

emeu news

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ACR HIGHLIGHTS



ACR 2016 WASHINGTON

- Oral presentations and posters
- Mentor/Mentee meetings
- Networking event

EDUCATIONAL EVENTS

ACR/EULAR EXCHANGE PROGRAM

Dear young rheumatologists and researchers in rheumatology,

We are happy to present you a new issue of EMEUNews about the Highlights of this year's ACR annual meeting.

The ACR 2016 Congress was a great scientific event and in this issue we provide a selection of oral presentations and posters that have been presented in the various clinical and research areas of our discipline. The selection is totally personal and therefore very limited and incomplete, but it still might give an overview of hot topics that have been discussed in each field.

In addition we included impressions of the events organized by EMEUNET including the EMEUNET business meeting to discuss the activities and programs of our subgroups.

ACR Congress was also an opportunity to meet and an EMEUNET networking event was organized.

EMEUNET is now active in social media hubs such as Facebook and Twitter, while maintaining the traditional website and the important physical (and personal) presence at major Rheumatology scientific events.

If this is your first contact with EMEUNET, we invite you to explore more and join us. If you are already part of our community, we kindly remind you that sharing is caring. Spread the word about our activities and work, and help us reach more young rheumatologists and researchers.

We hope that you enjoy reading this Newsletter and would be happy to receive any comments or contributions for future issues.

We wish you relaxing and pleasant Christmas holidays.

Francesco Carubbi, Mike Becker, Richard Conway and Alessia Alunno

on behalf of the Newsletter Subgroup



DIRECTORY

ACR 2016: ORAL PRESENTATIONS & POSTERS

4

Basic Research I
 Basic Research II
 RA I
 RA II
 RA III
 Psoriatic Arthritis
 Axial Spondyloarthritis
 SLE and APS
 Other connective tissue diseases
 Imaging
 Crystal Arthropathies
 Osteoarthritis & Osteoporosis
 Pediatric Rheumatology
 Rare and Autoinflammatory Diseases

MENTOR MENTEE MEETINGS

17

IMPRESSIONS FROM ACR 2016

18

THE 2016 ACR/EULAR EXCHANGE PROGRAM

19

THE EULAR IMAGING COURSE

20

NEWS FROM SOCIAL MEDIA AND COUNTRY LIAISON

21

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Javier Rodriguez Carrio

MSc, PhD is a postdoctoral researcher at the University of Oviedo (Spain). His major research interests are focused on the role of the immune system in endothelial activation, lipoprotein dysfunction and early atherosclerosis development in rheumatic autoimmune diseases.

BASIC RESEARCH I & II

Genetics, cartilage/synovium, osteoimmunology, animal models, immunity, immunology

Javier Rodriguez Carrio

A number of epigenetic studies provided new clues on the underlying mechanisms of rheumatic diseases. **Ai et al (3119)** presented the results of the first genome-wide analysis of the transcriptome, methylome and histone marks in fibroblast-like synoviocytes (FLS) from RA. Combining three different approaches (gene expression by RNA-seq for differentially expressed genes, epigenetic modification of histones by ChIP-seq and DNA methylation analysis by Illumina chips), they identified 19 biological pathways including “Macrophages, Fibroblasts and Endothelial Cells in RA”, “JAK family kinases in IL-6-type Cytokine Signaling” and “Cytokine Regulation in Macrophages and Th Cells by IL-17A/F” which can provide a rationale for the development of novel therapeutic targets for drug discovery. Similarly, **Yau et al (3122)** presented a pioneer work of the genome-wide DNA methylation sites associated with hand osteoarthritis (OA). Performed on the Framingham Study Cohort, this study identified 7 methylated regions, none of them being previously linked to OA. This study suggests a role for some genes such as PARP3, IFFO1 or ARHGEF3 as potential players in OA pathogenesis. **Damen et al (69)** presented a very interesting poster analyzing the associations between genetic variants, lipid profiles and cardiovascular disease in RA. By studying the allelic distribution of a functional SNP on IL-32 promoter, they reported a positive association between HDL levels and the C allele. Further studies are warranted to understand its potentially protective role in CVD. On the other hand, **Batu et al (2036)** presented their results on the elucidation of the genetic basis of early onset SLE. Using a whole exome approach, different mutations on complement proteins (C1q, C1s/r) were identified in most of the cases. However, larger studies are needed to understand the biological significance of these variants as well as the potential as biomarkers. Osteoimmunology is a continuously growing field. In this congress, several related abstracts were presented. **Humphrey et al (2996)** revealed a pivotal role of TLR4 activation in the progression of OA upon high fat diet, thus proposing TLR4 inhibition as a therapeutic target in this scenario and proposing a mechanistic link between obesity, inflammation and OA. Using mice models of RA, **Sun et al (917)** found that B cells secrete osteoblast inhibitors and impaired osteoblast differentiation in vitro, NFkB pathway being involved. Therefore, B cells are directly involved in bone loss and joint

BASIC RESEARCH I & II

(continued)

erosion in RA, whereas B-cell directed therapy abrogated these mechanisms. **Kasper et al (3109)** provided new insight into the regulatory T cells (Treg) deficiencies in the context of autoimmune diseases. By means of a sophisticated design of transgenic mice, they demonstrated the central role of protein phosphatase 2A (PPA2) for the maintenance of these regulatory functions, as mice lacking this gene exhibited decreased Foxp3 expression (master Treg transcription factor) and acquired ability to produce IL-17 by Treg. Type I interferons have received a notable interest during this congress. On the one hand, **Antiochos et al (184)** identified the IFI16-STING-IRF3 pathway as candidate to explain the production of type I IFN in salivary glands from SS patients. **Cooles et al (185)** demonstrated a link between increased type I IFN expression in peripheral blood and poor clinical response in RA patients upon conventional DMARD treatment. Also, **Liu et al (1827)** expanded the current knowledge of the relevance of the type I IFN signature in SLE. A major topic in this congress was the microbiome and its connections with immunity and autoimmunity. In this sense, several authors have focused on the study of the microbiota and the immune dysfunction which underlies systemic rheumatic diseases. Using a mice model of RA (CIA), **Rogier et al (1915)** demonstrated a role for microbiota on IL-17 production, Th17 expansion and disease severity. Furthermore, no effect was observed in a T-cell independent mice model. The authors concluded that the intestinal microbiota are linked to an aberrant Th17 response, but elucidation of the actual mediators involved is needed. Similarly, **Bosello et al (1889)** presented an interesting study of the intestinal microbiota in SSc patients, both reporting an increase in the Firmicutes/Bacteroidetes ratio (the two most important bacterial taxa) as well as in several genera such as Lactobacillus, Roseburia and Faecalibacterium, thus strengthening previous findings in this field. Finally, Dr. Noah Palm (session “Autoimmunity and the microbiome”) performed an outstanding summary on the current trends in the analysis of the interactions host-microbiota. Through easy to understand, clear and concise slides (which I strongly recommend to revise in the congress App), he made an excellent overview on the elegant studies performed in their lab changing the analysis of the microbiome from a classical taxonomic-driven approach, towards a functional classification of the gut microbiota (IgA-SEQ approach). Although only tested in IBD until date, it is very likely we will soon hear on this novel approach in rheumatic diseases, which undoubtedly may shed new light on this continuously evolving field.



Diederick De Cock

PhD, is a Belgian epidemiologist currently working in Manchester, UK. His PhD focused on the efficacy of different intensive treatment strategies in early rheumatoid arthritis in the context of the Flemish CareRA trial. His post-doctoral work focuses on safety of biological therapy in more established rheumatoid arthritis. His other areas of interest are steroid safety and treatment delay.

RA I

Epidemiology, clinics and non biologics

Diederick De Cock

One of the highlights of this year's ACR was the Great Debate on tapering biologic therapy. Professor Emery stated that tapering was possible in both early and late disease. He focused especially on early disease, suggesting that if all patients, even those with moderate disease activity would be treated intensively from the start, tapering would form no problem and most patients would stay in remission. Also the favorable cost effectiveness was given as a benefit from tapering early in disease. On the other hand, Professor Kavanaugh saw the glass half empty. Tapering will leave a minority of patients as more difficult to treat while before disease was controlled in these patients. Moreover, he underlined the current inability to predict who can be tapered and cannot. In daily practice, this is not acceptable, he argued. **Bergstra et al (953)** showed another advantage of treating intensively early in the disease course. Ten year follow up in the BeST trial demonstrated that more patients achieved persistent low disease activity on initial combination therapy with prednisone or infliximab than on MTX monotherapy. However, rapidly achieving remission or low disease activity itself seems more crucial for determining long-term outcome in RA than treatment choice. On the same day, **Gross et al (1040)** showed the more the patient experienced stress, the greater was the risk of developing RA. Clinicians should look for stressful life events in the history-taking of patients with early arthritis. **Meißner et al (1993)** demonstrated in a nested case control study that the risk of stroke in RA patients in the German biologics register RABBIT may be driven by precedent serious adverse events requiring hospitalization. In addition, untreated cardiovascular disease was a significant risk factor for a future stroke. A better management of comorbidities is needed in RA patients. A randomized controlled trial presented by **Park et al (2054)** revealed that short-term discontinuation of MTX improves the immunogenicity, and hence the efficacy of seasonal influenza vaccination in RA patients. A descriptive study by **Druce et al (3067)** tried to unravel treatment decisions following cancer diagnosis in patients receiving TNFi in the British biologic register BSRBR-RA. These decisions were highly variable and differed by the site of cancer diagnosis. Patients with longer survival were more likely to continue or restart a biologic. If biologics were restarted, most patients started an alternative class of drug.



Alessia Alunno

MD, is a Rheumatologist and PhD candidate at the Rheumatology Unit, University of Perugia, Italy. Her main interests are Sjögren's syndrome, rheumatoid arthritis and autoantibodies. She is a member of the EULAR Study Group on Sjögren's syndrome and one of the founders of the Italian Study Group on research in Sjögren's syndrome (GRISS). Alessia is the leader of the EMEUNET Newsletter Subgroup.

RA II

Biological therapies: anti-TNF

Alessia Alunno

Despite the high amount of data about biologic therapies in RA, head-to-head comparisons are still very few. **Frisell et al (597)** reported data from the Nationwide Swedish Register 2010-2015 about all patients (n° 6149) receiving an anti-TNF agent as first line biologic therapy. The purpose of the study was to identify possible differences among different compounds but all the anti-TNF agents evaluated (infliximab, adalimumab, etanercept, certolizumab, golimumab) showed comparable efficacy as assessed by the EULAR response and a similar retention rate. Another study aimed at head-to-head comparison was reported by **Fleischmann et al (602)** who evaluated the efficacy and safety of switching between certolizumab pegol and adalimumab after primary anti-TNF failure. The EXXELERATE trial is an investigator-blind head-to-head superiority study and at 104 weeks no differences in efficacy and safety could be detected in certolizumab failure switched to adalimumab versus adalimumab failure switched to certolizumab. Furthermore, the immediate switch without washout did not increase the rate of adverse events. In this context, **Lopez Olivo et al (617)** performed a systematic review and meta-analysis of randomized controlled trials about therapy in rheumatoid arthritis patients with inadequate response to anti-TNF agents. Currently available data support the concept that the failure of one anti-TNF does not necessarily imply the failure of other anti-TNF agents, therefore switching to another anti-TNF is an option to consider as an alternative to the change of mechanism of action. **Tesser et al (625)** performed an interesting post hoc analysis of the GO-FURTHER trial to investigate possible differences in response to golimumab plus methotrexate according to age (>65 years versus younger patients). Clinical response, retention rate and safety profile were comparable in patients >65 years compared to younger patients. The prevalence of concomitant steroid treatment resulted similar in the 2 groups but the dose was slightly higher in younger patients. Therefore, this therapeutic strategy may be employed in clinical practice independently of patients' age. However, as pointed out by **Tweehuysen et al (633)** the cytokine profile in golimumab treated patients is similar to that of adalimumab treated patients. This may at least in part explain why golimumab was found to be less effective after adalimumab failure compared to biologic naïve patients.



RA III

Other biologics and new drugs beyond biologics

Jan Leipe

Jan Leipe

MD, board-certified rheumatologist, has completed specialist training in rheumatology and general internal medicine and is currently an attending physician at University of Munich, Germany. His major research interests include early rheumatoid arthritis and the role of T cells in the pathogenesis of autoimmune arthritis.

Fleischman et al (650) and **Genovese et al (3225)** presented data from phase II trials and an open label extension phase on dual cytokine inhibition with ABT-122, a bispecific antibody targeting TNF α and IL-17, in active RA. After 12 weeks (RCT) and 24 weeks (OLE) the highest dose of ABT-122 (120mg every other week, eow) showed a trend towards higher ACR70 response compared to standard dose adalimumab (40mg eow), however, the differences were not statistically significant. Of note, no safety signals were observed with ABT-122, proving for the first time in a RCT a combination cytokine blockade to be safe. Although the authors stated that Abbvie will not move on to phase III trials, data from this study might lead to a revival of combination biologic therapies, given that it seems safe (after this field was abandoned following increased SAEs with a combination of abatacept and etanercept). Another presentation by **Weinblatt et al (1619)** was remarkable since efficacy data from phase IIb study investigating mavrilimumab, a GM-CSF receptor α antibody, in active RA, in comparison to golimumab were shown for the first time (EARTH EXPLORER 2). This is the first treatment directly targeting macrophages as an important cell in synovial inflammation. Whereas in DMARD-IR (DMARD inadequate responders) mavrilimumab 100 mg eow demonstrated slightly lower ACR responses compared to golimumab, results were comparable between the two agents in the TNF-IR. Importantly, no safety signals were observed for mavrilimumab (which was a concern when the studies were started since macrophages are of importance for the defense against bacterial infections). The presenting author mentioned that the dose used in the current trial might be not appropriately high since 100 mg mavrilimumab demonstrated suboptimal efficacy when compared to 150 mg in the EARTH EXPLORER 1 trial. **Taylor et al (3222)** presented efficacy and safety data from a phase III trial of sirukumab, an anti-IL-6 antibody, compared with adalimumab monotherapy in biologic-naïve, active RA. Efficacy of sirukumab at week 24 was higher compared to adalimumab for DAS28 (ESR), but not for ACR20 response. Safety of sirukumab was comparable to adalimumab. Finally **Behrens et al (954)** reported data on the first RCT evaluating a therapy regimen with rituximab in combination with leflunomide versus leflunomide alone. As expected, the combination of rituximab and leflunomide was superior indicating that leflunomide can be used in combination with rituximab when methotrexate is ineligible.



PSORIATIC ARTHRITIS

Antonis Fanouriakis

Antonis Fanouriakis

MD, completed his residency in Internal Medicine and Rheumatology in 2014 and is currently working as a consultant rheumatologist in "Attikon" University Hospital of Athens. He has completed a MSc program in Molecular Medicine and his thesis on neuropsychiatric systemic lupus erythematosus, both in the University of Crete. His scientific interests focus on systemic autoimmune diseases, mainly pathogenesis and treatment of SLE

Regarding treatment of psoriatic arthritis (PsA), **Mease et al (958)** presented the results of a phase II study regarding the use of a TNF α and IL-17 dual inhibitor as the first biologic agent in PsA patients with incomplete response to methotrexate. ABT-122 was superior to placebo and similar to adalimumab in most outcomes, including ACR20 and PASI90, with an acceptable safety profile. In a phase IIa study of guselkumab, a monoclonal Ab against IL-23, **Deodhar et al (4L)** reported a 40% difference in ACR20 responses compared to placebo (58% vs. 18%), and similar responses in other parameters, without significant safety concerns. Similar results were shown in a phase 3 study of tofacitinib in PsA patients with incomplete response to anti-TNF agents presented by **Gladman et al (10L)**, as well as in a similar study of abatacept in biologic-naïve active PsA by **Mease et al (1041)**.

In an interesting real-life observation, **Metyas et al (1725)** reported their experience on combining apremilast with a biologic agent in PsA, in terms of safety and, secondarily, efficacy. The authors found no increased safety issues in 22 patients treated with such a combination, albeit with the limitation of a relatively short follow-up (mean 8 months).

In the field of pathogenesis, **Baldwin et al (3040)** described an interesting observation, wherein the recruitment of Th17 cells in vitro in the synovial fluid of active PsA patients is peculiarly promoted by regulatory T-cells, in striking contrast to what is observed in the healthy state. **Giles et al (3098)** identified a specific major histocompatibility class I haplotype to be associated with the development of a devastating complication of PsA, arthritis mutilans, indicating that particular subtypes within this disease may actually be guided by genetic determinants.

Coates et al (3095) compared different definitions of low disease activity in PsA, in an effort to identify the most suitable target for a "treat-to-target" approach in the disease. The authors found that Very Low Disease Activity (VLDA, defined as fulfilling all criteria for minimal disease activity of the TICOPA study) is more stringent than remission variants of DAPSA and thus, closer to true remission.



AXIAL SPONDYLOARTHRITIS

Alexandre Sepriano

Alexandre Sepriano

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Outcomes-research was on the spotlight at this year ACR. Several, high quality, studies assessing long-term outcome in patients with axial spondyloarthritis (axSpA) with special focus on imaging outcomes and predictors thereof (including therapy) were presented. **Gensler et al (1956)** presented an elegant longitudinal analysis from a large (N=527) observational cohort of axSpA patients fulfilling the modified New York criteria (mNY). This analysis has shown a lower radiographic progression (mSASSS) in those under TNFi treatment vs those not under TNFi in patients with a high NSAID intake over a mean follow up of 4 years. Another (smaller) observational cohort also including axSpA patients fulfilling the mNY, by **Maas et al (724)** has shown that spinal radiographic progression tends to decrease over time (non-linear course) in patients under TNFi. Data from a long-term extension of a clinical trial (RAPID-axSpA) presented by **van der Heijde et al (1042)**, has also shown that spinal radiographic progression is larger during the first 2 years as compared to the subsequent two, both in patients with non-radiographic axSpA (nr-axSpA; mNY-negative) and radiographic axSpA (r-axSpA; mNY-positive or ankylosing spondylitis). This trial further demonstrated how difficult it is to ascertain radiographic sacroiliitis changes over time, as apparently a similar number of patients progressed from nr-axSpA to r-axSpA as in the opposite direction. Alternative imaging techniques to assess the sacroiliac joints (SIJ) and spine in patients with axSpA have been proposed. **Baraliakos et al (682)** has shown computerized tomography (CT) and magnetic resonance imaging (MRI) superiority over conventional radiographs in detecting structural changes in the SIJ in patients with r-axSpA. While **Lambert et al (3159)** assessed the detection of SIJ structural lesions on MRI against CT; and **Bruin et al (3160)** has shown impressive reliability of 'low-dose CT' in detecting syndesmophytes in the whole spine of patients with r-axSpA. Early and reliable detection of imaging abnormalities may promote early diagnosis and timely institution of therapy, which has been shown by **Sieper et al (735)** to increase the likelihood of response to TNFi. **van der Heijde et al (1045)** presented the 2016 Update of the ASAS-EULAR Management Recommendations for Axial Spondyloarthritis that for the first time target the entire spectrum of axSpA (nr-axSpA and r-axSpA). In the same line, **Sieper et al (712)** contributed to the increasing body of evidence showing similar response to TNFi between patients with r-axSpA and nr-axSpA especially in those with objective signs of inflammation (either elevated CRP and/or sacroiliitis on MRI) for the latter group.



SLE AND APS

Katja Lakota

Katja Lakota

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Two abstract analyzed risk factors for thrombosis in APS patients and suggested physicians to control for those additional risk factors to evaluate the risk of thrombosis re-occurrence by calculating a thrombotic risk score. **Unlu et al (1072)** showed that patients with thrombotic APS (571 patients from 24 centers) have a higher frequency of hypertension, hyperlipidemia, obesity and a sedentary lifestyle as compared to only obstetric APS or asymptomatic aPL carriers. **Žigon et al (2093)** evaluated 585 patients with autoimmune inflammatory rheumatic diseases and found that, besides conventional risk factors, also BMI, hyperlipidemia, arterial hypertension, thrombocytopenia and oral contraceptive use along with LA, aCI (IgG, IgA), anti-β2 GPI (IgG, IgA) and aPS/PT (IgG, IgM, IgA) significantly associated with thrombotic risk. **Van den Hoogen et al (2087)** confirmed that type I IFN signature is present in monocytes of APS patients albeit in lower extent than in SLE and accordingly to a reported decreased frequency of pDC. Concordant with type I IFN induced signaling the first GWAS performed on two cohorts of primary APS by **Gensterblum et al (1961)** that found a genetic association between common autoimmunity locus STAT4 and APS and identified HLA-DQA1 and PLEK (pleckstrin) as susceptibility locuses for APS. Furthermore RNA seq of neutrophils performed by **Knight et al (1962)** showed overexpression of IFN regulated genes, TLR signaling pathway and adhesion molecules (where they identified PSGL as required for APS IgG mediated acceleration of thrombosis in a mouse model). However, analysis of T and B cell subsets using flow cytometry by **Hisada et al (2089)** found Th2 cells increased and decreased resting Treg and memory B cells in APS (the same work also reports association between decreased post-switch B memory and TLR7 SNP rs3853839, the SNP found to be associated with extent of type I IFN signature in SLE). **Ruff et al (920)** showed that gut microbiome, specifically *Roseburia intestinalis*, could be the trigger for autoreactivity via cross-reactivity for major APS antigen β2-GPI and β2-GPI of specific memory CD4+ T cells that recognize the domain V epitope and may bind APS derived β2-GPI anti-domain I monoclonal antibodies. Two abstracts presented by **Lopez-Pedreira et al. (2099)** suggest crucial role of deregulated miRNA and miRNA biogenesis related molecules found in neutrophils and monocytes of APS and SLE. In vitro aPL-IgG and anti-dsDNA were able to reproduce those perturbations in levels of miRNA and miRNA biogenesis related molecules and monocyte transfection with downregulated pre-miR-124a and miR-125a decreased expression of molecules involved in atherothrombotic process in APS and SLE.



OTHER CONNECTIVE TISSUE DISEASES

Including systemic sclerosis, myositis, vasculitis

Barbara Ruaro

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MD, works in the Division of Rheumatology at the University of Genoa and currently is a PhD applicant in Immunology. Her main interest area focuses on connective tissue diseases.

In their work **McMahan et al (974)** demonstrate that male sex, diffuse cutaneous disease, and myopathy are significantly associated with severe systemic sclerosis gastrointestinal dysmotility.

In their abstract **Namas et al (3248)** show that systemic sclerosis patients treated with mycophenolate mofetil and cyclophosphamide have a significant improvement from baseline in mRSS in the subset of patients with dcSSc over a 24-month period. **Hsu et al (972)** conducted a large prospective study of systemic sclerosis patients at risk for pulmonary hypertension (inclusion criteria: echocardiogram systolic pulmonary arterial pressure >40mmHg, or diffusion lung capacity of carbon monoxide < 55% predicted or ratio of % forced vital capacity/ lung capacity of carbon monoxide > 1.6 measured by pulmonary function testing). Though survival was better than those with incident pulmonary hypertension, male sex, low lung capacity of carbon monoxide, exercise oxygen desaturation and pericardial effusion, were similarly associated with worse outcomes. The retrospective work of **van Roon et al (1867)** shows that systemic sclerosis-like nailfold capillary microscopy pattern is common in connective tissue disease patients and appears to be associated with a greater prevalence of organ involvement. The authors underline the importance of assessing nailfold capillary microscopy in Raynaud's phenomenon patients to evaluate the risk for organ involvement in connective tissue disease other than systemic sclerosis, already in early stages of the disease. **Ali et al (1928)** demonstrate that a significant percentage of the very elderly patients can benefit from immunosuppression therapy for anti-neutrophil cytoplasmic antibody associated vasculitis, despite the higher risks of adverse effects from these medications. **Castro et al (2669)** in their study have evaluated biological treatments in primary Sjögren's syndrome. They reported the absence of clinical controlled studies demonstrating efficacy and safety, biological frequently used in patients with primary Sjögren syndrome. The most widely used biological agent is rituximab. Its use is associated with the presence of musculoskeletal, neurological, pulmonary and haematological manifestations, hospitalization for disease activity and a high EULAR Sjogren's syndrome disease activity index. **Delli et al (2685)** demonstrate that ultrasound of the major salivary glands is reliable in diagnosing Sjögren's syndrome. The authors observed that some discrepancies between observers there might be in assessing the severity of ultrasound findings. In conclusion they advised that patient is scored by the same ultrasonographer at every time point.



Joanna Zalewska

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IMAGING

Joanna Zalewska

Møller-Bisgaard et al (934) investigated the predictive value of baseline MRI inflammatory and damage parameters on 2 year MRI and X-ray damage progression in an early RA cohort following a non biologic treat-to-target strategy. This trial reports that MRI joint space narrowing independently predicts both X-ray and MRI damage progression in early RA. In the authors' opinion further studies are needed to confirm early MRI-determined cartilage damage as predictor of progressive joint destruction in RA. **Ammitzbøll-Danielsen et al (1973)** compared the efficacy of intramuscular versus ultrasound (US)-guided peritendinous glucocorticoid injection in providing disease control after 2, 4 and 12 weeks in rheumatoid arthritis patients with tenosynovitis. Fifty RA patients with tenosynovitis were randomised into two double-blind groups: "intramuscular group, receiving intramuscular injection of betamethasone and US-guided peritendinous isotonic saline injection and "peritendinous group" receiving saline intramuscularly and US-guided peritendinous betamethasone injection. In a result, in this randomised double-blind clinical trial, RA patients with tenosynovitis responded significantly better to US guided peritendinous glucocorticoid injection than to intramuscular glucocorticoid injection, both at 4 and 12 weeks follow up. The first *in vivo* demonstration of TNF abundance in erosive OA was undertaken by **Wittoek et al (3200)**. They investigated the uptake of radiolabeled Certolizumab pegol in patients with erosive OA and study associations with other markers of active disease. They found strong associations with presence of clinical swelling. The strongest association with TNF was found in the remodeling phases. Salivary gland dysfunction is one of the most common features of Sjögren' syndrome. **Garcia-Gonzalez et al (3201)** aimed to describe glandular involvement patterns and quantitative scintigraphic indices, mainly excretion fraction (EF%). They have also compared diagnostic accuracy of scintigraphic indices and biopsy of salivary glands. Patients fulfilling SS criteria showed lower submandibular EF% compared to those who do not. In the authors' opinion diagnostic accuracy of submandibular EF% is better than qualitative sSC and similar to biopsy. **Martire et al (3202)** evaluated the characteristics of joint involvement in a cohort of patients with systemic sclerosis assessed by clinimetric and ultrasonographic (US) measures. 40 consecutive patients with systemic sclerosis were included. The US findings were: 47.5% of patients presented at least one finding by ultrasound, 32.5% proliferative synovitis grade II in the radiocarpal joint and 2.5% grade III. They underline that the joint involvement in systemic sclerosis was frequent, evaluated both clinically and by ultrasound. This manifestation should be considered in daily care in patients with systemic sclerosis.



METABOLIC AND CRYSTAL ARTHROPATHIES

Richard Conway

Richard Conway

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There are significant opportunities for broader health interventions in gout patients due to the frequent occurrence of unidentified co-morbid conditions. **Ordoñez et al (233)** again highlighted the high frequency of unidentified cardiovascular co-morbidities in this population, with screening revealing at least one previously unknown co-morbidity in half of patients. **Rai et al (3125)** reported that the premature mortality gap that exists in gout patients has not improved over the past 16 years, in contrast to rheumatoid arthritis, highlighting the need for improved management of gout and its co-morbidities in this population. One factor contributing to this persistent premature mortality is the suboptimal interaction between this patient group and health services in general. **Khanna et al (3130)** report the development of a novel web-based educational tool designed to address the educational needs of this population. Dual energy computed tomography allows quantification of tophus burden, a better marker of the total body urate burden than serum urate. **Ellmann et al (3128)** demonstrated the potential utility of this modality in monitoring the response to urate lowering therapy. Concern over potential adverse events can lead to unnecessary avoidance of effective treatment options. The risk of myopathy associated with colchicine, in particular in patients co-prescribed other agents such as statins, has been a worry. **Kwon et al (1013)** presented evidence from over 600 Korean patients treated with colchicine demonstrating no evidence of an increased risk of myopathy in patients taking statins. The optimal use and safety of allopurinol in severe chronic kidney disease and in particular in haemodialysis patients remains to be defined. **Doogue et al (3129)** demonstrated that oxypurinol, the active metabolite of allopurinol, is cleared by haemodialysis to an extent similar to a patient with normal renal function. The implications of this are two-fold, firstly that allopurinol should be administered post-dialysis, and secondly that the reluctance to use allopurinol in this patient population may be unfounded. Finally they demonstrated a rapid decrease in serum urate post-dialysis, followed by an increase to baseline over 42 hours, suggesting that serum urate samples should be drawn prior to haemodialysis. The short half-life of anakinra has limited its potential application as an intra-articular treatment for gout flare. **Pancoast et al (3076)** presented preliminary evidence of a novel matrix-binding interleukin-1 receptor antagonist fusion which had extended residence while retaining potency.



OSTEOARTHRITIS AND OSTEOPOROSIS

Ida Haugen

Ida Haugen

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Dietary fiber reduced risks of metabolic diseases in part by reducing systemic inflammation and body weight. These factors are both likely to contribute to causing osteoarthritis (OA). **Zhaoli et al (1018)** used data from the Osteoarthritis Initiative, which is a prospective longitudinal cohort of 4796 men and women with or at risk of knee OA. Self-reported dietary total fiber was inversely associated with incident symptomatic knee OA and pain worsening, partially mediated through reduced BMI. The strongest association was found at the highest quartile of fiber intake, which is in line with the recommended daily fiber of 25 grams for Americans. The purpose of meniscus repair, beyond short time symptom relief and restoration of knee biomechanics, is to reduce the risk of later knee OA. However, the long-term consequences of meniscus repair have not been sufficiently investigated. In a Swedish healthcare register, **Englund et al (1022)** found that the point estimates of knee OA suggested about 20-50% lower risk of knee OA in patients after meniscus repair as compared to patients with acute meniscus repair. However, the consultation rate for OA after repair was still at least 2.5 times higher as compared to the general population. OA and diabetes commonly co-occur. Potential explanations include common risk factors (aging, obesity) or the effects of OA-related disability on diabetes risk factors (e.g., sedentary behavior exacerbating metabolic syndrome). In a large population-based cohort, **Kendzierska et al (1019)** explored the associations between baseline knee and hip OA (based on joint symptoms) and subsequent incident diabetes as with data from health administrations. After controlling for multiple confounders, the presence and burden of hip and knee OA was a significant independent predictor of incident diabetes, which was explained largely by OA-related walking limitation. Pain is a major symptom in hand osteoarthritis (OA), and many patients use analgesics. Patients with OA who do not respond to conventional analgesics may have 'sensitization', or heightened pain symptoms which are centrally mediated. **Sofat et al (3131)** performed a prospective, randomized, double-blind, placebo-controlled trial from 42 primary care and rheumatology clinics in the UK and 85 participants with symptomatic clinical hand OA were recruited. Pregabalin 300 mg was significantly more effective in improving pain and function after 12 weeks compared with duloxetine or placebo and may be an alternative for OA pain in sensitized patients. **Conaghan et al (3134)** presented data from the HERO study, in which 243 persons with symptomatic and radiographic hand OA were randomized to hydroxychloroquine (HCQ) or placebo for 12 months. HCQ was not more effective than placebo in reducing symptoms or radiographic progression in persons with moderate to severe hand pain and radiographic OA, and HCQ can therefore not be recommended for this patient group.



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PEDIATRIC RHEUMATOLOGY

Alberto Sifuentes

Simonini et al (950) assessed the risk for flares after discontinuing biological therapy in a retrospective, multicenter study that included 135 juvenile idiopathic arthritis (JIA) patients (103 females; median age 15 years) treated with their first cycle of biologics (87 etanercept, 27 adalimumab, 12 infliximab, 7 anakinra, 1 rituximab, 1 abatacept) who achieved remission and could discontinue them. Patients with positive ANA test and those who stopped treatment before 2 years of remission had a higher chance of relapsing. The probability of maintaining remission was higher in patients with systemic-onset JIA and enthesitis-related arthritis (ERA).

Horneff et al (3010) presented the results of a 48-week, randomized, placebo-controlled trial (24-week open label period followed by 24-week randomized double-blind withdrawal period) on efficacy of etanercept in ERA. Etanercept was highly effective on peripheral disease as well as on spinal inflammation; a high rate of patients achieved JADAS remission, BASDAI 50, BASFI50, no spinal pain and no tender enthesitis points after 24 weeks of treatment. However, the study was underpowered to demonstrate differences between etanercept and placebo at week 48.

Although the main indication for anti-TNF therapy is JIA, 2 studies demonstrated the efficacy of these drugs in other autoimmune/autoinflammatory disorders. **Campanilho-Marques et al (1364)** evaluated the efficacy and safety of anti-TNF agents in 67 patients with juvenile dermatomyositis (61% females, median age at beginning of anti-TNF 10.1 years, median disease duration 3.2 years) included in a UK Cohort. Both muscle (CMAS and MMT8 values) and skin involvement significantly improved after anti-TNF treatment. **Ombrello et al (3207)** assessed the ability of anti-TNF treatment to reduce the number of ischemic attacks in patients with deficiency of adenosine deaminase type 2 (DADA2). They included 22 DADA2 patients, 15 of them with a history of ischemic stroke, and found that anti-TNF agents were highly effective in reducing stroke risk (recurrence rate 0) and improving acute phase reactants levels.

The potential role of Pentraxin 3 (PTX3) in patients with juvenile scleroderma was assessed by **Adrovic et al (2386)**. They compared 24 patients with juvenile systemic sclerosis (JSS) and 20 with juvenile localized scleroderma (JLS) with 41 health controls. Mean serum level of PTX3 were significantly higher in JSS (10.63 ± 8.61 ng/ml) and JLS (11.75 ± 9.11 ng/ml) compared to healthy children (2.76 ± 1.338 ng/ml) ($p < 0.001$), but no significant difference between JSS and JLS. There also was a positive correlation of PTX3 level with the modified Rodnan skin score in JSS patients ($Rho = 0.497$, $p = 0.030$).



RARE AND AUTOINFLAMMATORY DISEASES

Paul Studenic

Paul Studenic

MD, is a medical resident and clinical research fellow at the division of rheumatology of the Medical University Vienna in Austria. His main interests are outcomes assessment in RA and PsoA, patient reported outcomes, predictors of disease activity, biomarkers and elderly patients.

Yamada et al (241) presented the results of a retrospective observational study on the prevalence of malignancies in patients with immunoglobulin G4-related diseases (IgG4-related diseases). IgG4-related diseases comprise a collection of disorders, that share similar pathologic, clinical and serological findings. These diseases are increasingly diagnosed and linked together but evidence on all features of the disease as well as treatment is lacking. In 18 of 84 patients malignancies before or after the diagnosis of IgG4-related disease was identified. The most prevalent were colon cancer, lung cancer and lymphoma. No specific differences between patients with or without malignancies could be found. **Hoffman et al (255)** highlighted the long-term follow-up safety and efficacy of canakinumab in patients with Cryopyrin-associated periodic syndromes (CAPS), analysed from the Beta-Confident registry. This is the largest registry for canakinumab, following up patients for at least one year. The median follow-up time was 4.3 years for 288 patients and 1114 adverse events were reported in 223 patients, most commonly infections and infestations. After analysis of this registry data, no new safety signals for canakinumab were picked up and it supported data on long term efficacy of canakinumab.

Brito-Zerón et al (3081) reported their data of the REGHEM registry about prognostic factors for patients with hemophagocytic syndrome and risk of death. 61 of 116 patients died and survival was significantly limited in males with neoplasia, severe cytopenia and high ferritin. Furthermore, patients with chronic infections as the underlying illness had the best survival, whereas those with neoplasia the poorest. **Lim et al (236)** presented their findings of intrathoracic manifestations of IgG4-related diseases. Although pancreatitis, retroperitoneal fibrosis and salivary gland involvement are the most common features, all organs can be involved. This study of Lim et al. focused on pathological findings of the lung in a cohort of 143 patients and found 27 patients, with involvement of pleura or lung. Despite a wide variety of identified pathologies and a strong burden of these, many patients were relatively asymptomatic. In a part of the patients, records on response to rituximab were available and 10 of 11 patients treated with rituximab improved or attained stable disease. **Ungprasert et al (260)** showed that patients with sarcoidosis are at higher risk for cardiovascular disease compared to a sex and age-matched comparison group, when adjusting for life style and classic risk factors of cardiovascular disease.

THE MENTOR-MENTEE MEETINGS AT ACR 2016

The 7th mentor-mentee meeting was held with a great success at the ACR 2016 in Washington. We had 2 excellent mentors (Prof. Ronald van Vollenhoven and Prof. Margreet Kloppenburg) and 8 mentees. Below some feedback from the participants:

“I found it a very fun and informal meeting with an important individual in the rheumatology community. It was good to talk to him in a 1v1 way with a lot of time and hear about his career and his ideas of science.”

“I really enjoyed the Mentor-Mentee meeting. I feel it is an ideal platform to get exposed to the insights of established scientist and rheumatologist in the field. It is a safe place to ask any question you find relevant and to verify your ideas with a specialist that is not your direct supervisor. I really enjoyed talking with Prof van Vollenhoven”



Your EMEUNET Peer Mentoring Subgroup

THE EMEUNET NETWORKING EVENT AT ACR 2016

Our networking activities did not stop on the other side of the ocean. More than 40 EMEUNET members participated to our meet-up. We had a social gathering at the Penn Social Bar, a truly American sports bar. Below you can see some highlights from the night. We are looking forward to the next EMEUNET social event for the EULAR 2017 in Madrid 14-17 June 2017 SAVE THE DATE!

Your EMEUNET Visibility Subgroup



EMEUNET members leaving the conference together



At the Penn Social

EMEUNET @ TWEET-UP MEETING AT ACR 2016

American Rheumatologists have established a two-monthly journal club on twitter and EMEUNET is contributing to these brilliant discussions with rheumatology researchers world-wide. At the ACR, Paul Studenic and Diederik de Cock from the EMEUNET Social Media Subgroup had the opportunity to meet the twitter community and this time to discuss and talk in person as an alternative.



THE 2016 ACR-EULAR EXCHANGE PROGRAM

This year's ACR/EULAR Exchange program in Washington was hosted by Prof. Richard Siegel, Director of the National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIAMS) at the NIH in Bethesda. Ten enthusiastic researchers had the possibility to visit the NIAMS, present their own research, listen to the lectures of brilliant senior researchers and discuss face-to-face with them.



HERE IS THE OPINION OF SOME PARTICIPANTS:

"The ACR/EULAR Exchange program in Washington was a brilliant experience. The team of rheumatology fellows were a great mix of researchers doing clinical, epidemiological and basic research. I found it very easy to interact and got both new ideas and new potential collaborators. Also, the senior hosts and invited speakers were all highly influential researchers but still took their time to sit down and give good advice, and we were even invited for a private dinner. Thanks to the ACR and EULAR for arranging this program" (*Tue Kragstrup, Denmark*)

"I consider the ACR/EULAR Exchange program a great opportunity to interact with colleagues from other centers in Europe and USA and to get the chance to establish collaborations. It was a fascinating experience to visit the NIH, get to know the ongoing research and listen to presentations from experts in the field. It was a truly inspiring experience. (*Katerina Chatzidionysiou, Sweden*)

"I would recommend the ACR/EULAR Exchange program to every researcher in rheumatology. Not only you meet the American experts in their field in a formal and informal manner, but you also meet like minded researchers out of Europe! Great and inspiring experience" (*Diederick De Cock, Belgium, United Kingdom*)

"It was a huge experience to take a part in the ACR/EULAR Exchange program and I am very honored I could visit NIH. Lectures from senior researchers were brilliant, very informative and interesting. Also the presentation from exchange program colleagues were versatile, interesting and inspiring. We were also rewarded with a tour around the National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIAMS) at NIH" (*Polona Žigon, Slovenia*)

"Inspiring, fascinating and contagious research environment, excellent networking opportunity, an opportunity to not miss. If you are a young researcher in rheumatology, try to not miss the opportunity to join the ACR/EULAR Exchange program, even if you need to apply more than once, it's worth it!" (*Sofia Ramiro, Portugal/The Netherlands*)

"A friendly environment where worldwide renowned American senior researchers share their experience with young European colleagues and give them the opportunity to present their own research. I was fascinated by the visit to the National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIAMS) at NIH and I strongly recommend to apply for the program and take the chance to be involved in such an inspiring experience " (*Alessia Alunno, Italy*)

THE EULAR IMAGING COURSE



For Rheumatology trainees and Rheumatologists, this is a comprehensive new course on conventional radiography, magnetic resonance (MR), computerized tomography (CT) and ultrasonography (US). The course will further focus on lectures and workshops. The lectures will convey the possibility of questions and interactive discussion with the faculty in the end. The workshops will consist of interactive learning and practical training, discussing clinical cases and images (some of which selected from participant's applications).

This course aims to enrich the current EULAR educational curriculum, being useful for both the basic and the advanced training of any Rheumatologist, either involved in clinical practice, clinical or translational research.

Registration requires participants applying for the course to send 5 radiography pathology images, 3 MR pathology images, 2 CT scan pathology images and 3 ultrasound pathology images

**The 1st EULAR Imaging Course will take place on
30 March-1 April 2017 in Lisbon, Portugal**

EULAR grants 5 bursaries at 600 EUR each

For more information and to register: http://www.eular.org/eular_imaging_course.cfm

EMEUNET GOES LINKEDIN

We are proud to announce that EMEUNET now is on LinkedIn, the biggest professional network worldwide. EMEUNET LinkedIn was 'born' on the 25th October and we have already 156 connections (as of 30th November 2016). It is a wonderful way to stay in touch with international colleagues and friends! So why not sign up and get connected?'



EMEUNET AT THE ITALIAN SOCIETY OF RHEUMATOLOGY CONGRESS

The Italian Society of Rheumatology (SIR) national meeting was held on 23-26 November 2016 in Rimini, Italy. We had for the third year a Session for Young Rheumatologists where a lecture on how to conduct a systematic literature review was held and young fellows engaged in a national Master degree reported their experience. In addition, we reported about the growth of our Italian Young Rheumatologists Group since we established it at last year's Congress. During the session, several young rheumatologists joined our group that is now including over 150 people. EMEUNET was highlighted in this session as a powerpoint presentation was given to explain aims and organization of EMEUNET and to encourage young Italian rheumatologists to join our expanding network. EMEUNET flyers were also circulated to provide attendees with all information at a glance.

Sara Monti, EMEUNET Country Liaison for Italy
Alessia Alunno, EMEUNET Working Group member

