical signs and symptoms. However, we rheumatologists very often rely on serological and proteomic biomarkers that help to our pure clinical judgement, which is a central element of medical profession. Identifying biomarkers that can contribute the diagnosis, efficacy measurement, prognosis and treatment selection will be described in this paper. Personalized treatment strategy in the daily clinic using genomic, transcriptomic and proteomic screening is the era of the future medicine.

However, heterogeneous manifestations of rheumatic diseases make interpreting of some conflicting results on biomarkers difficult. Therefore, multibiomarker approach may prove useful.

In this paper, several well-established and novel biomarkers that have already been incorporated to the routine clinical setting or that are just studied for diagnostic and prognostic purposes will be discussed.

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**Disclosure:** None

## BIOMARKERS IN AXIAL SPONDYLOARTHRITIS

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Axial spondyloarthritis (axSpA) is a common chronic inflammatory rheumatic disease affecting predominantly axial skeleton. Long-term duration of the disease causes bone erosions, new bone formation and can gradually lead to ankylosis of the joints. Despite new possibilities for detection of early disease, the delay from the occurrence of the first symptom(s) to the diagnosis is still striking. Recent studies have focused on biomarkers that would help to diagnose the disease earlier, to determine disease activity and to select patients with potential rapid progression.

To this date the only widely used biomarker with some diagnostic value is HLA-B27 antigen. Other potential biomarkers can be found among acute-phase reactants. Some of them have been already well studied (calprotectin).

tin, IL-27), however some are newly discovered (defensin-2, lipocalin-2). Recently even relations between biomarkers of fat metabolism (triglycerides, glycerol) and fatty MRI lesions were studied for diagnostic utility. Second presented group could be entitled as disease activity biomarkers, where C-reactive protein (CRP) together with active magnetic resonance imaging (MRI) lesions are used as common indicators of disease activity. Other inflammatory biomarkers are serum amyloid A, some interleukins and tissue turnover biomarkers (metalloproteinases and their products of degradation). The last part of the presentation will be related to prognostic biomarkers. Except for already mentioned biomarkers (e.g. CRP or MMPs), vasoactive endothelial growth factor (VEGF) together with vimentin fragments, biomarkers of bone remodelling (DKK-1 and sclerostin) and some adipokines have been found to predict radiographic progression. Recently altered microRNAs (miRNAs) expression and target gene dysregulation have been shown to potentially predict progression of the disease.

Several biomarkers have been identified as potential diagnostic candidates, disease activity reflectors or markers of disease prognosis. The problem of inadequate sensitivity and specificity of these biomarkers however still remains and therefore future studies are needed for further validation.

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**Disclosure:** None

## MIRNAS AS BIOMARKERS IN AUTOIMMUNE RHEUMATIC DISEASES

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MicroRNAs (miRNAs) are small non-coding single-stranded RNAs of about 22 nucleotides in length that act as post-transcriptional regulators of gene expression. Depending on the complementarity between miRNA and target mRNA, cleavage or destabilization of mRNA or translational suppression occurs within the RISC complex. As gene expression regulators, miRNAs are involved in a variety of biological functions. Dysregulation of miRNAs and their target genes contribute to pathophysiology of many disorders including autoimmune rheumatic diseases. For example, dysregulation of miR-155, miR-146a or miR-203 have been known for a long time to contribute to aggressive behavior of synovial fibroblasts and inflammatory milieu in rheumatoid arthritis. Dysregulation of miR-155 or miR-130b influence inflammatory or resident renal tubular cells in systemic lupus erythematosus. MiR-29 appears a key regulator of collagen expression in systemic sclerosis. Many miRNAs have been shown to be of therapeutic potential in *in vivo* animal models.

MiRNAs are also present extracellularly in body fluids. Their incorporation into membrane vesicles or protein complexes with Ago2, HDL or nucleophosmin 1 protects them against RNases. Cell-free miRNAs can be delivered to another cell *in vitro* and maintain their functional potential. Therefore, miRNAs can be considered mediators of intercellular communication. Remarkable stability of cell-free miRNAs makes them accessible in body fluids. However, their origin, target tissue/organ or mechanism of action at the targeted site remains to be elucidated.

We aim to summarize growing pieces of evidence supporting diagnostic and prognostic potential of cell-free miRNAs in autoimmune rheumatic diseases such as rheumatoid arthritis, axial spondyloarthritis, systemic lupus erythematosus, systemic sclerosis, idiopathic inflammatory myopathies or Sjögren's syndrome.

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**Disclosure:** None





## SELECTED ORAL COMMUNICATIONS / IZABRANA ORALNA PRIOPĆENJA

### THE DIFFERENCES BETWEEN CLINICAL MANIFESTATIONS AND COMORBIDITIES BETWEEN WOMEN AND MEN WITH SLE TREATED IN UNIVERSITY HOSPITAL OF SPLIT FROM JANUARY 2007 TO DECEMBER 2017

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**Background:** SLE is chronic multisystem autoimmune disease with numerous clinical manifestations. Many comorbidities have significant impact on clinical course of SLE. They are partly mediated by the primary disease; some are partly caused by the treatment and some of the comorbidities are the result of genetic susceptibility, independently of the main disease.

**Objectives:** The aim of this study was to determine the differences between clinical manifestations and comorbidities in women and men with SLE treated in University Hospital Centre Split from January 2007 to December 2017.

**Methods:** The study included 268 patients with SLE diagnosis from the beginning of 2007 to the end of 2017. The data were collected from outpatient clinics, stationers and daily hospital of the Department of Rheumatology and Clinical Immunology of the Clinic for Internal Diseases of University Hospital Centre Split. During the collection process, the data were included in the Microsoft Office program package, or in Microsoft Excel, a program designed to create a table of budgets. For statistical analysis, SPSS 25 was used. We used  $\chi^2$  test and multivariate logistic regression.

**Results:** Among 268 SLE patients, there were 26 (10%) males and 242 (90%) females. The median age of the patients was 52 years (min-max: 22–88 years; Q1-Q3: 41-62.75 years). We explored the association of individual clinical manifestations and comorbidities with gender with the  $\chi^2$  test. A statistically significant association was obtained for Sjögren's syndrome and associated neoplasms with female gender, and for antiphospholipid syndrome (APS) and vasculitis with male gender. According the median age we divided our respondents into three groups. In the oldest age group >70 years there were no males, so we excluded patients > 70 years. The  $\chi^2$  test showed statistically significant association between younger age and skin changes and lupus nephritis. In older patients, statistical significant relation was found for dyslipidemia, hypertension, osteoporosis, gastritis and heart involvement. In multivariate logistic regression with the age and gender as independent variables, significantly higher frequency of Sjogren's syndrome ( $P = 0.04$ ) and associated neoplasms ( $P = 0.004$ ) were found in females, while vasculitides ( $P = 0.014$ ) and APS ( $P = 0.003$ ) were more frequent in males with SLE.

**Conclusions:** Women with SLE are more frequently affected by Sjögren's syndrome and associated neoplasms, while men with SLE suffer more frequently of vasculitis and APS. Lupus nephritis and skin changes usually occur in both sexes in younger patients. Dyslipidemia, hypertension, heart failure, osteoporosis and gastritis are more frequent in older patients than in younger patients with SLE.

**Disclosure:** None declared

## CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS OVER THE LAST 25 YEARS: PREDICTING ORGAN DAMAGE

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**Background:** Childhood-onset systemic lupus erythematosus (cSLE) is a chronic autoimmune disease with the course often more severe than in adults, and the activity of the disease widely being evaluated by SLE Disease Activity Index (SLEDAI 2K) and damage by the SLICC/ACR damage index (SDI).

**Objectives:** To explore the correlation between the SLEDAI-2K disease activity index at the time of diagnosis and the SLICC/ACR damage index of patients at their last follow up and to predict the risk of organ damage occurrence in time.

**Methods:** The retrospective study included children treated for cSLE from January 1991 to September 2017 at Department of Pediatrics, UHC Zagreb. All children were diagnosed according to the ACR 1997 and SLICC 2012 criteria.

**Results:** The disease development of 93 children (74 females) with cSLE was examined in this study. The median (range) follow up time was 7 (0.5–24) years and the median (range) age at diagnosis was 13 (5–19) years. Mean (SD) SLEDAI-2K was 18.3 (9.0) at the disease onset. 35 children (38 %) had organ damage at the last follow up with the median (range) SDI 0 (0–7). The first organ systems damaged in affected patients were renal (28%), musculoskeletal (22%), ocular (19%), neuropsychiatric (17%), cardiovascular (11%) and peripheral vascular (2.8%). A statistically significant positive correlation was found between SLEDAI-2K at the disease onset and SDI ( $\tau_b = 0.252$ ,  $p = 0.003$ ). No significant correlation was determined between the duration of the disease ( $\tau_b = 0.042$ ,  $p = 0.628$ ) or follow up period ( $\tau_b = 0.111$ ,  $p = 0.191$ ) and SDI, nor in SDI in regard to gender ( $p = 0.574$ ). Using Kaplan-Meier method we estimated the decrease in ratio of patients without organ damage since diagnosis or the occurrence of the first symptoms. Since the estimated ratio of patients with organ damage at the endpoint was less than 50%, we could not estimate the time required for damage development in 50% of patients. However, we are 95% sure that the damage is not happening in the first 9 years after diagnosis.

**Conclusions:** The high correlation detected between SLEDAI-2K and SDI indicated that the presentation of the cSLE at onset can be prognostic of the course and long-term prognosis of lupus. Our findings suggest that it is unlikely that organ damage will occur in 50% of patients in the first nine years of the disease course.

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**Disclosure:** None

## COGNITIVE DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS IS MORE ASSOCIATED WITH NON-INFLAMMATORY MECHANISM THAN INFLAMMATION

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**Introduction:** Neuropsychiatric involvement in systemic lupus erythematosus (NPSLE) includes a heterogeneous variety of neurological and psychiatric syndromes involving central, peripheral and autonomic nervous system. Neuropsychiatric lupus is associated with increased morbidity and mortality, and NPSLE has been proven to have a profound effect on health-related quality-of-life. Cognitive impairment is one of the most common manifestations of NPSLE. The aim of our study was to assess cognitive dysfunction and its association with an inflammatory and non-inflammatory mechanism in a cohort of NPSLE patients.

**Methods:** One-hundred patients with the diagnosis of systemic lupus erythematosus (SLE) were enrolled in our study. All patients underwent clinical neuro-psychological and psychiatric examinations and based on the results the diagnosis of cognitive dysfunction was established according to the ACR classification of NPSLE. In the study, the presence of serum autoantibodies and promising molecule tumour necrosis factor-like weak inducer of apoptosis (TWEAK), which supposed to be involved in the pathogenesis of NPSLE, were evaluated.

**Results:** Cognitive dysfunction (a moderate to severe degree of a cognitive deficit) was found in fifty-seven percent of SLE patients. Of the examined biomarkers including TWEAK, none showed a significant association with cognitive impairment. The only antibodies associated with cognitive dysfunction were antiphospholipid antibodies. The antiphospholipid antibodies were two times higher in a group with cognitive dysfunction than in the group without cognitive impairment and the prevalence of the antiphospholipid syndrome was significantly higher in NPSLE patients (28.1% vs. 20.9%;  $p < 0.05$ ). **Conclusion:** Cognitive dysfunction significantly decreased the mental performance of patients with SLE. The presence of antiphospholipid antibodies indicates that cognitive dysfunction is probably associated with non-inflammatory mechanism rather than inflammation. Supported by MHCR 023728.

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**Disclosure:** None

## DISEASE ACTIVITY AND TREATMENT PATTERNS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CROATIA

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**Background:** Access to biologic treatment differ in EU countries and is influenced by different factors. In CEE countries 1%–5% of all RA patients are treated with biological therapy. Factors influencing prescriptions of biologics in CEE are mostly macroeconomic conditions and restrictive treatment guidelines but also shortage of specialist prescribers, administrative hurdles and availability of care. [1]. There are published data on access to biologic treatment in Central and Eastern EU countries but there currently is no data in Croatia.

**Objectives:** The aim of this study was to assess and compare patient care and access to biologic therapy for rheumatoid arthritis (RA) treated in secondary and tertiary institutions in Croatia.

**Methods:** Non-interventional, multicenter study with retrospective chart review to collect demographics and clinical characteristics from patient's history and a cross-sectional study on date of visit to the rheumatologist with evaluation of DAS28 score and therapeutic interventions taken at this cross-sectional visit. Study was conducted in 398 RA patients from Balkan region and this subanalysis is showing results on 130 RA patients from 8 sites in Croatia.

**Results:** Results here are obtained from Non-interventional, Multicenter, Cross-sectional Study to Estimate Disease Activity and Treatment Patterns in Patients with Rheumatoid Arthritis in the Balkan Region and assessing information about cross-sectional status of DAS28 score and access to biologic therapy in 130 patients from 8 sites in Croatia. Average age was 56.4 years, and 85.4% were female. Results of the DAS28 cross-sectional status showing that 34,6% of patients are in status of moderate and 16% are in active disease. (Fig. 1) Mean time to introduction of biological therapy was 8.2 years. In a total of 28 (21.5%) subjects who had biologic treatment the mean DAS28 score at the time of start of biologic treatment was 5.5 (median 5.45; range 2.7–7.9). The mean time to introduction of biologic therapy was 8.2 years.

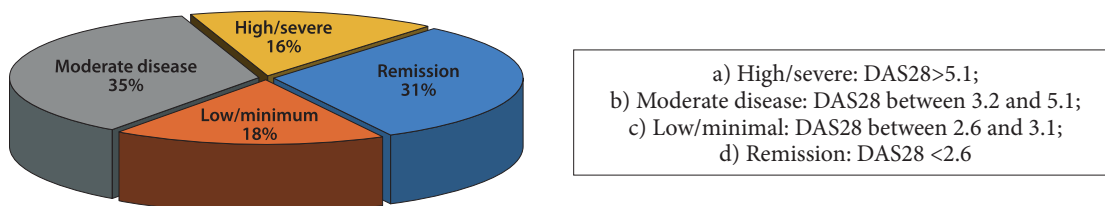


FIGURE 1. Distribution of disease categories

**Conclusions:** In this study, a half of patients despite treatment had moderate to active disease. The time to introduction of biologic therapy is very long. This clearly shows a treatment gap regarding timely introduction of biologic therapy.

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**Disclosure:** None

## DIFFICULT TO TREAT – A PATIENT WITH RHEUMATOID ARTHRITIS AND T-CELL LARGE GRANULAR LYMPHOCYTE LEUKEMIA (T-LGLL)

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**Introduction:** According to ultrasound studies, up to 52% of rheumatoid arthritis (RA) patients will have splenomegaly due to various reasons. Those, with leukopenia, will be diagnosed with Felty's syndrome (FS). However, a percentage of these patients will in fact have large granular lymphocyte leukemia, which in RA is almost always T-cell type (T-LGLL).

**Report:** A male patient born in 1963, came to our Clinic in 2016 due to a 5-year history of symmetric polyarthritis. At the time he had increased inflammatory markers, leukopenia, positive rheumatoid factor, cyclic citrullinated peptide antibodies and positive ANA and anti-DNA antibodies. He also had hepatosplenomegaly. There was a dilemma whether it was RA with FS, RA associated with systemic lupus (RUPUS) or even a paraneoplastic disorder due to microcytic anemia and weight loss. After a thorough workup, including CT scans, sternal puncture and bone marrow biopsy (showing a polyclonal T-lymphocyte hyperplasia), a diagnosis of FS was made. He was treated with methotrexate (MTX) and prednisone. However neutropenia, lymphocytosis and hepatosplenomegaly persisted. A second broad CT scan revealed a multifocal lymphadenopathy with nodes up to 2 centimeters in size. A repeated bone marrow biopsy was characteristic of a lymphoproliferative disorder. A T-cell clonality test was performed from peripheral blood and the patient was diagnosed with T-LGLL. Although the initial recommended treatment for T-LGLL associated with autoimmune disease is MTX with prednisone, the patient did not respond to this treatment. Tofacitinib was also tried, with lacking effect, and at the moment a trial with rituximab is planned.

**Conclusion:** About one third of T-LGLL patients have RA. However only 0.6% of RA patients have LGLL. A strong connection between these entities and HLA-DR4 has been observed. LGLL is in most cases a chronic,

indolent disease, without a standardised treatment protocol. Symptomatic patients and patients with associated autoimmune diseases require therapy, most often MTX with prednisone as the initial treatment. This case is an example that all neutropenic RA patients with splenomegaly should be carefully evaluated, especially if the triad of FS occurs early in the disease course, and also that thanks to clonality tests, a percentage of FS will most likely be reclassified to LGLL.

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Disclosure: None

## GIANT CELL ARTERITIS IN POLAND. HOW TO INCREASE DIAGNOSTIC RATE?

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**Background:** The incidence rate of giant cell arteritis (GCA) in Department of Rheumatology, Internal Medicine and Geriatrics was raised 10 folds between 2000 and 2016.

**Objectives:** In this presentation a practical question: "how to increase GCA diagnostic rate?" was addressed, and illustrated with some clinical cases.

**Methods:** GCA referrals to Department of Rheumatology in Szczecin were analyzed. Additionally GCA epidemiology in Poland was analyzed based on national insurance registry and compared with distribution of fast track GCA clinics.

**Results:** Increase of diagnostic rate was due to mainly 2 factors:

1. Development of effective temporal / large vessels visualization techniques and introduction of fast track GCA diagnostics.
2. Better cooperation with ophthalmologist and other specialists (Table 1.)

TABLE 1. GCA (confirmed cases) referrals to Department of Rheumatology in Szczecin, Poland (2000 to 2016).

Referral from:	N=119	%
general practitioners and emergency departments	31	26
ophthalmologists	24	20
internal medicine doctors	20	17
rheumatologists	19	16
neurologists	10	8
infectious diseases specialists	5	4
angiologists/vascular surgeons	4	3
cardiologists	3	3
other	3	3

Visualization techniques introduced were temporal/large arteries Doppler ultrasound (fast track) sometimes supported by large arteries computed tomography, occasionally by temporal artery biopsy and marginally by PET-CT. Based on national insurance registry, that we've analyzed, GCA diagnostic rate in Poland improved in recent years. This seems to correlate with increased interest in GCA in some sites that organized fast track GCA clinics.

**Conclusions:** Increase of GCA diagnostic rate requires further efforts.

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## THE OCCURRENCE OF PARANEOPLASTIC SYNDROMES IN PATIENTS WITH POLYMYALGIA RHEUMATICA TREATED AT THE UNIVERSITY HOSPITAL CENTER OSIJEK

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**Background:** Polymyalgia rheumatica (PMR) is an inflammatory rheumatic disease that occurs in an elderly person, usually over fifty years of age. Disease is characterized by pain, discomfort, and tenderness of shoulder, throat and hip muscles, elevated erythrocyte sedimentation values, and a fast and effective therapeutic response to the applied glucocorticoid therapy. Clinical image of PMR may resemble the presentation of many malignant diseases, given that it is of great importance to do extensive diagnostic treatment of the patient.

**Objectives:** The aim of this study was to investigate the occurrence of paraneoplastic syndromes in patients with PMR, treated at the Department of Rheumatology, Clinical Immunology and Allergology of the University Hospital Center of Osijek (UHCO).

**Methods:** The study included PMR patients treated at the UHCO in the period from 1/2013. to 10/2018. A study was conducted using data from the General Practice Research Database of the UHCO.

**Results:** In 46 patients with PMR the occurrence of paraneoplastic syndrome was 8.7% (N=4) with a 95% confidence interval of 2.42%–20.79%. The median age of the detection of the paraneoplastic syndrome was 73 (65–85) years, and the mean time of detection of the syndrome since the diagnosis of PMR was  $1 \pm 1$  years. In total number of diagnosed, there is an equal number of male and female patients (N=2,  $p > 0.999$ ). Among males, the occurrence of paraneoplastic syndrome was 15.38%, and among women 6.02% ( $p = 0.585$ ). The mean age of discovery of male paraneoplastic syndrome was  $75 \pm 14.14$ , and in women  $64 \pm 7.07$  godina ( $p = 0.699$ ). There was no statistically significant difference in the age of PMR patients ( $76.17 \pm 6.93$ ) compared to those with paraneoplastic syndrome ( $71.5 \pm 9.11$ ),  $p = 0.213$ .

**Conclusions:** According to the results of our research the time to diagnose paraneoplastic syndrome is approximately one year after the diagnosis of PMR. Therefore, more extensive diagnostic processing and disease control during the first year from the diagnosis of the PMR will reduce the risk of non-recognition of malignant disease disguised as a clinical image of PMR. In addition, the occurrence of paraneoplastic syndromes was 8.7% in the population of PMR patients included in this five-year study.

**Key words:** Polymyalgia rheumatica; Paraneoplastic syndromes; Occurrence

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**Disclosure:** None

## DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS

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Granulomatosis with polyangiitis (GPA), previously known as Wegener's granulomatosis, is a rare form of systemic vasculitis of unknown etiology, commonly associated with serum cANCA. Typical manifestations include necrotizing vasculitis and granulomatous inflammation which occur in the upper and lower respiratory tracts and kidneys, however the range of clinical manifestations of GPA can involve almost any organ. Epidemiological studies suggested that prevalence of GPA in Poland is 36/1,000,000 and is slightly lower than in other European

countries. A statistically significant decrease in the GPA incidence was found within 2011–2015. Both sexes are affected equally, and a mean age at diagnosis is 40 yrs.

Clinical manifestations are heterogeneous and the following presentation of the disease should be taken into consideration: cutaneous (leucocytoclastic vasculitis, purpura, digital infarcts and gangrene), oral (ulcers, granulomatous lesions, gingival hyperplasia with strawberry-like aspect), ocular (episcleritis, scleritis, conjunctivitis, keratitis, uveitis, retinal vasculitis or thrombosis, blindness, proptosis and orbital granulomatous masses), auricular (sensorineural hearing loss and conductive hearing loss), cardiovascular (small vessel vasculitis, occlusive vascular disease, pericarditis, cardiomyopathy, valvular heart disease, ischemic heart disease, heart failure), gastrointestinal (acute abdomen secondary to peritonitis or bowel ischemia), neurological (meningitis, seizures, cerebrovascular accidents, spinal cord lesions, cranial nerve palsies, sensory or motor peripheral neuropathy, mononeuritis multiplex, cerebral mass lesions) as well as musculoskeletal involvements.

Therapy should be adjusted to individual patient. Various programs have been proposed for the induction of remission and its maintenance, and management of relapses. Glucocorticoids and cyclophosphamide are the most commonly used medication although rituximab is particularly useful in patients with refractory or relapsing disease, women of childbearing potential, and patients previously treated with cyclophosphamide as well as is more effective than cyclophosphamide for treating relapses. Azathioprine is also used for remission maintenance. Plasma exchange is indicated in patients with alveolar hemorrhage.

**Disclosure:** None

## CLINICAL COURSE OF SYSTEMIC SCLEROSIS PATIENTS

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**Background:** Systemic sclerosis is a rare multisystem inflammatory connective tissue disorder of unclear etiology, characterized by progressive fibrosis of skin and internal organs as well as systemic vascular dysfunction. Disease severity is determined by the degree of internal organ involvement, especially pulmonary hypertension, interstitial lung disease, and peripheral vasculopathy.

**Objectives:** The aim of this study was to analyze a group of patients diagnosed with systemic sclerosis.

**Methods:** We retrospectively analyzed a group of 70 patients (42 women and 28 men) treated in the Department of Internal Medicine and Rheumatology, SUM, Katowice, Poland between 2013 and 2016. Patients were an average of 54.0 years old (+/–, range). Our study examined the incidence of cardiovascular and musculoskeletal symptoms as well as basic blood chemistry and imaging studies. We also assessed the degree of skin thickness by the Modified Rodnan Skin score (mRSS).

**Results:** Among study group participants, 67 patients tested positive for ANA, 51- Scl-70, 6-ACA antibodies while 3 patients were not tested. Most patients had an abnormal nailfold capillaroscopy with a sclerodermal pattern, joint pain and features of interstitial lung disease on HRCT. 30% of patients demonstrated pulmonary hypertension and anemia, 7.1% chronic kidney disease, and 15.7% finger ulcers.

Most patients were treated with immunosuppressants, and 9 subjects underwent autologous of stem cell transplantation from peripheral blood.

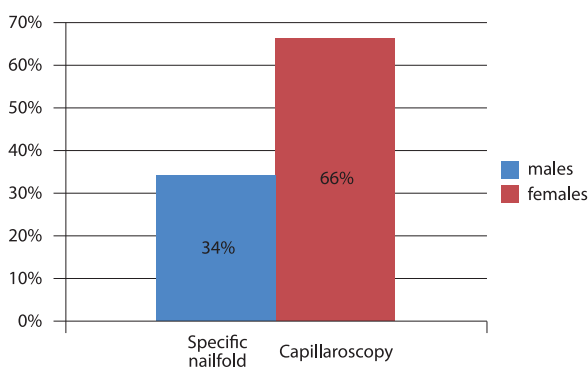


FIGURE 1. Distribution of specific nailfold capillaroscopy according to gender

TABLE 1. Results of Modified Rodnan skin score

Modified Rodnan skin score (MRSS)	Males	Females	Examined group
0	7,00%	12,00%	10,00%
1–14	47,00%	72,00%	61,00%
15–29	43,00%	14,00%	26,00%
30–39	3,00%	2,00%	3,00%
>= 40	0	0	0

TABLE 2. Occurance of pulmonary hypertension

Pulmonary hypertension	Females	Males
present (+)	52,00%	48,00%
nonpresent (–)	64,00%	36,00%

**Conclusions:** Our results are comparable to other similar studies seen in the literature. A team based approach involving physicians of different specialties as well as immunosuppressive therapy (cyclophosphamide, mycophenolate mofetil) and autologous transplantation of stem cells from peripheral blood, can greatly increase quality of life and survival of patients with systemic sclerosis. It is clear that systemic sclerosis requires further extensive study.

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**Disclosure:** None

## HSP90 PLASMA SEVELS ARE INCREASED IN PATIENTS WITH SYSTEMIC SCLEROSIS ESPECIALLY WITH INTERSTITIAL LUNG INVOLVEMENT AND SKIN FIBROSIS

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**Background:** Our previous study demonstrated that Heat shock protein 90 (Hsp90) is overexpressed in the skin of patients with systemic sclerosis (SSc), in cultured SSc fibroblasts and preclinical models of SSc in a TGF- $\beta$  dependent manner.

**Objectives:** The aim of this study was to evaluate Hsp90 in the circulation of SSc patients and characterize its potential association with skin changes and SSc-related features.

**Methods:** A total of 91 patients (78 females; mean age 52.7; disease duration 6.0 years; diffuse cutaneous (dc)SSc/limited cutaneous (lc)SSc = 38/53) who met the ACR/EULAR 2013 classification criteria for SSc and 85 age-/sex-matched healthy individuals were included. Plasma Hsp90 was measured by ELISA (eBioscience, Vienna, Austria). Data are presented as median (IQR, 25. – 75. percentile).

**Results:** Plasma Hsp90 levels were increased in SSc patients compared to healthy controls [12.5 (9.6–17.9) vs. 9.9 (7.9–12.6) ng/mL,  $p = 0.001$ ], but no difference between lcSSc and dcSSc was detected [13.1 (9.4–18.1) vs. 11.5 (9.5–17.5) ng/mL,  $p = 0.316$ ]. Hsp90 levels in all patients positively correlated with CRP ( $r = 0.313$ ,  $p = 0.006$ ). Fur-



thermore, Hsp90 was increased in patients with interstitial lung disease (ILD) compared to those without ILD [12.8 (10.2–17.9) vs. 10.3 (8.6–16.6) ng/mL,  $p = 0.045$ ] and was negatively associated with functional parameters of ILD: FVC ( $r = -0.299$ ,  $p = 0.011$ ), FEV1 ( $r = -0.256$ ,  $p = 0.031$ ), DLCO ( $r = -0.303$ ,  $p = 0.009$ ) and SpO2 ( $r = -0.317$ ,  $p = 0.038$ ). In addition, only in patients with dcSSc, Hsp90 levels positively correlated with the mRSS ( $r = 0.437$ ,  $p = 0.006$ ). Hsp90 concentrations were not significantly affected by other main clinical parameters of SSc.

**Conclusions:** We demonstrated higher plasma levels of Hsp90 in SSc patients compared to healthy controls. Concentrations of Hsp90 increase with higher inflammatory activity, with deteriorated lung functions and also with the skin involvement in patients with diffuse cutaneous SSc. These data further highlight the role of Hsp90 as a significant regulator of fibroblast activation and tissue fibrosis in SSc.

**Acknowledgement:** Supported by AZV – 16-33542A, MHCR 023728 and SVV – 260373.

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## IMPAIRED SEXUAL FUNCTIONING IN WOMEN WITH SYSTEMIC SCLEROSIS

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**Background:** Systemic sclerosis (SSc) is a chronic autoimmune disease leading to various physical and psychological impairments including sexual dysfunction.

**Objectives:** The aim of this study was to assess sexual functions/quality of life and pelvic floor function in female SSc patients compared to age-/sex-matched healthy controls (HC), and to analyze the potential impact of disease activity, fatigue, physical activity and depression.

**Methods:** In total, 41 women with SSc (mean age: 50.9, disease duration: 5.8 years, lcSSc/dcSSc: 18/23, mRSS: 13.6, ESSG activity index: 2.5), who fulfilled the ACR/EULAR 2013 criteria, and 41 healthy controls (mean age: 50.9) filled in 12 well-established and validated questionnaires assessing sexual function/quality of life, pelvic floor function, fatigue, physical activity and depression. Full names of questionnaires are listed in the table. Data are presented as mean±SEM.

**Results:** Compared to HC, patients with SSc had significantly higher prevalence and greater severity of sexual dysfunction (FSFI, BISF-W: in all subscales as well as total scores), dysfunction of pelvic floor (PISQ-12, PFIQ7), and worse sexual quality of life (SQol-F) (table). Worse scores in SSc patients were associated with higher disease activity [ESSG activity index: SQol-F ( $r = -0.364$ ,  $p = 0.0443$ ), PFIQ7-gynaecological subscale ( $r = 0.492$ ,  $p = 0.0036$ )], greater fatigue [all three questionnaires FSS/FIS/MAF correlated negatively with FSFI, BISF-W], more severe depression [BDI-II: FSFI ( $r = -0.553$ ,  $p = 0.0002$ ), BISF-W ( $r = -0.514$ ,  $p = 0.0007$ ), PFIQ7 ( $r = 0.495$ ,  $p = 0.0010$ )], deteriorated quality of life [SHAQ: FSFI ( $r = -0.536$ ,  $p = 0.0003$ ), BISF-W ( $r = -0.563$ ,  $p = 0.0001$ ), SQol-F ( $r = -0.338$ ,  $p = 0.0382$ ), PISQ-12 ( $r = 0.563$ ,  $p = 0.0051$ ), PFIQ7 ( $r = 0.380$ ,  $p = 0.0142$ )], and worse ability to perform physical activities [HAP: FSFI ( $r = 0.407$ ,  $p = 0.0082$ ), BISF-W ( $r = 0.409$ ,  $p = 0.0078$ )].

TABLE 1. Comparison of the questionnaires of interest scores for the group of patients with systemic sclerosis and healthy controls.

Questionnaire: score range	Systemic sclerosis (n=41)	Healthy controls (n=41)	p-value
<b>FSFI:</b> Female Sexual Function Index: 2(worst)–36(best)	15.2±1.7	25.0±1.7	$p < 0.001$
<b>BISF-W:</b> Brief Index of Sexual Function for Women: –16(worst)–75(best)	17.5±2.8	29.7±2.8	$p = 0.003$
<b>PISQ-12:</b> Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form: 0(best)–48(worst)	13.9±0.9	8.5±0.7	$p < 0.001$
<b>PFIQ7:</b> Pelvic Floor Distress Inventory Questionnaire – short form 7: 0(best)–300(worst)	26.4±5.9	7.1±2.2	$p = 0.009$
<b>SQol-F:</b> Sexual Quality of Life Questionnaire – Female: 0(worst)–100(best)	56.7±3.9	78.8±3.3	$p < 0.001$
<b>FSS:</b> Fatigue Severity Scale: 9(best)–63(worst)	40.7±2.2	6.9±1.0	$p < 0.001$
<b>FIS:</b> Fatigue Impact Scale: 0(best)–160(worst)	59.2±4.9	28.8±4.3	$p < 0.001$
<b>MAF:</b> Multidimensional Assessment of Fatigue Scale: 1(best)–50(worst)	26.0±1.6	13.6±1.3	$p < 0.001$
<b>BDI-II:</b> Beck's Depression Inventory II: 0(best)–63(worst)	14.2 ±1.3	4.8± 0.8	$p < 0.001$
<b>HAP:</b> Human Activity Profile–adjusted activity score: 0(worst)–94(best)	49.4±3.7	81.1±1.5	$p < 0.001$
<b>HAQ:</b> Health Assessment Questionnaire: 0(best)–3(worst)	0.9±0.1	0.1±0.0	$p < 0.001$

**Conclusions:** Women with SSc reported significantly impaired sexual function, sexual quality of life and pelvic floor function than age-matched healthy controls. Worse scores in SSc were associated with disease activity, physical activity, fatigue, depression and quality of life.

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**Disclosure:** None

## ABBERANCIES OF SPECIFIC PERIPHERAL BLOOD T-CELL AND MONOCYTE SUBPOPULATIONS IN ANKYLOSING SPONDILITIS CORRELATE WITH DISEASE ACTIVITY PARAMETERS

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**Background:** Autoimmunity is major driving force in pathogenesis of rheumatic diseases, including ankylosing spondylitis (AS). AS is associated with abnormal immune cell functions. Several recent studies stressed the role of T-cells and monocyte subpopulations in AS, but these mechanisms are significantly less understood compared to other rheumatic diseases (1).

**Objectives:** The aim was to compare the frequency of T-cell and monocyte subpopulations in AS patients and controls, and to correlate them with disease activity.

**Methods:** Mononuclear cells (MNC) were isolated from blood of healthy controls (n=110) and AS (n=65) patients. T-cell and monocyte phenotype of MNC was determined using flow cytometry for the following markers: Th1/2 (CD3+CD4+CCR6-), Th17 (CD3+CD4+CCR4+CCR6+), Tfh (CD3+CD4+CXCR5+), Tc (CD3+CD8+), memory Tc (CD3+CD8+CCR4+) double-positive (dp) Tc (CD3+CD4+CD8+); and monocytes (CD3-CD19-CD56-CD11b+CD14+). On lymphocytes IL21R, CD25 and CD11b were analyzed; while on monocytes chemokine receptors CCR1, CCR2, CCR4, CXCR4 and RANK. Frequencies of lymphocyte and monocyte subpopulations were correlated with ASDAS, BASDAI, VAS of pain in spine and peripheral joints, stiffness intensity and duration, ESR and CRP.

**Results:** Results showed decrease of memory Tc (p=0.022) and Tfh in AS (p=0.038) which correlated negatively with physician's assessment of disease activity. The frequency of dp Tc was unchanged, but negatively correlated with BASDAI and pain assessment. The frequency of monocytes was decreased in AS (p<0.001), while the subpopulation expressing RANK was increased (p=0.007). In monocytes; CCR1 correlated with BASDAI and pain assessment, CCR2 correlated with stiffness duration. CXCR4 expression was increased in AS (p<0.001) and correlated with BASDAI and stiffness intensity.

**Conclusions:** Results show changes in T-cells and monocyte subpopulations induced in AS and indicate their possible importance for AS pathogenesis. Peripheral blood dp Tc cells may be of particular interest as further research targets for novel therapeutic approaches, since their frequency is associated with disease activity and patient's pain assessment (2).

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**Disclosure:** None

## PLASMA LEVELS OF HSP90 ARE INCREASED IN AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS WITH STRUCTURAL CHANGES

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**Background:** Hsp90 is required for the proper conformation and activation of a number of cellular proteins. It also regulates activation of innate immunity and the induction of proinflammatory cytokines and chemokines. These properties predispose Hsp90 to its potential role in the pathogenesis of autoimmune inflammatory rheumatic diseases.

**Objectives:** The aim of this study was to assess Hsp90 in the plasma of axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) patients compared to healthy controls (HC) and to determine its potential associations with disease activity and clinical features.

**Methods:** A total of 80 axSpA patients (37 females; mean age 37.0 years; disease duration 9.9 years; non-radiographic (nr-axSpA): 40; radiographic (r-axSpA): 40) and 21 PsA patients (9 females, mean age 52.1 years, disease duration 25.8 years) and age-/sex- matched healthy individuals (80 and 21 respectively) were included. Plasma Hsp90 levels were measured by ELISA (eBioscience, Vienna, Austria). Data are presented as median (IQR).

**Results:** Plasma Hsp90 levels were significantly increased in axSpA patients compared to healthy controls [15.7 (10.5–19.8) vs. 8.3 (6.6–11.7) ng/mL,  $p < 0.001$ ], but no difference between nr-axSpA and r-axSpA subsets was detected [14.8 (9.2 – 19.7) vs. 16.1 (10.5 – 21.6) ng/mL,  $p = 0.513$ ]. Increased plasma levels of Hsp90 in PsA compared to HC did not reach statistical significance [11.23 (8.15–16.20) vs 8.54 (6.32–11.73) ng/mL,  $p = 0.066$ ]. Hsp90 levels in r-axSpA patients positively correlated with the MRI presence of active inflammatory lesions in sacroiliac joints (SPARCC MRI score for SI joints:  $r = 0.594$ ,  $p = 0.020$ ). Furthermore, increased Hsp90 levels in PsA patients were associated with the count of joint deformities ( $r = 0.526$ ,  $p = 0.025$ ). Plasma Hsp90 levels were neither significantly associated with other main clinical features of axSpA and PsA nor with markers of disease activity (e.g. ESR, CRP, BASDAI, ASDAS, DAPSA).

**Conclusions:** We demonstrated elevated plasma levels of Hsp90 in axSpA patients compared to healthy controls. In r-axSpA, Hsp90 may represent an independent marker of SI joint inflammation, whereas in PsA, plasma Hsp90 correlates with joint deformities. These data suggest that Hsp90 could become a potential biomarker of structural changes in SpA.

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## WHICH DEMOGRAPHIC DISEASE RELATED VARIABLES MAY BE PREDICTORS OF QUALITY OF LIFE IN PSORIATIC ARTHRITIS PATIENTS?

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Psoriatic arthritis (PsA) patients may face challenges other than skin disease, arthralgias, synovitis or dactylitis. These patients experience considerable disability and impaired quality of life, including sleep problems, depression/anxiety and problems in intimate life.

To assess if age at onset of PsA and psoriasis, duration of PsA and psoriasis severity of psoriasis, functional ability and disease activity are predictors of quality of life in PsA patients.

The study was conducted in two visits with five years period in between at the outpatient clinic of the rheumatology departments in two tertiary university hospitals, in Zagreb and Split. A total of 114 PsA patients (61 men, 53 women) were enrolled in the phase 1, while phase 2 included 104 patients (56 men, 48 women). Practising experienced rheumatologists collected demographic data and history of diseases (age, gender, age of diagnosis, duration of psoriasis and PsA). HAQ was used to assess function and DAS28 for disease activity. For assessing quality of life patients filled SF36. Methods of descriptive statistics and canonical regression were used in this research.

Mean age of patients in phase 1 was  $57,3 \pm 11,1$  years (men 57,81 years, women 56,83 years) and mean age of patients in phase 2 was  $60,1 \pm 11,3$  years (men 60,1 years, women 60,1 years). Mean duration of psoriasis in phase 1 was  $211,9 \pm 147,1$  months and in phase 2 was  $251,6 \pm 153,9$  months, while mean duration of PsA in phase 1 was  $132,5 \pm 113,6$  months and in phase 2 was  $171,7 \pm 108,4$  months. Canonical regression was performed in both phases and showed that age of PsA diagnosis and duration of PsA were significantly associated with worse functional ability, but not with the quality of life of PsA patients.

Based on the result of this research, functional ability of PsA patients depends on age at diagnosis and disease duration which could be considered as the predictors of functional ability in PsA patients.

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**Disclosure:** None

## COMPARISON OF COMPUTERIZED COLOR TELETHERMOGRAPHY AND NAILFOLD CAPILLAROSCOPY IN DIAGNOSTICS OF SECONDARY RAYNAUD'S PHENOMENON IN CHILDREN

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**Background:** Raynaud's phenomenon (RP) is a condition characterized by periodical vasospasm in response to cold temperatures or emotional stress exposure. To distinguish between primary and secondary RP, clinical examination, laboratory findings, nailfold capillaroscopy (NC) and computerized color telethermography (CCTT) are necessary.

**Objectives:** To analyze RP features in children in correlation with the most frequently associated laboratory tests, CCTT and NC.

**Methods:** This study included children clinically recognized as RP in the period from 2011–2017 at the Referral Center for Pediatric and Adolescent Rheumatology Republic of Croatia. Laboratory data included serum level of IgG, C3, C4, CH50, RF, presence of ANA and ANCA.

**Results:** CCTT, performed in 188 patients, classified 15 as primary RP, 57 as secondary RP, while in 47 no classification could be made. Among patients classified as secondary RP on CCTT, the most of them, 14 (24.6%), were diagnosed with juvenile idiopathic arthritis (JIA). There were 5 patients (8.8%) with systemic sclerosis (SSc), 2 (3.5%) with mixed connective tissue disease (MCTD), 1 (1.7%) with systemic lupus erythematosus, 11 (19.3%) with undifferentiated connective tissue disease (UCTD), whilst 24 (42.1%) had no evident other disease. The appearance of abnormal capillaroscopic pattern was found in 17 out of 89 patients and nonspecific capillaroscopic alterations were noticed in 27. Among patients with the appearance of abnormal capillaroscopic pattern, 5 (29.4%) were diagnosed with SSc, 3 (17.6%) with JIA, 2 (11.8%) with MCTD, 1 (5.9%) with dermatomyositis, 2 (11.8%) with UCTD, whilst 4 (23.5%) had no evident rheumatic disease. All patients with RP diagnosed with SSc and MCTD had both the appearance of abnormal capillaroscopic pattern and CCTT findings consistent with secondary RP. No statistically significant difference between NC and CCTT in predicting the diagnosis of secondary RP was determined (McNemar's test,  $\chi^2 = 0.042$ ,  $p = 0.838$ ) nor was there significant difference between NC and CCTT in regard to the results of laboratory findings ( $\chi^2 = 1.042$ ,  $p = 0.307$ ).

**Conclusions:** We found that nailfold capillaroscopy and CCTT were equally effective in the diagnosis of secondary RP in children. There was no difference between them in regard to the results of immunological laboratory findings distinctive with secondary RP.

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**Disclosure:** None



## APPLICATION OF FRAX AND TRABECULAR BONE SCORE IN PATIENTS WITH PSORIATIC ARTHRITIS

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**Background:** Studies evaluating BMD in PsA provides inconsistent and conflicting results, and there are a limited number of studies that evaluated bone microarchitecture and low BMD – related fragility fractures. Degenerative changes of the spine may limit accurate assessment of BMD using DXA. According to our knowledge, this is the first study that estimates bone microarchitecture measured by TBS –DXA in PsA patients.

**Objectives:** The first aim of the study was to evaluate if application of FRAX tool can identify more patients who are under risk for major osteoporotic fractures and hip fractures and therefore modify treatment for osteoporosis. The second aim was to evaluate which clinical and bone parameters are associated with low TBS.

**Methods:** The study included 54 female patients with PsA who fulfilled the CASPAR criteria. PsA-related and osteoporosis risk factors data were obtained and FRAX was calculated for each patient. Spine (L1-L4) and hip BMD were assessed by DXA. TBS was calculated from L1-L4 spine BMD.

**Results:** The patients aged 61.28 ±9.02 (mean, SD) yrs, while the mean duration of PsA was 13.45±9.09 yrs. Osteoporosis (T-score ≤ -2.5) was detected in 13 patients (24.1%) and 15 (27.8%) reported nontraumatic fracture: 8 pts out of them had X-ray detected vertebral fractures. After applying the FRAX tool among patients with a T-score above -2.5, in 3 pts osteoporosis treatment would be required due to FRAX-HF > 3%. The patients were further divided into tertiles according to TBS results (1.359±0.09). Those with TBS in the lowest tertile (TBS ≤ 1.320, n=18) were compared with patients having TBS in the 2 upper tertiles (TBS > 1.320, n=36). Among vari-

TABLE 1 Comparison of two groups of PsA patients according to TBS values.

	Low TBS (< 1.320) N=18	High TBS (>1.320) N=36
Age (years)	63.6±9.95	60.11±8.42
BMI (kg/m <sup>2</sup> )	34.53±3.84	28.65±5.02
BMI >25 (overweight) (%)	16 (88.9)	19 (52.8)
BMI > 30 (%)	10 (52.8)	10 (27.8)
PsA disease duration (years)	11.94±8.81	8.06±9.09
Menopause duration (years)	(N=16) 16.00±8.49	(N= 32) 12.06±9.04
T score ≤ -2.5 SD at 1 site or more (%)	8 (44.4 %)* *all pts at L-spine	5(13.9 %)
Both axial and peripheral bone involvement of the disease (%)	7(38.9)	9(25)
Smoking history-ever (%)	6 (27.3)	16(44.4)
Current	4	11
previous	2	5
DMARDs (%)	9 (50)	27 (75)
Glucocorticoids > 3 months (%)	3 (16.7)	6 (16.7)
ESR mm/1st hour	26.90±14.76	21.67±12.34
CRP mg/L	7.62±8.74	6.73±5.53
Previous fracture (%)	7 (38.9)	8 (22.2)
Vertebral (%)	3 (16.7)	5 (13.9)
FRAX -HF > 3%	3 (16.7)	5 (13.9)

Mean±SD or n, %; <sup>a</sup> Number (%); <sup>b</sup> Mean (SD)

ables of interest patients with lower TBS ( $\leq 1.320$ ) had more often osteoporosis (44.4% vs. 13.9%) and non-traumatic fractures (38.9 % vs. 22.2%), longer duration of the disease ( $11.94 \pm 8.81$  vs.  $8.06 \pm 9.09$  yrs), longer menopause duration ( $16.00 \pm 8.49$  vs.  $12.06 \pm 9.04$  yrs) and higher body mass index (BMI) ( $34.53 \pm 3.84$  vs.  $28.65 \pm 5.02$ ) (Table 1).

**Conclusions:** According to results of our study application of FRAX tool would modify treatment decision in minority of patients with PsA. The TBS measurement enabled recognition of some clinical factors and parameters of the disease associated with lower TBS. Further studies involving larger number of PsA patients and healthy controls are required to investigate additional determinants of a low TBS and its importance in PsA.

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**Disclosure:** None

## PROGRESSION OF PAIN, STIFFNESS, FUNCTION CHANGES, AND ULTRASOUND DETECTED SYNOVITIS AND OSTEOPHYTE FORMATION IN PATIENTS WITH HAND OSTEOARTHRITIS OVER THREE YEARS

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**Background:** Hand osteoarthritis (HOA) is a common and frequent cause of pain. HOA is a heterogeneous group of disorders with two main subsets including non-erosive and erosive disease. Few studies demonstrated inflammatory ultrasound changes and more severe clinical symptoms in patients with erosive compared with non-erosive disease, however the results are inconsistent.

**Objectives:** The aim of this study was to evaluate progression of pain, stiffness, physical impairment and ultrasound features in patients with erosive and non-erosive HOA in a three years longitudinal study.

**Methods:** Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. Joint pain and swelling, the Australian/Canadian OA hand index (AUSCAN), radiographs and ultrasound. of both hands were assessed. Patients were examined at baseline and at the and third year of follow up.

**Results:** Altogether, 97 patients (7 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2018. Out of these patients, 57 had erosive disease. The number of painful and clinically swollen joints ( $p < 0.05$ ) was significantly higher in patients with erosive compared with non-erosive disease at baseline and still remains statistically higher ( $p < 0.01$ ) at the third year of follow up in patients with erosive disease. According to the AUSCAN, patients with erosive disease had more pain ( $p < 0.05$ ) and stiffness ( $p < 0.01$ ) at baseline. Pain ( $p < 0.01$ ), stiffness ( $p < 0.05$ ) and also function ( $p < 0.01$ ) worsened in patients with erosive disease at the third year of follow up. US-detected pathologies such as gray-scale synovitis ( $p < 0.001$ ), intensity of PDS ( $p < 0.01$ ) and number of osteophytes ( $p < 0.01$ ) were significantly higher in patients with erosive disease at baseline. Patients with erosive disease also worsened after the third year of follow up ( $p < 0.01$ ).

**Conclusions:** The findings of this study show that pain and number of clinically swollen joints associated with US-detected synovial changes and osteophyte formation is more severe in patients with erosive HOA than in patients with non-erosive disease. In addition, osteophyte formation is more likely to progress independent of synovial inflammation.

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## EXPRESSION OF CXCL16 IN PERIPHERAL BLOOD OF INDIVIDUALS IN THE PRE-CLINICAL PHASE OF RHEUMATOID ARTHRITIS

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**Background:** Individuals with arthralgia and positivity of anti-citrullinated protein antibodies (ACPA) are considered at high risk of developing rheumatoid arthritis (RA). The altered expression of miRNAs is involved in the development and maintenance of autoimmune diseases.

**Objectives:** We aimed to analyse miRNAs and expression of their target genes in individuals in the pre-clinical phase of RA.

**Methods:** The initial study included 19 individuals with arthralgia (all were ACPA+) and 20 healthy controls (HC). Total RNA from peripheral blood mononuclear cells (PBMC) was isolated. A comprehensive analysis of miRNAs was performed using TaqMan® Low Density Array (TLDA) in 5 samples per group. Single assay analysis of miR-451a and CXCL16 at mRNA level was performed in remaining samples. dCt was used for relative quantification. The expression of CXCL16 at protein level in different subpopulations of leukocytes was analysed by flow cytometry in a validation cohort of 16 individuals with arthralgia and 13 HC.

**Results:** TLDA analysis as well as single assay analysis revealed 2.43-3.19x higher levels of miR-451a in individuals with arthralgia compared to HC. Levels of miR-451 positively correlated with DAS28-CRP and SDAI clinical activity scores. Online tools predicted CXCL16 as a direct target of miR-451a. The expression of CXCL16 at mRNA level was 1.51x higher in patients with arthralgia compared to HC and positively correlated with the expression of miR-451a. There was no difference in plasma levels of CXCL16. Flow cytometry analysis of different subpopulations of leukocytes revealed the expression of CXCL16 on the surface of granulocytes, monocytes and NK cells. The expression of CXCL16 was lower in patients with arthralgia compared to HC in granulocytes and monocytes while there was no difference in NK cells.

**Conclusions:** MiR-451a is of higher expression in PBMC of individuals with arthralgia compared to healthy controls and positively correlates with increased expression of chemokine CXCL16 at transcriptional level. Importantly, low protein expression of CXCL16 in granulocytes and monocytes in individuals with arthralgia is suggestive of direct regulation of CXCL16 by miR-451a. We therefore hypothesize a role of CXCL16 in the preclinical phase of RA.

**Acknowledgement:** Project AZV-17-32612A.

**Disclosure:** None

## INVESTIGATING THE POTENTIAL OF MEAN LYMPHOCYTE VOLUME AND MEAN MONOCYTE VOLUME AS BIOCHEMICAL MARKERS FOR DIAGNOSIS AND FOLLOW UP OF RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

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**Background:** The evolution of automated haematological analysers provides insight into mean cell volumes of leukocyte subpopulations. The changes in cell volumes have already been investigated as markers for inflammation response and sepsis. The focus of this research was set on rheumatoid arthritis (RA) and ankylosing spondylitis (AS) since both conditions initiate an inflammatory response and activate different cell populations.

**Objectives:** The aim of this research project was to determine the usefulness of mean monocyte volume (MCV Mo) and mean lymphocyte volume (MCV Ly) as biochemical markers for RA and AS, with the specific objectives:

1. To compare MCV Mo and MCV Ly between diagnosed patients and control group in active disease and remission
2. To investigate the relationship between these parameters and conventional biomarkers (CRP, SE, DAS28)
3. To explore these parameters as predictors of therapy effectiveness

**Methods:** This was a retrospective analysis from January 2016 to January 2017 which included a total of 183 blood samples from patients diagnosed with RA or AS at the Centre for Clinical Immunology and Rheumatology, Department for Internal Medicine at University Hospital Centre Zagreb, Croatia and 32 blood samples within the control group. The analysis was done on the automated haematology system Beckman Coulter DxH800. Data was collected and analysed in MedCalc Software.

**Results:** There is a statistically significant difference between MCV Mo and MCV Ly in patients with RA and AS compared to control group, as well as in active RA and remission. A significant moderate positive correlation was found between MCV Ly and CRP in RA ( $r=0.43$ ,  $p=0.001$ ), MCV Ly and DAS28 in active RA ( $r=0.48$ ,  $p=0.044$ ), as well as MCV Mo and SE ( $r=0.58$ ,  $p=0.000$ ) and MCV Mo and CRP ( $r=0.53$ ,  $p=0.000$ ) in AS. Patients receiving anti-TNF $\alpha$  therapy had statistically higher values of both parameters. Differences are observed in MCV Mo of patients receiving over 5mg of corticosteroids compared to lower doses.

**Conclusions:** The distribution and differences of investigated parameters could be used in longitudinal patient follow-up, thus enabling clinicians to track the disease state. The conventional biochemical markers give clinicians a broad picture of the inflammation process. Although investigated parameters cannot replace CRP, SE or DAS28 in RA and AS diagnosis, they could provide additional insight into the inflammatory process.

**Disclosure:** None

## PLASMA LEVELS OF HSP90 ARE INCREASED IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS PATIENTS

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**Background:** Hsp90 is required for the proper conformation and activation of a number of cellular proteins. It also regulates activation of innate immunity and the induction of proinflammatory cytokines and chemokines. These properties predispose Hsp90 to its potential role in the pathogenesis of autoimmune inflammatory rheumatic diseases.

**Objectives:** The aim of this study was to assess Hsp90 in plasma of rheumatoid arthritis (RA) patients and osteoarthritis (OA) patients compared to healthy controls (HC). Secondly, potential associations of plasma Hsp90 levels with disease activity and clinical features were determined.

**Methods:** A total of 35 RA patients (25 females; mean age 54.6 years; disease duration 13.0 years) and 36 OA patients (22 females, mean age 66.8 years, disease duration 6.7 years) and age-/sex- matched healthy individuals (35 and 36 respectively) were included. Plasma Hsp90 levels were measured by ELISA (eBioscience, Vienna, Austria). Data are presented as median (IQR).

**Results:** Plasma Hsp90 levels were significantly increased in RA patients compared to HC [41.4 (22.1–68.9) vs. 9.3 (7.7–14.3) ng/mL,  $p<0.0001$ ]. Furthermore, plasma Hsp90 levels correlated with serum low-density lipoproteins (LDL), high-density lipoproteins (HDL) levels and atherogenic index (AI) ( $r=0.35$ ,  $p=0.05$ ;  $r=-0.35$ ,  $p=0.05$ ;  $r=0.45$ ,  $p=0.009$ , respectively). Plasma Hsp90 levels were significantly increased in OA patients compared to HC [45.6 (42.5–53.1) vs. 10.2 (7.8–14.4) ng/mL,  $p<0.0001$ ]. Furthermore, Hsp90 plasma levels correlated with body mass index (BMI) ( $r=-0.71$ ,  $p<0.0001$ ). Concentrations of Hsp90 in plasma were neither significantly associated with other main clinical parameters nor with inflammatory/disease activity or RA/OA-related patient reported outcomes (e.g. ESR, CRP, DAS28, WOMAC, HAQ).

**Conclusions:** We demonstrated elevated plasma concentrations of Hsp90 in RA and OA patients compared to HC. In RA, Hsp90 may have a potential role in the link between inflammation and lipid metabolism, whereas in OA, Hsp90 may have a potential role in the link between obesity and progression of cartilage degradation.

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**Disclosure:** None

## ORAL COMMUNICATIONS – YOUNG RHEUMATOLOGISTS / ORALNA PRIOPČENJA – MLADA REUMATOLOGIJA

### THE INCIDENCE RATE AND CLINICAL CHARACTERISTICS OF RHEUMATOID ARTHRITIS IN SLOVENIA

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**Background:** Most epidemiological studies in RA stem from Western countries, suggesting an incidence rate of 24–45 per 100,000 person-years. However, epidemiological data for rheumatoid arthritis (RA) differ by ethnicity and geographical region. Data for Slovenia are lacking.

**Objectives:** Our objectives were to determine the incidence rate and the clinical characteristics of RA in Slovenia.

**Methods:** We analyzed prospectively collected data of adult patients diagnosed with RA from 2014 through 2016 at the Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia. The department provides rheumatology services to a well-defined region with a population of 704,000 adult residents. The patients are referred to our department by general practitioners or other specialists. We have an early interventional clinic where patients considered urgent by the referring doctor reach a rheumatologist within 24 hours from the referral from Monday through Friday, excluding national holidays.

**Results:** Between 1 January 2014 and 31 December 2016, we identified 341 incipient cases of RA (75.1% females, median age 64 (IQR 52.0–75.4) years), resulting in an estimated annual incidence rate of 16.0 per 100,000 adults (95% CI 14.5–17.9), in females 23.6 (95% CI 20.8–26.7) per 100,000 and in males 8.3 (95% CI 6.6–10.2) per 100,000, and a female to male ratio of 2.8 (Figure 1). After the age of 80 years the incidence rate again decreased. Thirty percent of all patients were identified in spring, while only 19% came in winter ( $p = 0.001$ ). Among the 341 new RA cases 323 (94.7%) fulfilled the ACR/EULAR 2010 classification criteria. Seventy four percent were ACPA positive. The ACPA positive patients were significantly younger ( $p < 0.001$ ) and more likely ever smokers ( $p < 0.001$ ); they were found to have lower disease activity at presentation (including swollen/tender joint counts and CRP) than their ACPA negative counterparts.

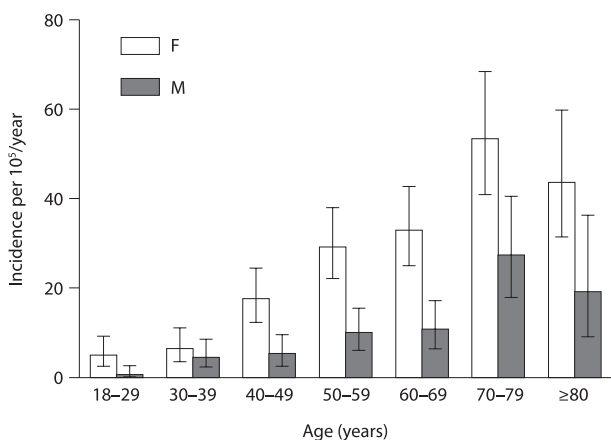


FIGURE 1. Age stratified gender specific incidence of RA in Slovenia. Data are given as incidence rates  $\pm$  95% confidence interval.

**Conclusions:** In Slovenia, the estimated incidence rate was in line with available epidemiological data. We found a significant seasonal variation in RA incidence. The ACPA-negative group in our study presented with a higher disease activity, a higher number of affected joints and higher CRP levels.

**Disclosure:** None

## VALIDATION OF SLICC-12 AND ACR-97 CLASSIFICATION CRITERIA IN A PATIENT COHORT WITH SLE TREATED IN UNIVERSITY HOSPITAL CENTRE ZAGREB

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**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease of multi-organ nature, heterogeneous clinical presentations and slow accumulation of typical symptoms, thus often hard to diagnose in early stages. Most widely used ACR classification from 1997 (ACR-97) shows high specificity and acceptable sensitivity in classifying patients with established SLE, but its value declines in early stages and in milder cases. The gold standard for diagnosing SLE and most rheumatic diseases is the experienced rheumatologist's assessment. Efforts are now put in validation and redefining current classification rules. SLICC group has published the results of multiannual revision of the ACR-97 criteria in 2012. The new (SLICC-12) criteria have shown higher sensitivity, but lower specificity than the ACR-97 criteria (97% vs 83% and 84% vs 96%, respectively).

**Objectives:** The objective of this study was to validate SLICC-12 and ACR-97 classification criteria on a patient cohort from UHC Zagreb. Overall sensitivity and specificity, as well as sensitivity and specificity according to disease duration were compared between the two sets of criteria. The value of every criterium and its contribution to diagnosing SLE was calculated.

**Methods:** This retrospective observational study comprised 308 patients with SLE (n=146) and SLE-allied conditions (n=162). All patient-history charts were evaluated by expert rheumatologists to confirm clinical diagnosis, regardless of the number of the ACR-97 criteria met. Value of the SLICC-12 and ACR-97 classification criteria was analyzed and compared using logistic regression and ROC curves.

**Results:** A clear distinction between SLICC-12 and ACR-97 criteria is observed. While sensitivity of the SLICC-12 criteria is significantly higher with a tendency to rise as SLE progresses, ACR-97 criteria have shown higher specificity. Specificity of the SLICC-12 criteria is low and declines with disease progression. Analysing and comparing the overall value of the new SLICC-12 classification rule to the ACR-97 criteria, the new criteria show superiority in our patients, with areas under the ROC curve (AUC) 0,79 and 0,70, respectively.

**Conclusions:** Although SLICC-12 criteria show superiority to ACR-97, and are more successful in diagnosing SLE in early stages, the specificity in our population is too low. Our results contribute to the current initiative for developing new criteria for SLE.

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**Disclosure:** None



## SOCIAL MEDIA USE FOR HEALTH-RELATED PURPOSES BY PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

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**Background:** Smartphone applications and social media (SM) transform the way in which people communicate, representing novel opportunities and challenges for people with rheumatic and musculoskeletal diseases (RMDs). **Objectives:** To explore the use of SM for health related purposes and perspectives of using SM.

**Methods:** A questionnaire-based survey, co-designed in English by rheumatologists and patient research partners, translated into 6 languages, then distributed via patient organisations and SM platforms. We report on interim data analyses after 5 months of data collection.

**Results:** A total of 809 participants were included in analyses from 57 countries. 40% rated to have good experience in social media. More than half were between 35 and 54 years, 90% were female, 38% had >1 RMD, 61% of participants were multimorbid.

96% were using SM and 75% reported using SM for health-related purposes, in particular to connect with other people living with the same condition (53%), via Facebook, YouTube and Google+ being the top 3 used platforms. The greatest advantage of SM is to acquire different experiences and exchange knowledge with peers. More than half voiced concerns regarding confidentiality.

SM use and education was comparable between groups with different levels of multimorbidity, although health was poorer ( $p=0.001$ ), they were older ( $p=0.001$ ) and more frequently considered that information provided by primary care physicians was inadequate ( $p=0.035$ ).

**Conclusions:** This study demonstrates that use of SM for health-related purposes is widespread among people with RMDs, mainly as a means to connect and exchange knowledge and experience. Despite concerns about confidentiality the use of SM represents new avenues for health care.

## INCREASE IN NON-CLASSICAL SUBPOPULATIONS OF MONOCYTES AND DECREASE IN NUMBERS OF NK CELLS IN THE PRE-CLINICAL PHASE OF RHEUMATOID ARTHRITIS

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**Background:** Anti-citrullinated protein antibodies (ACPA) are detectable long before the first manifestation of rheumatoid arthritis (RA). EULAR defined a clinical characteristic of individuals with arthralgia suspicious for progression to RA (clinically suspect arthralgia, CSA). The alteration of monocyte subpopulations in patients with established RA has been described.

**Objectives:** We aimed to study subpopulations of monocytes and lymphocytes in individuals in the preclinical phase of RA.

**Methods:** Our study enrolled 34 individuals with arthralgia and 80 healthy controls (HC). Leukocytes from peripheral blood were analysed by flow cytometry. Lymphocyte subpopulations were defined as CD19+CD3-, CD3+CD4+, CD3+CD8+ and CD16/56+CD3- (NK) cells, monocytes were segregated into classical (CD14+CD16-), intermediate (CD14+CD16+/++) and non-classical (CD14-/dimCD16++) subsets. Data were analysed using t-test and Spearman's correlation.

**Results:** Out of 34 patients with arthralgia, 27 were ACPA+ and 17 met CSA definition (10 were ACPA+). Individuals with arthralgia had higher %CD3 and %CD3CD8 T cells and lower %NK and absolute count of NK cells compared to HC. This was confirmed in a subgroup of ACPA+ individuals. The count of tender joints correlated

positively with %CD3 and %CD3CD8 T cells and negatively with %NK cells. Five individuals developed RA within 3–9 months of follow up. These individuals had higher baseline %CD3 cells with the trend for lower %NK cells. Expansion of intermediate and non-classical monocytes with reduction of classical monocytes were demonstrated in all individuals with arthralgia compared to HC. Importantly, ACPA+ individuals had higher non-classical and lower classical monocytes compared to ACPA-group. Similarly, ACPA+ individuals had higher intermediate or non-classical and lower classical monocytes compared to HC, while no differences were seen between ACPA- individuals and HC.

**Conclusions:** We demonstrate lower NK cells, expansion of intermediate and non-classical monocyte subpopulation in individuals in the preclinical phase of RA, especially with ACPA positivity. Our data suggest their role even in early phases of RA development. These subpopulations of leukocytes could be considered as prognostic biomarkers for further development of RA.

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**Disclosure:** None

## HEMOPHAGOCYtic LYMPHOHISTIOCYTOSIS

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Hemophagocytic lymphohistiocytosis (HLH) is a rare disorder in which the immune response is dysregulated due to elevated levels of proinflammatory cytokines while the activity of NK-cells and cytotoxic T cells is impaired. The pathogenesis of HLH might be associated with genetic risk factors, infections, autoimmune disorders and neoplasms. A 24-year-old man with suspected Still's disease was admitted to the Department of Internal and

TABLE 1. Laboratory results

	End 2014	April/May 2015	May 2015	Start of treatment May / June 2015	August 2016
HGB [g/dl]	14.3	15.2	10.9	10.4	15.8
PLT [ $\times 10^3$ /ul]	241	214	79	24	217
Granulocytes	rod cells 3%. segments cells 58%	rod cells 11%. segments cells 74%		segments cells 78%	segments cells 69.8%
Triglycerides[mg/dl]	78	155	778	568	340
Fibrinogen [g/dl]		0.95	0.40	0.43	
Ferritin [ng/ml]	1404	705	>2 000	>40 000	1480
WBC [ $\times 10^3$ /ul]	6.8	7.48	2.41	0.18	10.24
ALT [U/l]	21.3	321	275	192	116
AST [U/l]	19.3	472	224	636	54
ALP [U/l]	63	341	416	444	59
GGTP [U/l]	22.7	931		950	76
Bilirubin [mg/dl]	0.31	1.06	2.5	7.96	0.86
ESR [mm/h]	57	30/59	–	–	–
CRP [mg/l]	73.42	35.3	10.8	6.03	
PCT [ng/ml]	0.06	0.09			
Na [mmol/l]	139	138	130	130	137
LDH [U/l]	635.6	436		2402	
Creatinine [mg/dl]	0.82	0.80	1.1	1.79	0.89
Uric acid [mg/dl]	6.7	6.6	–	7.1	7.5
d-dimers[ng/ml]	860	1220.28	1330	3880	–
PT	1.11	3.1	1.77	1.3	–
APTT	30.2		44.9		–
TSH [uIU/ml]	2.83	1.450	–	1.12	–



TABLE 2. Diagnostic imaging

EXAMINATION	RESULT
CHEST X-RAY	No abnormalities detected
CHEST CT	No abnormalities detected
ECHOCARDIOGRAPHY	EF 60%, trace tricuspid regurgitation. Otherwise – no abnormalities detected
ABDOMINAL ULTRASOUND	Liver – up to 191 mm and of increased echogenicity, spleen – normal size; large amount of fluid in the peritoneal cavity
ABDOMINAL CT	Liver enlarged and of reduced attenuation, large amount of fluid in the abdominopelvic cavity, pancreatic head enlargement, an increase in the density of mesenteric fat. Spleen – no abnormalities detected. Otherwise – no abnormalities detected.
MR CHOLANGIOGRAPHY	Large amount of fluid in the peritoneal cavity; slight amount of fluid in the pleural cavities
PORTAL VEIN DOPPLER	Portal vein – patent, splenic vein stenosis behind mesenteric vein outlet to the portal vein
PANENDOSCOPY	February 2015 – erosive esophagitis (LA-B). Otherwise – no abnormalities detected May 2015: sliding hiatal hernia. Otherwise – no abnormalities detected
COLONOSCOPY	The Boston bowel preparation (3/3/3). Instrument inserted in the caecum and terminal ileum. No abnormalities detected

Rheumatic Diseases, Medical University of Silesia, Katowice. The patient had a history of hypertension (of several months' duration following the institution of prednisolone therapy) and teeth extraction. The following clinical manifestations had been present for a few months: generalized purpuric papules, recurrent episodes of fever (up to 40°C) with elbow and knee pain. The symptoms were initially attributed to respiratory / urinary infection. Laboratory and bacteriological tests, diagnostic imaging and bone marrow biopsy were all performed; consultations by several specialists were also ordered. Despite the treatment (antibiotics, anti-inflammatory drugs, glucocorticoids), only transient improvement was observed. Due to several abnormalities of laboratory results including features of liver failure (MELD score 19), renal insufficiency, pancytopenia and CRP oscillations as well as aggravation of general condition, the patient underwent specialist examination by an infectious disease specialist and gastroenterologists. After a repeat hematology consultation, the patient was transferred to the Department of Hematology and Bone Marrow Transplantation, Medical University of Silesia. Following detailed hematology testing, the preliminary diagnosis of hemophagocytic lymphohistiocytosis was confirmed and treatment modified (cyclosporin A, etoposide, glucocorticoids). The patient's condition improved and laboratory results returned to normal except slight elevation of fibrinogen levels and ALT activity.

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**Disclosure:** None

**RESPONSIVENESS OF ARTICULAR DISEASE ACTIVITY INDICES IN PATIENTS WITH SYSTEMIC SCLEROSIS**

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**Background:** We have recently completed a cross sectional study for validation of articular disease activity indices (DAIs) in 77 patients with systemic sclerosis (SSc). Disease Activity Score of 28 Joints using Erythrocyte Sedimentation Rate (DAS28-ESR) showed the best construct validity and reliability.

**Objectives:** We performed a follow-up study to explore the responsiveness of the different DAS28 scores in patients with SSc.

**Methods:** One year follow-up results of 72 patients with SSc and 38 patients with RA were compared to baseline values. The change of articular disease activity in patients with SSc was blindly categorised by two rheumatolo-

gists as improved, stable or increased disease activity. These particular categories were used as references for the determination of effect size (ES) and standardised response mean (SRM). The patient charts data contained swollen and tender joint counts, laboratory signs of inflammation, and visual analogue scales referring to articular disease activity and pain.

**Results:** According to the physicians' opinion of the SSc group, improvement of articular disease activity was present in 15 patients, deterioration in 12 patients and no change in articular disease activity in 45 patients. Correlation between change of DAS28-ESR, Disease Activity Score of 28 Joints using C-reactive protein (DAS28-CRP), Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI) measurements and the physicians' opinion of articular disease activity change was high ( $r>0.68$ ;  $p<0.001$ ). All four articular DAIs were responsive to change in articular disease activity ( $ES\geq 1$ ;  $SRM>1$ , Table 1). Out of our 38 RA patients with one-year follow-up data, disease activity decreased in 9, increased in 6 and stagnated in 23 patients based on their DAS28-ESR values.

TABLE 1. Responsiveness of disease activity indices in systemic sclerosis

Articular disease activity indices	Subgroups based on change of articular disease activity by physician consensus <sup>a</sup> (number of patients)	Articular disease activity mean (SD <sup>b</sup> )			Data of responsiveness	
		Baseline visit	1 year follow-up visit	Change over 1 year	Effect size	Standardised response mean
DAS28-ESR	improvement (n=15)	4.13 (1.32)	2.85 (1.48)	-1.29 (1.16)	-0.98	-1.11
	no change (n=45)	2.43 (1.32)	2.53 (1.28)	0.09 (0.70)	0.07	0.13
	deterioration (n=12)	3.54 (1.05)	4.71 (1.13)	1.17 (0.58)	1.11	2.03
DAS28-CRP	improvement (n=15)	3.92 (1.26)	2.54 (1.40)	-1.38 (1.01)	-1.10	-1.37
	no change (n=45)	2.04 (1.08)	2.07 (1.07)	0.03 (0.57)	0.03	0.06
	deterioration (n=12)	2.90 (1.01)	3.99 (1.10)	1.09 (0.61)	1.08	1.79
SDAI	improvement (n=15)	19.3 (10.7)	8.3 (9.8)	-11.1 (9.5)	-1.04	-1.17
	no change (n=45)	5.2 (8.5)	5.1 (8.6)	-0.1 (2.4)	-0.01	-0.05
	deterioration (n=12)	10.8 (7.1)	21.3 (12.6)	10.5 (7.8)	1.48	1.35
CDAI	improvement (n=15)	18.5 (9.8)	8.0 (9.7)	-10.5 (8.7)	-1.07	-1.20
	no change (n=45)	4.9 (8.6)	4.8 (8.6)	-0.1 (2.2)	-0.01	-0.05
	deterioration (n=12)	10.6 (7.1)	20.8 (12.7)	10.2 (8.0)	1.44	1.27

<sup>a</sup> over 1 year based on blinded evaluation of patient charts, <sup>b</sup> standard deviation

**Conclusions:** One third (38%) of the patients with SSc showed clinically significant change in articular disease activity which was similar to cases with RA (39%). All four DAIs showed good responsiveness in SSc patients with clinically meaningful change in articular disease activity.

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## POSTERS / POSTERI

### ADVANCES IN MANAGEMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Survival and prognosis of patients with SLE was improved markedly. Progress is not only in new therapeutic modalities but also in early diagnostics, assessment of activity, prognosis and monitoring focused on effects and adverse effects of therapy, and comorbidities.

For treatment of the most serious forms as neuropsychiatric lupus, lupus nephritis (LN), pulmonary alveolar haemorrhagy are indicated high doses of glucocorticoids (GC) or pulse therapy (PT) of metylprednisolone and cyclophosphamide. In refractory forms of lupus high doses of immunoglobulins, plasmapheresis, immunoadsorption is indicated. Bone marrow ablative chemotherapy and transplantation with stem cell reconstruction is seldom used method of therapy. Biologic therapy with rituximab is the most frequent used biological therapy in severe forms of lupus. In maintenance phase is proved biological therapy with belimumab, mycophenolate mofetil, azathioprine, methotrexate and calcineurin inhibitors. Belimumab is used in moderate forms of SLE. Hydroxychloroquine is appropriate to combination with other therapy in all patients with SLE. New biologics are targeted to I IFN $\alpha$ , IL-12/23 and JAK-STAT inhibition. After suppression of SLE activity is necessary to reduce of GC to the lowest effective dosages.

Morbidity and mortality in late stages of lupus is caused by organ damages (estimated by SLICC Damage Index) and comorbidities. It is associated with age, duration of the disease, number of relapses and high doses of GC. Cardiovascular diseases are the most frequent complications of SLE. On them participate diabetes, hypertension, hypercholesterolemia, metabolic syndrome, nephropathy, hyperhomocysteinaemia and premature menopause. Statins are prevention for thromboses in patient with antiphospholipid antibodies ; statins aren't risk factor for clinical worsening of SLE.

Aim of SLE therapy is low activity or remission with as low as possible dosages of GC.

Management of SLE requires monitoring activity, damage index, prevention and therapy cardiovascular complications and comorbidities. Tight monitoring leads to stabilization of damage index and prognosis improvement.

**Disclosure:** None

### WHEN A RHEUMATOLOGIC DISEASE GETS A HEAD START. A CASE REPORT OF SERONEGATIVE ANTIPHOSPHOLIPID SYNDROME

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We present a case report of a 56 year old woman with an established diagnosis of systemic lupus erythematosus and a history of multiple thrombotic events, i.e. two ischaemic strokes, myocardial infarction and recurrent deep

venous thrombosis. The patient tested negative for routinely examined antiphospholipid syndrome antibodies, that is lupus anticoagulant, anticardiolipin and anti-beta-2-glycoprotein antibodies.

She was admitted to our Department due to severe thrombocytopenia accompanied by skin and mucosal purpura. The patient was on aspirin therapy for secondary prevention of cardiovascular incidents. A couple of days prior to admission, longterm anticoagulation with heparin was switched to rivaroxaban due to the suspicion of heparin-induced thrombocytopenia.

On a second day of hospitalization, the patient had a fresh stroke that turned out ischaemic on CT scan. For the first time, the diagnosis of seronegative syndrome was proposed and adequate therapy introduced.

This case highlights how the seronegative antiphospholipid syndrome must always be suspected in patients with autoimmune conditions and recurrent thrombosis in the absence of routinely identified antiphospholipid antibodies. We discuss the seronegative antiphospholipid diagnosis and management, including antithrombotic therapy and immunotherapy, in the light of current knowledge.

**Key words:** seronegative antiphospholipid syndrome, recurrent thrombosis, antiphospholipid antibodies

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**Disclosure:** None

## NEUTROPHIL TO LYMPHOCYTE RATIO (NLR) IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND RHEUMATOID ARTHRITIS (RA)

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**Background:** Neutrophil to lymphocyte ratio (NLR) has in recent years emerged as a potential marker of systemic inflammation in numerous malignant, cardiovascular, autoimmune and other diseases. Previous studies have found a positive correlation between NLR and disease activity in RA patients, while findings for SLE are contradictory.

**Objectives:** To examine the mechanisms behind the NLR change in SLE and RA and correlation with disease activity.

**Methods:** This is a historical study. Subjects are patients with SLE (n=146) and patients with RA (n=181). Patients were divided in two groups, a group in remission and a group with active disease, with a cut-off value of SLEDAI=3 for SLE and DAS28CRP=2.6 for RA (tables 1 and 2).

**Results:** In patients with SLE, NLR is in positive, and lymphocyte count in peripheral blood in negative correlation with SLEDAI (NLR:  $r=0.165, p=0.046$ ; lymphocyte count:  $r=-0.173, p=0.037$ ) and plasma concentration of CRP (NLR:  $r=0.233, p=0.005$ ; lymphocyte count:  $r=-0.287, p=0.001$ ), while a change in neutrophil count is insignificant.

TABLE 1. Clinical characteristics of SLE patients.

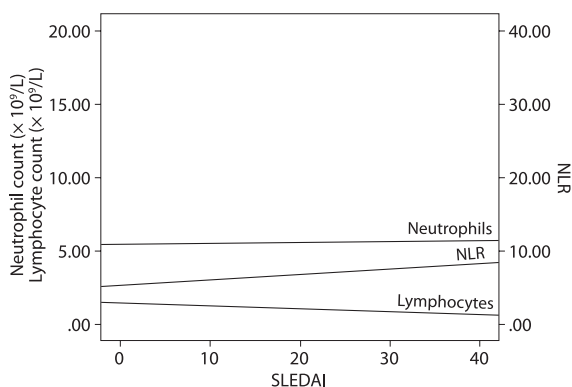
Characteristics	( )	( )	value
C3 (g/L)	1.03 (0.82–1.13)	0.73 (0.54–0.92)	<0.001
C4 (g/L)	0.18 (0.13–0.26)	0.11 (0.06–0.19)	<0.001
Neutrophil count (x10 <sup>9</sup> /L)	4.63 (3.37–6.34)	4.62 (3.31–7.41)	0.7
Lymphocyte count (x10 <sup>9</sup> /L)	1.12 (0.78–2.08)	1.09 (0.67–1.6)	0.166
NLR	2.88 (2.15–6.15)	4.65 (2.75–7.06)	0.062
CRP (mg/L)	3.1 (1.125–11.2)	4.5 (1.175–12.675)	0.534
SLEDAI	2 (0–2)	9 (6–14)	<0.001

NLR – neutrophil to lymphocyte ratio

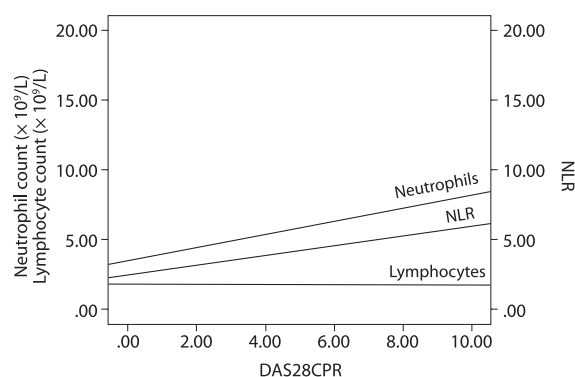
TABLE 2. Clinical characteristics of RA patients.

Characteristics	( )	( )	value
Neutrophil count (x10 <sup>9</sup> /L)	4.0 (2.63–5.33)	5.3 (4.1–7.2)	<0.001
Lymphocyte count (x10 <sup>9</sup> /L)	1.66 (1.15–2.22)	1.6 (1.27–2.2)	0.691
NLR	2.39 (1.4–4.08)	3.1 (1.96–4.54)	0.018
CRP (mg/L)	1.6 (0.45–4.0)	9.45 (2.8–24.5)	<0.001
Swollen joint count	0	4 (1–11)	<0.001
Tender joint count	0 (0–1)	8 (3–18)	<0.001
DAS28CRP	2.0 (1.39–2.315)	4.655 (3.405–6.005)	<0.001

NLR – neutrophil to lymphocyte ratio



GRAPH 1A. Regression analysis between SLEDAI and neutrophil count in peripheral blood ( $r=0.007, p=0.868$ ), lymphocyte count ( $r=-0.021, p=0.038$ ) and NLR ( $r=0.074, p=0.322$ ) in SLE patients. NLR – neutrophil to lymphocyte ratio



GRAPH 1B. Regression analysis between DAS28CRP and neutrophil count in peripheral blood ( $r=0.472, p<0.001$ ), lymphocyte count ( $r=-0.003, p=0.94$ ) and NLR ( $r=0.352, p=0.52$ ) in RA patients. NLR – neutrophil to lymphocyte ratio

nificant. NLR and neutrophil count in peripheral blood of patients with RA are in positive correlation with DAS-28CRP (NLR:  $r=0.254, p<0.001$ ; neutrophil count:  $r=0.328, p<0.001$ ) and plasma concentration of CRP (NLR:  $r=0.716, p<0.001$ ; neutrophil count:  $r=0.417, p<0.001$ ), while a change in lymphocyte count is insignificant.

**Conclusions:** NLR is a good marker of systemic inflammation in SLE and RA. However, two different mechanisms are responsible for the change in NLR. In response to increased disease activity, in SLE NLR increases due to elevated lymphocyte count in peripheral blood with insignificant change in neutrophil count, while in RA NLR increases due to elevated neutrophil count with insignificant change in lymphocyte count (graph 1a and 1b).

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**Disclosure:** None

**DEFICIENCY OF MARGINAL-ZONE-LIKE B CELL ABSOLUTE VALUES IN PERIPHERAL BLOOD IN SYSTEMIC LUPUS ERYTHEMATOSUS – A TWELVE-MONTH FOLLOW-UP STUDY**

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**Background:** Systemic lupus erythematosus (SLE) is a disease associated with a risk of serious infections, in case of hyposplenism/asplenia incl. fulminant sepsis. In SLE after splenectomy a profound deficiency of marginal-zone-like B cells in peripheral blood (PB) was observed (1); recent data are suggestive for this disorder also in non-splenectomised SLE (2).



**Objectives:** Investigation of marginal-zone-like (CD19+ CD27+ IgM+) B cells in PB as a possible member of pathway associated with a risk of infection in non-splenectomised SLE.

**Methods:** Sixty adult SLE (ACR/1982, updated 1997) pts at a level LLDAS (lupus low disease activity state; 3) and 10 age and sex-matched healthy controls (HC) were enrolled in month 0', and 56 pts persistently at LLDAS also repeatedly after twelve-month-period, i. e. month 12'; overlap syndromes, infection, renal failure and monoclonal gammopathy in SLE under study were excluded. The DuraClone IM panel (Beckman Coulter) was used to identify CD19+ CD27+ IgM+ B cell subpopulation in PB samples by flow cytometry Navios (Beckman Coulter) with software analysis using Kaluza version 1.2; data obtained were expressed not only in relative % of PB lymphocytes, but also in absolute values x10<sup>6</sup> /L, and statistically processed using Medcalc-Statistical Software programme.

**Results:** Significant differences ( $p < 0.001$ ) were obtained between absolute values of CD19+ CD27+ IgM+ B cells in HC (median 31.36, 95%CI:24.49-63.35) and SLE month 0' (median 9.82, 95%CI:6.01-14.26) and also SLE month 12' (median 9.82, 95%CI:7.12-14.42), but not between values obtained in SLE month 0' and month 12' ( $p > 0.05$ ); not significant differences were found in analysis using relative % PB lymphocytes ( $p > 0.05$ ).

**Conclusions:** The data obtained demonstrated significant and persistent character of deficiency of marginal-zone-like B cell absolute values in peripheral blood in LLDAS SLE. In this connection is suggested that the change observed should be a component of pathway associated with a risk of infections in SLE, but further studies are necessary.

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**Disclosure:** None

## EFFICACY OF BIOLOGIC TREATMENT ON QUALITY OF LIFE IN RHEUMATOID ARTHRITIS PATIENTS IN CROATIA: RESULTS FROM A NON-INTERVENTIONAL, MULTICENTER, CROSS-SECTIONAL STUDY TO ESTIMATE DISEASE ACTIVITY AND TREATMENT PATTERNS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Achieving optimal QoL is the ultimate goal of any therapeutic intervention, including biologic therapy, in patients with RA.

**Objectives:** To assess the efficacy of biologic therapy on QoL in RA patients in Croatia.

**Methods:** There were 130 patients included (19 men, 111 women) with established diagnosis of RA based on 1984 ACR criteria. Patients were consequently selected from eight rheumatology centers across Croatia. Practising rheumatologist collected demographic information, information about medications (both conventional and biologic disease modifying antirheumatic drugs). DAS28 was used to assess disease activity. All the patients filled SF-12 questionnaire, as a measure of QoL.



**Results:** The age of patients was 56,4 +/- 11,22 years. In our cohort, 102 patients were taking cDMARDs while 28 patients were on bDMARDs. Mean DAS28 score was 3.4 +/- 1,51. The QoL was assessed using SF-12 questionnaire subscores. For Q1 about general health, 48.5% patients stated it was very good or good, 37.7% fair health and 13.8% stated to have poor health. For Qs 2A and 2B approximately 50% of patients stated they were limited a little in performing while 20–25% were limited a lot. For Qs 3A and 3B (patient’s physical life). most of patients answered that they accomplished less than expected some of the time (41.9%) and they were limited in work/activities some of the time (39.8%). As for patient’s emotional life (Qs 4A and 4B), most of them answered that they accomplished less than expected some of the time (36.4%) and they were limited in work/activities some of the time (40.9%). For Q5 (interference of pain on patient’s normal work), 34.4% patients stated that it affected their work quite a bit. Qs 6A-6C (patients mental state as well as well-being), 32.6% patients stated they were peaceful and calm some of the time, while 41.9% answered most of the time. As for having a lot of energy, 65.9% of them answered they stated they had most of the time or some of the time. 65.3% patients stated they felt depressed a little bit of time or some of the time. Q7 (social activities), 66.6% stated that physical health or emotional problems affected their social activities some of the time or a little of the time.

**Conclusions:** In our group of patients with RA, treatment with both cDMARDs and bDMARDs improved QoL in some of SF-12 subscores.

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**Disclosure:** None

## ASSOCIATION BETWEEN ICF BRIEF CORE SET FOR HAND CONDITIONS AND GRIP STRENGTH IN RHEUMATOID ARTHRITIS PATIENTS

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**Background:** International Classification of Functioning Disability and Health (ICF) core set for hand conditions is based on biopsychosocial approach and is used to comprehensively describe functioning and disability of patients with conditions that affect hand. Rheumatoid arthritis (RA) is a progressive inflammatory rheumatic disease in which hands and wrists are affected in 80–90% of cases resulting in its decreased function and loss of muscle strength.

**Objectives:** In this cross-sectional study of patients with RA we studied the association between dynamometric parameters of hand grip with dimensions of ICF.

**Methods:** We included 43 patients (39 women, 4 men) with established RA and hand involvement, age 35–60 years, mean disease duration 92 months (range 58-156). Maximal grip force of dominant and non-dominant hand was measured by electronic dynamometer and patients were all evaluated by giving qualifiers to the 23

TABLE 1 The correlation between non-dominant and dominant hand grip force with results in the categories of International Classification of Functioning, Disability and Health (ICF).

	Non-dominant hand		Dominant hand	
	τ	p	τ	p
Body functions (b)	-0.38	0.002	-0.25	0.042
Body structure (s)	-0.20	0.090	-0.23	0.058
Activity and participation (d)	-0.40	0.001	-0.41	0.001
Environmental factors (e)	0.02	>0.897	-0.01	0.920

Legend: τ=Kendallov Tau-b correlation coefficient; p=significance level

TABLE 2 The correlation between left and right hand grip force with results in the categories of International Classification of Functioning, Disability and Health (ICF).

	Left hand		Right hand	
	$\tau$	p	T	p
Body functions (b)	-0.37	0.002	-0.26	0.034
Body structure (s)	-0.17	0.164	-0.26	0.034
Activity and Participation (d)	-0.40	0.001	-0.40	0.001
Environmental factors(e)	0.00	>0.999	0.00	0.991

Legend:  $\tau$ =Kendallov Tau-b correlation coefficient; p=significance level

components of ICF core set for hand conditions. ICF categories are divided into 4 domains: Body Functions (b), Body Structure (s), Activity and Participation (d), and Environmental Factors (e), and each category is encoded in the alphanumeric system.

**Results:** The ICF categories related to Body function (b) and Activity and Participation (d) were statistically significantly related to the grip force of both hands in the way that the greater difficulties in these two ICF categories were associated with a lower grip force (Table 1). Body function was associated with the grip force of the dominant hand ( $\tau$  -0.25; P=0.042) and non-dominant hand ( $\tau$  -0.38; P=0.002). Also, there was a strong association with categories of Activity and Participation for both hands ( $\tau$  -0.41; P=0.001 – dominant hand and  $\tau$  -0.40; P=0.001 – non-dominant hand). Similar results were obtained for right and left hand. (Table 2). For category of Body structure right hand showed negative correlation ( $\tau$  -0.26; P=0.034), while results for left hand were lower and not statistically significant (Table 2).

**Conclusions:** In our group of patients with established RA by evaluating them through the dimensions of ICF, categories Body function and Activity and Participation showed good correlation with the hand grip strength.

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**Disclosure:** None

## ASSOCIATION OF RS17004921 ADORA2A GENE POLYMORPHISM WITH EFFICACY OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Adenosine A2A receptors (ADORA2A) are part of the adenosine-mediated antiinflammatory pathway. These receptors are over-expressed in peripheral blood leukocytes of patients with rheumatoid arthritis (RA). Methotrexate (MTX), the gold standard for therapy, exerts its antiinflammatory effects via increased release of adenosine into the extracellular space. Adenosine binds to ADOR A2A and A3 and initiates an antiinflammatory response. Therefore, ADOR gene polymorphisms could have an impact on MTX therapy outcome.

**Objectives:** To examine the role of adenosine receptor 2A gene (ADORA2A, rs 17004921) polymorphism on outcome of MTX treatment in RA.

**Methods:** A total of 123 patients with RA (mean age 56.5±10.73, 91 (74%) female), treated with MTX for 6 months (mean dose 12.22±3.20/weekly) were enrolled in a prospective study. Genotyping within ADORA2A gene was performed using the KASP genotyping assays. MTX efficacy assessment was based on the changes in the Disease activity score (DAS28) after 6 months of treatment according to the EULAR response criteria. Patients

with good and moderate response were classified as „responders“, whereas patients with poor response were considered „nonresponders“. Data of adverse effects were collected during this period. MTX efficacy and toxicity were compared among patients with different genotypes.

**Results:** Median DAS 28 at the beginning of MTX treatment was  $7.43 \pm 0.89$ . According to EULAR response criteria, 111 (90.2%) patients with RA were classified as responders. Among all RA patients, 97 (78.9%) had CC, 20 (16.3%) CT and 6 (4.9%) TT genotype. The distribution of ADORA2 genotypes in responders (CC 77.5%, CT 17% and TT 5.4%) was not significantly different from nonresponders (CC 91.7%, CT 8.3%),  $p > 0.05$ . After 6 months, 26 carriers of T allele (CT+TT) had higher reduction DAS 28 (7.16 vs. 3.88) in comparison to other 97 patients (7.50 vs. 4.64,  $p = 0.013$ ). Adverse effects were reported in 24 (19.5%) patients. Most of patients had hepatotoxicity and nausea, 14 (58%) and 9 (37%) respectively. No statistically significant association between ADORA2A genotype and side events has been observed ( $p > 0.05$ ).

**Conclusions:** According to our results, T allele of ADORA2A rs17004921 polymorphism may have favourable influence on efficacy in RA patients treated with methotexatate.

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**Disclosure:** None

## TREATMENT OPTIONS IN PATIENT WITH RHEUMATOID ARTHRITIS AND HISTORY OF MALIGNANCY – INTRACRANIAL CHONDROSARCOMA/OSTEOCHONDROMA

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**Background:** Biologics are routinely being used as therapy for rheumatoid arthritis (RA), but there aren't many available studies that include enough data about their safety in treatment of patients with prior malignancy (1). We are presenting a patient with RA and intracranial chondrosarcoma/osteochondroma treated with rituximab (RTX). Intracranial chondrosarcoma of the sellar region is an extremely rare tumor with only few cases described in literature (1).

**Methods:** A 47-year old male patient with a positive family history of RA (mother) was diagnosed with a low grade malignancy chondrosarcoma with the elements of osteochondroma of the left parasellar region and cavernous sinus in 2006. He underwent the microneurosurgical procedure where tumor was reduced. After that, he was treated with Gamma knife (18 Gy) and continued regular follow-ups. Two years after, he developed pain and swelling of small joints of his hands and was diagnosed with seropositive (RF and ACPA) erosive RA.

**Results:** Patient was treated with NSAIDs, low dose prednisone and methotrexate (MTX). Sulphasalazine (SSZ) was added due to high disease activity (DAS28ESR=5.76). Although arthritis was controlled with high doses of prednisone (0.3–0.5 mg/kg), the disease remained active, and severe side-effects glucocorticoids started to occur. Because of the patient's prior malignancy, the treatment was thoroughly discussed with the colleagues from the Oncology Department. In a 10 years' follow-up period there was no relapse of malignancy, therefore due to high disease activity (DAS28ESR=6.1) it was decided that RA should be treated more aggressively. The patient started the treatment with RTX (1000 mg per application; two applications two weeks apart). His symptoms were improved and the disease activity decreased (DAS28ESR=2.51). Prednisone was excluded from the treatment, while he continued to use MTX and SSZ. On the last check-up the disease activity was low (DAS28ESR=1.9), the patient is without symptoms and there is no sign of malignancy.

**Conclusions:** Treatment of RA in patients with prior malignancy is challenging and there is still not enough evidence to generally recommend one specific treatment strategy (1). We believe that close communication between the rheumatologist, oncologist, and the patient are necessary to find the best individual therapeutic management.

**References:**

1. *Annals of Rheumatic Disease*, UpToDate

**Disclosure:** None

## THE ASSOCIATION BETWEEN PATIENT REPORTED OUTCOMES AND CLINICAL MEASURES AMONG RHEUMATOID ARTHRITIS PATIENTS: ANALYSES USING PHASE 3 CLINICAL TRIALS OF UPADACITINIB

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**Background:** Patient-reported outcomes (PROs) in RA are important to evaluate total disease impact and may guide treatment decisions.

**Objectives:** The purpose of this analysis was to determine the association between PROs and composite outcomes in RA patients receiving the JAK1-selective inhibitor, upadacitinib (UPA), with prior inadequate responses (IR) to conventional synthetic (cs) or biologic (b) DMARD(s).

TABLE 1. Association between PROs and clinical outcomes

	SELECT-NEXT (csDMARD-IR)			SELECT-BEYOND (bDMARD-IR)	
	Substantial improvement in pain (≥50%)	Normative HAQ-DI (≤0.25)	Normative FACIT-fatigue (≥43.6)	Substantial improvement in pain (≥50%)	Normative HAQ-DI (≤0.25)
Improvement from baseline to wk 12, Odds ratio (95% CI)					
TJC68	1.04 (1.03–1.06)***	1.05 (1.03–1.07)***	1.04 (1.02–1.05)***	1.04 (1.02–1.06)***	1.04 (1.02–1.06)***
SJC66	1.04 (1.02–1.06)***	1.05 (1.02–1.07)***	1.04 (1.01–1.06)**	1.04 (1.02–1.07)***	1.05 (1.02–1.08)**
MDGA	1.04 (1.03–1.05)***	1.03 (1.02–1.04)***	1.04 (1.02–1.05)***	1.03 (1.02–1.04)***	1.05 (1.03–1.07)***
hsCRP	1.02 (1.01–1.03)***	1.02 (1.01–1.04)***	1.02 (1.01–1.03)**	1.01 (1.00–1.02)*	1.02 (1.01–1.04)**
HAQ-DI	6.98 (4.63–10.53)***	NE	6.56 (4.12–10.45)***	8.76 (5.30–14.50)***	NE
PtGA	1.11 (1.09–1.14)***	1.04 (1.03–1.05)***	1.04 (1.03–1.05)***	1.10 (1.08–1.12)***	1.04 (1.03–1.06)***
AM stiffness duration	1.00 (1.000–1.00)**	1.00 (1.00–1.00)**	1.00 (1.00–1.00)	1.00 (1.00–1.01)***	1.00 (1.00–1.00)*
AM stiffness severity	1.56 (1.43–1.70)***	1.34 (1.22–1.48)***	1.36 (1.24–1.48)***	1.66 (1.50–1.84)***	1.69 (1.45–1.97)***
Response at wk 12, odds ratio (95% CI)					
ACR20	12.67 (8.18–19.64)***	8.81 (4.88–15.91)***	4.98 (3.06–8.11)***	13.30 (7.95–22.25)***	7.84 (3.39–18.12)***
ACR50	38.57 (22.94–64.86)***	8.52 (5.02–14.46)***	5.22 (3.31–8.23)***	60.15 (30.64–118.06)***	12.18 (5.79–25.65)***
ACR70	62.59 (22.49–174.16)***	14.35 (7.84–26.29)***	7.31 (4.31–12.40)***	96.16 (22.97–402.56)***	14.47 (6.73–31.14)***
DAS28-CRP ≤3.2	11.27 (7.56–16.78)***	6.75 (4.07–11.18)***	3.95 (2.53–6.15)***	9.43 (5.90–15.07)***	7.09 (3.52–14.30)***
DAS28-CRP <2.6	11.07 (6.85–17.90)***	4.75 (2.93–7.71)***	3.99 (2.53–6.32)***	12.11 (6.91–21.23)***	7.39 (3.85–14.18)***
CDAI ≤10	12.36 (8.09–18.87)***	4.75 (2.97–7.58)***	3.61 (2.34–5.57)***	12.99 (7.83–21.53)***	8.76 (4.44–17.29)***
CDAI ≤2.8	27.90 (8.43–92.30)***	6.18 (3.07–12.45)***	9.14 (4.44–18.82)***	NE	6.76 (3.01–15.20)***
Odds ratio, 95% CI, and P-values were calculated using univariate logistic regression model with treatment group, baseline value, and corresponding clinical outcome. ***, **, and * statistically significant at <0.001, <0.01, and <0.05 levels, respectively. NE, estimate not possible.					



**Methods:** Data were analyzed from two 12-week (wk), phase 3, RCTs in csDMARD-IR (SELECT-NEXT) and bDMARD-IR (SELECT-BEYOND) patients receiving UPA 15 or 30 mg daily (QD) or placebo and background csDMARD therapy; and from a third trial (SELECT-MONOTHERAPY), in which MTX-IR patients received UPA monotherapy or MTX for 14 wks. Moderate and substantial improvements in pain ( $\geq 30\%$  and  $\geq 50\%$  improvement from baseline [ $\Delta$ BL], respectively), and normative values in HAQ-DI ( $\leq 0.25$ ) and functional assessment of chronic illness therapy-fatigue (FACIT-F:  $\geq 43.6$ , SELECT-NEXT only) were evaluated. Associations between clinical outcomes and PROs were evaluated through Pearson correlations and a univariate logistic model, controlling for treatment group and BL value.

**Results:** In general,  $\Delta$ BL in pain and HAQ-DI scores were marginally correlated with individual physician-derived measures (SELECT-NEXT: pain, 0.161–0.537, HAQ-DI, 0.081–0.425; SELECT-BEYOND: pain, 0.131–0.511, HAQ-DI, 0.052–0.409); moreover, moderate to high correlations were observed between pain, HAQ-DI and PtGA in both RCTs (SELECT-NEXT: pain, 0.835–0.851, HAQ-DI, 0.418–0.518; SELECT-BEYOND: pain, 0.828–0.871, HAQ-DI, 0.479–0.520). In regression analyses, improvements in individual disease assessments were associated with significant improvements in pain at Wk12 across RCTs (Table). Patients with improvement in composite measures were more likely to report substantial improvements in pain. Similar associations were evident for HAQ-DI scores at Wk12 across RCTs (including SELECT-MONOTHERAPY), as well as for FACIT-F in SELECT-NEXT.

**Conclusions:** Achieving substantial improvements in pain, physical function, and fatigue was associated both with individual physician-derived measures and with composite disease outcomes. These data support the use of PROs in RCTs and also imply that, although PROs may be included in composite endpoints, they are distinct parameters that provide additional insights into the true impact of RA.

**Disclosure:** None

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## A PHASE 3, RANDOMIZED CONTROLLED TRIAL COMPARING UPADACITINIB MONOTHERAPY TO MTX MONOTHERAPY IN MTX-NAÏVE PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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**Background:** N/A

**Objectives:** To compare the clinical efficacy, including inhibition of structural damage, and safety of upadacitinib (UPA), a JAK1-selective inhibitor, as monotherapy, vs methotrexate (MTX) monotherapy, in MTX-naïve patients (pts) with moderate to severely active rheumatoid arthritis (RA).



TABLE 1. Efficacy at Weeks 12 and 24 and treatment-Emergent Adverse Events Summary Through Week 24

	WEEK 12 MTX N=314	WEEK 12 UPA 15 MG QD N= 317	WEEK 12 UPA 30 MG QD N=314	WEEK 24 MTX N=314	WEEK 24 UPA 15 MG QD N= 317	WEEK 24 UPA 30 MG QD N=314
ACR20, %	54.1	75.7***	77.1***	58.6	78.9***	78.0***
ACR50, %	28.3	52.1***	56.4***	33.4	60.3***	65.6***
ACR70 %	14.0	32.5***	36.9***	18.5	44.5***	49.7***
DAS28CRP≤3.2, %	28.3	53.3***	54.8***	32.2	59.9***	65.0***
DAS28CRP<2.6, %	13.7	35.6***	40.8***	18.5	48.3***	50.0***
CDAI≤2.8 (REM), %	6.4	16.1***	21.3***	10.5	28.4***	29.3***
ΔmTSS	NA	NA	NA	0.67	0.14**	0.07***
No radiographic progression, %	NA	NA	NA	77.7	87.5**	89.3***
Any Adverse Event (AE), n (%)	NA	NA	NA	205 (65.3)	203 (64.0)	224 (71.3)
Serious AE, n (%)	NA	NA	NA	13 (4.1)	15 (4.7)	20 (6.4)
AE Leading To Discontinuation Of Study Drug, n (%)	NA	NA	NA	16 (5.1)	14 (4.4)	12 (3.8)
Deaths*	NA	NA	NA	1 (0.3)	2 (0.6)	3 (1.0)
Infection, n (%)	NA	NA	NA	103 (32.8)	104 (32.8)	115 (36.6)
- Serious Infection, n (%)	NA	NA	NA	4 (1.3)	5 (1.6)	8 (2.5)
- Opportunistic Infection, n (%)	NA	NA	NA	0	1 (0.3)	1 (0.3)
- Herpes Zoster <sup>‡</sup> , n (%)	NA	NA	NA	1 (0.3)	7 (2.2)	7 (2.2)
Malignancy (including NMSC) <sup>‡</sup> , n (%)	NA	NA	NA	1 (0.3)	3 (0.9)	0
MACE (adjudicated) <sup>§</sup> , n (%)	NA	NA	NA	1 (0.3)	1 (0.3)	2 (0.6)

Efficacy: Values are LS mean unless otherwise specified. Δ, Change from baseline; QD, once daily; ACR20/50/70, 20/50 or 70% improvement in ACR criteria; CDAI, clinical disease activity index; DAS28CRP, 28-joint disease activity score using C-reactive protein; mTSS, modified total Sharp score; REM, remission.  
 Results are based on following analyses: binary endpoints, NRI; DAS28CRP and HAQ-DI, ANCOVA with Multiple Imputation; mTSS, ANCOVA with linear extrapolation.  
 \*\*,\*\*\* p<.01, p<.001 for UPA vs MTX  
 Safety: AE, adverse event; NMSC, non-melanoma skin cancer; VTE, venous thromboembolic events; PE, pulmonary embolism. DVT, deep vein thrombosis.  
 \*Deaths: MTX: 1 sudden cardiovascular (CV) death; UPA 15, 1 CV death, 1 death due to metastatic malignant melanoma; UPA 30, 1 CV death, 1 death due to pneumonia and sepsis, 1 death due to peritonitis (also counted under GI perforation)  
<sup>‡</sup>Herpes zoster: All non-serious, 12 were single dermatome  
<sup>‡</sup>Malignancies: MTX: 1 ovarian cancer; UPA 15: 1 metastatic malignant melanoma, 1 squamous cell carcinoma of the lung, 1 uterine carcinoma in situ  
<sup>§</sup>MACE, major adverse cardiovascular events (adjudicated): MTX, 1 CV death; UPA 15, 1 non-fatal myocardial infarction (MI), CV death due to other CV causes; UPA30, 1 non-fatal MI and 1 CV death (sudden).

**Methods:** In SELECT-EARLY, MTX-naïve pts with active RA who were positive for both RF and ACPA and/or had ≥1 joint erosion were randomized 1:1:1 to once-daily (QD) UPA at 15mg or 30mg, or weekly MTX. Separate primary endpoints were ACR50 at Wk12 (FDA), or the proportion of pts achieving DAS28CRP<2.6 at Wk24 (EMA). Secondary endpoints included mean changes from baseline (Δ BL) in modified Total Sharp Score (mTSS) and proportion of pts with no radiographic progression (mTSS≤0) at Wk24.

**Results:** Of 947 randomized pts, 945 received study drug; 840 (88.7%) completed Wk24. ~50% had an RA diagnosis of <6 months and RA symptoms <2 years. Of the 945 pts, 874 (92.5%) had no prior MTX exposure; 706 (74.7%) had no prior csDMARD exposure. Both primary endpoints were met. Significantly more patients receiving UPA 15 and 30mg vs MTX achieved ACR50 responses at Wk12, DAS28CRP<2.6 at Wk24 and all ranked secondary endpoints were met (Table). At Wk24, significantly more pts had no radiographic progression on UPA 15 and 30mg vs MTX. LDA and remission by various criteria at Wks12 and 24 were achieved in more pts on UPA vs MTX (nominal p<.001 for all). Up to Wk24, treatment-emergent adverse events (AEs) and serious AEs were similar in the UPA 15mg and MTX arms, and slightly higher in the UPA 30mg arm. A numerically higher proportion of pts on UPA 30mg reported serious infections vs MTX and UPA 15mg, and there were more cases of herpes zoster in the UPA vs MTX arms. Four malignancies, 4 major adverse cardiovascular events, and 6 deaths were reported (Table 1). Two gastrointestinal perforations (on UPA 30mg) and two venous thromboembolic

events were reported (1 pulmonary embolism on MTX, 1 deep vein thrombosis on UPA 30mg). Laboratory abnormalities were consistent with other Phase 2 and 3 studies with UPA.

**Conclusions:** In MTX-naïve pts, UPA 15 and 30mg QD demonstrated significant and clinically meaningful improvements in RA signs & symptoms vs MTX. Radiographic progression was significantly less with UPA vs MTX. Safety events were consistent with Phase 2 and 3 studies with UPA in RA to date.

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### A PHASE 3, RANDOMIZED, DOUBLE-BLIND STUDY COMPARING UPADACITINIB TO PLACEBO AND TO ADALIMUMAB, IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO METHOTREXATE

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**Background:** N/A

**Objectives:** To assess efficacy, including inhibition of radiographic progression, and safety with upadacitinib (UPA), a JAK1- selective inhibitor, vs placebo (PBO) and active comparator, adalimumab (ADA), in patients (pts) with active rheumatoid arthritis (RA) continuing on prior methotrexate (MTX).

**Methods:** In SELECT-COMPARE, pts with active RA despite MTX were randomized 2:2:1 to once-daily (QD) UPA 15mg, PBO, or ADA 40mg every other week (wk) in a double-blind manner, while continuing stable background MTX. Primary endpoints were ACR20 and the proportion of pts achieving DAS28CRP<2.6 (NRI) at Wk12. Key secondary endpoints included non-inferiority (and superiority) of UPA vs ADA at Wk12 (for ACR50,

TABLE 1. Efficacy Endpoints at Weeks 12 and 26.

Endpoint	WEEK 12			WEEK 26		
	PBO N=651	UPA 15MG QD N=651	ADA 40MG EOW N=327	PBO N=651	UPA 15MG QD N=651	ADA 40MG EOW N=327
ACR20 (%)	36.4	70.5*** #	63.0	35.6	67.4*** ##	57.2
ACR50 (%)	14.9	45.2*** ###	29.1	20.9	53.9*** ###	41.9
ACR70 (%)	4.9	24.9*** ###	13.5	9.5	34.7*** ###	22.9
DAS28CRP ≤3.2 (%)	13.8	45.0*** ###	28.7	18.0	54.7*** ###	38.5
DAS28CRP <2.6 (%)	6.1	28.7*** ###	18.0	9.2	40.9*** ###	26.9
CDAI ≤10 (LDA) (%)	16.3	40.4*** ##	30.0	22.1	52.7*** ###	38.2
CDAI ≤2.8 (CR) (%)	3.1	13.4*** ##	7.6	5.5	23.0*** ###	13.8
SDAI ≤11.0 (LDA) (%)	15.2	40.4*** ##	30.0	22.1	53.9*** ###	38.8
SDAI ≤3.3 (CR) (%)	2.8	12.1*** #	7.3	4.8	24.3*** ###	13.8
Boolean remission	2.0	9.8*** ##	4.0	3.8	18.1*** ###	9.8
ΔPain	-15.69	-32.10 *** ###	-25.61	-18.60	-36.75*** ##	-31.86
ΔHAQ-DI	-0.28	-0.60 *** ##	-0.49	-0.33	-0.69*** ##	-0.57
ΔmTSS Wk 26				0.92	0.24***	0.10
Δ JE	NA	NA	NA	0.44	0.03***	0.02
Δ JSN				0.58	0.22***	0.14
No Radiographic Progression Wk 26 (%)	NA	NA	NA	76.0	83.5**	86.8

Values are LS mean unless otherwise specified. Δ, Change from baseline; QD, once daily; ACR20/50/70, 20/50 or 70% improvement in ACR criteria; CR, Clinical remission; DAS28-CRP, 28-joint disease activity score using C-reactive protein; HAQ-DI, health assessment questionnaire disability index; JE, joint erosion; JSN, joint space narrowing; LDA, low disease activity; mTSS, modified total Sharp score; SF-36 PCS, short form 36- physical component score.  
 Results are based on following analyses: binary endpoints, NRI; mTSS, ANCOVA with linear extrapolation; other continuous endpoints, ANCOVA with rescue handling via LOCF.  
 \*\*, \*\*\* p<.01 and .001 for UPA vs PBO; #, ##, ### p<.05, .01 and .001 for UPA vs ADA. Black symbols indicate comparisons that were pre-specified for multiplicity control; lighter gray symbols indicate comparisons that were not pre-specified for multiplicity control

DAS28CRP≤3.2, change from BL (Δ) in Pain, and ΔHAQ-DI), and radiographic inhibition (ΔmTSS) for UPA vs PBO at Wk26. Pts with <20% improvement in TJC and SJC were rescued between Wks14- 26 (from PBO to UPA, UPA to ADA, or ADA to UPA).

**Results:** Of 1629 randomized pts, 91% completed Wk26.(including rescued pts). BL characteristics were similar across arms. All primary and key secondary endpoints were met (Table 1). Superiority was met for UPA vs ADA at Wk12 for ACR50, DAS28CRP≤3.2, ΔPain and ΔHAQ-DI, differences were maintained through Wk26. At Wk26, pts on UPA vs PBO had significantly less radiographic progression (Table). At Wk26, more pts on UPA vs PBO or ADA achieved low disease activity or remission by various criteria (nominal p<.001). Up to Wk26, the proportion of pts with adverse events (AEs) and serious infections, censored at rescue, was higher for UPA vs PBO but similar vs ADA. The proportion of pts with SAEs and AEs leading to discontinuation for UPA was numerically higher vs PBO and lower vs ADA. Herpes Zoster was numerically higher in UPA vs ADA and PBO. Three malignancies, 5 major adverse cardiovascular events, and 4 deaths were reported, none on UPA. Six venous thromboembolic events (VTEs) were reported (1 on PBO, 2 on UPA and 3 on ADA). For pts who were rescued, no deaths, adjudicated MACE, or adjudicated VTE were observed between rescue and Wk26.

**Conclusions:** UPA 15mg QD showed superiority on improvement in RA signs & symptoms vs PBO and ADA in this MTX-IR population. Radiographic progression was significantly lower with UPA vs PBO. Safety events were consistent with Ph 2 and 3 studies in RA to date.

**References:** N/A

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BMS, Sanofi, Eli Lilly A Ostor: Speaker, consulting fees and/or research: BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Eli Lilly, Novartis M Genovese: Consultant for, and has received grants from AbbVie, Lilly, Pfizer, Galapagos, Gilead AL Pangan, Y Li, Y Zhou, A Othman and I-H Song are employees of AbbVie and may own stock/options Acknowledgements: AbbVie and the authors thank the patients, study sites and investigators who participated in this clinical trial. AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. Medical writing support was provided by Naina Barretto, PhD, of AbbVie, Inc.

## THE EFFICACY OF SUBCUTANEOUS APPLICATION OF TOCILIZUMAB IN A PATIENT WITH LONG STANDING LARGE VESSEL VASCULITIS RELAPSE, A CASE REPORT

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The term large vessel vasculitis (LVV) encompasses the spectrum of primary vasculitides that causes chronic granulomatous inflammation predominantly of the aorta and its major branches. Two major categories of LVV are giant cell arteritis (GCA) and Takayasu arteritis (TA). Considering the fact that there is a great unmet need for better treatments in that field, we present a case of the patient with a long standing LVV, that has been recently administered tocilizumab (TCZ), a humanised monoclonal antibody against the interleukin-6 receptor, with a satisfactory short-term outcome.

A 56 old female patient has been diagnosed with LVV in the age od 36. Initial presentation was tinnitus and progressive irreversible hearing loss, raised ESR, anemia, further investigation showed aortic insufficiency and the right subclavian artery occlusion. Systemic glucocorticoids (GC) and cyclophosphamide were initially introduced. Surgical replacement with a mechanical aortic valve was performed, as well as a pulmonary vein isolation with radiofrequency ablation. A few months after GC was omitted from therapy, she has undergone multiple hospitalizations. Evaluation revealed pulmonary hypertension, tricuspid insufficiency, right heart failure, predominantly of diastolic dysfunction, and a small pulmonary embolism. In 6/2017 occurred a relapse of vasculitis proven by laboratory findings showing anemia, accelerated ESR, increase in CRP, elevated ferritin levels and PET CT scan (picture enclosed) that demonstrated diffuse enhanced vascular uptake in the area of ascending aorta and the aortic arch. Oral GC was reintroduced, followed by i.v. methylprednisolone pulses with inadequate clinical and laboratory improvement. Therefore in 12/2017 biological therapy with TCZ started in addition to GC therapy, first application i.v. and further on subcutaneously, in a dose of 162 mg, which has been followed by a

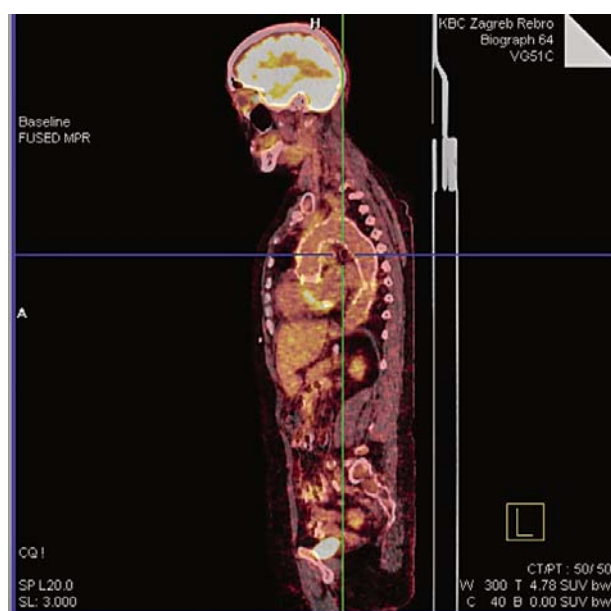


FIGURE 1. Patient's PET CT scan (June 2017)



clinical and laboratory remission. Regarding LVV, IL-6 multiple activities include the induction of antibody production, activation of Th17 cells, and increase of hepcidin, which is responsible for anemia (1). IL-6 is upregulated in inflamed arteries of patients with GCA and TA (2). Therefore it is to be expected that a treatment with TCZ is promising effective and safe solution for a refractory LVV, as it has been shown in available data obtained from limited clinical studies (3,4,5).

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**Disclosure:** None

## CHILDHOOD-ONSET OF HENoch-SCHÖNLEIN PURPURA NEPHRITIS IN CROATIA: A STUDY CONDUCTED IN FIVE TERTIARY CARE CENTRES OVER NINE YEARS

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**Background:** Henoch-Schönlein purpura nephritis (HSPN) is the most severe complication of Henoch-Schönlein purpura (HSP) that includes isolated microscopic/macrosopic hematuria, mild/heavy proteinuria with/without nephrotic syndrome, renal failure and hypertension.

**Objectives:** The aim was to determine a possible prognostic factor for earlier HSPN onset, to explore indications for kidney biopsy according to urine analysis and the correlation between 24-h urinary protein levels and biopsy findings, as well as biopsy findings and patient outcome.

**Methods:** The cross-sectional study included all children with HSPN diagnosed by EULAR/ PRES/PRINTO criteria from 2009 to 2017 at 5 tertiary care centres in Croatia.

**Results:** Out of 522 patients diagnosed with HSP, 101 children developed HSPN (19.35%). Median (range) age of HSP diagnosis was 7.5 (2–17.5) years. Nephritis was present in 7.9% of cases at the HSP onset. No positive correlation was found between the time of HSP diagnosis to HSPN onset and gender, age, purpura distribution, joint and gastrointestinal involvement. Kidney biopsy was done in 30 patients: 3 had isolated persistent hematuria, 3 isolated proteinuria and 24 patients had both hematuria and proteinuria. Median (range) 24-h urinary protein levels in biopsied patients was 1.11 (0–7.46) g/dU. The leading indication for biopsy was simultaneous hematuria and proteinuria ( $p < 0.001$ ). Biopsy findings were graded with different classifications (Oxford, Haas, ISKDC). No positive correlation was found between 24-h urinary protein levels and biopsy findings. 60.4% of HSPN patients were treated with corticosteroids. Most patients had good outcome, with normal physical exam findings and no signs of renal disease in laboratory tests (79.2%), or with microhematuria and proteinuria  $< 1\text{g/dU}$  (15.8%), while only 4 patients had a more severe outcome with proteinuria  $> 1\text{g/dU}$ . No positive correlation was found between biopsy findings and patient outcome ( $p = 0.017$ ).

**Conclusions:** Simultaneous hematuria and proteinuria was a statistically significant factor for kidney biopsy. However, while isolated proteinuria was not the sole determining factor, excessive levels of 24-h urinary proteins should be taken in consideration. Due to the small number of patients and no uniform classification generally used in grading biopsy findings, a statistically significant correlation in regard to outcome could not be confirmed.

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**Disclosure:** None



## POTENTIAL MARKERS OF SKIN FIBROSIS IN SYSTEMIC SCLEROSIS

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**Background:** Skin fibrosis is a hallmark of systemic sclerosis (SSc). There are no widely accepted biomarkers of skin involvement in this condition. Several serum or plasma markers have been studied in patients with SSc – monocyte chemoattractant protein-1 (MCP-1), chemokine (C-X-C motif) ligand 8 (CXCL8), interleukin-13 (IL-13), and some more recognized such as – platelet derived growth factor (PDGF), transforming growth factor-beta 1 (TGF-beta 1), epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF).

**Objectives:** The aim of this study was to assess several circulating biomarkers which may be relevant to the fibrosing process and further to correlate the obtained data with clinical indicators specific for SSc skin involvement.

**Methods:** 59 SSc patients (M/F 9/50; mean age 52.1 years, mean disease duration 6.7 years, 36 patients with limited cutaneous SSc and 23 with diffuse cutaneous SSc. As a control group 36 healthy individuals matched to sex and age were examined.

Serum concentrations of bFGF, granulocyte-colony stimulating factor (G-CSF), granulocyte-macrophage-colony stimulating factor (GM-CSF), MCP-1, PDGF, IL-8 and 13 were analysed using commercial multiplex kit. The following clinical examinations were performed: modified Rodnan skin score (mRSS), Hand Mobility in Scleroderma Test (assessing hand function) (HAMIS), Cochin Hand Function Scale (hand function) (CHFS), Delta Finger-to-Palm Distance (extension-flexion) (dFTP), Inter-lip Distance (inter-lip), Inter-incisor Distance (inter-incisor), and Mouth Handicap in Systemic Sclerosis Scale (mouth opening) (MHISS). For statistical evaluation Spearman's correlation coefficient was used.

**Results:** When compared with healthy controls serum concentrations of bFGF ( $p < 0.001$ ), G-CSF ( $p < 0.0001$ ), GM-CSF ( $p < 0.0001$ ), MCP-1 ( $p < 0.0001$ ), IL-8 ( $p < 0.0001$ ), and IL-13 ( $p < 0.001$ ) were significantly elevated in SSc cohort. PDGF levels were increased in SSc patients with only a lower significance ( $p < 0.01$ ). bFGF, G-CSF, MCP-1 and IL-8 levels correlated significantly ( $p < 0.05$ ) with mRSS and HAMIS. GM-CSF levels correlated with mRSS and HAMIS and there was only a trend for negative correlation with inter-incisor. There was no correlation of IL-13 and PDGF levels with the evaluated clinical data.

**Conclusions:** Our results have shown that G-CSF, GM-CSF and IL-8 play a substantial role in SSc fibrosing process. Potential biomarkers as bFGF, G-CSF, MCP-1 and IL-8 correlated with a few clinical indices of SSc skin involvement.

**Acknowledgement:** Study was supported by research grants AZV 16-33574A and AZV 16-33542A.

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**Disclosure:** None

## INFLAMMATION-RELATED PROTEINS AS POTENTIAL MARKERS OF DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Introduction:** Systemic sclerosis (SSc) is a multiorgan autoimmune connective tissue disease with varying manifestations. Several serious clinical prognostic factors are investigated. Serum markers reflecting clinical activity are not yet well known.

**Methods:** We investigated the serum levels of 92 inflammation-related proteins in 52 Czech patients with SSc and 24 age/gender-matched healthy control subjects using a highly sensitive innovative multiplex PEA (Olink Bioscience, Sweden). Disease activity was determinate by EUSTAR activity index of >2.25. Subgroups were formed based on the disease activity (non-active SSc, n=14; active SSc, n=38). Statistics were performed using GenEx (Sweden).

**Results:** Top-ranked proteins distinguishing SSc and healthy controls ( $P_{corr} < 0.00001$ ) were sTNFSF14, axin 1, sulfotransferase 1A1, CCL7, caspase 8, sTGF $\alpha$ , FGF23, and CXCL10. Of them, upregulation of axin 1, sulfotransferase 1A1, caspase 8, and FGF23 has not been reported in SSc yet. When comparing SSc patients with active and non-active disease, upregulation of IL-6, CCL7, IL-10, sTGF $\alpha$ , FGF21, CCL23, oncostatin M, EN-RAGE, CSF1, sHGF, GDNF, CCL11, and downregulation of sTNF $\beta$  was associated with disease activity ( $P < 0.05$ ). Moreover, serum levels of IL-6, CCL7, IL-10, CSF1, sHGF positively correlated ( $r > 0.353$ ,  $P < 0.009$ ) and sTNF $\beta$  negatively correlated ( $r = -0.374$ ,  $P < 0.006$ ) with levels of C-reactive protein. Further multivariate analysis is needed to identify pattern associated with high disease activity. **Conclusions:** This study showed, that serum markers IL-6, CCL7, IL-10, CSF1, sHGF, and sTNF $\beta$ , can be potential new markers for evaluation of the disease activity of patients with SSc. Larger cohorts, comparison with other autoimmune disease and multivariate analysis will be needed to prove their usefulness as biomarkers for active SSc. Grant support: MZ CR VES15-28659A, SG-III. IK IGA UP\_2018\_010 MH CZ – DRO (FNOL, 00098892)

**Disclosure:** None

### SYSTEMIC SCLEROSIS AND IMMUNOGLOBULIN THERAPY: OUR EXPERIENCE IN THE LAST 5 YEARS.

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Systemic sclerosis (SSc) is a rare chronic disease that is characterized by pathologic collagen deposits in the skin and internal organs. Although it is considered as autoimmune disease, immunosuppressants have a limited effect on SSc. Intravenous immunoglobulins (IVIG) have shown favorable effects in patients with SSc by suppressing action of profibrotic cytokines.

The aim of this study was to present immunomodulatory role of intravenous immunoglobulins (IVIG) in the therapy of refractory SSc in our center in last 5 years (from 2011 to 2016). We analyzed the medical documentation and included in study all patients with SSc who were treated with IVIG at a dose of 0.4 g/kg for 3 to 5 days per month (it represents one cycle). We included only patients that received at least 3 cycles of IVIG.

Twelve patients were treated with IVIG (0.4 g/kg/month), two of them had progressive skin diseases, four patients had interstitial lung diseases (ILD), and another six had combination of skin and lung involvement. In 11 cases

TABLE 1. Characteristics of the patients treated with IVIG.

Sex and age	Disease duration (y)	SSc variant	IVIG cycles	Reason for application IVIG	Outcome
62, F	19	Diffuse	13x	DU, ILD	Healing of DU, decrease in mRSS (-5)
50, F	13	Diffuse	3x	ILD, skin thickening	Decrease in mRSS (-2)
48, F	5	Diffuse	3x	ILD, DU	Healing of DU, Radiologic progression of lung fibrosis
50, F	13	Limited	7x	DU, skin thickening	Healing of DU
30, F	7	Diffuse	4x	ILD, DU	Improvement of DLCO (+10%), less dyspnoic
69, F	5	Diffuse	3x	ILD, skin thickening	Improvement of DLCO (+12%), less dyspnoic
66, F	7	Diffuse	3x	ILD	Improvement of 6MWT, less dyspnoic
62, F	18	Diffuse	3x	ILD	Less dyspnoic
58, F	13	Diffuse	3x	ILD	Less dyspnoic
66, F	32	Diffuse	3x	ILD, esophageal stenosis	Less dyspnoic
70, F	5	Diffuse	3x	Skin thickening	Subjectively better
69, F	18	Diffuse	8x	ILD, Skin thickening	No effect

(91.7%) some kind of improvement was documented. The best results were achieved in skin changes, where we recorded complete healing of digital ulcers (DU) in 3 cases (75%) and improvement of skin thickening in 4 cases (80%).

This retrospective observational study suggests that IVIG may be an effective therapy option for refractory SSc in patients who have failed other therapies, but further studies on the exact role of IVIG in the treatment of SSc are required.

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**Disclosure:** None

## EFFICACY OF AN INTENSIVE 24-WEEK PHYSICAL-OCCUPATIONAL THERAPY PROGRAM WITH SUBSEQUENT 24-WEEK FOLLOW-UP IN PATIENTS WITH SYSTEMIC SCLEROSIS – PRELIMINARY DATA FROM A SINGLE-CENTER CONTROLLED STUDY

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**Background:** Involvement of the skin and musculoskeletal system in patients with systemic sclerosis (SSc) decreases their quality of life. Data on the effectiveness of non-pharmacological interventions in SSc are limited due to heterogeneity of studied interventions/outcomes.

**Objectives:** The aim of our study was to minimize the limitations of available studies and to determine the effect of our physical-occupational therapy (POT) program in cohorts with a substantial number of SSc patients.

**Methods:** Patients were consecutively recruited into two groups, intervention (IG) and control (CG) group, they fulfilled the ACR/EULAR classification criteria from 2013 and had skin involvement of the hands and face. Both groups received educational material for home exercises, but only the IG underwent a 24-week intensive POT program with a subsequent 24-week follow-up. All patients were evaluated by a physician and physiotherapist blinded to intervention at 0, 12, 24 and 48 weeks. All of them also filled out patient reported outcomes/questionnaires and provided blood for routine laboratory analysis and biobanking. Data analysis was performed between groups and within the group.

**Results:** 25 patients were included in the IG and 30 into the CG. Compared to the observed statistically significant deterioration in CG, we found a statistically significant improvement in IG in objectively assessed function and strength of hand, distance between incisors and lips and also subjectively assessed functional ability (SHAQ). During the follow-up period there was a significant deterioration or stagnation of the achieved results in the IG. Only numerical improvements in IG compared to numerical deterioration in CG, but not statistically significant, were observed, during the intervention period, in subjectively evaluated parameters assessing hand/face function, functional ability (HAQ), and some domains of (SF-36).

**Conclusions:** Our program led to a significant improvement in the observed parameters that were clinically relevant in a substantial proportion of patients with SSc (in the IG) and prevented the natural course of progressive deterioration in hand/face function (observed in the CG).

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**Disclosure:** None

TABLE 1. The main outcomes of the variables of interest in the intervention and the control group.

Parameter (unit)	Intervention group Mean ± SEM	Control group Mean ± SEM	Intra-group analysis (Friedman+Dunn)		Inter-group analysis (2WA)
			Intervention gr.	Control group	
dFTP, dominant hand (cm)	m0: 5.7 ± 0.5	m0: 6.8 ± 0.5	m0-3: p<0.01	m0-3: NS	p<0.0001
	m3: 6.2 ± 0.5	m3: 6.2 ± 0.4	m3-6: p<0.05	m3-6: NS	
	m6: 6.8 ± 0.6	m6: 5.9 ± 0.4	m0-6: p<0.0001	m0-6: p<0.0001	
	m12: 6.0 ± 0.6	m12: 5.6 ± 0.4	m6-12: p<0.0001	m6-12: NS	
Hand grip strength, dominant hand (kg)	m0: 17.2 ± 1.8	m0: 16.5 ± 1.2	m0-3: p<0.05	m0-3: NS	p<0.0001
	m3: 19.2 ± 1.9	m3: 14.9 ± 1.3	m3-6: NS	m3-6: NS	
	m6: 19.7 ± 1.9	m6: 13.8 ± 1.2	m0-6: p<0.001	m0-6: p<0.01	
	m12: 17.5 ± 2.0	m12: 14.2 ± 1.3	m6-12: p<0.05	m6-12: NS	
HAMIS, dominant hand	m0: 9.8 ± 1.3	m0: 3.9 ± 1.1	m0-3: p<0.01	m0-3: NS	p<0.0001
	m3: 7.1 ± 1.3	m3: 6.3 ± 1.2	m3-6: p<0.001	m3-6: p<0.001	
	m6: 4.1 ± 0.9	m6: 8.9 ± 1.1	m0-6: p<0.0001	m0-6: p<0.0001	
	m12: 7.2 ± 1.2	m12: 9.8 ± 1.2	m6-12: p<0.001	m6-12: NS	
Inter-lip distance (cm)	m0: 3.92 ± 0.16	m0: 4.18 ± 0.11	m0-3: p<0.01	m0-3: NS	p<0.0001
	m3: 4.24 ± 0.17	m3: 4.03 ± 0.12	m3-6: NS	m3-6: NS	
	m6: 4.46 ± 0.18	m6: 4.02 ± 0.13	m0-6: p<0.0001	m0-6: NS	
	m12: 4.25 ± 0.20	m12: 3.88 ± 0.13	m6-12: NS	m6-12: NS	
Inter-incisor distance (cm)	m0: 2.9 ± 0.2	m0: 3.3 ± 0.1	m0-3: p<0.01	m0-3: p<0.01	p<0.0001
	m3: 3.2 ± 0.2	m3: 3.1 ± 0.1	m3-6: NS	m3-6: NS	
	m6: 3.5 ± 0.2	m6: 3.0 ± 0.1	m0-6: p<0.0001	m0-6: p<0.001	
	m12: 3.2 ± 0.2	m12: 3.0 ± 0.1	m6-12: p<0.01	m6-12: NS	
SHAQ (mm)	m0: 28.8 ± 3.9	m0: 21.5 ± 2.1	m0-3: NS	m0-3: NS	p=0.0015
	m3: 21.5 ± 3.4	m3: 24.6 ± 2.6	m3-6: NS	m3-6: NS	
	m6: 22.0 ± 3.5	m6: 24.9 ± 2.9	m0-6: p<0.05	m0-6: NS	
	m12: 23.4 ± 3.7	m12: 27.5 ± 3.3	m6-12: NS	m6-12: NS	

**Acronyms:** SEM, standard error of the mean; Friedman, Friedman's test; Dunn, Dunn's post hoc test; 2WA, two way ANOVA, dFTP, delta finger to palm; HAMIS, Hand Mobility in Scleroderma; m0, month 0 (= at the baseline); m3, month (= in the middle of the intervention period); m6, month 6 (= at the end of intervention); m12, month 12 (= at the end of the 6-month follow up period); p, p-value; NS, not significant

## DIFFERENCES IN BODY COMPOSITION IN SCLERODERMA PATIENTS AND HEALTHY CONTROLS AND ASSOCIATION WITH DISEASE ACTIVITY, PHYSICAL ACTIVITY AND SERUM LEVELS OF INFLAMMATORY CYTOKINES.

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**Background:** Fibrosis of the skin and visceral organs, especially digestive tract, and musculoskeletal involvement in systemic sclerosis (SSc) can have a negative impact on body composition and physical activity.

**Objectives:** To assess body composition and physical activity of SSc patients and healthy controls (HC) and the association with selected inflammatory cytokines in SSc.

**Methods:** 59 SSc patients (50 females; mean age 52.5; disease duration 6.7 years; lcSSc:34/dcSSc:25) and 59 age-/sex-matched HC (50 females, mean age 52.5) were included. SSc patients fulfilled ACR/EULAR 2013 criteria. We assessed body composition (densitometry: iDXA Lunar, bioelectric impedance: BIA-2000-M), physical activity (Human Activity Profile questionnaire, HAP), disease activity (European Scleroderma Study Group Activity

Score, ESSG) and serum levels of 27 cytokines (commercial multiplex ELISA kit, Bio-Rad Laboratories). Data are presented as mean±SD.

**Results:** Compared to HC, SSc patients had significantly lower body mass index (BMI), body fat % (BF%) and visceral fat weight (VF), and significantly decreased lean body mass (LBM), and bone mineral density (BMD). Compared to HC, SSc patients had increased extracellular mass/body cell mass (ECM/BCM) ratio, reflecting deteriorated nutritional status and worse muscle predispositions for physical activity (Table 1). Increased ECM/BCM in SSc positively correlated with disease activity (ESSG), skin score (mRSS) and inflammation (CRP, ESR), and was associated with worse quality of life (HAQ, SHAQ), fatigue (FSS), and decreased physical activity (HAP). ESSG negatively correlated with BF%. HAP positively correlated with BMD. Increased serum levels of several inflammatory cytokines were associated with alterations of body composition (Table 2).

TABLE 1. Body composition in SSc and HC.

Correlated parameters	SSc (n=59)	HC (n=59)	p-value
BMI (Body Mass Index) (kg/m <sup>2</sup> ); VF (Visceral Fat) (kg)	22.4±4.3; 0.5±0.5	27.4±8.3; 1.0±0.8	<0.001; <0.001
BF% (Body Fat %) iDXA; BIA	32.6±8.2; 24.3±7.9	38.0±7.6; 31.3±7.6	<0.001; <0.001
LBM (Lean Body Mass) (kg), iDXA; BIA	47.8±7.0; 40.9±6.8	51.9±8.4; 45.4±7.3	0.005; 0.005
ECM/BCM (Extracellular Mass/Body Cell Mass ratio); BMD (Bone Mineral Density) (g/cm <sup>2</sup> )	1.28±0.4; 1.0±0.1	1.03±0.1; 1.2±0.1	<0.001; <0.001
HAP (Human Activity Profile)	64.1±17.2	84.7±6.6	<0.001

TABLE 2. Correlation of body composition parameters and clinical features of SSc, and serum levels of inflammatory cytokines (pg/mL).

Correlated parameters	r	p-value
ESSG: ECM/BCM; BF% (iDXA)	0.273; -0.324	0.044; 0.014
ECM/BCM: mRSS (modified Rodnan Skin Score); CRP; ESR	0.371; 0.292; 0.302	0.005; 0.028; 0.023
ECM/BCM: HAQ (Health Assessment Questionnaire); SHAQ (Scleroderma HAQ)	0.438; 0.268	0.001; 0.044
ECM/BCM: FSS (Fatigue Severity Scale)	0.366	0.004
HAP: ECM/BCM; BMD	-0.644; 0.280	<0.001; 0.032
LBM (kg, iDXA; BIA):IL-1b / LBM (kg, iDXA; BIA):IL-6	0.347; 0.289 / 0.275; 0.280	0.009; 0.034 / 0.035; 0.035
LBM (kg, iDXA; BIA):IL-17 / LBM (kg, iDXA; BIA):EOTAXIN	0.387; 0.388 / 0.267; 0.299	0.002; 0.003 / 0.041; 0.024
LBM (kg, iDXA; BIA): TNF	0.284; 0.267	0.031; 0.047
BMR (Basal Metabolic Rate) (kcal): IL-b1; IL-6; IL-17; EOTAXIN; TNF	0.339; 0.282; 0.383; 0.258; 0.288	0.011; 0.03; 0.003; 0.048; 0.028
TBW (Total Body Water) (%): IL-1b; IL-6; IL-5; IL-8; EOTAXIN	0.441; 0.314; 0.361; 0.367; 0.338	<0.001; 0.017; 0.009; 0.005; 0.01
TNF: VF (kg); FFM (Fat Free Tissue) (kg); A/G (Android/Gynoid ratio); BMD (g/cm <sup>2</sup> )	0.299; 0.287; 0.369; 0.262	0.023; 0.029; 0.004; 0.047

**Conclusions:** Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our SSc patients, which are associated with the disease activity and physical activity, and could reflect their nutritional status, and gastrointestinal and musculoskeletal involvement. Serum levels of certain inflammatory cytokines were associated with alterations of body composition in SSc patients.

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**Disclosure:** None



## IMPAIRED SEXUAL FUNCTIONING IN WOMEN WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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**Background:** Idiopathic inflammatory myopathies (IIM) are characterized by inflammation and atrophy of skeletal muscles, pulmonary and articular involvement, which leads to functional impairment, reduced quality of life including sexual life.

**Objectives:** The aim of this study was to assess sexual functions/quality of life and pelvic floor function in female IIM patients compared to age-/sex-matched healthy controls (HC).

**Methods:** In total, 22 women with IIM [mean age: 55.1, disease duration: 7.9 years, dermatomyositis (DM, 8)/ polymyositis (PM, 10)/ necrotizing myopathy (IMNM, 3)/ inclusion body myositis (IBM, 1)], who fulfilled the Bohan/Peter 1975 criteria for DM/PM, and 22 healthy controls (mean age: 55.1 years) filled in 12 well-established and validated questionnaires assessing sexual function/quality of life, pelvic floor function, fatigue, physical activity and depression. Data are presented as mean  $\pm$ SEM.

**Results:** Compared to HC, patients with IIM had significantly higher prevalence and greater severity of sexual dysfunction (FSFI, BISF-W: in all subscales as well as total scores), dysfunction of pelvic floor (PISQ-12), and worse sexual quality of life (SQoL-F) (table). Worse scores in IIM patients were associated with elevated muscle enzyme levels [lactate dehydrogenase: FSFI ( $r=-0.524, p=0.0123$ ), BISFW ( $r=-0.528, p=0.0115$ )], greater fatigue [FIS: FSFI ( $r=-0.434, p=0.0438$ ), BISF-W ( $r=-0.488, p=0.0211$ ), SQoL-F ( $r=-0.488, p=0.0070$ ), PISQ-12 ( $r=0.643, p=0.0013$ )], more severe depression [BDI-II: PISQ-12 ( $r=0.474, p=0.0258$ )], deteriorated quality of life [HAQ: PISQ-12 ( $r=0.476, p=0.0252$ )], and worse ability to perform physical activities [HAP: FSFI ( $r=0.437, p=0.0417$ ), BISF-W ( $r=0.451, p=0.0351$ ), PISQ-12 ( $r=-0.494, p=0.0195$ )].

**Conclusions:** Women with IIM reported significantly impaired sexual function, sexual quality of life and pelvic floor function than age-matched healthy controls. Worse scores in IIM were associated with disease activity, physical activity, fatigue, depression and quality of life.

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**Disclosure:** None

## NEGATIVE CHANGES OF BODY COMPOSITION IN MYOSITIS PATIENTS COMPARED TO HEALTHY CONTROLS AND ASSOCIATIONS WITH MYOSITIS-RELATED CLINICAL MANIFESTATIONS

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**Background:** Skeletal muscle, pulmonary and articular involvement in idiopathic inflammatory myopathies (IIM) limits the mobility/self-sufficiency of patients, and can have a negative impact on body composition.

**Objectives:** To assess body composition and physical activity of IIM patients and healthy controls (HC).

**Methods:** 54 patients with IIM (45 females; mean age 57.7; disease duration 5.8 years; PM: 22 / DM: 25 / IMNM: 7) and 54 age-/sex-matched HC (45 females, mean age 57.7) were included. PM/DM patients fulfilled Bohan/Peter criteria for PM/DM. Anthropometric parameters and body composition (by densitometry: iDXA Lunar, and by bioelectric impedance: BIA2000-M), and physical activity (by Human Activity Profile questionnaire, HAP) were assessed. Routine biochemistry analysis was performed after 8 hours of fasting. Disease activity was evaluated by MITAX and MYOACT activity score, muscle involvement by manual muscle test (MMT-8) and functional index 2 (FI2). Data are presented as mean  $\pm$ SD.

**Results:** Compared to HC, patients with IIM had increased body fat % (BF%) but significantly decreased lean body mass (LBM), and increased extracellular mass/body cell mass (ECM/BCM) ratio, which reflects worse

muscle predispositions for physical activity and deteriorated nutritional status. Compared to HC, IIM patients had significantly lower bone mineral density (BMD) (Table 1). Disease duration negatively correlated with BMD and LBM (assessed by BIA). Disease activity assessed by MITAX and MYOACT positively correlated with LBM (assessed by both BIA and DXA), as well as with basal metabolic rate (BMR), and fat free mass (FFM). CRP was positively associated with BF% (iDXA and BIA). Higher BF% (iDXA) was associated with worse physical endurance (FI2) and worse ability to perform physical activity (HAP). MMT-8 score negatively correlated with ECM/BCM ratio (Table 2).

TABLE 1. Body composition in IIM and HC.

Correlated parameters	IIM (n=54)	HC (n=54)	p-value
BF% (Body Fat %) (iDXA)	42.4±7.1	39.9±7.1	0.077
LBM (Lean Body Mass) (kg, iDXA)	40.6±7.2	45.6±8.1	<0.001
LBM (Lean Body Mass) (kg, BIA)	48.7±9.5	52.6±8.8	0.023
ECM/BCM (Extracellular Mass/Body Cell Mass ratio)	1.44±0.42	1.06±0.15	<0.001
BMD (Bone Mineral Density) (g/cm <sup>2</sup> )	1.1±0.1	1.2±0.1	<0.001

TABLE 2. Correlation of body composition parameters and clinical features of IIM – disease duration and activity, physical endurance and activity, and muscle involvement.

Correlated parameters	r	p-value
BMD (iDXA):Disease duration	-0.392	0.004
LBM (BIA):Disease duration	-0.272	0.047
LBM (BIA):MITAX; MYOACT	0.294; 0.335	0.031; 0.013
LBM (iDXA):MITAX; MYOACT	0.341; 0.368	0.012; 0.007
BMR:MITAX; MYOACT	0.336; 0.351	0.014; 0.010
FFM:MITAX; MYOACT	0.338; 0.356	0.014; 0.009
CRP: BF%-iDXA; BF%-BIA	0.276; 0.306	0.035; 0.025
BF%-iDXA:FI2	-0.311	0.026
BF%-iDXA:HAP	-0.292	0.032
ECM/BCM:MMT8	-0.385	0.006

**Conclusions:** We found significant negative changes of body composition of our IIM patients compared to healthy age-/sex-matched individuals, associated with their disease activity and duration, inflammatory status, skeletal muscle involvement, and physical activity. These data could reflect their impaired nutritional status and predispositions for physical exercise, aerobic fitness and performance.

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**Disclosure:** None

## EFFICACY OF AN INTENSIVE 24-WEEK SPECIALIZED ADL EXERCISE PROGRAM WITH SUBSEQUENT 24-WEEK FOLLOW-UP IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES – PRELIMINARY DATA FROM A SINGLE-CENTER CONTROLLED STUDY

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**Background:** Involvement of muscles in idiopathic inflammatory myopathies (IIM) leads to reduced strength and endurance, decreasing patients' quality of life. Data on the effectiveness of exercise in IIM are limited due to heterogeneity of studied interventions/outcomes.

**Objectives:** The aim of our study was to minimize the limitations of available studies and to determine the effect of our specialized ADL exercise program in cohorts with a substantial number of IIM patients.

**Methods:** Patients were consecutively recruited into two groups, intervention (IG) and control (CG) group, they fulfilled the diagnostic criteria from 1975 and had impaired muscle strength. Both groups received educational material for home exercises, but only the IG underwent a 24-week intensive ADL (activities of daily living) and muscle strength exercise program with a subsequent 24-week follow-up. All patients were evaluated by a physician and physiotherapist blinded to intervention at 0, 12, 24 and 48 weeks. All of them also filled out patient reported outcomes/questionnaires and provided blood for routine laboratory analysis and biobanking. Data analysis was performed between groups and within the group.

**Results:** 27 patients were included in the IG and 23 patients in the CG. Compared to the observed statistically significant deterioration in the CG over the period of 0–24 weeks, we found a statistically significant improvement in IG in objectively assessed muscle strength and endurance as well as in subjectively assessed functional abilities and depression. During the follow-up period, there was a significant deterioration or stagnation of the achieved results in the IG. However, improved functional abilities during the intervention period persisted in the IG even in the follow-up period. Only numerical improvements in the IG compared to numerical deterioration in CG, that did not achieve statistical significance during the intervention period, were observed in some subjectively assessed patient reported outcomes assessing quality of life and fatigue.

TABLE 1. The main outcomes of the variables of interest in the intervention and the control group.

Parameter (unit)	Intervention group Mean ± SEM	Control group Mean ± SEM	Intra-group analysis (Friedman+Dunn)		Inter-group analysis (2WA)
			Intervention gr.	Control group	
MMT-8	m0: 54.7 ± 2.6	m0: 63.6 ± 2.0	m0-3: p<0.01	m0-3: p<0.05	p<0.0001
	m3: 60.7 ± 2.4	m3: 57.9 ± 1.8	m3-6: p<0.0001	m3-6: NS	
	m6: 69.1 ± 1.9	m6: 54.2 ± 1.9	m0-6: p<0.0001	m0-6: p<0.0001	
	m12: 64.0 ± 2.5	m12: 56.5 ± 2.2	m6-12: p<0.05	m6-12: NS	
FI-2 (%)	m0: 30.0 ± 4.4	m0: 38.3 ± 5.3	m0-3: p<0.01	m0-3: NS	p<0.0001
	m3: 46.9 ± 4.7	m3: 29.6 ± 4.6	m3-6: p<0.0001	m3-6: NS	
	m6: 70.6 ± 4.9	m6: 26.1 ± 4.1	m0-6: p<0.0001	m0-6: p<0.01	
	m12: 58.4 ± 5.8	m12: 25.7 ± 3.6	m6-12: p<0.05	m6-12: NS	
HAQ	m0: 0.9 ± 0.2	m0: 1.3 ± 0.2	m0-3: NS	m0-3: NS	p=0.0002
	m3: 0.7 ± 0.1	m3: 1.4 ± 0.2	m3-6: NS	m3-6: NS	
	m6: 0.6 ± 0.1	m6: 1.4 ± 0.2	m0-6: p<0.01	m0-6: NS	
	m12: 0.8 ± 0.2	m12: 1.5 ± 0.2	m6-12: p<0.05	m6-12: NS	
BDI-II	m0: 11.9 ± 2.1	m0: 13.0 ± 1.4	m0-3: NS	m0-3: NS	p=0.0025
	m3: 10.7 ± 1.7	m3: 14.3 ± 1.7	m3-6: NS	m3-6: NS	
	m6: 8.9 ± 1.5	m6: 15.7 ± 1.1	m0-6: p<0.05	m0-6: NS	
	m12: 10.5 ± 2.0	m12: 16.0 ± 2.0	m6-12: NS	m6-12: NS	

**Acronyms:** SEM, standard error of the mean; Friedman, Friedman’s test; Dunn, Dunn’s post hoc test; 2WA, two way ANOVA, MMT-8, Manual muscle test-8; FI-2, Functional index-2; HAQ, Health assessment questionnaire; BDI-II, Beck’s depression inventory-II; m0, month 0 (= at the baseline); m3, month 3 (= in the middle of the intervention period); m6, month 6 (= at the end of intervention); m12, month 12 (= at the end of a 6-month follow up period); p, p-value; NS, not significant

**Conclusions:** Our program led to a significant improvement in the observed parameters that was clinically significant in a substantial proportion of patients, and to prevention of the expected worsening in muscle strength and endurance.

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## OCULAR MANIFESTATIONS IN ANKYLOSING SPONDYLITIS AND RHEUMATOID ARTHRITIS

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Ocular manifestations occur in 10–50% of the patients with ankylosing spondylitis (AS)(1). Keratoconjunctivitis sicca occurs in 10 to 20 % patients with rheumatoid arthritis (RA)(2). It is known that the biomechanical properties of the cornea may change in some inflammatory diseases (3). The objective of the study was to evaluate corneal morphology and thickness in patients with AS and RA and to investigate the correlations between corneal alterations and disease activity.

24 patients with AS and 28 patients with RA underwent ophthalmologic and physical examination. All patients were treated with biologic therapy. Corneal hysteresis(CH) and corneal resistance factor(CRF) were evaluated. The BASDAI for AS and DAS28CRP for RA were recorded. Significant pathology changes of CH and CRF in both groups were not found. Moreover, correlations between disease activity and corneal changes were not found. Corneal morphology and thickness in patients with AS and RA could be changed, but the correlation between disease activity and the severity of changes has to be further investigated.

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**Disclosure:** None

## THE RELATIONSHIP BETWEEN HLA-B27 AND OCULAR INVOLVEMENT IN MALE ALBANIAN PATIENTS WITH ANKYLOSING SPONDYLITIS.

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**Background:** It is well-known the prevalence of uveitis and iritis in patients diagnosed with ankylosing spondylitis. Patients with positive HLA-B27 are more susceptible to seronegative arthropathies and in particular mode to ankylosing spondylitis.

**Objectives:** The aim of this study is to evaluate the relationship between ocular involvement and HLA-B27 in male albanian patients suffering from ankylosing spondylitis.

**Methods:** Patients included in this study were albanian males diagnosed with ankylosing spondylitis and ocular involvement. All patients were completed with clinical, laboratory and imaging exams. Every patient was evaluated for HLA-B27 and consulted by an ophthalmologist for their ocular disorders.

**Results:** Thirty-four patients (59.65%) were diagnosed with ocular involvement (iritis, uveitis). From those patients, 25 patients (73.53%) were found with positive HLA-B27. After statistically analyzing all data, it was found a significant relationship between ocular involvement and positive HLA-B27 ( $p < 0.001$ ).

**Conclusions:** It was found that in patients with AS-related ocular involvement (iritis and uveitis), positive HLA-B27 was very prevalent. It was shown that there is a strong statistical relationship between ocular involvement and HLA-B27.

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Spondylarthropathies: Pathogenesis and Clinical Features pg 299; EULAR Textbook On Rheumatic Diseases

**Disclosure:** None

## ANTI-JAK TREATMENT AND INFECTION IN A PATIENT WITH SPONDYLOARTHRITIS

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Ankylosing spondylitis (AS) is a chronic inflammatory disease involving mainly the sacroiliac and axial joints. The current recommendations for the treatment considered the non-steroidal anti-inflammatory drugs (NSAIDs), disease modifying antirheumatic drugs, biological agents, analgesics, surgical interventions. (1)

Janus kinase (JAK) inhibitor is an alternative option for those patients who do not respond to classical treatment. By inhibition of multiple cytokines it might be a new potential strong strategy. (2)

We describe a case of a 43 year-old patient with AS human leukocyte antigen B27-positive treated with Baricitinib.

The patient was admitted for painful walking. Previous year he underwent a total hip replacement of the left side due to bacteraemia.

Examination revealed his hip range of motion restricted and scanner found an accumulation around the right femoral shaft.

The diagnosis of infection of the right hip prosthesis and a proximal femur osteomyelitis was confirmed by aspiration.

The patient went through a total hip replacement in two-steps, following with 3 months of antibiotherapy.

JAK inhibitor was suspended during the investigation of the infection but persistence of inflammatory syndrome made it necessary to resume the treatment.

The efficacy of JAK inhibitors is due to blocking the cytokine signaling, stability in laboratory parameters and long-term safety resulting in decrease of disease activity. (3)

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**Disclosure:** None

## SPONTANEOUS BICEPS FEMORIS RUPTURE HEMATOMA WITH SECONDARY INFLAMMATION IN A PATIENT WITH PSORIATIC ARTHRITIS TREATED WITH SECUKINUMAB DEVELOPING MYELODYSPLASTIC SYNDROME (MDS) – CASE REPORT

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory disease, a member of a spondyloarthritis (SpA) group associated with psoriasis. Treatment is based on non-steroidal anti-inflammatory drugs (NSAID), glucocorticoids, conventional and targeted disease modifying anti-rheumatic drugs (DMARDs) and biological agents. Arrival of biologics and targeted synthetic drugs has enabled more comprehensive treatment to target of all domains of the psoriatic disease. More aggressive treatment approach of complex patients with many comorbidities presents an additional adverse event risk.

**Case report:** A sixty-five year old diabetic male patient with longstanding severe psoriasis and psoriatic arthritis, treated sequentially with conventional DMARDs, ustekinumab and secukinumab, developed myelodysplastic syndrome and spontaneous partial rupture of the biceps femoris muscle complicated with inflamed hematoma, caused by *S.aureus* infection.



**Conclusion:** The aim of this paper is to present a patient in a long-lasting persistent remission induced and maintained on biologics, developing rare serious side effect related to disease, comorbidities and the treatment itself. Further treatment options are discussed.

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**Disclosure:** None

## INHIBITION OF IL-17 BY SECUKINUMAB LEAD TO THE REMISSION OF SEVERE PSORIATIC ARTHRITIS AND SYMPTOMS OF PEMPHIGUS VULGARIS IN A PATIENT CONCIDENCE OF THESE CONDITIONS

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**Background:** IL-17 plays an important role in the pathogenesis of psoriasis and psoriatic arthritis (PsA) and its inhibition improves both, the skin and articular symptoms of the disease. Pemphigus vulgaris is a rare autoimmune disease which may be also IL-17 mediated based on preclinical data (1), but anti-IL17 agents have not been tested in pemphigus yet (2).. Coincidence of psoriasis and pemphigus vulgaris is exceptional.

**Objectives:** To describe a rare case of severe psoriatic arthritis with preceding pemphigus vulgaris successfully treated with anti-IL17 therapy (secukinumab).

**Methods:** We have observed a 43-years old man with a two years' history of pemphigus vulgaris having been treated with continuous oral cyclophosphamide (CPM, 100 mg daily) and glucocorticoids (prednisone 10 mg daily) who developed psoriasis and severe psoriatic arthritis despite this treatment.

**Results:** At the diagnosis of PsA CPM was stopped and replaced with methotrexate (MTX) up to the dose of 25 mg weekly, prednisone was increased up to 20 mg QD, several painful joints were injected with GC. Three months of this intensive treatment had only low impact on the activity of PsA and the patients was indicated for biological therapy. Because of the previous treatment with high cumulative dose of CPM and possible risk of malignancies of the combination of CPM and TNF inhibitors, we preferred secukinumab (150 mg weekly/ monthly) as the first line biological. The treatment went promptly to the diminution of symptoms, decrease of inflammatory markers (ESR, CRP) and after several weeks to the resolution of skin symptoms as well as arthritis. Symptoms of pemphigus vulgaris have not been observed more despite tapering prednisone off.

**Conclusions:** In our patient, we have observed not only a successful treatment of psoriatic arthritis, but thanks to the coincidence with pemphigus vulgaris also for the very first time the possible impact of this therapy on the course of pemphigus which was in remission throughout the durations of observation. In agreement with pre-clinical data our case report suggests the possible effect of anti-IL17 therapy also on pemphigus vulgaris.

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**Disclosure:** None

## APREMILAST AS A TREATMENT OF CHOICE FOR PSORIATIC ARTHRITIS IN A PATIENT WITH DIFFICULT TO TREAT AUTOIMMUNE HEPATITIS

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The complexity of multiple coexisting illnesses, the interactions of several different recommended treatment options and the attempts to avoid various side effects and contraindications, classify this case as one of the more challenging as well as interesting of the ones a physician may encounter. Although similar constellations of diseases are rather uncommon, the reason for presenting this case lies in its value as a teaching tool for specialists and non-specialists alike.

To introduce an approach to a complex patient with a rheumatic disease and multiple comorbidities to a wider population of clinicians.

A 56-year-old female patient suffering from psoriasis, psoriatic arthritis (PsA) and autoimmune hepatitis (AIH) was referred to the rheumatology outpatient clinic at the University Hospital Centre Zagreb, Croatia. In spite of the remission of AIH due to the administered immunosuppressant therapy (tacrolimus, glucocorticoids), the patient experienced an exacerbation of PsA symptoms, including worsened arthralgia and dactylitis. Taking into account the referring gastroenterologist's stance on contraindications regarding conventional PsA therapy, due to potential progression of hepatic fibrosis, hepatotoxicity, and severe drug interactions with tacrolimus, an alternative treatment regime needed to be decided upon. The optimal treatment option, due to additional immunosuppressive effects with fewest expected interactions with tacrolimus, was decided to be apremilast, a novel oral inhibitor of the enzyme phosphodiesterase-4 (PDE-4). At a follow-up two months since the beginning of treatment the patient's state improved significantly, in terms of alleviated joint pain and reduced psoriatic plaques.

This case report highlights the importance of a multidisciplinary approach in the care for patients with rheumatic diseases. Apremilast significantly mitigates the symptoms of enthesitis in addition to relieving pain, diminishing fatigue, and increasing work productivity in patients with active PsA.

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## INNATE IMMUNITY GENE EXPRESSION SIGNATURE IN PATIENTS WITH AUTOIMMUNE DISEASES IN ACTIVE DISEASE STAGE: RA, SLE, SSC

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**Background:** Mounting evidence indicates that innate immunity, especially Toll-like-receptors (TLR) and interleukin (IL)-1/IL-1R families, play essential roles in the pathogenesis of autoimmune diseases. The differential innate expression pattern associated with disease activity in systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and systemic sclerosis (SSc) has not been established.

**Objective:** To elucidate the underlying differences in innate immunity signatures associated with disease activity in major autoimmune diseases.

**Methods:** We investigated gene expression of TLR1-10, 7 members of IL-1/IL-1R family, and interleukin 8 (IL-8/CXCL8) in peripheral blood mononuclear cells from patients with autoimmune disorders taken at time of active disease: SLE (n=28, SLEDAI>6), RA (n=36, DAS28≥3.2), and SSc (n=22, revised EUSTAR index>2.25) using high-throughput SmartChip Real-Time-qPCR system (WaferGen). Statistics were performed by R statistical software, P-value<0.05 was considered as significant. Results: RA (a chronic joint inflammatory disease) differed from SLE (a multisystem inflammatory disease) and SSc (typical by tissue fibrosis of the skin and internal organs)

by the upregulated expression of six genes (TLR2, TLR3, TLR5, SIGIRR, IL-1RAP, and IL-18R1;  $P < 0.05$ ). Active SLE and SSc showed high similarity in term of immunity gene expression signatures. In SSc, downregulated expression of IL-18R1 ( $P < 0.05$ ) was observed when compared to SLE and RA. In SLE, downregulated expression of IL-1R1 ( $P < 0.05$ ) was detected when compared to RA and upregulation of IL-18R1 ( $P < 0.05$ ) when compared to SSc. Conclusions: Innate immune gene expression signature in patients with autoimmune diseases in active disease stage was identified, showing high similarity between SLE and SSc. Grant support: MZ CR VES15-28659A, IGA UP\_2018\_010

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## S100A11 (CALGIZZARIN) INDUCES INFLAMMATION VIA TLR-4 SIGNALLING AND STIMULATES SECRETION OF ANGIOGENIC FACTORS IL-8 AND VEGFs BY MONONUCLEAR CELLS IN RHEUMATOID ARTHRITIS

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**Background:** S100A11 (calgizzarin), S100 protein family member, is known to participate in oncogenesis via regulating number of biologic functions. It has also been described as inflammatory mediator associated with rheumatoid arthritis (RA).

**Objectives:** Given the fact that inflammation evolves in parallel with angiogenesis, we aimed to assess the role of S100A11 in immune response and angiogenesis.

**Methods:** For in vitro experiments, peripheral blood mononuclear cells (PBMCs) were obtained from patients with RA (n=6–12). Expression and protein synthesis were analysed by RT-PCR, ELISA and LUMINEX. The co-expression of S100A11 and TLR-4 receptor were analysed in synovial tissues from RA patients (n=6) by immunohistochemistry and immunofluorescence. Receptor involvement was investigated using antibodies against RAGE, TLR-4, and inhibitor of MyD88. Intracellular signalling pathways were determined by use of inhibitors of NF $\kappa$ B, p38, erk1/erk2, and jnk.

**Results:** PBMCs from patients with RA exposed to S100A11 increased the mRNA expression of pro-inflammatory cytokines IL-6, TNF $\alpha$  and chemokine IL-8 ( $p < 0.05$ ,  $p < 0.01$  and  $p < 0.01$ ) as well as their secretion ( $p < 0.01$ ,  $p < 0.001$  and  $p < 0.01$ ). Moreover, S100A11 triggered the release of angiogenic factors VEGF-C and VEGF-D ( $p < 0.05$  and  $p < 0.01$ ) by PBMCs but did not modify their mRNA expression. No changes in IL-6 secretion by PBMCs were observed after blocking the receptor for advanced glycation products (RAGE) prior to S100A11 treatment. More importantly, PBMCs pre-treated with antibody against TLR-4 before S100A11 stimulation reduced the secretion of IL-6 by 92% ( $p < 0.05$ ). Inhibition of MyD88 adaptor protein also lead to a significant decrease of IL-6 release by 55% ( $p < 0.05$ ). To support the implication of TLR-4 in S100A11 signalling, we demonstrated the co-expression of S100A11 and TLR-4 in the RA synovial tissue. Furthermore, S100A11 mediated IL-6 secretion was partially down-regulated by all selected inhibitors of cell signalling such as NF $\kappa$ B, erk1/2, jnk, p38 ( $p < 0.05$  for all).

**Conclusions:** We are the first to show that S100A11 may participate in regulation of angiogenesis and stimulates inflammation via TLR-4 dependent pathway. These findings indicate more complex role of S100A11 in the pathogenesis of RA.

**Acknowledgement:** This work received support from research project 15-34065A of the Agency for Healthcare Research of the Czech Republic

**Disclosure:** None

## INTERACTION OF P.Q141K VARIANT IN ABCG2 GENE WITH CLINICAL DATA AND CYTOKINES LEVELS IN PRIMARY HYPERURICEMIA AND GOUT

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**Background:** Gout is multifactorial disorder caused by many conditions including genetic background. One of the well-established genes linked to gout is ABCG2 and its common missense variant p.Q141K which has negative influence on urate excretion (1). Long lasting hyperuricemia leads to formation of monosodium urate crystals in joints and tissues. Immune response to these crystals is triggered by NLRP3 inflammasome and subsequent production of proinflammatory cytokines which results in escalation of immune reaction.

**Objectives:** The aim of our study was to analyse the possible differences in age, BMI, CRP and GFR as risk factors/symptoms for gout and immunological parameters between hyperuricemic, gouty and acute gouty arthritic patients who had known genetic background in risk allele p.Q141K.

**Methods:** Gene ABCG2 was sequenced in cohort of 69 primary hyperuricemic and 177 gout patients. Variant p.Q141K was examined in 132 normouricemic controls using tetra primer ARMS-PCR method. Afterwards we determined plasma levels of 27 cytokines using human multiple cytokine assay in subcohort of 42 patients with primary hyperuricemia, 131 gout patients including 17 acute gouty arthritis patients and 132 controls.

**Results:** We have found differences between diagnostic groups for disease onset, BMI, CRP and GFR. In addition, homozygotes p.Q141K were significantly younger ( $p = 0.019$ ) and had earlier onset of disorder ( $p = 0.011$ ) than wild-type and heterozygotes. Homozygotes p.Q141K tended to have lower BMI ( $p = 0.020$ ) and CRP ( $p < 0.001$ ). Heterozygous and mainly homozygous carriers of p.Q141K variant had significantly higher GFR ( $p = 0.022$ ). Levels of IL-1 $\beta$ , IL-1ra, IL-4, IL-6, IL-7, IL-8, IL-9, IL-13, IL-17, FGF basic, IFN $\gamma$  and TNF $\alpha$  were significantly increased in patients with acute gouty arthritis. Eotaxin, MCP-1 and RANTES were decreased in all patient groups compared to controls. We did not find any impact of p.Q141K on cytokine amount.

**Conclusions:** Variant p.Q141K is related to earlier onset, lower BMI, lower CRP and higher GFR at patients with primary hyperuricemia and gout. Levels of 19 cytokines were significantly higher mainly in patients with acute gouty arthritis compared to other groups without correlation to presence of p.Q141K.

**Acknowledgement:** Supported by AZV 15-26693A and RVO 00023728.

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**Disclosure:** None

## REAL LIFE EXPERIENCE WITH GOLIMUMAB IN CROATIA

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**Background:** Golimumab (GLM) is a human monoclonal antibody indicated in the treatment of adults with active RA, PsA and AS who have had an inadequate response to conventional therapies. There are some data that persistence with GLM in immune-mediated rheumatic disease may be higher than with other TNF- $\alpha$  agents and may be lower in biologic-experienced compared with biologic-naive patients. Efficacy of golimumab through 3 and 5 years of treatment in patients with RA, PsA and AS was consistent with other TNF- $\alpha$  antagonist.

**Objectives:** The aim of this study was to evaluate the efficacy and the retention of golimumab (GLM) in treating patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) in a real-world setting.



**Methods:** This was a retrospective cohort study on patients with RA (11), PsA (20) and AS (23) who had active disease despite prior treatment with c DMARDs, NSAIDs or biological drugs. Efficacy of GLM was evaluated at weeks 12, 36 and 52 after starting GLM treatment. Golimumab drug retention rate at 2 and 5 years of treatment was determined for all patients and additionally for each indication (RA, PsA, AS) and according to TNF $\alpha$  naivety. Statistical significance was determined at the level of 0.05. Kaplan-Meier analysis was used to assess drug retention.

**Results:** GLM demonstrated significant efficacy in terms of decreasing disease activity in RA, PsA and AS patients already at week 12. The results were held even at week 36 and 52. Overall 2 and 5 years retention rate was 77% and 60%, the highest being in AS patients – 90% in 2 and 5 years. Two-year retention rate for GLM in PsA and RA patients was 75% and 55%. Five-year retention rate for GLM in PsA and RA patients was 57% and 37%. TNF $\alpha$  naïve patients had higher retention rate in comparison to non-naïve patients (66% vs 34%).

**Conclusions:** In this retrospective study in a real-life setting it was demonstrated that GLM is an effective drug for RA, PsA and AS patients with a high retention rate. GLM retention rate was higher in AS patients compared to RA and PsA patients and in TNF $\alpha$  naïve patients compared to patients previously treated with TNF $\alpha$  inhibitors.

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**Disclosure:** None

## EFFICACY AND SAFETY OF SWITCHING FROM ORAL TO SUBCUTANEOUS METHOTREXATE IN EVERYDAY CLINICAL PRACTICE: RESULTS OF THE SIX-MONTH OBSERVATIONAL PROSPECTIVE STUDY IN CROATIA

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**Background:** Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are chronic debilitating inflammatory rheumatic conditions with the major impact on quality of life (QoL). csDMARDs are the basic pharmacological option for these patients, and choice of DMARDs depends on many factors.

**Objectives:** The objective of this study was to evaluate the changes in disease activity, QoL, adverse events when switching from oral to subcutaneous methotrexate (MTX) in patients with RA and PsA, addressing also the adherence to treatment.

**Methods:** This was an observational prospective longitudinal study of patients with RA and PsA on csDMARDs who switched from oral to s.c. MTX. Consecutive patients with established diagnosis of RA and PsA were enrolled from the outpatient clinics of 6 centres in Croatia. There were 48 patients (79.2% women), of median age 61 (range 39–79), and with the median of disease duration of 120 months. Data were collected at baseline (T0) including retrospective data collection for the previous 3 months (on oral MTX), at day 90 ( $\pm 10$  days) (T1) and at day 180 ( $\pm 10$  days) (T2) for the previous periods (both of them during s.c. MTX treatment). Dose of MTX remained stable during the study. Domains of interest were: DAS28, level of pain, PtGHA and PhGHA, QoL (EQ-5Q) and physical function (HAQ-DI). Adherence to treatment and safety data were recorded, too.

**Results:** In a comparison between T0 and T1/T2 there was more chance for patients having low to moderate disease activity after 3 and 6 months of s.c. MTX (8.0; 95%CI 1.9-32.0) and less chance to have high disease activity (0.25; 95%CI 0.11-0.48) in comparison to the baseline DAS 28 (on oral MTX). Adjusted mean values for intensity of pain, PtGHA and PhGHA showed significant decrease for T1 and T2 versus T0 assessment (–1.46; 95%CI



-1.55 to -0.35; -1.12; 95%CI -1.50 to -0.73; -1.15; 95%CI -1.50 to -0.80, respectively). Also, in the same comparison EQ-5D global health showed significant improvement (8.6; 95%CI 4.00 to 13.3), as well as HAQ-DI (-0.25; 95%CI -0.32 to -0.17). In the retrospective analysis there were more missed doses of oral compared to s.c. MTX, while on the other hand adverse events were less frequent with s.c. compared to oral MTX.

**Conclusions:** In the group of patients with RA and PsA who switched from oral to s.c. MTX improvement was observed in multiple outcomes including disease activity, QoL and safety as well as better adherence.

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**Disclosure:** None

## INFECTIONS AND MALIGNANCIES IN PATIENTS TREATED WITH BIOLOGICAL DISEASE MODIFYING ANTIRHEUMATIC DRUGS- OUR EXPERIENCE

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**Background:** Over the past century the treatment of inflammatory rheumatic diseases has moved from an entirely empiric approach, based on the use of aspirin, gold salts and glucocorticoids, through evidence-based approaches with conventional synthetic disease modifying antirheumatic drugs (cs DMARDs), to mechanism-based regimens with biologic disease modifiers. Biological disease-modifying antirheumatic drugs (bDMARDs) have become standard treatment option with a major safety issue related to increased risk of infections<sup>1</sup>.

**Objectives:** The objective of the research was to determine prevalence of infections and malignancies in patients with inflammatory rheumatism treated with bDMARDs in our Department.

**Methods:** Data on one hundred seventeen (117) patients with rheumatoid arthritis (RA, N=50), psoriatic arthritis (PsA, N=18), ankylosing spondylitis (AS, N=42), undifferentiated spondylarthritis (N=7) were analysed retrospectively. Patients were mainly treated with tumour necrosis factor (TNF)-inhibitors (N=103) (adalimumab, certolizumab, etanercept, golimumab, infliximab) and tocilizumab (N=14) from 2004 until September 2018. Descriptive statistical analysis was used.

**Results:** Total number of patients experiencing any documented infection during treatment with bDMARDs was 27 (23,1%), mostly prevalent among patients with RA (N=16; 59,3%), less in patients with AS (N=7; 25,9%) and PsA (N=4; 14,8%). One patient was diagnosed with solid tissue malignancy (hepatocellular carcinoma).

**Conclusions:** Infections were more often diagnosed among RA patients possibly due to nature of the disease itself and immunosuppressive effects of concomitant treatment. Only one patient was diagnosed with solid tissue carcinoma which seems to be in concordance with published data on risk of malignancy during biologic treatment<sup>2</sup>. This study serves as a basis for further bDMARDs safety monitoring in our Department. It is necessary to increase the sample size and continue follow up to before making any definite conclusions.

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**Disclosure:** None

## CLINICAL OUTCOMES OF MACROPHAGE ACTIVATION SYNDROME IN UNIVERSITY HOSPITAL CENTRE

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**Background:** Macrophage activation syndrome (MAS) is an inflammatory, potentially life-threatening process that accompanies autoimmune diseases. It is more common in children than in adults. Outcome success depends on early diagnosis and prompt treatment.

**Objectives:** To evaluate causes and clinical features of MAS, and to discuss clinical pitfalls, with respect to available 2016 classification criteria (EULAR/ACR PRINTO for MAS in JIA)1.

**Methods:** Retrospective study (2012–2018) included 6 patients. The basic characteristics (age, gender, comorbidities), laboratory findings, biopsy (bone marrow, lymph node, liver) results, treatment, underlying disease, clinical course of illness and outcome were reported.

**Results:** Four female and two male patients, age (26–71), were diagnosed with MAS. MAS was the first manifestation of autoimmune disease in one patient, Adult onset Still disease (AOSD), and appeared in previously known Rheumatoid arthritis (RA) and Undifferentiated Connective Tissue Disease (UCTD). Trigger infections were Cytomegalovirus (CMV) and Chlamydia pneumoniae. In one patient, antibodies to Sjogren syndrome (SS) and Primary biliary cirrhosis occurred after one year of follow up. Laboratory abnormalities included elevated liver enzymes and LDH and thrombocytopenia. The hallmark was ferritin level above 5000 [ug/L]. Poorer outcomes were observed in cases of delayed diagnosis ( $\geq 20$  days) and in elderly patients with comorbidities. All patients were treated with glucocorticoids and cyclosporin, and if necessary etoposide. One patient had refractory disease without any evidence of infectious, malignant or autoimmune background despite additional therapy with IVIG, IL-1 and IL-6 inhibitors, and probably had a primary form. Three patients had a lethal outcome. More detailed information are shown in Table 1.

**Conclusions:** A combination of symptoms and laboratory findings of high fever, increased ferritin level, elevated liver function tests and thrombocytopenia should always arouse suspicion of MAS in patient with known predisposing factors. Recognising triggers and aggressive treatment could significantly improve survival outcomes.

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**Disclosure:** None

## LYME DISEASE. MOST FREQUENT OBSERVED SYMPTOMS. IS ARTHRALGIA AMONG THEM?

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**Background:** A Tick born Lyme disease is one of the reasons which can cause reactive arthritis. Lyme disease is very common disease in the world, It has spread into the whole of Europe, except for the warmest and dry areas in the south and the coldest areas in the north. The annual incidence of Lyme disease in the USA is 8/100 000 and

in central Europe and in Scandinavia varies from 0.3 to 155/100 000 (Schnarr et al, 2006\*), in Lithuania (central Europe) it's frequency is 101.6/100 000 (2016 years). Infection usually begins with an expanding skin lesion, known as erythema migrans.

**Objectives:** To find out how often rheumatic symptoms appears in patients with Lyme disease in Lithuania.

**Methods:** We have analyzed data from Center for Communicable Diseases and Aids of Lithuania, of persons who were diagnosed with Lyme disease in 2014–2016 years. Total number of cases is 7424 (2791 males, 4633 females).

**Results:** 996 patients assumed to be symptomatic, the rest 6428 were asymptomatic either information about clinical disease manifestation is not known. Erythema migrans was the most frequently appeared symptom (n = 753, 75,6 %), arthralgia was the second one (220, 22,1 %), the following symptoms were headache (151, 15,2%), general weakness (124, 12,4%), fever (101, 10,1%), myalgia (78, 7,8%), head dizziness (64, 6,4%).

**Conclusions:** In symptomatic patients rheumatic symptoms (arthralgia and myalgia) appears often and Lyme disease should be in rheumatologists minds, especially those who works in endemic zones.

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**Disclosure:** None

## TRAPS (TUMOR NECROSIS FACTOR RECEPTOR – ASSOCIATED PERIODIC SYNDROME)

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Periodic/recurrent fever syndromes belong to group of autoinflammatory syndromes diseases. Familial Mediterranean Fever and Tumor necrosis factor receptor – associated periodic syndrome are most often from them, a less are : HIDS – Hyper IgD Syndrome, MKD – Mevalonate Kinase Deficiency, CAPS: Cryopyrin-Associated Autoinflammatory Syndromes, NALP12-associated periodic fever.

TRAPS is the second often hereditary syndrome of periodic fever (after Familial Mediterranean Fever). There are approximately 1000 peoples with TRAPS, mostly from Middle and South Europe, from northern countries, from America, Japan. There are recurrent fever episode with duration days to months, abdominal pain, myalgia, skin rash – mostly at limbs in clinical pictures. Sometimes there could appear arthralgia, ocular syndrome (periorbital oedema, conjunctivitis, uveitis, iritis). The amyloidosis could occur and lead to renal failure. During childhood disease could manifest as juvenile idiopathic arthritis, systemic form (fever, rash, IBD).

In TRAPS is mutation in gene TNFRSF1A, which insure interaction for TNF receptor 1. After mutation incorrect configuration of TNFR protein is producing, which could not bind at cell surface, could not bind to TNF.

There are use non-inflammatory drugs, glucocorticoids, kolchicin in therapy of TRAPS. After identification of mutation of TNFRSF1A gene biological therapy start to use: etanercept, anakinra

Casuistic: Now 30 years old patient with juvenile idiopathic arthritis with systemic form from 1998 (from 11 years of age). Her mother had amyloidosis of kidneys and died as 43 years old. At year 2009 patient was diagnostic primary amyloidosis of heavy form. At 2012 was done biopsy, deposits of amyloid at vessel. After chemotherapy the autologous transplantation of bone marrow was done. At 2014 was done rebiopsy with finding of AA amyloidosis. From 2015 therapy by etanercept was begin. In successive steps quantitative proteinuria was fall (tab.1).

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**Disclosure:** None

## THE RELATIONSHIP BETWEEN THE DURATION OF METHOTREXATE / ETANERCEPT THERAPY AND SERUM ANTI-SPP IGG ANTIBODIES IN PATIENTS WITH JIA WITHOUT SYSTEMIC MANIFESTATIONS.

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**Background:** Juvenile idiopathic arthritis (JIA) is a chronic disease with unknown etiology, a complex immunoproggressive pathogenesis characterized by a steadily progressing course, the development of destruction of the connective tissue of the joints, a wide spectrum of severe extra-articular manifestations, leading to an early disability of patients. Currently, the prevention of infectious diseases in children with juvenile idiopathic arthritis under conditions of immunosuppressive and biological therapy is of particular importance, since it requires resolving the issue of getting out of the vicious circle of prejudice to vaccination. The decision to immunize a child with JIA implies a special responsibility of pediatricians and children's rheumatologists. Systematic reviews of the results of vaccination of patients with rheumatic diseases against infectious diseases summarize that most vaccines are effective and safe even when patients receive immunosuppressive drugs.

**Objectives:** To analyze the incidence of infectious complications, prescribing antibacterial drugs and adherence to antirheumatic therapy in patients with JIA without systemic manifestations before and after immunization of 13 PCV.

**Methods:** During the prospective cohort study, five groups were formed: children with JIA in remission phase with methotrexate (group 1) or etanercept (group 2), with JIA in the active phase prior to the appointment of methotrexate (group 3) or etanercept (group 4), control group (conditionally healthy children). 13-valent PCV was injected once in 0.5 ml subcutaneously against therapy in patients in the remission phase, or 3 weeks before the appointment of methotrexate or etanercept in patients in the active phase. In the course of the study, the frequency of acute infectious complications, the frequency of prescribing antibacterial drugs in patients with JIA, as well as adverse events against vaccination was assessed.

**Results:** Before the vaccination of 13 PCV, the incidence of infectious complications, the morbidity rate and the frequency of administration of antibiotics in children with JIA who received methotrexate or etanercept (Ia and Ib group, respectively) were significantly higher ( $p = 0.001$ ) than in patients not treated with an immunosuppressant (IIa group), inhibitor of TNF- $\alpha$  (IIb group) and in children of the control group (Figure 2, 3). After immunization with 13 PCV, the incidence of infectious complications, the morbidity rate and the frequency of administration of antibiotics decreased ( $p = 0.001$ ) and did not significantly differ from those of the control group.

**Conclusions:** The severity of the vaccine response in patients in the phase of drug remission of JIA depends on the duration of antirheumatic therapy: the longer the children are treated with methotrexate ( $r = -0.876$ ) and etanercept ( $r = -0.776$ ), the lower the serum level of anti-SPP IgG antibodies after 4 weeks after vaccination 13 PCV. Reduction of the level of immune response is observed when using antirheumatic drugs for more than 8 months.

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## STRUCTURE MODIFICATION IN OA AND PRESENT AND FUTURE PERSPECTIVES

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Therapy of OA has been considered as purely symptomatic at present. Despite of that, several RCT have been performed and published, which have documented positive effect of active drug compared to placebo. The evidence was shown in studies with glukosamine 1), chondroitin sulphate, combination of glucosamine and chondroitin sulphate, diacerhein, piascalidin, hyaluronic acid and tetracyklin. In 2 year controlled study, chondroitin sulphate against celecoxib, chondroitin documented less decrease of medial compartment cartilage volume when using special quantitative MRI methodology2)

New therapeutic tested alternatives in OA are: autologous conditioned serum, platelet rich plasma (PRP), mesenchymal stem cells, fibroblast growth factor 18 (FGF-18), inhibitors MMP, inhibitors of aggrecanase, K-inhibitors cathepsin, inhibitors MAP kinases, inhibitors nitric oxide synthase (i NOS).

Recent metaanalysis didn't confirm structure modification by bone marrow derived, mesenchymal stem cells. Methodological and ethical problems in long-term studies in OA will be discussed.

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**Disclosure:** None

## HYPOKALEMIC PARALYSIS AS A PRESENTING MANIFESTATION OF PRIMARY SJÖGREN'S SYNDROME: CASE REPORT

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**Background:** Primary Sjögren's syndrome is a chronic autoimmune disease primarily characterized by a progressive lymphocytic infiltration of the exocrine glands with varying degrees of systemic involvement. In case of renal involvement, the most common manifestation is renal tubular acidosis, resulting from tubular dysfunction due to tubulointerstitial nephritis

**Objectives:** We present a case of a patient with hypokalemic quadriparesis due to tubulointerstitial nephritis and renal tubular acidosis, as a manifestation of Sjögren's syndrome

**Methods:** A 41-year-old woman, was admitted to the emergency room due to weakness, muscle pain, difficulties walking and moving all four limbs. Laboratory results showed extreme hypokalemia with metabolic acidosis, increased erythrocyte sedimentation rate, hyperchloremia and hypernatremia. Urin sample analysis revealed proteinuria semi-quantitative 2–3, ketonuria. Immunoserologic tests confirmed the presence of speckled ANA with the presence of anti SSA and anti SSB antibodies. High values of muscle enzymes were identified (CPK, Troponin, CK). In the left kidney, initial hydronephrosis with calcification in the lower half of the size up to 4mm was found

**Results:** Hypokalemia and metabolic acidosis were treated with parenteral administration of sodium bicarbonate and thiazide diuretic. Immunofluorescent microscopy of the renal biopsy sample revealed a densely infiltrated hypercellular interstitial segment without presence of immunofluorescent deposits within the glomerulus; the finding of light microscopic analysis fits into the clinical picture of tubulointerstitial nephritis.

The patient was given pulse doses of corticosteroids with cyclophosphamide intravenously in monthly intervals and is on regular outpatient follow up, with a stable remission of the underlying disease

**Conclusions:** The presence of hypokalemia and consequent symptoms, such as quadriparesis, needs to be thoroughly analyzed and further investigated for a possible cause

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**Disclosure:** None



## A RHEUMATOLOGIC DISEASE OR A PARANEOPLASTIC SYNDROME WITH A RHEUMATIC MANIFESTATION? CASE REPORT

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We present a case report of a 66 year old woman meeting the diagnostic criteria of rheumatoid arthritis and also observed for systemic lupus erythematosus and allergic urticaria. The patient was admitted to our Department due to passing fits of facial and fingertips' skin flush with concomitant sweating, tachycardia, rise in arterial blood pressure and edema of multiple joints triggered by specific foods (bananas, citrus, chocolate, cheese, wine), stress and exertion.

Multiple laboratory and imaging tests were performed and a number of diseases excluded before the abdominal CT scan showed an ileum tumor accompanied by two focal liver changes. Hormonal and histopathologic tests revealed the carcinoid tumor.

This case highlights how carcinoid tumor may present for many years with non-specific symptoms that may easily be mistaken for symptoms of a rheumatologic disease. Patient history must always be taken very carefully and clinical vigilance maintained even in patients with established rheumatologic diagnoses in order not to overlook an underlying neoplasia.

**Disclosure:** None

## SEVERE COURSE OF POLYARTERITIS NODOSA PRESENTING WITH ASYNCHRONOUS SPONTANEOUS RETROPERITONEAL HEMORRHAGE AND SPONTANEOUS HEPATIC RUPTURE: CASE REPORT AND LITERATURE REVIEW

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**Background:** Spontaneous internal organ ruptures occur either as a first presentation of polyarteritis nodosa (PAN) or during the disease course in a patient already diagnosed with this condition.

**Objectives:** We report on an unusually rapid course of PAN in a 75-year old Caucasian male, complicated by spontaneous renal hemorrhage and spontaneous hepatic hemorrhage leading to two hemodynamic shocks, two consecutive surgical interventions and renal failure. Angiographic and histopathologic findings were consistent with the diagnosis of PAN. Regardless of the delay in the accurate diagnosis, methylprednisolone and cyclophosphamide combined therapy resulted in improvement of clinical symptoms and improvement in laboratory markers and functional imaging findings.

**Methods:** A systematic literature search for cases of PAN presenting with renal or hepatic hemorrhage has been conducted.

**Results:** Patients with either renal or hepatic hemorrhage have been described (twelve cases of hepatic hemorrhage, thirty-two cases of renal hemorrhage), but the occurrence of both disease manifestations has been reported in five cases to the best of our knowledge.

**Conclusions:** Clinicians should consider PAN in differential diagnosis of spontaneous retroperitoneal hemorrhage or hepatic rupture, in younger as well as the elderly, comorbid patients.

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**Disclosure:** None

## ASEPTIC SYSTEMIC ABSCESSSES SYNDROME – CASE REPORT

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**Background:** Aseptic systemic abscesses syndrome is a rare inflammatory disorder with a fewer than 50 cases reported so far. It is characterized by formation of deep aseptic abscesses, most commonly localized in the abdomen, recurrent fever attacks and leucocytosis. Etiology is still unknown, but it shares some features with inflammatory bowel diseases and neutrophilic dermatoses which suggests a correlation with auto-inflammatory disorders. Lesions are consisted of central necrosis formed by polymorphonuclear cells and surrounded by palisading histiocytes. The diagnosis is based on a combination of a typical clinical and radiological presentation, the pathohistological findings and the exclusion of other differential diagnosis, especially infective agents. Antibiotics are ineffective, while corticosteroid and immunosuppressive therapy leads to a rapid improvement.

**Case report:** we are presenting a forty-five year old female patient who manifested features suggestive of the aseptic systemic abscesses syndrome, developing recurrent aseptic abscesses in the abdominal lymphnodes, spleen and the liver.

**Conclusions:** the aim of this case report is to draw attention to the aseptic systemic abscesses syndrome as a possible differential diagnosis in a patients with unclear etiology of aseptic suppurative intra-abdominal lesions.

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**Disclosure:** None

## ARTHRITIS OF THE ANKLES AS A MAJOR MANIFESTATION OF PONCET'S DISEASE – CASE REPORT

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A 22-years old black male presented to our university hospital complaining of bilateral painful swelling of the ankles. He had no known comorbid illnesses. His complaints started about a month ago. He described the pain as more pronounced on the insertion of the Achilles tendons, worsening when subjected to active or passive motion of the joint, and improving when at rest. Over-the-counter anti-inflammatories did not alleviate the pain. At the very beginning of his condition, he presented with a short bout of emetizing cough that remitted spontaneously after three days. He also referred intermittent fever, of up to 39 °C, during the period. Two days previously to his visit, he also started complaining ofodynophagia located to the right side of the throat. On physical examination, he was febrile (38,2 °C), had an aphtous ulcer on his right peritonsillar space, and presented non-pitting bilateral edema of the ankles. Thorax auscultation was unremarkable. X-ray images of both feet showed no findings. It was visualized a small effusion on his left ankle on USG study. An attempt was made to perform arthrocentesis, which yielded a dry tap, nonetheless. He had a marked elevated CRP of 128 mg/L, and a mildly elevated ESR of 41 mm. UA was 2.5 mg/dL. RF and FAN were negative. A hypothesis of either reactive arthritis or sarcoidosis Lofgren syndrome was made. In order to corroborate the latter, a thorax CT was ordered, which uncovered a cavitory lesion measuring 3 x 1.7 cm on the apex of his left lung, surrounded by micronodules or branching lesions (tree-in-bud sign). Given the typical aspect of tuberculosis on CT, a bronchoscopy was performed. BAL

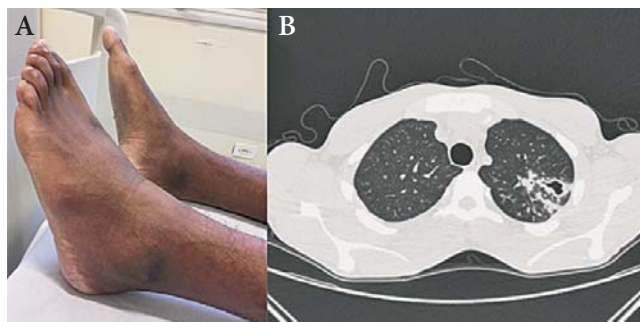


FIGURE 1. In (A), the patient's swollen ankles at presentation. In (B), typical lesion seen on chest CT.

revealed a richly cellular fluid, with predominance of lymphocytes (30%) and macrophages (58%). AFB testing resulted negative, but both RMT and culture for BK were positive. The patient was initiated on RIPE treatment, and improved of symptoms after 15 days. The typical presentation of bilateral ankle swelling and resolution of symptoms after RIPE treatment allowed the final diagnosis of Poncet's disease.

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Disclosure: None

## GENERALIZED TELANGIECTASIA MISINTERPRETED AS VASCULITIS – CASE REPORT

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Paraneoplastic syndromes (PNS) are defined as tumor-associated symptoms and signs that are a result of tumor secretion of functional peptides, hormones, and cytokines or immune cross-reactivity between tumor and normal host tissues. Autoimmunity can be one of the presentations of PNS. Gastrointestinal stromal tumor (GIST) is rarely described as a cause of PNS. We present 81 – year old female patient with bizarre, generalized telangiectasia on her trunk and legs with subcutaneous indurated plaques of variable size (Figure) and positive immunological lab results (anti SSA, SSB, anti-centromeres, and anti-histones). The diagnosis of vasculitis and unknown connective tissue disease (UCTD) was made, although patient did not have other symptoms that would accompany collagenosis. Skin biopsy revealed isolated telangiectasia with no signs of inflammation and necrosis that would support the diagnosis of vasculitis. Due to abrupt clinical start and the age of the patient paraneoplastic syndrome was suspected. Unfortunately, due to poor health and other comorbidities, the patient died. The autopsy revealed GIST in her intestines, as a cause of PNS.

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**Disclosure:** None

## EDUCATIONAL EXPECTATIONS OF THE POLISH PATIENTS WITH RHEUMATIC DISORDERS TREATED WITH BIOPHARMACEUTICALS

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**Background:** Biopharmaceuticals are still considered by patients as a new and partially enigmatic tool for management of rheumatic diseases.

**Objectives:** The study was designed to evaluate educational expectations and sources of knowledge in patients with rheumatic diseases treated with biologics.

**Methods:** Anonymous questionnaires were distributed in 23 Polish rheumatological centers involved in the treatment. Responses were received from 606 patients with rheumatoid arthritis, 427 with ankylosing spondylitis, 117 psoriatic arthritis, and 62 adult patients with juvenile idiopathic arthritis (in whom administration of the drugs had been introduced before they were 18-year-old).

**Results:** Almost all the patients had learnt for the first time on biologics from their rheumatologist (93%). Few only patients had got such data from internet or from other patients. Likewise, most of the patients got majority of educational data on treatment with biologics from rheumatologist who was supervising the therapy (82%). Remaining sources included internet (8%) and other patients (5%). Relative low number of patients was educated by nurses (2%). Most of the patients (87%) were looking for more details on biological treatment. The patients with rheumatic disease lasting less than 10 yrs. were more interested in the management than those suffering longer. Most of the patients (94%) considered their rheumatologist as the main person responsible for their education on biologics. There was no difference between patients with various rheumatic diseases as well as no difference was found between female and male patients. Biological treatment attracted more interest in younger than older patients.

**Conclusions:** Education is still a challenge in patients receiving biopharmaceuticals. Most of the patients represented traditional attitude to health education, expecting almost all educational data to be provided by their physician. We were surprised that role of the nurses was found to be rather low. An increase in role of nurses seems to be the future aim of the educational efforts in Polish rheumatology.

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**Disclosure:** None



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Radovi se ne objavljuju prema redoslijedu prispjeća rukopisa u uredništvo časopisa. Rukopisi i ostali dostavljeni materijali ne vraćaju se pošiljateljima.

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## NASLOVNA STRANICA

Na naslovnoj stranici treba biti naslov rada (mora biti sažet, jasan i informativan) na hrvatskom i engleskom jeziku te puno ime svakog od autora. U sljedećem retku treba navesti puni naziv ustanove, ulicu i broj, grad i državu autora. Ako su u izradi rada sudjelovali autori iz različitih ustanova, za svakog od njih poslije imena i prezimena te prije navoda ustanove treba napisati odgovarajući broj u superskriptu.

Slijedi ime i prezime te puna adresa autora za dopisivanje u vezi s radom, njegov/njezin telefonski broj, broj faksa i e-mail adresa.

## SAŽETAK I KLJUČNE RIJEČI

Druga stranica treba sadržavati sažetak na hrvatskom i engleskom jeziku (do 300 riječi) u kojem su navedeni cilj studije ili istraživanja, osnovni postupci, najvažnija otkrića te osnovni zaključci.

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U radovima koji se bave eksperimentima na ljudima jasno treba navesti da su postupci provedeni sukladno etičkim standardima institucijskog ili regionalnog odbora odgovornog za izvođenje eksperimenata na ljudima te u skladu s Helsinškom deklaracijom iz 1975. godine, revidiranom 1983. godine. Ne smije se navoditi ispitanikovo ime i/ili prezime, osobito u ilustrativnim materijalima. U radovima koji se bave eksperimentima na životinjama treba navesti da je poštovan institucionalni ili nacionalni pravilnik o brizi za laboratorijske životinje i njihovu upotrebu.

## STATISTIČKA OBRADA

Treba iscrpno opisati statističke metode kako bi se obradovanom čitatelju koji ima pristup originalnim podatcima omogućilo da potvrdi navedene rezultate. Gdje god je to moguće zaključke treba kvantificirati i prezentirati odgovarajućim indikatorima pogreške ili odstupanja od mjerenja. Treba navesti upotrijebljeni računalni program.

## REZULTATI

Rezultati se izlažu logičnim slijedom u tekstu, tablicama i ilustracijama. U tekstu se ne ponavljaju svi podatci iz tablica ili ilustracija već se naglašavaju ili sažimaju samo bitna opažanja.

## RASPRAVA

Treba naglasiti nove i bitne aspekte studije te zaključke koji iz nje proistječu. Ne preporučuje se detaljno ponavljati podatke ni bilo koje druge materijale koji su navedeni u uvodnom dijelu ili u dijelu s rezultatima. U dijelu za raspravu treba objasniti važnost dobivenih rezultata i njihova ograničenja, uključujući i implikacije vezane uz buduća istraživanja, ali uz izbjegavanje izjava i zaključaka koji nisu potpuno potvrđeni dobivenim podatcima. Opažanja iz ove studije treba usporediti s ostalim relevantnim studijama. Kad je potrebno, mogu se navesti nove hipoteze uz jasno naglašavanje da su nove.

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Zaključci se izvode na osnovi vlastitih rezultata, odvojeno od rasprave.

## KRATICE

Treba rabiti samo standardne kratice. Puni pojam za koji se rabi kratica mora biti naveden pri prvoj uporabi kratice u

tekstu, osim ako je riječ o standardnim kraticama mjernih jedinica. Kratice treba izbjegavati u naslovu rada.

## SIMBOLI

U tekstu se simboli moraju objasniti. U dodatku se može navesti iscrpan popis simbola.

## TABLICE

Tablice se pišu s dvostrukim proredom na posebnoj stranici. Tablice se ne smiju slati kao fotografije. Svaka tablica mora imati naslov i redni broj prema redoslijedu pojavljivanja u tekstu. Tablica mora biti pregledna i jednostavna. Primjedbe trebaju biti napisane ispod tablice, uz oznaku u tablici malim slovima u superskriptu. Tablice ne bi trebale ponavljati rezultate koji su prezentirani bilo gdje drugdje u radu (npr., u grafikonu).

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Sve ilustracije trebaju biti profesionalno nacrtane ili snimljene. Slova, brojevi i simboli moraju biti čitki i u smanjenom obliku u kojem će se objaviti. Svaka fotografija mora imati broj prema redoslijedu pojavljivanja u tekstu, ime autora i označenu gornju stranu. Svaki crtež mora imati broj prema redoslijedu pojavljivanja u tekstu i označenu gornju stranu. Crteži trebaju biti izrađeni ili otisnuti crnom tintom na bijelom papiru. Otisci u boji ili fotokopije nisu pogodni za reprodukciju. Fotokopije fotografija nisu prihvatljive. Fotografije osoba mogu se objavljivati samo uz pismeno dopuštenje osobe na fotografiji ili osoba mora biti neprepoznatljiva. Preuzete slike i tablice iz drugih izvora treba popratiti dopuštenjem njihova izdavača i autora.

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## IZJAVA O SUKOBU INTERESA

Autori moraju izjaviti postoji li financijski odnos između njih i organizacije/tvrtke koja je sponzorirala istraživanje. Ova bilješka mora se dodati u odvojenom odjeljku prije popisa literature. Ako nema sukoba interesa, autori trebaju napisati: "Autori izjavljuju da nisu u sukobu interesa."

## LITERATURA

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Literaturu u tekstu, tablicama i legendama treba navoditi arapskim brojevima u zagradi, prema redoslijedu pojavljivajuća. Ako brojeva ima više, odvajaju se zarezima.

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[Primjer] Članak iz časopisa, više od šest autora:

1. Ćurković B, Babić-Naglić Đ, Morović-Vergles J, i sur. Prijedlog primjene bioloških lijekova u reumatoidnom artritisu. *Reumatizam*. 2010;57(1):29-35.

[Primjer] Članak iz časopisa, kontinuirana paginacija:

2. Ritchlin CT. From skin to bone: translational perspectives on psoriatic disease. *J Rheumatol*. 2008;35:1434-7.

[Primjer] Članak iz suplementa:

3. Gladman DD, Antoni C, Mease P, Clegg DO, Nash P. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis*. 2005;64(Suppl 2):ii14-7.

## Knjige

Obavezatno se navode mjesto izdanja, izdavač i godina izdanja. Brojevi stranica navode se samo kada se citira dio knjige.

[Primjer] Knjiga (autori):

4. Walker JM, Helewa A. *Physical rehabilitation in arthritis*. 2. izd. St. Louis: Saunders; 2004.

[Primjer] Knjiga (urednici):

5. Isenberg DA, Maddison PJ, Woo P, Glass D, Breedveld FC, urednici. *Oxford textbook of rheumatology*. 3. izd. New York: Oxford University Press; 2004.

[Primjer] Poglavlje u knjizi:

6. Vasey FB, Espinoza LR. Psoriatic arthritis. U: Calin A, urednik. *Spondyloarthropathies*. Orlando: Grune and Stratton; 1984. str. 151-85.

## Izlaganje na znanstvenom skupu

Ako je izlaganje objavljeno u časopisu ili suplementu, treba slijediti upute za časopis ili suplement. Ako su izlaganja objavljena u knjizi, nakon naslova knjige dodaje se napomena „Zbornik izlaganja na“, naziv skupa te vrijeme, mjesto i država održavanja.

[Primjer] Izlaganje na znanstvenom skupu, objavljeno u suplementu:

7. Matucci Cerinic M, Pignone A. The early diagnosis of rheumatoid arthritis (RA). *Reumatizam*. 1997;44 (Suppl):1.

[Primjer] Izlaganje na znanstvenom skupu, objavljeno u knjizi:

8. Babić-Naglić Đ. Fizička aktivnost i vježbe. U: Ivanišević G, urednik. *Talasoterapija, kineziterapija i aromaterapija u Hrvatskoj*. Zbornik izlaganja na 14. lošinjskoj školi prirodnih ljekovitih činitelja; 2013. Ružica 6-7; Veli Lošinj, Hrvatska. Zagreb: Hrvatski liječnički zbor; 2013. str. 49-55.

[Primjer] Zbornik izlaganja na znanstvenom skupu (knjiga):

9. Gordon DA, urednik. *Immune reactions and experimental models in rheumatic diseases*. Zbornik izlaganja na Četvrtoj kanadskoj konferenciji o istraživanju reumatskih bolesti; 1970. Lis 15-17; Toronto, Kanada. Toronto: University of Toronto Press; 1972.

## Mrežne publikacije

Citati mrežnih publikacija trebaju uključivati URL i datum pristupa, osim ako je riječ o publikaciji koja ima DOI.

[Primjer] Članak iz časopisa na internetu:

10. Mak A, Kow NY. The pathology of T cells in systemic lupus erythematosus. *J Immunol Res* [Internet]. 2014; 2014:419029. Dostupno na: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4017881>. [Pristupljeno: 25. 5. 2014.].

[Primjer] Članak iz časopisa na internetu, sadrži DOI:

11. Vivar N, Van Vollenhoven RF. Advances in the treatment of rheumatoid arthritis. *F1000Prime Rep*. 2014. Svi 6;6:31. doi: 10.12703/P6-31. PubMed PMID: 24860653; PubMed Central PMCID: PMC4017904.

[Primjer] Knjiga/monografija na internetu:

12. Chen Q, urednik. *Osteoarthritis – diagnosis, treatment and surgery* [Internet]. Rijeka: InTech; 2012. Dostupno na: <http://www.intechopen.com/books/osteoarthritis-diagnosis-treatment-and-surgery>. [Pristupljeno: 8. 10. 2013.].

[Primjer] Mrežna stranica:

13. Hrvatsko reumatološko društvo [Internet]. Zagreb: Hrvatsko reumatološko društvo HLZ-a; c2014. Dostupno na: <http://www.reumatologija.org/Pocetna.aspx>. [Pristupljeno: 1. 4. 2014.].

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# IZJAVA O PUBLICISTIČKOJ ETICI I PUBLICISTIČKOJ ZLOUPOTREBI

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U liječenju odraslih bolesnika s umjerenim do teškim reumatoidnim artritismom (RA) kad metotreksat više nije dovoljno učinkovit<sup>1</sup>

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Reference: 1. Sažetak opisa svojstava lijeka Olumiant 27. rujna 2018. 2. Smolen et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update, Ann Rheum Dis Published Online First: 6 March 2017. doi:10.1136/annrheumdis-2016-210715. 3. Taylor PC et al. N Engl J Med. 2017 Feb 16;376(7):652-662

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≥ 75 godina, a može biti prikladna i za bolesnike koji u anamnezi imaju kronične ili rekurentne infekcije. Doza od 2 mg jedanput na dan može se razmotriti i u bolesnika koji su dozom od 4 mg jedanput na dan postigli održanu kontrolu aktivnosti bolesti i koji su kandidati za postupno smanjivanje doze. Liječenje se ne smije započeti u bolesnika s apsolutnim brojem limfocita (ABL) manjim od  $0,5 \times 10^9$  stanica/l, apsolutnim brojem neutrofila (ABN) manjim od  $1 \times 10^9$  stanica/l ili vrijednošću hemoglobina manjom od 8 g/dl. Liječenje može započeti nakon što se vrijednosti vrate iznad tih granica. Primjena lijeka Olumiant ne preporučuje se u bolesnika s klirensom kreatinina < 30 ml/min niti u bolesnika s teškim oštećenjem jetrene funkcije. **Pedijatrijska populacija** Sigurnost i djelotvornost lijeka Olumiant u djece i adolescenata u dobi od 0 do 18 godina još nisu ustanovljene. **Način primjene:** Za peroralnu primjenu. Olumiant se primjenjuje jedanput na dan, uz hranu ili bez nje, a može se uzeti u bilo koje doba dana. **Kontraindikacije:** Preosjetljivost na djelatnu tvar ili neku od pomoćnih tvari. Trudnoća. **Posebna upozorenja i mjere opreza pri uporabi:** **Infekcije** – Baricitinib je, u usporedbi s placebom, povezan s povišenom stopom infekcija kao što su infekcije gornjih dišnih putova. U prethodno neliječenih bolesnika, kombinacija s metotreksatom povećala je učestalost infekcija u usporedbi s monoterapijom baricitinibom. U bolesnika s aktivnim, kroničnim ili rekurentnim infekcijama potrebno je pažljivo razmotriti rizike i koristi liječenja lijekom Olumiant prije početka njegove primjene. Ako se razvije infekcija, bolesnika treba pažljivo nadzirati, a liječenje lijekom Olumiant privremeno prekinuti ako bolesnik ne odgovara na standardnu terapiju. Liječenje lijekom Olumiant ne smije se nastaviti dok se infekcija ne povuče. **Tuberkuloza** Prije početka liječenja lijekom Olumiant u bolesnika treba provesti probir na tuberkulozu (TBC). Olumiant se ne smije davati bolesnicima s aktivnim TBC-om. U bolesnika s prethodno neliječenim latentnim TBC-om potrebno je razmotriti antituberkuloznu terapiju prije početka liječenja lijekom Olumiant. **Ponovna aktivacija virusa** U kliničkim je ispitivanjima prijavljena ponovna aktivacija virusa, uključujući slučajeve ponovne aktivacije virusa herpesa (npr. herpes zoster, herpes simpleks). Herpes zoster češće se prijavljivao u bolesnika u dobi od ≥ 65 godina koji su prethodno bili liječeni i biološkim i konvencionalnim antireumatskim lijekovima koji modificiraju tijek bolesti (engl. *disease-modifying anti-rheumatic drug*, DMARD). Ako se u bolesnika razvije herpes zoster, liječenje lijekom Olumiant mora se privremeno prekinuti dok se epizoda ne povuče. Prije početka liječenja lijekom Olumiant potrebno je provesti probir na virusni hepatitis u skladu s kliničkim smjernicama. Ako se utvrdi prisutnost HBV DNK, treba se savjetovati sa specijalistom za jetrene bolesti kako bi se utvrdilo treba li prekinuti liječenje. **Cijepljenje** Ne preporučuje se primjena živih, atenuiranih cjepiva tijekom ili neposredno prije liječenja lijekom Olumiant. Preporučuje se da prije početka liječenja lijekom Olumiant svi bolesnici obave sva potrebna cijepljenja u skladu s važećim smjernicama za cijepljenje. **Lipidi** U usporedbi s placebom, u bolesnika liječenih baricitinibom prijavljena su o dozi ovisna povišenja vrijednosti lipidnih parametara. Primjena terapije statinima dovela je do spuštanja povišene vrijednosti LDL-kolesterola na razinu na kojoj je bila prije liječenja. Lipidne parametre treba odrediti

približno 12 tjedana nakon početka liječenja lijekom Olumiant, nakon čega bolesnike treba liječiti u skladu s međunarodnim kliničkim smjernicama za hiperlipidemiju. Učinak tih povišenja vrijednosti lipidnih parametara na pobol i smrtnost od kardiovaskularnih bolesti još nije utvrđen. **Povišenja vrijednosti jetrenih transaminaza** Ako se tijekom rutinskih mjera skrbi u bolesnika primijete povišenja vrijednosti ALT-a ili AST-a i posumnja na lijekom izazvano oštećenje jetre, primjenu lijeka Olumiant treba privremeno prekinuti dok se ta dijagnoza ne isključi. **Zloćudna bolest** Rizik od zloćudnih bolesti, uključujući limfom, povećan je u bolesnika s reumatoidnim artritismom. Imunomodulacijski lijekovi mogu povećati rizik od zloćudnih bolesti, uključujući limfom. **Venska tromboembolija** U bolesnika liječenih baricitinibom prijavljeni su slučajevi duboke venske tromboze (DVT) i plućne embolije (PE). Olumiant treba primjenjivati uz oprez u bolesnika s faktorima rizika za DVT/PE, kao što su starija dob, pretilost, DVT/PE u povijesti bolesti, te u bolesnika u kirurškoj obradi i imobilizaciji. Ako se pojave klinički znakovi DVT-a/PE-a, potrebno je privremeno prekinuti liječenje lijekom Olumiant i odmah ocijeniti stanje bolesnika te potom uvesti odgovarajuće liječenje. **Imunosupresivni lijekovi** Ne preporučuje se primjena u kombinaciji s biološkim DMARD-ovima ili drugim inhibitorima Janus kinaze (JAK) jer se ne može isključiti rizik od aditivne imunosupresije. Podaci o primjeni baricitiniba zajedno sa snažnim imunosupresivima (npr. azatioprinom, takrolimusom, ciklosporinom) su ograničeni pa je kod primjene tih kombinacija potreban oprez. **Interakcije s drugim lijekovima i drugi oblici interakcija:** *In vitro*, baricitinib je supstrat organskog anionskog prijenosnika (OAT)3, P-glikoproteina (P-gp), proteina koji uzrokuje otpornost raka dojke na liječenje (engl. *breast cancer resistance protein*, BCRP) i proteina za izlučivanje više lijekova i toksina (engl. *multidrug and toxin extrusion transporter*, MATE)2-K. Predlijelek leflunomid brzo se pretvara u teriflunomid, koji je slab inhibitor OAT3, pa može povećati izloženost baricitinibu. **Plodnost, trudnoća i dojenje:** **Trudnoća** Olumiant je kontraindiciran u trudnoći. Žene reproduktivne dobi moraju koristiti učinkovitu metodu kontracepcije tijekom liječenja i još najmanje tjedan dana po njegovu završetku. Ako bolesnica zatrudni dok uzima Olumiant, roditelje treba upozoriti na mogući rizik za plod. **Dojenje** Ne može se isključiti rizik za novorođenčad/dojenčad i stoga se Olumiant ne smije uzimati tijekom dojenja. **Plodnost** Ispitivanja na životinjama upućuju na to da bi baricitinib mogao smanjiti plodnost žena tijekom liječenja, dok učinka na spermatogenezu nije bilo. **Nuspojave:** Najčešće prijavljene nuspojave lijeka koje su se javile u ≥ 2% bolesnika liječenih lijekom Olumiant u monoterapiji ili u kombinaciji s konvencionalnim sintetskim DMARD-ovima bile su povišene vrijednosti LDL-kolesterola (33,6%), infekcije gornjih dišnih putova (14,7%) i mučnina (2,8%). Infekcije prijavljene kod liječenja lijekom Olumiant uključivale su herpes zoster. **Broj i datum odobrenja za stavljanje lijeka u promet:** EU/1/16/1170/004, EU/1/16/1170/012 od 13. veljače 2017. **Način i mjesto izdavanja lijeka:** Lijek se izdaje na recept. **Naziv i adresa nositelja odobrenja za stavljanje gotovog lijeka u promet:** Eli Lilly Nederland B.V, Papendorpseweg 83, 3528 BJ Utrecht, Nizozemska **Datum revizije Sažetka opisa svojstava lijeka:** 27. rujna 2018.

Važno: Lijek Olumiant izdaje se na recept. Prije propisivanja lijeka Olumiant molimo pročitajte zadnji odobreni sažetak opisa svojstava lijeka i uputu o lijeku. Detaljnije informacije o ovom lijeku dostupne su na internetskoj stranici Europske agencije za lijekove: <http://www.ema.europa.eu>



Za bolesnike koji ne postižu terapijske ciljeve  
**ZAUSTAVLJENA**  
**PROGRESIJA RA**<sup>2,3,4</sup>



# KEVZARA<sup>®</sup>

## NOVO, HUMANO MONOKLONSKO PROTUTIJELO KOJE INHIBIRA RECEPTORE INTERLEUKINA-6

- Uvjerljivi i dosljedni rezultati u različitim populacijama bolesnika (nedovoljno dobar odgovor na MTX, nedovoljno dobar odgovor na inhibitore TNF, monoterapija)<sup>2,3,4</sup>
- Brzo ublažavanje znakova i simptoma RA<sup>2,3,4</sup>
- Snažna inhibicija progresije oštećenja zglobova<sup>3</sup>

### PREDVIDLJIVO, FLEKSIBILNO DOZIRANJE

Primjena svaka  
2 tjedna<sup>1</sup>

2

2 doze,  
kod odstupanja  
u laboratorijskim  
nalazima<sup>1</sup>

2

### PRAKTIČNOST ZA BOLESNIKE

2 pomagala  
za primjenu:  
brizgalica bez  
tipke  
i štrcaljka<sup>1</sup>

2

Stabilan  
2 tjedna na  
sobnoj  
temperaturi<sup>1</sup>

2

SANOFI GENZYME 

Sažetak opisa svojstava lijeka KEVZARA dostupan je na informativnom štandu Sanofi Genzyme i Regeneron surađujući na globalnom programu razvoja i tržišne dostupnosti lijeka KEVZARA.

\* Nakon što se izvadi iz hladnjaka, KEVZARA se mora primijeniti unutar 14 dana te se ne smije čuvati na temperaturi iznad 25°C.

1. Sažetak opisa svojstava lijeka Kevzara, kolovoz 2017., [www.ema.europa.eu](http://www.ema.europa.eu).
2. Fleischmann R, van Adelsberg J, Lin Y, et al. Sarilumab and nonbiologic disease-modifying antirheumatic drugs in patients with active rheumatoid arthritis and inadequate response or intolerance to tumor necrosis factor inhibitors. *Arthritis Rheum.* 2017;69:277-290.
3. Genovese MC, Fleischmann R, Kivitz AJ, et al. Sarilumab plus methotrexate in patients with active rheumatoid arthritis and inadequate response to methotrexate: results of a Phase III study. *Arthritis Rheumatol.* 2015;67(6):1424-1437.
4. Burmester GR, Lin Y, Patel R, et al. Efficacy and safety of sarilumab monotherapy versus adalimumab monotherapy for the treatment of patients with active rheumatoid arthritis (MONARCH): a randomised, double-blind, parallel-group phase III trial *Ann Rheum Dis* 2017; 76:840-847

**KEVZARA<sup>®</sup>**  
(sarilumab) injekcija  
150 mg | 200 mg



▼ Ovaj je lijek pod dodatnim praćenjem. Time se omogućuje brzo otkrivanje novih sigurnosnih informacija. Od zdravstvenih djelatnika se traži da prijave svaku sumnju na nuspojavu za ovaj lijek. Upute za prijavljivanje dostupne su na [www.halmed.hr](http://www.halmed.hr).

**SKRAĆENI SAŽETAK OPISA SVOJSTAVA - 1. NAZIV LIJEKA I SASTAV:** Kevzara 150 mg i 200 mg otopina za injekciju u napunjenoj štrcaljki i brizgalici. Jedna jednodozna napunjena štrcaljka ili brizgalica sadrže 150 mg ili 200 mg sarilumaba u 1,14 ml otopine. **2. TERAPIJSKE INDIKACIJE:** Kevzara je u kombinaciji s metotreksatom (MTX) indicirana za liječenje umjerenog do teškog oblika aktivnog reumatoidnog artritisa (RA) u odraslih bolesnika koji nisu dovoljno dobro odgovorili na jedan ili više antireumatika koji modificiraju tijek bolesti ili koji nisu podnosili takve lijekove. Kevzara se može primjenjivati i kao monoterapija u slučaju nepodnošenja MTX-a ili kada liječenje MTX-om nije prikladno. **3. DOZIRANJE I NAČIN PRIMJENE:** Preporučena doza iznosi 200 mg jedanput svaka 2 tjedna supkutanom injekcijom. Smanjenje doze s 200 mg jedanput svaka 2 tjedna na 150 mg jedanput svaka 2 tjedna preporučuje se za zbrinjavanje neutropenije, trombocitopenije i povišenih vrijednosti jetrenih enzima. Potrebno je odgoditi primjenu lijeka Kevzara u bolesnika u kojih se razvije ozbiljna infekcija. Ne preporučuje se započeti liječenje lijekom Kevzara u bolesnika s apsolutnim brojem neutrofila (ABN) manjim od  $2 \times 10^9/l$  i kod onih kojima je broj trombocita manji od  $150 \times 10^3/\mu l$ . **Oštećenje funkcije bubrega:** Nije potrebno prilagođavati dozu u bolesnika s blagim do umjerenim oštećenjem funkcije bubrega. Kevzara se nije ispitivala u bolesnika s teškim oštećenjem funkcije bubrega. **Oštećenje funkcije jetre:** Sigurnost i djelotvornost lijeka Kevzara nisu se ispitivale u bolesnika s oštećenjem funkcije jetre. **Starije osobe:** Nije potrebno prilagođavati dozu u bolesnika starijih od 65 godina. **Pedijatrijska populacija:** Nema dostupnih podataka. **Način primjene** Cjelokupan sadržaj (1,14 ml) napunjene štrcaljke/brizgalice treba primijeniti supkutanom injekcijom. **4. KONTRAINDIKACIJE:** Preosjetljivost na djelatnu tvar ili neku od pomoćnih tvari. Aktivne, teške infekcije. **5. POSEBNA UPOZORENJA I MJERE OPREZA PRI UPORABI:** Naziv i broj serije primijenjenog lijeka treba jasno zabilježiti. Tijekom liječenja bolesnike treba pažljivo nadzirati zbog moguće pojave znakova i simptoma infekcije. Kevzara se ne smije primijeniti bolesnicima s aktivnom infekcijom, uključujući lokalizirane infekcije. Prije početka liječenja lijekom Kevzara razmotrite rizike i koristi liječenja u bolesnika koji imaju kroničnu ili rekurentnu infekciju, ozbiljne ili oportunističke infekcije u anamnezi, HIV infekciju, podležuća stanja zbog kojih mogu biti podložniji infekciji, su bili izloženi tuberkulozi ili su živjeli u područjima ili putovali u područja gdje su tuberkuloza ili mikoza endemske bolesti. Primjenu lijeka Kevzara potrebno je odgoditi ako se u bolesnika razvije ozbiljna ili oportunistička infekcija. U bolesnika u kojeg se tijekom liječenja lijekom Kevzara razvije infekcija također treba odmah provesti cjelovite dijagnostičke pretrage prikladne za imunokompromitiranog bolesnika. **Tuberkuloza** Prije početka liječenja lijekom Kevzara potrebno je provesti procjenu faktora rizika za tuberkulozu i testirati bolesnike na latentnu infekciju. Bolesnike s latentnom ili aktivnom tuberkulozom treba liječiti standardnom antimikobakterijskom terapijom prije nego što se uvede Kevzara. Potrebno je razmotriti terapiju za tuberkulozu prije uvođenja lijeka Kevzara u bolesnika koji u anamnezi imaju latentnu ili aktivnu tuberkulozu, a u kojih se ne može potvrditi provedba odgovarajućeg liječenja, kao i u bolesnika s negativnim nalazom testa na tuberkulozu koji imaju faktore rizika za tu bolest. Bolesnike treba pažljivo nadzirati zbog mogućeg razvoja znakova i simptoma tuberkuloze, uključujući bolesnike koji su prije početka liječenja imali negativan nalaz testa na latentnu tuberkulozu. **Ponovna aktivacija virusa** U kliničkim ispitivanjima lijeka Kevzara primijećeni su slučajevi herpesa zoster. U kliničkim ispitivanjima nisu prijavljeni slučajevi ponovne aktivacije virusa hepatitisa B; međutim, bolesnici u kojih je postojao rizik od ponovne aktivacije nisu bili uključeni u ispitivanja. **Laboratorijski parametri** **Broj neutrofila** Liječenje lijekom Kevzara bilo je povezano s višom incidencijom pada ABN-a. Pad ABN-a nije bio povezan s višom incidencijom infekcija. **Broj trombocita** U kliničkim ispitivanjima liječenje lijekom Kevzara bilo je povezano s padom broja trombocita. Pad broja trombocita nije bio povezan s događajima krvarenja. **Jetreni enzimi** Liječenje lijekom Kevzara bilo je povezano s višom incidencijom porasta vrijednosti transaminaza. U kliničkim ispitivanjima taj porast bio prolazan i nije doveo ni do kakvog klinički primjetnog oštećenja jetre. Ne preporučuje se započeti liječenje lijekom Kevzara u bolesnika s povišenim vrijednostima transaminaza, ALT-a ili AST-a više od  $1,5 \times$  GGN. U bolesnika u kojih je ALT  $> 5 \times$  GGN liječenje lijekom Kevzara treba prekinuti. Odstupanja u vrijednostima lipida Liječenje lijekom Kevzara bilo je povezano s porastom vrijednosti lipidnih parametara kao što su LDL-kolesterol, HDL-kolesterol i/ili trigliceridi. **Gastrointestinalna perforacija** Lijek Kevzara treba primjenjivati uz oprez u bolesnika koji u anamnezi imaju ulceracije crijeva ili divertikulitis. **Zloćudne bolesti** Utjecaj liječenja lijekom Kevzara na razvoj zloćudnih bolesti nije poznat, no zloćudne su bolesti prijavljene u kliničkim ispitivanjima. **Reakcije preosjetljivosti** Najčešće reakcije preosjetljivosti bile su osip na mjestu injiciranja, osip i urtikarija. **Oštećenje funkcije jetre** Ne preporučuje se liječenje lijekom Kevzara u bolesnika s aktivnom bolešću jetre ili oštećenjem funkcije jetre. **Cijepljenje** Treba izbjegavati istodobnu primjenu živih cjepiva kao i živih atenuiranih cjepiva tijekom liječenja lijekom Kevzara. Prije uvođenja lijeka Kevzara preporučuje se da svi bolesnici prime sva cjepiva predviđena važećim smjernicama za imunizaciju. **Kardiovaskularni rizik** Budući da bolesnici s RA imaju povećan rizik od kardiovaskularnih poremećaja, njihove faktore rizika treba liječiti u sklopu uobičajene standardne skrbi. **6. INTERAKCIJE S DRUGIM LIJEKOVIMA I DRUGI OBLICI INTERAKCIJA:** Citokini i modulatori citokina mogu utjecati na ekspresiju i aktivnost specifičnih enzima citokroma (CYP) P450 (CYP1A2, CYP2C9, CYP2C19 i CYP3A4). Povišene vrijednosti interleukina-6 (IL-6) mogu smanjiti aktivnost CYP enzima u bolesnika s RA i tako povisiti razine lijeka u odnosu na ispitanih koji nemaju RA. Blokada signalizacije putem IL-6 izazvana djelovanjem antagonista IL-6Ra, kao što je sarilumab, može neutralizirati inhibicijski učinak IL-6 i ponovno uspostaviti aktivnost CYP enzima te tako izmijeniti koncentracije lijekova. Nakon uvođenja ili prekida liječenja lijekom Kevzara u bolesnika koji se liječe supstratom CYP enzima potrebno je kontrolirati terapijski učinak (npr. varfarina) ili koncentraciju lijeka (npr. teofilina) i po potrebi prilagoditi dozu lijeka. Potrebno je oprez u bolesnika koji započnu liječenje lijekom Kevzara dok primjenjuju supstrate enzima CYP3A4 (npr. oralne kontraceptive ili statine). **7. PLODNOST, TRUDNOĆA I DOJENJE:** Žene reproduktivne dobi moraju koristiti učinkovitu kontracepciju tijekom liječenja i do 3 mjeseca po njegovu završetku. **Trudnoća** Nema podataka ili su podaci o primjeni sarilumaba u trudnica ograničeni. Kevzara se ne smije primjenjivati tijekom trudnoće, osim u slučajevima kada kliničko stanje žene zahtijeva liječenje sarilumabom. **Dojenje** Nije poznato izlučuje li se sarilumab u majčino mlijeko niti apsorbira li se sistemski nakon ingestije. Budući da se IgG1 izlučuje u majčino mlijeko, treba donijeti odluku o tome hoće li se prekinuti dojenje ili liječenje sarilumabom, uzimajući u obzir korist dojenja za dijete i dobrobit liječenja za ženu. **Plodnost** Nema dostupnih podataka o učinku sarilumaba na plodnost u ljudi. **8. UTJECAJ NA SPOSOBNOST UPRAVLJANJA VOZILIMA I RADA NA STROJEVIMA:** Kevzara ne utječe ili zanemarivo utječe na sposobnost upravljanja vozilima i rada sa strojevima. **9. NUSPOJAVE:** Vrlo često: neutropenija. Često: infekcija gornjih dišnih putova, infekcija mokraćnih putova, nazofaringitis, oralni herpes, trombocitopenija, hiperkolesterolemija, hipertrigliceridemija, povišene vrijednosti transaminaza, eritem na mjestu injiciranja, pruritus na mjestu injiciranja. **10. PREDOZIRANJE:** Dostupni su ograničeni podaci o predoziranju lijekom Kevzara. Ne postoji specifično liječenje za predoziranje lijekom Kevzara. U slučaju predoziranja potrebno je pažljivo nadzirati bolesnika i liječiti ga simptomatski te po potrebi uvesti potporne mjere. **11. FARMAKODINAMIČKA SVOJSTVA:** Farmakoterapijska skupina: imunosupresivi, inhibitori interleukina, ATK oznaka: L04AC14. **12. NOSITELJ ODOBRENJA:** sanofi-aventis groupe, 54, rue La Boétie, 75008 Paris, Francuska **13. BROJ(EVI) ODOBRENJA ZA STAVLJANJE GOTOVOG LIJEKA U PROMET:** EU/1/17/1196/001-012. **14. NAČIN I MJESTO IZDAVANJA:** Na recept, u ljekarni. Detaljnije informacije o ovom lijeku dostupne su na web stranici Europske agencije za lijekove <http://www.ema.europa.eu/>.

Ovo je skraćeni Sažetak opisa svojstava lijeka te sukladno Pravilniku o načinu oglašavanja o lijekovima (Narodne Novine broj 43/15) molimo prije propisivanja lijeka Kevzara pročitajte zadnji odobreni Sažetak opisa svojstava lijeka i Uputu o lijeku.





# SVAKI DAN

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ona preuzima odgovornost  
za svoju budućnost

Kineret<sup>®</sup> (anakinra) je indiciran u odraslih, adolescenata, djece i dojenčadi u dobi od 8 mjeseci i starije s tjelesnom težinom od 10 kg ili više za liječenje Stilllove bolesti, uključujući sistemski juvenilni idiopatski artritis (SJIA) i Stillovu bolest odrasle dobi (AOSD), s prisutnim sistemskim značajkama umjerene do visoke aktivnosti bolesti ili u bolesnika u kojih aktivnost bolesti traje i nakon liječenja nesteroidnim protuupalnim lijekovima (NSAIL) ili glukokortikoidima.



AOSD

## Kineret<sup>®</sup> 100 mg/0,67 ml otopina za injekciju u napunjenoj štrcaljki

Skraćena uputa za propisivanje. Molim pogledajte sažetak opisa svojstava lijeka (SPC) prije propisivanja

**Sastav:** Djelatna tvar je antagonist receptora humanog interleukina-1 (r-methHuL-1ra) proizveden na stanicama *E. coli* tehnologijom rekombinantne DNK. Svaka kalibrirana napunjena štrcaljka sadrži 1000 mg anakinre u 0,67 ml (150 mg/ml).

**Indikacije:** Kineret je indiciran za liječenje reumatoidnog artritisa, periodičnog sindroma povezanog s kriopirinom (CAPS) i Stilllove bolesti u odraslih, adolescenata, djece, dojenčadi u dobi  $\geq 8$  mjeseci i težine  $> 10$  kg, sam (SJIA) ili u kombinaciji s drugim DMARD-ovima (AOSD).

**Doziranje i način primjene (Stillova bolest):**

tjelesna težina  $\geq 50$  kg: 100 mg/dan  
tjelesna težina  $\leq 50$  kg: 1-2 mg/kg/dan

U djece s neodgovarajućim odgovorom dozu povisiti do 4 mg/kg/dan. U bolesnika s teškim oštećenjem bubrega ( $CL_{cr} < 30$  ml/min) ili u završnom stadiju bubrežne bolesti, uključujući dijalizu, Kineret primjenjivati svaki drugi dan. Kalibrirana napunjena štrcaljka omogućuje supkutanu primjenu doza od 20 do 100 mg.

Nije prikladno za pedijatrijske bolesnike tjelesne težine manje od 10 kg. Za jednokratnu primjenu. Ne trestil! Omogućiti da napunjena štrcaljka postigne sobnu temperaturu prije injiciranja.

**Kontraindikacije:** Preosjetljivost na djelatnu tvar, neku od pomoćnih tvari ili na proteine porijeklom iz *E. Coli*; neutropenija ( $ABN < 1,5 \times 10^9/l$ )

**Posebna upozorenja i mjere opreza pri uporabi:** **Alergijske reakcije** (anafilaktičke reakcije, angioedem) prijavljene su manje često. **Hepatički događaji** (neinfektivni hepatitis, akutno zatajenje jetre) zabilježeni su u prvom mjesecu liječenja Stilllove bolesti. Oprez je potreban u bolesnika s predisponirajućim čimbenicima ili onih koji razviju simptome koji upućuju na disfunkciju jetre. **Ozbiljne infekcije** zabilježene u bolesnika s RA uglavnom pogađaju dišni sustav. Infekcijama su sklonije osobe starije životne dobi. Liječenje Kineretom ne smije se započinjati u bolesnika s aktivnim infekcijama. Ako dođe do ozbiljne infekcije, liječenje Kineretom u bolesnika s RA treba prekinuti, a u bolesnika s CAPS-om razmotriti obzirom da postoji rizik ponovnog izbijanja bolesti. Kod pojave simptoma infekcije ili pogoršanja Stilllove bolesti može doći do **sindroma aktivacije makrofaga (MAS)**.

**Interakcije:** Konkomitantna primjena lijeka Kineret i etanercepta u bolesnika s RA povećava rizik od ozbiljnih infekcija i neutropenije te se ista ne smatra opravdanom. Obzirom da Kineret povećava raspoloživost CYP450 supstrata male terapijske širine (varfarin, fenitoin), potrebno je

terapijsko praćenje učinka i koncentracija u plazmi.

**Nuspojave:** U kliničkim ispitivanjima i postmarketinškom praćenju glavobolja, reakcije na mjestu primjene i povišeni kolesterol u krvi zabilježeni su vrlo često, a ozbiljne infekcije, neutropenija i trombocitopenija često, neovisno o indikaciji. Sigurnosni profil u pedijatrijskih bolesnika bio je sličan onomu u odrasloj populaciji te nisu primijećene klinički značajne nuspojave.

**Inkompatibilnosti:** Zbog nedostatka ispitivanja kompatibilnosti ovaj lijek se ne smije miješati s drugim lijekovima.

**Način izdavanja lijeka:** Lijek se izdaje na ograničeni recept.

**Broj(evi) odobrenja za stavljanje lijeka u promet:** EU/1/02/203/005-007.

**Pakiranje:** 1, 7 ili 28 napunjenih štrcaljki, u kutiji.

**Nositelj odobrenja za stavljanje lijeka u promet:** Swedish Orphan Biovitrum AB (publ), SE-112 76 Stockholm, Švedska. Lokalni predstavnik za Hrvatsku: Swedish Orphan Biovitrum s.r.o., Glavna podružnica Zagreb, Ulica Matka Baštijana 54, 10000 Zagreb.

**Broj dokumenta:** PP-4863

**Datum pripreme:** rujan 2018.



## SHORTENED SUMMARY OF PRODUCT CHARACTERISTICS<sup>1</sup>:

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

**Name of the medicinal product:** Cosentyx 150 mg solution for injection in pre-filled pen (secukinumab).  
**Therapeutic indications:** Plaque psoriasis: Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. Psoriatic arthritis: Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate. Ankylosing spondylitis: Cosentyx is indicated for the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy. **Posology and method of administration:** Plaque psoriasis: The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as two subcutaneous injections of 150 mg. Psoriatic arthritis: For patients with concomitant moderate to severe plaque psoriasis or who are anti-TNF $\alpha$  inadequate responders (IR), the recommended dose is 300 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as two subcutaneous injections of 150 mg. For other patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg. Ankylosing spondylitis: The recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. For all of the above indications, available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks. **Contraindications:** Severe hypersensitivity reactions to the active substance or to any of the excipients. Clinically important, active infection (e.g. active tuberculosis). **Special warnings and precautions for use:** Infections: Serious infections have been observed in patients receiving Cosentyx in the post-marketing setting. Caution should be exercised when considering the use of Cosentyx in patients with a chronic infection or a history of recurrent infection. Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and Cosentyx should not be administered until the infection resolves. Cosentyx should not be given to patients with active tuberculosis. Anti-tuberculosis therapy should be considered prior to initiation of Cosentyx in patients with latent tuberculosis. Inflammatory bowel disease: Cases of new or exacerbations of Crohn's disease and ulcerative colitis have been reported. Patients treated with Cosentyx, who have inflammatory bowel disease, including Crohn's disease and ulcerative colitis, should be closely monitored. Hypersensitivity reactions: In clinical studies, rare cases of anaphylactic reactions have been observed in patients receiving Cosentyx. If an anaphylactic or other serious allergic reactions occur, administration of Cosentyx should be discontinued immediately and appropriate therapy initiated. Latex-sensitive individuals: The removable cap of the Cosentyx pre-filled pen contains a derivative of natural rubber latex. Vaccinations: Live vaccines should not be given concurrently with Cosentyx. **Fertility, pregnancy and lactation:** Pregnancy: As a precautionary measure, it is preferable to avoid the use of Cosentyx in pregnancy. Breast-feeding: Because of the potential for adverse reactions in nursing infants from secukinumab, a decision on whether to discontinue breast-feeding during treatment and up to 20 weeks after treatment or to discontinue therapy with Cosentyx must be made taking into account the benefit of breast-feeding to the child and the benefit of Cosentyx therapy to the woman. **Undesirable effects:** Very common ( $\geq 1/10$ ): upper respiratory tract infections. Common ( $\geq 1/100$  to  $< 1/10$ ): oral herpes, rhinorrhoea, diarrhoea. Uncommon ( $\geq 1/1,000$  to  $< 1/100$ ): oral candidiasis, tinea pedis, otitis externa, neutropenia, conjunctivitis, urticaria. **Interaction with other medicinal products and other forms of interaction:** Live vaccines should not be given concurrently with Cosentyx. In a study in subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate). No interaction was seen when Cosentyx was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis). **Legal status:** Prescription medication. **Marketing authorization holder:** Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, Dublin 4, Ireland. For any information about this medicine, please contact the local representative of the Marketing Authorization Holder in your country. **Marketing authorization numbers:** EU/1/14/980/004-005, 007. **Note:** Before prescribing, please read latest approved Summary of Product characteristics and package leaflet. This promotional material contains essential information in line with the approved Summary of Product characteristics as defined by article 15. of the Ordinance on the Manner of Advertising Medicinal Products (Official Gazette No. 43/15).

Literature: 1. Cosentyx, Novartis Europharm Limited, latest approved Summary of Product characteristics 2. <http://www.ema.europa.eu/ema>



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SPONDYLITIS (AS)<sup>1</sup>



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