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Helsinki Cathedral with harbor view and the Scandic Marina Congress Center located on waterfront.

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ABSTRACTS

ORAL PRESENTATIONS

THURSDAY SESSION

Pain in arthritis patients

OP01

Unacceptable, refractory pain despite inflammation control in early rheumatoid arthritis and its relation to treatment strategy: results from the randomized controlled SWEFOT trial

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Objectives: Pain is a major concern of rheumatoid arthritis (RA) patients and earlier work has defined the level considered not acceptable by patients [unacceptable pain according to the patient acceptable symptom state (PASS)] (1). The aim of this study was to investigate the prevalence of unacceptable pain despite inflammation control during the first 2 years after treatment start in new-onset RA patients and to compare the impact of biological vs conventional combination therapy on the occurrence of this pain state.

Methods: The SWEFOT (SWedish FarmacOTherapy) trial was designed as a randomized, active-controlled, open-label study, enrolling early [40 mm (1–100) with C-reactive protein < 10 mg/L (2) and ≤ 1 swollen joint (of 28)]. Differences in prevalence were analysed by McNemar’s test, while differences between patients randomized to infliximab (IFX) vs sulphasalazine (SSZ) + hydroxychloroquine (HCQ) as well as between EULAR response groups were estimated by logistic regression, adjusting for age, gender, and visual analogue scale (VAS) pain at baseline.

Results: In the whole material (including all three groups, n = 405), the frequency of unacceptable pain despite inflammation control increased gradually from inclusion, reached 12% at 1 year (difference from inclusion; p < 0.001), and then remained stable until the 2 year follow-up; at that point accounting for more than half of all unacceptable pain (Figure OP01). The frequency was unrelated to EULAR response from inclusion to the 2 year follow-up (11.4% of good responders vs 10.4% of non-responders, p = 0.95). Furthermore, no difference in unacceptable pain despite inflammation control at 2 years was found between patients randomized to IFX versus SSZ + HCQ (adjusted odds ratio 1.1, 95% CI 0.5–2.4; p = 0.75).

Conclusions: After 2 years of early active treatment in new-onset RA patients, a substantial portion had unacceptable pain despite inflammation control. This pain status was as common in EULAR good responders as in non-responders, and no difference was found in patients randomized to IFX compared to SSZ + HCQ. These data are in line with insufficient effects of current treatment strategies to prevent development of inflammation-independent pain in a subgroup of patients, strongly warranting alternative treatment strategies in these patients.

References


FRIDAY SESSIONS

Systemic lupus erythematosus

OP02

Systemic lupus erythematosus subgroups, with features of antiphospholipid or Sjögren’s syndrome, differ in molecular signatures and treatment perspectives

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Objectives: Previous studies and our own clinical observations of patients with systemic lupus erythematosus (SLE) suggest that SLE harbours distinct immunophenotypes/subgroups. Based on these experiences, we explored biochemical pathways in two predefined SLE subgroups and in controls to further characterize these subgroups and identify biomarkers for personalized medicine.

Methods: Our cross-sectional study includes 378 well-characterized SLE patients and 316 individually matched population controls. Based only on patients’ autoantibody profile, we selected a core of an anti-phospholipid-like SLE subgroup (aPL-positive, n = 66) and a Sjögren’s syndrome-like SLE subgroup (SSA/SSB positive, n = 63). Carefully selected proteins (n = 281) were analysed by affinity-based proteomics and complementary immunoassays in the entire cohort. The predicting performance of proteins was evaluated by receiver operating characteristics (ROC) curve analysis.

Results: The protein with the highest predicting power (ROC, area under the curve = 0.89) for separating the aPL-positive and SSA/SSB-positive SLE subgroups was integrin beta-1 (ITGB1) and was detected at higher levels in the SSA/SSB-positive subgroup. Proteins with the lowest p-values comparing the two suggested SLE subgroups were ITGB1, SLC13A3, and CERS5, and were all increased in the SSA/SSB-positive subgroup. Complement activation was more pronounced in the aPL-positive subgroup, and biomarkers indicating systemic inflammation, i.e. fibrinogen, α1-antitrypsin, neutrophils, and triglycerides, were significantly increased in this subgroup.

Conclusions: Our observations indicate underlying pathogenic differences between SSA/SSB-positive and aPL-positive SLE. Stratification of SLE patients could be a way forward to understanding the underlying pathophysiology and to improve selection of patients for treatment, clinical trials, and drug development.

Genetics and gene expression

OP03

Widespread regulation of gene expression by glucocorticoids in chondrocytes from osteoarthritis patients as determined by next generation sequencing-based genome-wide expression analysis

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Objectives: In osteoarthritis (OA), chondrocytes display changes in their gene expression profile. Glucocorticoids (GCs) can counteract some of the harmful changes, and intra-articular GC injections are widely used in the treatment of OA. However, there are also concerns about their potentially harmful effects, and their comprehensive effects on chondrocytes remain poorly understood. We carried out a genome-wide expression analysis on the effects of GCs in OA chondrocytes.

Methods: Chondrocytes were isolated from cartilage obtained from OA patients undergoing knee replacement surgery. The cells were cultured with or without the GC dexamethasone for 24 h. Total mRNA was sequenced, and functional analysis was performed against the Gene Ontology (GO) database. We also separately studied the 54 genes linked to OA in genome-wide association studies (1, 2), and the 19 genes found to be differentially expressed in OA affected vs preserved cartilage in genome-wide expression analysis (RAAK study) (3).

Results: In dexamethasone-treated chondrocytes, 896 genes were downregulated and 685 upregulated in a statistically significant manner with a fold change > 2.0. In the GO analysis, genes involved in inflammation, cell proliferation and adhesion, extracellular matrix organization, collagen catabolism and anabolism, and lipid and glucose metabolism were enriched among the significantly affected genes. Of note was the downregulation of several matrix-degrading enzymes and pro-inflammatory factors, but also cartilage-specific collagens. Conversely, several anti-inflammatory and anti-oxidative genes were upregulated. Notably, 11 of the 54 genes linked to OA in GWAS were significantly affected by dexamethasone. Also, two of the 19 genes identified to be upregulated in OA vs normal cartilage in the RAAK study were downregulated by dexamethasone.

Conclusions: The results indicate that GCs regulate the expression of a wide range of genes in OA chondrocytes. In addition to clear anti-inflammatory and anti-catabolic effects, GCs affect lipid and glucose metabolism in chondrocytes, an observation that may be particularly important in the metabolic phenotype of OA.
References


OP04

Shared and unique patterns of DNA methylation in primary Sjögren’s syndrome and systemic lupus erythematosus

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Objectives: Epigenetic modifications have emerged as contributory factors in the pathogenesis of primary Sjögren’s syndrome (pSS) and systemic lupus erythematosus (SLE). In the current study we investigated DNA methylation in healthy controls and in patients with pSS and SLE with the aim of identifying shared and unique methylation signatures in pSS and SLE.

Methods: DNA extracted from blood from 100 patients with pSS, 347 with SLE, and 400 healthy blood donor controls was analysed on the HumanMethylation 450k array, targeting 485 000 CpG sites across the genome. The logistic regression model included age, gender, and cell type distribution as covariates, and differentially methylated CpG sites (DMCs) were defined as p < 1.3 × 10−5 for association based on Bonferroni correction and an absolute average difference in methylation beta of Δβ > 0.05.

Results: Differential DNA methylation between patients with pSS compared to SLE was identified at 2227 CpG sites, where the majority of DMCs showed increased methylation in pSS compared to SLE. In pSS we typically found methylation levels which were intermediary to those of healthy individuals and patients with SLE; for example at CpG site cg21549285 located in the promoter region of the MX1 gene, where controls had an average methylation level of 0.83, patients with SLE showed distinctly decreased methylation (β = 0.40) and in-between levels were observed for patients with pSS (β = 0.57). We further noted that hypomethylation at interferon-induced genes in pSS was mainly driven by patients who were positive for Sjögren’s syndrome antigen A/B (SSA/SSB) antibodies (average β at cg21549285 in MX1 of 0.49 compared to 0.79 for antibody-negative patients). Analysis of methylation variation unique for pSS identified a DMC at the proteasome subunit beta type 8 gene (PSMB8, p = 1.8 × 10−9) with decreased methylation in pSS, while no differential methylation between patients with SLE and controls was found at this CpG site.

Conclusions: Comparative analyses of DNA methylation between pSS and SLE facilitates identification of shared and unique molecular patterns across systemic inflammatory autoimmune diseases. Our results suggest variation in DNA methylation in pSS as a starting point for development of pSS-specific biomarkers.

Spondylarthritis and seronegative arthritis

OP05

Low rates of major adverse cardiac events, malignancies, and serious infections in subjects with psoriasis and psoriatic arthritis treated with apremilast for ≥ 156 weeks: pooled analysis from the ESTEEM and PALACE 1–3 phase 3 trials

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Objectives: Apremilast (APR), an oral phosphodiesterase-4 (PDE4) inhibitor, was effective in phase 3, randomized, placebo (PBO)-controlled trials in moderate to severe plaque psoriasis (ESTEEM 1 and 2) and psoriatic arthritis (PsA) (PALACE 1–3). We report on major advanced cardiovascular events (MACE), malignancies, and serious infections (SIs; opportunistic and non-opportunistic) in subjects receiving apremilast (APR) 30 mg b.i.d. (APR30) for ≥ 156 weeks in a pooled analysis.

Methods: Incidence rates and exposure-adjusted incidence rates (EAIRs)/100 subject-years of MACE, malignancies, SIs, and serious opportunistic infections (SOIs)

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are reported for 0 to 16 weeks, 0 to ≤ 52 weeks, and the APR exposure period (0 to ≥ 156 weeks) for subjects receiving APR30 during the studies until February 2015; ~30% of subjects received > 3 years of exposure.

Results: In total, 2242 subjects were included in safety analyses for 0 to 16 weeks [PBO n = 913, subject-years exposure (sy) = 260.2; APR30 n = 1329, sy = 377.8]; 1905 received APR30 during the APR exposure period (3527.5 sy). Exposure during 0 to ≤ 52 weeks was 1524.5 sy. At baseline, 64.2% of APR30 subjects with PsA (PALACE 1–3) were receiving concomitant disease-modifying anti-rheumatic drugs, including methotrexate.

Table OP05.

<table>
<thead>
<tr>
<th>Treatment period</th>
<th>APR exposure period</th>
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<tr>
<td>0 to ≤ 52 weeks</td>
<td>APR exposure period</td>
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<tr>
<td>Relationship</td>
<td>0 to ≥ 156 weeks</td>
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<tr>
<td>Cumulative events*</td>
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<td>APR30 (n = 1905)</td>
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<td>Subject-years</td>
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<td>Subject-years</td>
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Major adverse cardiac events†
- Acute myocardial infarction 0.1 0.1
- Myocardial infarction 0.1 0.1
- Subarachnoid haemorrhage 0.1 0.1
- Cardiac arrest 0.0 0.1
- Cerebral infarction 0.0 0.1

Malignancies
- Haematological 0.0 0.1
- Non-melanoma skin cancer 0.9 0.5
- Solid tumours† 0.3 0.4

Serious infections
- Pneumonia 0.75 1.0
- Urinary tract infection 0.1 0.1
- Appendicitis 0.1 0.1
- Diverticulitis 0.1 0.1
- Sepsis 0.0 0.1
- Bronchitis 0.0 0.1

*Each subject’s total exposure is defined as the time interval between the date of the first and last doses of APR30, regardless of when treatment was initiated, until February 2015.
†No adjudication of major adverse cardiac events for the APR exposure period.
‡Including malignant melanoma.
§Serious infections occurring in subjects included pneumonia (n = 2), urinary tract infection (n = 2), appendicitis (n = 1), and diverticulitis (n = 1).
||Serious infections occurring in at least subjects included pneumonia (n = 5), appendicitis (n = 3), bronchitis (n = 3), diverticulitis (n = 2), sepsis (n = 2), and urinary tract infection (n = 2).

APR30, apremilast 30 mg b.i.d.; EAIR, exposure-adjusted incidence rate.

MACE incidence with APR30 was low and comparable to PBO during 0 to 16 weeks (PBO-controlled period). During 0 to ≤ 52 weeks and the APR-exposure period, MACE incidence remained low (Table OP05). EAIRs/100 subject-years of haematological malignancies, non-melanoma skin cancers, and solid tumours were similar with PBO (0.0, 1.2, 0.4) and APR30 (0.0, 1.3, 0.3) during 0 to 16 weeks; rates remained low during 0 to ≤ 52 weeks and the APR exposure period (Table OP05). During 0 to 16 weeks, SI rates with APR30 were low and comparable to PBO; no SOIs were reported. During 0 to ≤ 52 weeks, the overall SI rate was low (0.6%; EAIR/100 subject-years: 0.7). The SI rate remained low (1.8%; EAIR/100 subject-years: 1.0) during long-term cumulative APR exposure (0 to ≥ 156 weeks) (Table OP05). No clustering of any event was noted with respect to SIs. No clinical reactivation of tuberculosis was reported (0 to ≥ 156 weeks). The rate of marked haematological abnormalities remained low with long-term APR exposure.

Conclusions: The incidence of MACE, malignancies, and SIs was low in subjects with psoriasis and PsA receiving APR30 for ≥ 156 weeks. No new safety signals or SOIs were observed.

Innate immunity in arthritis

OP06

Apremilast specifically inhibits interleukin-12/interleukin-23p40 production in human arthritic ex vivo models

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Objectives: Apremilast (Otezla®) is a phosphodiesterase-4 (PDE4) inhibitor approved for the treatment of psoriasis and psoriatic arthritis (PsA), but the reason why apremilast shows clinical effect in PsA is not fully understood. The objective of this study was to study the downstream effects of apremilast on cells of the inflamed joint in ex vivo models of immune-mediated inflammatory arthritis.

Methods: Synovial fluid was obtained from a study population consisting of patients with active rheumatoid arthritis, PsA, or peripheral spondyloarthritis with at least one swollen joint (n = 18). Synovial fluid mononuclear cells (SFMCs) cultured for 48 h were used to study the effect of apremilast and the tumour necrosis factor-α (TNF-α) inhibitor adalimumab on secretion of a large panel of cytokines, chemokines and growth factors. Further, we used fibroblast-like synovial cells (FLSs), SFMCs cultured for 21 days (inflammatory osteoclastogenesis and macrophage differentiation), an osteoclast pit formation assay, and a mineralization assay.
Results: In SFMCs cultured for 48 h, apremilast decreased the production of interleukin (IL)-12/IL-23p40 (the shared subunit of IL-12 and IL-23) (p < 0.00001), colony stimulating factor 1 (p = 0.009), CD6 (p = 0.03), CD40 (p = 0.04), and monocyte chemoattractant protein-1 (p = 0.02), and increased the production of C-X-C motif chemokine 5 (p = 0.003) dose dependently. Further, apremilast had a very different response signature compared with adalimumab, e.g. with a much greater inhibition of IL-12/IL-23p40 (p = 0.01) and less inhibition of IL-8 (p = 0.0001) (Figure OP06). In SFMCs cultured for 21 days apremilast increased the secretion of IL-10 (p = 0.04) and in FLS cultures apremilast decreased matrix metalloproteinase-3 production (p = 0.005). Apremilast decreased osteoclast pit formation but did not change mineralization by human osteoblasts.

Conclusions: This study reveals the downstream effects of apremilast in ex vivo models of arthritis with a strong inhibition of IL-12/IL-23p40. Our findings could explain some of the efficacy of apremilast seen in IL-12/IL-23-driven immune-mediated inflammatory diseases such as psoriasis and PsA.

OP07

Mitogen-activated protein kinase phosphatase-1 (MKP-1) as a target of anti-inflammatory drug treatment: anti-inflammatory effects of the glucocorticoid dexamethasone are mediated by MKP-1 in murine models

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Objectives: Rheumatoid arthritis and other chronic inflammatory diseases are characterized by a prolonged and uncontrolled inflammatory response. Mitogen-activated protein (MAP) kinases are a major signalling pathway in inflammation, upregulating the expression of inflammatory genes and the immune response. MAP kinase phosphatases (MKPs) are also activated in inflammation, and they negatively regulate MAP kinases by dephosphorylation to suppress and limit inflammatory responses. MKP-1 is the best characterized member of MKPs, and its expression has been shown to be upregulated by glucocorticoids. In the present study, we investigated the role of MKP-1 as a mediator of the anti-inflammatory effects of glucocorticoids.

Methods: The effect of dexamethasone on carrageenan-induced paw inflammation was studied in MKP-1-deficient (knockout, KO) and wild-type (WT) mice. In addition, suppression of inflammatory gene expression by dexamethasone was investigated in peritoneal macrophages and cartilage explants from WT and MKP-1 KO mice as well as in murine H4 chondrocytes in which MKP-1 was downregulated with siRNA.

Results: Carrageenan-induced paw inflammation was more severe in MKP-1 KO mice than in WT mice. Dexamethasone significantly suppressed the inflammatory response in WT mice but its effect was considerably impaired in MKP-1 KO mice. Following stimulation with lipopolysaccharide, the expression of inflammatory genes interleukin-6 (IL-6) and inducible nitric oxide synthase (iNOS) was higher in peritoneal macrophages and cartilage explants from WT and MKP-1 KO mice as well as in murine H4 chondrocytes in which MKP-1 was downregulated with siRNA.

Figure OP06. Secretion of interleukin-12 (IL-12)/IL-23p40 and IL-8 by synovial fluid mononuclear cells (SFMCs) cultured for 48 h untreated (UT) or treated with DMSO control, apremilast, or adalimumab. Data are presented as normalized protein expression (NPX) values, which is an arbitrary unit on log2 scale. A decrease of 1 NPX corresponds to a two-fold decrease in concentration. *p < 0.05, ***p < 0.001, ****p < 0.0001.
expression of inflammatory/catabolic factors IL-6 and matrix metalloproteinase-3 in murine chondrocytes. **Conclusions:** The results reveal the significant mediator role of MKP-1 in the anti-inflammatory effects of the glucocorticoid dexamethasone in murine models and underline the potential of MKP-1 as a target of anti-inflammatory drug development.

## Hyperuricaemia and gout

**OP08**

The challenges of managing gout in primary care: results of a best practice audit

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**Objectives:** The majority of gout management occurs in primary care and may be suboptimal. While community-based clinical trials have reported improvements, whether such improvements can be replicated in routine clinical care is unknown. The aim of this study was to determine the effects of a package of care (POC) for gout in a real-life primary care setting.

**Methods:** A POC was developed reflecting current gout management guidelines including patient education, a structured approach to the management of gout flares and urate-lowering therapy (ULT), and screening for comorbidities. An audit of gout management in a single rural general practice was undertaken before (2012) and after (2015) introduction of the POC.

**Results:** In 2012, 120 people with gout and in 2015 171 people with gout were identified. After the introduction of the POC, more people with gout were prescribed ULT [79/120 (65.8%) vs 127/171 (74.5%); p = 0.12] and there was a significant increase in the median (IQR) number of prescriptions per individual over the 12 month period [1 (0–4) vs 3 (0–4); p < 0.001] (Figure OP08). There was a significant increase in the number of individuals commenced on allopurinol ≤ 100 mg daily and a corresponding decrease in the number commenced on ≥ 200 mg daily (p < 0.001) (Figure OP08). There was a significant increase in the frequency of urate testing between 2012 and 2015 [(median (range) 1 (0–3) vs 2 (0–10), respectively; p < 0.001). Of those individuals who had at least one urate measurement, the proportion of individuals who never achieved target urate reduced from 43/67 (64.2%) in 2012 to 52/133 (39.1%) in 2015 (p = 0.001). With the exception of smoking, screening for important comorbidities improved significantly after introduction of the POC.

**Conclusions:** A structured POC can improve gout management in primary care, although allopurinol dose escalation remains challenging.

## The past and present of clinical rheumatology

**OP09**

Less pain over two years with biological compared to conventional combination therapy in early rheumatoid arthritis: results from the randomized controlled SWEFOT trial

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Pain course in the different treatment groups. SSZ, abstracts

**Objectives:** Pain is a common and debilitating feature of rheumatoid arthritis (RA) and a level > 40 mm on a visual analogue scale (VAS) of pain (scale 0–100 mm) has been suggested as a measure of unacceptable pain (1). The aim of this study was to investigate pain development and unacceptable pain over 2 years after the start of biological compared to conventional combination therapy in early RA patients.

**Methods:** The multicentre SWEFOT (SWedish FarmacO Therapy) trial was designed as a randomized, active-controlled, open-label study, enrolling new-onset RA patients. Unacceptable pain (> 40 mm) at 2 year follow-up and area under the curve (AUC) for VAS pain were used as outcome measures. Statistical analyses were performed by logistic regression for unacceptable pain and analysis of covariance for AUC for VAS pain, adjusting for age, gender, and VAS pain at randomization.

**Results:** The study enrolled 487 RA patients, of whom 258 [who did not respond sufficiently to methotrexate (MTX)] were randomly allocated to either addition of infliximab (IFX) (n = 128) or sulphasalazine (SSZ) + hydroxychloroquine (HCQ) (n = 130). Baseline characteristics were similar between the two groups. Of the patients assigned to IFX, 32% had unacceptable pain at 2 year follow-up (21 months after randomization), while the same figure for SSZ + HCQ (n = 130) was 45% (adjusted odds ratio 0.41, 95% CI 0.23–0.73; p = 0.003). Serial VAS pain measurements are displayed in the Figure OP09. An AUC analysis for mean VAS pain levels from randomization to 2 year follow-up confirmed significantly lower levels for patients randomized to IFX compared to SSZ + HCQ (p = 0.01).

**Conclusions:** Despite early active treatment, a large share of new-onset RA patients showed unacceptable pain after 2 years. Both the fraction of patients with unacceptable pain and assessment of pain over time were substantially lower for patients randomized to addition of IFX compared to SSZ + HCQ, contrasting with earlier SWEFOT reports where significant between-group differences at 2 year follow-up for disease activity and health-related quality of life were not seen (2, 3). This suggests a better effect on long-term pain for the biological therapy, which could be taken into account when choosing treatment strategy in patients responding insufficiently to MTX.

**References**


**OP10**

Pain-associated factors and administration of pain medication in the elderly Finnish population

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**Objectives:** The overall consensus among professionals has long highlighted underassessment and undertreatment/mistreatment of persistent pain in the elderly (1). The aim of this public-based study was to examine Finnish seniors’ self-reported pain severity and interference and their association with demographic factors, life habits, obesity, and morbidity. Administration of pain medication was of particular interest.

**Methods:** This cross-sectional substudy of the Good Ageing in Lahti region (GOAL) cohort study, in which...
questionnaire-provided data from aged citizens were collected in a 10 year follow-up (2002–2012), focused on the endpoint data from 2012. In total, 1420 seniors aged 62–86 years answered questions regarding intensity and interference due to experienced pain during the previous month. Additional questionnaire-provided, clinical, and blood sample data were scrutinized. Data regarding administration of pain medication during the previous and following 6 months were retrieved from the national prescription database.

**Results:** The vast majority of seniors had endured pain. Four groups were formed based on both pain intensity and interference: group I (moderate to very severe pain, moderate to extreme harm caused by pain) to group IV (no pain at all, no harm at all). Low socio-economic status, obesity, and depression were found to independently associate with pain intensity and interference. During the scrutinized time interval, 84% had used some pain medication, 77% had used non-steroidal anti-inflammatory drugs (NSAIDs) (92% in group I, 70% in group IV), and opioids were liberally used in all pain groups (52% in group I, 23% in group IV).

**Conclusions:** Low socio-economic status, obesity, and depression were found to independently associate with pain intensity and interference. This public-based study showed that the majority of seniors had experienced pain despite the ample administration of analgesic drugs. NSAID administration was remarkable in all pain groups and opioids were commonly used among participants in pain. These results underline the importance of increasing attention of medical professionals to pain management in the elderly, especially considering the non-pharmacological modalities.

**Reference**


**OP11**

**Validity of polymyalgia rheumatica diagnoses and classification criteria in primary healthcare**

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**Objectives:** Polymyalgia rheumatica (PMR) is an inflammatory disorder that mainly affects elderly women, and usually is diagnosed in primary healthcare (PHC). The ACR/EULAR classification criteria (1) were developed in a cohort of patients recruited from rheumatology clinics. The objective was to examine the validity of PMR diagnoses in primary care, and to validate the use of classification criteria for PMR in a retrospective survey of a PHC cohort. **Methods:** All patients at two PHC centres with a registered diagnosis of PMR between 2000 and 2013 were identified (N = 305). Electronic case records were reviewed up to June 2015. Patients with a diagnosis of PMR prior to 2000, or at another care facility, and those with an incorrectly registered PMR diagnosis code, were excluded. In a structured review of the case records, information required for classification according to the ACR/EULAR criteria and several other criteria sets (Table OP11) was extracted. For the ACR/EULAR criteria, a modified version, in which patients who had never been tested for rheumatoid factor and anti-citrullinated protein antibody only required 2 points to be classified as having PMR, was used. The reference method was an independent review, with assessment of the long-term disease course and differential diagnoses, by an experienced rheumatologist.

**Results:** Among 188 with an incident PMR diagnosis at the study sites during the study period, 49 (26%) fulfilled the modified ACR/EULAR criteria, whereas greater proportions fulfilled the Bird criteria and the Healey criteria (Table OP11). The PMR diagnosis was verified using the reference method in 60% of cases overall, and in 84% of patients fulfilling the modified ACR/EULAR criteria, with lower proportions for the Bird criteria (2) and the Healey criteria (3) (Table OP11).

**Conclusions:** In this study of patients with PMR diagnosed in PHC, the diagnosis could be verified in 60% of the patients. This underlines the heterogeneity of PMR patients and related diagnostic procedures in PHC. A modified version of the ACR/EULAR criteria can be used to identify patients with a valid PMR diagnosis in retrospective surveys, but does not capture all PMR patients. The modified ACR/EULAR criteria appear to be more stringent than some of the older criteria sets.

**References**


| Table OP11. Characteristics of patients with a new diagnosis of polymyalgia rheumatica in the study, by fulfilment of classification criteria. |
|---------------------------------|-----------------|-----------------|-----------------|
|                                | Fulfilled         | Fulfilled         | Fulfilled         |
|                                | ACR/EULAR criteria | Bird criteria    | Healey criteria  |
| n (%)                          | All              | 49 (26)          | 145 (77)         | 93 (49)          |
| Female gender                  | 75%              | 70%             | 73%             | 70%             |
| Age at diagnosis (years)       | 75.8 ± 9.9       | 74.4 ± 7.8      | 78.8 ± 8.7      | 74.5 ± 9.8      |
| Verified by reference method   | 60%              | 84%             | 66%             | 74%             |

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Patients with psoriatic arthritis who are not eligible for randomized clinical trials for tumour necrosis factor inhibitors have similar treatment response and drug survival

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Objectives: We have recently reported that a majority of patients with psoriatic arthritis (PsA) who are being treated with tumour necrosis factor inhibitors (TNFi) would not have been eligible for randomized clinical trials (RCTs) (1). The most common reasons for exclusion are insufficient numbers of swollen joints (45%) and various comorbidities (16%). Here, we seek to determine whether patients with PsA who did not fulfill the inclusion criteria (group B) in RCTs receive similar benefits and drug survival from TNFi as patients who would have fulfilled the inclusion criteria (group A).

Methods: The ICEBIO registry covers 98% of all patients with PsA treated with biological originator disease-modifying anti-rheumatic drugs (boDMARDs) in Iceland (2). On 1 February 2016, there was information on 1058 individuals in ICEBIO, of whom 329 had PsA. Of the 274 patients receiving TNFi, 231 received first line treatment and could be classified according to the inclusion criteria of the respective pharmaceutical RCT (1). Information on disease activity at baseline [visual analogue scale pain/global, swollen and tender joint counts (SJC and TJC), Disease Activity Score based on 28-joint count–C-reactive protein (DAS28-CRP), and Health Assessment Questionnaire (HAQ)] was collected and we estimated the treatment response at 6 months (90–210 days) and 18 months (211–570 days) according to American College of Rheumatology 20% response (ACR20) and DAS28-CRP. We also analysed the drug survival rate.

Results: The groups were similar at baseline, although group A predictably had higher SJC (5.5 vs 3.8) and subsequently higher DAS28-CRP (4.6 vs 4.2). Out of 231 patients, we had sufficient data to determine ACR20 and DAS28-CRP response in 92 and 91 patients, respectively. Treatment response was better in group A with regard to HAQ and SJC (Table OP12), while drug survival was similar (Figure OP12).

Conclusions: Patients with PsA who would not have fulfilled the inclusion criteria in RCTs seem to respond to treatment effectively and have similar drug survival to patients who would have been included in RCTs. Thus, treatment outcomes for PsA from RCTs may probably be applied to daily clinical practice, whether patients would have fulfilled RCT criteria or not. However, more detailed long-term studies are needed on this issue.

References


Signal transduction pathways in arthritis

OP13

Transient receptor potential ankyrin-1 (TRPA1) as a novel factor in osteoarthritis: TRPA1 ion channel mediates monosodium iodoacetate (MIA)-induced acute inflammation and contributes to the development of cartilage degradation and joint pain in the MIA model of osteoarthritis

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Objectives: Intra-articular injection of monosodium iodoacetate (MIA) induces joint pathology mimicking osteoarthritis (OA) and is a widely used experimental model of OA. Transient receptor potential ankyrin-1 (TRPA1) is a cation channel which mediates nociception and neurogenic inflammation. It is activated by exogenous irritants but also by mediators formed in inflammation. We addressed the significance of TRPA1 in OA by investigating its role in MIA-induced acute inflammation and experimental OA.

Methods: Experimental OA was induced by MIA injection into the mouse knee at two doses (37.5 and 500 µg). Joint pain was estimated by weight-bearing tests weekly up to 4 weeks and final cartilage degradation was assessed histologically. The responses between wild-type (WT) and TRPA1-deficient (knockout, KO) mice were compared. Acute inflammation was induced by an MIA (400 µg) injection into the paw. Inflammatory oedema was measured with a plethysmometer up to 6 h. The paw tissue was analysed for substance P release. WT mice were compared to the TRPA1 blocker TCS5861528-treated and TRPA1 KO mice. The effects of the H\textsubscript{2}O\textsubscript{2}-decomposing enzyme catalase, the substance P receptor antagonist L703,606, and the control drug dexamethasone were studied.

Results: In the weight-bearing test, both doses of MIA caused spontaneous joint pain in the WT mice, whereas the effect was blunted in the TRPA1 KO mice. Also, the higher dose of MIA caused cartilage degradation in the WT mice, but not in the TRPA1 KO mice. MIA injection into the paw caused an acute inflammatory oedema, which was attenuated by TRPA1 blocker treatment and in the TRPA1 KO mice. Levels of substance P were measured as it mediates many of the inflammatory effects of TRPA1. MIA injection increased the substance P levels in the inflamed paw tissue in the WT mice, but much less in the TRPA1 KO and WT mice receiving TRPA1 blocker. As expected, the inflammatory response was attenuated with catalase treatment as H\textsubscript{2}O\textsubscript{2} is an endogenous TRPA1 activator.

Conclusions: TRPA1 mediates the acute MIA-induced inflammation in a substance P-dependent manner and contributes to the subsequent cartilage degradation and joint pain. Hence, TRPA1 could be a potential mediator and drug target in OA.

Myositis and myopathy

OP14

Anti-Jo1-positive myositis patients display a specific immunoglobulin G Fc-glycan profile which is further enhanced in anti-Jo1 autoantibodies

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Objectives: Immunoglobulin G (IgG) Fc-glycans affect IgG function and are altered in autoimmune diseases and autoantibodies. Anti-histidyl tRNA synthetase autoantibodies (anti-Jo1) are frequent in myositis associated with interstitial lung disease (ILD). We tested whether total IgG Fc-glycans from Jo1+ vs Jo1− myositis patients and anti-Jo1-IgG showed characteristic differences, and whether particular Fc-glycan features could be associated with specific clinical manifestations.

Methods: Total IgG was isolated by affinity purification from serum of 44 myositis patients (19 Jo1+ and 25 Jo1−) and 24 age-/gender-matched healthy controls (HCs). Anti-Jo1-IgG was further purified from 11 patients using a recombinant Jo1-coupled affinity column. A shotgun proteomics approach was used to profile serum-derived IgG-Fc-glycans and IgG-chain distributions. Univariate and multivariate statistics were used to find characteristics and correlate data with clinical information.

Results: A high frequency of agalactosylated IgG\textsubscript{1} Fc-glycans was observed in myositis patients compared to HCs. Using intra-individual normalization of the main agalactosylated glycan (FA2) of IgG\textsubscript{1} vs FA2-IgG\textsubscript{3}, myositis and HC were distinguished with an area under the curve (AUC) of 79 ± 6%. For Jo1 or anti-synthetase syndrome/ILD patients (ASS/ILD, comprising both Jo1+ and Jo1− patients), the AUCs went up to 88 ± 6%. Bisected and afucosylated Fc-glycans were significantly lower in Jo1+ compared to Jo1− patients. Anti-Jo1 IgG contained even lower abundances of bisected, afucosylated, and galactosylated forms compared to matched total IgG. Factors such as ASS and ILD diagnosis were associated with the anti-Jo1+ profile via multivariate analysis.

Conclusions: Myositis IgG Fc-glycans contain specific features representative of a Jo1+ and/or ASS/ILD type of phenotype. These Fc-glycan properties may translate into a pro-inflammatory profile, and thereby contribute to the pathogenesis of myositis associated with ILD.
SATURDAY SESSIONS

Anti-citrulline and anti-carbamylated protein antibodies in rheumatoid arthritis

OP15

Inflammatory markers in relation to risk factors for cardiovascular disease in the pre-symptomatic phase of rheumatoid arthritis

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Objectives: Individuals have years before onset of rheumatoid arthritis (RA) increased frequencies of risk factors for cardiovascular disease (CVD). The relationships between CVD risk factors and inflammatory markers were analysed in individuals before the onset of symptoms and compared with controls.

Methods: This case–control study was based on population surveys from the Medical Biobank. By co-analysing registers of patients with RA and the Medical Biobank, 469 pre-symptomatic individuals [age 50.2 years; median pre-dating time 5.0 (IQR 6.0) years] and 234 controls (age 50.3 years) were identified. CVD risk factors were defined as: hypertension (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg), elevated apolipoprotein B/apolipoprotein A1 ratio (women ≥ 0.7, men ≥ 0.8), body mass index (BMI) ≥ 25 kg/m², diabetes, and ever smoking. Levels of eotaxin, interferon gamma-induced protein (IP-10), monocyte chemotactant-1 (MCP-1), macrophage-derived chemokine (MDC), and interleukins (IL-2, IL-4, IL-6, IL-8, and IL-10), were analysed in plasma using R&D systems assays (Minneapolis, MN, USA).

Results: Pre-symptomatic individuals had significantly higher levels of IL-6 compared with controls, in both genders. IL-10 was significantly higher in pre-symptomatic men than in controls. Cytokines/chemokines were significantly associated with the CVD risk factors in the cases, e.g. IL-6 with each of the risk factors, eotaxin with smoking, IP-10 with increased BMI, having diabetes or hypertension, while MDC was associated significantly with smoking and BMI ≥ 25 kg/m². After adjusting for gender and age, only eotaxin concentrations were significantly associated with ever smoking. In women, MDC was significantly associated with smoking, BMI ≥ 25 kg/m², and diabetes. Having a combination of several CVD risk factors was associated with significantly higher concentrations of MCP-1, MDC, and IL-6 in pre-symptomatic women. IL-6 further increased the relative risk for the combinations of CVD risk factors for the pre-symptomatic cases vs controls.

Conclusions: Increased levels of cytokines/chemokines were associated with CVD risk factors, particularly in the pre-symptomatic RA cases compared with controls. The pattern of associations varied between the risk factors and the gender of the cases.

Managing inflammatory arthritis today and tomorrow

OP16

The NORD-STAR trial in early rheumatoid arthritis: a head-to-head comparison of aggressive conventional therapy and three biological therapies and comparison of two de-escalation strategies in patients who respond to treatment

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Objectives: An important issue in the treatment of early rheumatoid arthritis (RA) is whether an early aggressive intervention leads to a stable disease state of remission which can be maintained applying the principle of induction–maintenance. In the NORD-STAR trial (1), the aim is to compare the efficacy of different initial treatment regimes in early RA and the effects of subsequent dose reduction and termination of all therapies except methotrexate (MTX).

Methods: This 80–160 week, randomized, multicentre, open-label, assessor-blinded, phase 4 study includes 800 patients with early RA (symptoms < 24 months). Patients are randomized to one of four different treatment arms with stratification for anti-cyclic citrullinated peptide antibody (anti-CCP) status and gender: aggressive conventional synthetic disease-modifying anti-rheumatic drug...
(csDMARD) therapy with MTX ± glucocorticoids (oral or intra-articular), MTX + certolizumab-pegol, MTX + abatacept, or MTX + tocilizumab. The primary clinical endpoint is the proportion of patients reaching Clinical Disease Activity Index (CDAI) remission at week 24. Patients in stable remission over 24 consecutive weeks after week 24 enter part 2 of the study (TP2) after 48 weeks at the earliest. Patients are then re-randomized to an immediate de-escalation strategy or delayed (after a further 24 weeks) tapering, followed by cessation of study medication. All patients remain on stable doses of methotrexate. Radiographic assessments are performed regularly, and blood and urine samples are stored in a biobank for later biomarker analyses.

**Results:** By April 2018, 678 of 800 patients had been recruited in the ongoing trial, from Sweden (359), Denmark (147), Norway (87), Finland (66), Iceland (11), and the Netherlands (8). Recruitment is expected to be completed in December 2018. In a pre-analysis (n = 252), 38% of all included patients reached remission after 24 weeks, and 41.3% fulfilled criteria (stable remission until week 48) for entering TP2.

**Conclusions:** NORD-STAR is globally one of the largest investigator-initiated trials in RA. The trial has the potential to identify which treatment strategy to apply in early RA to achieve optimized outcomes for both patients and society.

**Reference**


**POSTER PRESENTATIONS**

**BASIC SCIENCE**

**PP01**

**Expression of inducible microsomal prostaglandin E synthase-1 is regulated by mitogen-activated protein kinase phosphatase-1**

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**Objectives:** Microsomal prostaglandin E synthase-1 (mPGES-1) is a terminal enzyme downstream of cyclooxygenase-2 (COX-2) in the prostaglandin E2 synthesis pathway and it is overexpressed under inflammatory conditions, such as arthritis. mPGES-1 is an interesting drug target, as inhibition of COX enzymes affects the production of all prostanoids and the known adverse effects of non-steroidal anti-inflammatory drugs are considered to result from this (1). Mitogen-activated protein (MAP) kinase pathways are signalling cascades regulating cellular responses to inflammatory stimuli. MAP kinase phosphatase-1 (MKP-1) is an enzyme dephosphorylating (i.e. inactivating) MAP kinases JNK and p38, and therefore serves as an endogenous anti-inflammatory mechanism (2). MKP-1 is also known to mediate anti-inflammatory effects of glucocorticoids and some other anti-inflammatory drugs, including phosphodiesterase-4 (PDE4) inhibitors (3). We investigated the role of MKP-1 in the regulation of mPGES-1 expression and tested the hypothesis that glucocorticoids and PDE4 inhibitors downregulate the expression of mPGES-1 through increased MKP-1 expression and decreased MAP kinase phosphorylation.

**Methods:** Peritoneal macrophages from MKP-1-deficient (knockout, KO) and wild-type (WT) mice as well as J774 macrophage cell line were used. mPGES-1 and MKP-1 expression, and MAP kinase phosphorylation were investigated by real-time quantitative reverse transcription–polymerase chain reaction and Western blotting.

**Results:** Glucocorticoid dexamethasone and PDE4 inhibitor rolipram decreased mPGES-1 expression in activated peritoneal macrophages from WT mice. Their effects were abolished in macrophages from MKP-1 KO animals. Dexamethasone and rolipram also increased the expression of MKP-1 in activated macrophages. Further, dexamethasone

![Figure PP01. Proposed mechanism of the downregulation of microsomal prostaglandin E synthase-1 (mPGES-1) by the phosphodiesterase-4 (PDE4) inhibitor rolipram. Rolipram inhibits the expression of mPGES-1 and the inhibitory effect is mediated via increased expression of MAP kinase phosphatase-1 (MKP-1) and decreased phosphorylation of MAP kinase Jun N-terminal kinase (JNK).](image-url)
decreased the phosphorylation of both p38 and JNK whereas rolipram decreased the phosphorylation of JNK only. The selective JNK inhibitor SP600125 downregulated mPGES-1 expression whereas p38 inhibitor BIRB796 did not have any significant effect.

Conclusions: This study underlines the role of MKP-1 as an anti-inflammatory mechanism of glucocorticoids and PDE4 inhibitors and shows that the increased mPGES-1 expression in inflammatory conditions is downregulated by those drugs through increased MKP-1 expression and decreased activation of MAP kinase JNK.

References


PP02

Mitogen-activated protein kinase phosphatase-1 as a novel factor in the pathogenesis of scleroderma: an experimental study

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Objectives: Scleroderma is a chronic connective tissue disease of unknown aetiology. In early stages, vascular injury and inflammation lead to fibrosis of tissues, resulting in irreversible damage. Inflammation is believed to be necessary in order to activate fibroblasts to overproduce extracellular matrix components. At present, there is no effective standard treatment to reverse or slow down the progression of scleroderma, but one feasible approach is to target key inflammatory pathways that are involved in the pathogenesis of the disease. Mitogen-activated protein kinase phosphatase-1 (MKP-1) is a nuclear phosphatase present in most cell types and tissues. Studies with MKP-1-deficient mice have shown that MKP-1 is an important regulator of innate and adaptive immune responses and inflammation, but its role in fibrosing diseases has not been studied. In the present study we investigated the potential role of MKP-1 in a mouse model of scleroderma.

Methods: Bleomycin-induced dermal fibrosis in the mouse was used as an experimental model of scleroderma. Wild-type (WT) and MKP-1 knockout (KO) mice were injected subcutaneously with bleomycin every other day for 28 days. Dermal thickness and collagen accumulation were determined in bleomycin-injected skin by histological analyses. The expression of several inflammatory and profibrotic mediators was investigated by quantitative reverse transcription–polymerase chain reaction.

Results: Bleomycin-induced dermal thickness and lipodystrophy were increased in MKP-1 KO mice. Collagen accumulation in dermis and mRNA expression of collagens Col1A1 and Col3A1 were increased in the skin from MKP-1 KO mice compared to skin from WT animals. Affected skin from MKP-1-deficient mice presented an increase of interleukin-6, transforming growth factor-β1, chitinase-3-like protein-1 (YKL-40), fibronectin-1, monocyte chemoattractant protein-1, macrophage inflammatory protein (MIP-1α), and MIP-2 mRNA expression.

Conclusions: This study demonstrates, for the first time, that MKP-1-deficient mice develop more severe bleomycin-induced dermal fibrosis than their WT counterparts, indicating that MKP-1 plays a role in the inflammatory and fibrotic processes typical for experimentally induced scleroderma. Taken together, these findings suggest MKP-1 as a potential new target for the stage-specific modulation of the pathogenesis of scleroderma.

PP03

Transient receptor potential ankyrin-1 (TRPA1) as a factor in osteoarthritis: TRPA1 mediates interleukin-6 expression in chondrocytes

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Objectives: Transient receptor potential ankyrin-1 (TRPA1) is a membrane-bound cation channel primarily studied in neurons as a factor that mediates nociception and neurogenic inflammation. We have recently discovered that TRPA1 is also expressed in human osteoarthritis (OA) chondrocytes, where it mediates inflammatory and catabolic effects (1), and where its expression is downregulated by the anti-inflammatory drugs dexamethasone and aurothiomalate (2). We also showed that in monosodium iodoacetate-induced experimental OA, TRPA1 mediates inflammation, cartilage degradation, and pain (3). In this study, we aimed to investigate in chondrocytes the role of TRPA1 in joint inflammation.

Methods: Genome-wide expression analysis was performed using chondrocytes from wild-type (WT) and TRPA1 knockout (KO) mice. Next-generation RNA sequencing was carried out with Illumina HiSeq2500
and functional analysis was performed against the Gene Ontology (GO) database. Chondrocytes/cartilage from TRPA1 KO and WT mice, as well as primary human OA chondrocytes, were cultured with interleukin-1β (IL-1β) alone or together with the selective TRPA1 antagonist HC-030031. Expression of the genes of interest was confirmed by quantitative reverse transcription–polymerase chain reaction (qRT-PCR) and immunobassay.

**Results:** Based on GO analysis, genes involved in the regulation of IL-6 production were enriched among those significantly affected by TRPA1. IL-6 was one of the most prominently expressed cytokines in WT chondrocytes, and its expression was significantly downregulated in cells from TRPA1 KO mice. The results further showed that other members of the IL-6 family of cytokines, IL-11 and leukaemia inhibitory factor (Lif), were also significantly downregulated in chondrocytes from TRPA1 KO mice. The results were verified with qRT-PCR. Also, genetic deletion of TRPA1 in murine cartilage explants, and pharmacological inhibition of TRPA1 in WT murine chondrocytes and primary human OA chondrocytes, significantly downregulated the expression of IL-6.

**Conclusions:** The results revealed the significant role of TRPA1 in the regulation of IL-6 production in chondrocytes. These findings, together with our recent data on TRPA1 in cellular and animal models, support the concept of TRPA1 as a potential mediator and drug target in OA.

**References**


**PP04**

**Myositis-specific anti-histidyl tRNA synthetase (HisRS) autoantibodies display high reactivity against HisRS conformational epitopes and are associated with lung and joint involvement**

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**Objectives:** Autoimmune myositis associated with interstitial lung disease (ILD) and arthritis is strongly correlated with circulating anti-histidyl tRNA synthetase (HisRS aka Jo1) autoantibodies. The aims of this study were to investigate: (i) myositis immunoglobulin G (IgG) reactivity against HisRS conformational epitopes; and (ii) associations between the anti-HisRS reactivity profiles and clinical manifestations.

**Methods:** Serum IgG was isolated using a protein G affinity column (from 25 anti-HisRS− and 19 anti-HisRS+ myositis sera and 24 age-/gender-matched healthy controls, HC). An enzyme-linked immunosorbent assay was developed to investigate IgG reactivity against HisRS full-length protein and three HisRS conformational epitopes [WHEP domain, localized in the

**Figure PP04.** Anti-full-length anti-histidyl tRNA synthetase (HisRS) immunoglobulin G reactivity (high, low, or no reactivity) in myositis patients diagnosed with polymyositis (PM) or dermatomyositis (DM), and presenting manifestations of interstitial lung disease (ILD), skin rash, arthritis, and dysphagia.

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N-terminal; HisRS without WHEP (HisRS_WHEP); and ABD, anticodon-binding domain located in the C-terminal]. Correlations between diagnosis, clinical manifestations, and anti-HisRS IgG reactivity were evaluated.

**Results:** HisRS+ myositis IgG displayed stronger reactivity against full-length HisRS and HisRS_WHEP (median 372 ng/mL and 334 ng/mL, respectively), compared to WHEP and ABD (6.38 and 6.48 ng/mL). The highest levels of anti-full-length HisRS reactivity (> 372 ng/mL) were detected in patients presenting with ILD (100% of patients), arthritis (60%), and polymyositis (PM) (90%). In contrast, 36% of patients with no anti-HisRS reactivity presented with ILD, 28% arthritis, and 56% were diagnosed with PM. Patients with low anti-HisRS reactivity (< 23 ng/mL) presented a clinical phenotype in between those observed for high and no anti-HisRS reactivity (67% diagnosed with ILD, 56% arthritis, and 67% PM). Manifestations of dysphagia and skin rash were more prevalent in HisRS+ patients (24% and 36%) compared to patients displaying high anti-HisRS reactivity (10% for both dysphagia and skin rash). Similar associations were observed between the degree of anti-HisRS_WHEP, anti-WHEP, or anti-ABD reactivities and manifestations of ILD, arthritis, skin rash, or dysphagia, and dermatomyositis or PM diagnosis. No anti-HisRS reactivity was detected in HC.

**Conclusions:** This study provides evidence for a possible underlying role of anti-HisRS autoantibodies in the pathogenesis of myositis with ILD and joint involvement.

**PP05**

Pyrazine-fused triterpenoids block transient receptor potential ankyrin-1 (TRPA1) ion channel in vitro and inhibit TRPA1-mediated inflammation in vivo

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**Objectives:** Transient receptor potential ankyrin-1 (TRPA1) is a cation channel expressed mostly in non-myelinated nerve endings. TRPA1 has a significant role in sensing chemical and mechanical pain and, according to more recent findings, also in inflammation. We have recently shown that pharmacological blockade and genetic deletion of TRPA1 alleviate inflammation and pain in murine models of gout and (osteo)arthritis (1, 2). Furthermore, TRPA1 is expressed in human articular chondrocytes and synovial cells in inflammatory conditions and mediates inflammatory and catabolic responses in vitro (3). Triterpenoids are naturally occurring molecules, which have been discovered to have anti-inflammatory and anti-cancer properties. The objective of the present study was to synthesize a series of derivatives of the triterpenoid betulin (which is a bioactive molecule from birch bark) and investigate their effects on TRPA1-ion channel and TRPA1-mediated inflammation.

**Methods:** Fluo 3-AM intracellular Ca2+-measurement protocol was utilized to screen the triterpenoid derivatives for TRPA1-blocking activity. Whole-cell patch-clamp recording was used to study the TRPA1-inhibiting activity of the most potent TRPA1-blockers in further detail. To investigate drug effects on TRPA1-mediated inflammation in vivo, an AITC-induced mouse paw oedema model was used.

**Results:** In the initial screening based on Fluo 3-AM measurements, five out of the 14 tested triterpenoids had a significant blocking effect on TRPA1 at 10 μM concentration. In the further studies, the two most potent compounds (compounds 8 and 9) were found to have dose-dependent, reversible, and voltage-dependent blocking effects on TRPA1 at submicromolar concentrations based on whole-cell patch-clamp recordings. The TRPA1 antagonistic activity of these two triterpenoid derivatives was also translated to in vivo, as compounds 8 and 9 significantly attenuated TRPA1-mediated acute inflammatory paw oedema in mice.

**Conclusions:** The results introduce pyrazine-fused triterpenoid derivatives as effective novel blockers of TRPA1 with potential for treatment of TRPA1-mediated adverse conditions, such as arthritis and arthritis-related pain.

**References**


**PP06**

cAMP-enhancing drugs salbutamol and rolipram augment the alternative activation of murine macrophages through mitogen-activated protein kinase phosphatase-1

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**Objectives:** Macrophages possess remarkable plasticity and respond to environmental cues with distinct functional phenotypes. These phenotypes have traditionally been described by two main functional subsets: classically (M1) and alternatively (M2) activated macrophages. M1 macrophages are characterized by expression of high levels of pro-inflammatory cytokines, whereas M2 macrophages drive the resolution of inflammation. Aberrant activation of M1 macrophages is known to be involved in the pathogenesis of autoimmune diseases such as rheumatoid arthritis (RA). Mitogen-activated protein kinase phosphatase-1 (MKP-1) is known to have a regulatory role in M1 macrophage activation and it acts as an important endogenous mechanism to suppress and limit inflammation. In the present study, we investigated whether MKP-1 takes part in the interleukin-4 (IL-4) + IL-13-induced M2 activation. Since cAMP-enhancing drugs, such as the β2-agonist salbutamol and phosphodiesterase inhibitor rolipram, increase MKP-1 expression, we studied their effects on IL-4 + IL-13-induced M2 activation.

**Methods:** Peritoneal macrophages (PMs) derived from MKP-1-deficient and wild-type mice, and J774 macrophage cell line were used. Macrophage activation was studied by measuring the expression of M2 markers arginase 1, Ym-1, and MRC1 by polymerase chain reaction and Western blotting.

**Results:** In cultured murine macrophages, salbutamol, rolipram, and their combination enhanced IL-4 + IL-13-induced expression of M2 activation markers. They also increased MKP-1 mRNA and protein expression in untreated and IL-4 + IL-13-treated macrophages. The enhancing effects of salbutamol, rolipram, and their combination on M2 activation markers were abolished in PM cells from MKP-1-deficient mice, indicating a role for MKP-1.

**Conclusions:** Our data show that cAMP-enhancing drugs direct macrophage polarization towards the M2 phenotype and that this effect is, at least partly, mediated by MKP-1. These results provide new knowledge on the signalling pathways governing macrophage polarization and functional phenotypes. Redirecting M1 macrophages towards the resolution-inducing M2 phenotype affords a novel target for the development of drugs for autoimmune diseases such as RA.

**PP07**

**Anti-inflammatory properties of the β2-receptor agonist salbutamol and the phosphodiesterase-4 inhibitor rolipram are mediated by mitogen-activated protein kinase phosphatase-1**

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**Objectives:** Excessive inflammatory response is the main cause for symptoms and pathological findings in patients with arthritis and other chronic inflammatory diseases. p38 mitogen-activated protein kinase (MAPK) is involved in the regulation of immune responses and inflammation. MAPK phosphatase-1 (MKP-1) is a nuclear phosphatase that inactivates the p38 pathway and inhibits cytokine production and inflammation. Anti-inflammatory steroids increase MKP-1 expression, and many of their anti-inflammatory effects are mediated through enhanced MKP-1. In addition to a glucocorticoid response element, MKP-1 promoter is known to contain a cAMP-responsive element. That led us to hypothesize that in inflammatory conditions cAMP-enhancing drugs may upregulate MKP-1 expression, leading to suppression of the inflammatory response. In the present study, we tested that hypothesis by investigating the role of MKP-1 as a mediator of the anti-inflammatory effects of the β2-agonist salbutamol and the PDE4 inhibitor rolipram.

**Methods:** Peritoneal macrophages (PMs) and the J774 macrophage cell line were used in the study. MKP-1 and tumour necrosis factor (TNF) expression was measured by quantitative reverse transcription–polymerase chain reaction and Western blot/enzyme-linked immunosorbent assay, and p38 phosphorylation by Western blot. The effects of salbutamol and rolipram were investigated also in vivo in carrageenan-induced paw inflammation in MKP-1 knockout (KO) and wild-type (WT) mice.

**Results:** Salbutamol, rolipram, and cAMP analogue increased MKP-1 expression, reduced p38 phosphorylation, and inhibited the production of the pro-inflammatory cytokine TNF. The effect of rolipram on TNF production was attenuated in PMs from MKP-1 KO mice compared to WT mice. Salbutamol and rolipram alleviated carrageenan-induced paw inflammation in vivo. That effect of salbutamol was impaired in MKP-1 KO mice and the effect of rolipram was totally abolished.

**Conclusions:** The results show that the cAMP-enhancing compounds salbutamol and rolipram inhibit the production of the pro-inflammatory cytokine TNF in macrophages and possess anti-inflammatory properties in vivo. These effects were found to be mediated, at least partly, by increased expression of MKP-1. The results emphasize the potential of MKP-1 as a novel anti-inflammatory drug target.

**PP08**

**Self-reported and performance-based physical function in patients with knee osteoarthritis**

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**Objectives:** Knee osteoarthritis is one of the most prevalent chronic rheumatic diseases and is a leading cause
of pain and disability. The aim of this study was to investigate the correlations between self-reported and performance-based physical function in patients with knee osteoarthritis.

**Methods:** Patients with knee osteoarthritis answered the Western Ontario and McMaster Universities (WOMAC) osteoarthritis index and the physical functioning domain of the Medical Outcomes Study 36-item Short Form Health Survey (SF-36) for self-reported physical function. In addition, 10-Metre Walk Test, Timed Up and Go test (TUG), Sit to Stand test, and manual muscle tests of the left and right quadriceps femoris (QF) muscles were applied to assess the performance-based physical function.

**Results:** Twenty-eight knee osteoarthritis patients (mean age 60.17 ± 6.96 years) participated in this study. The WOMAC–physical function correlated with the physical functioning domain of SF-36 (r = −0.646 p = −0.000), 10-Metre Walk Test (r = −0.491 p = −0.009), TUG (r = 0.496 p = 0.008), and strength of the right-side QF (r = −0.481 p = 0.011). Correlations of the physical functioning domain of SF-36 with the parameters of performance-based physical function were poor (p > 0.05).

**Conclusions:** Our results indicated that while the scales (WOMAC and SF-36) which assessed the self-reported physical function were related to each other, only WOMAC–physical function was associated with performance-based physical function parameters, but SF-36–physical functioning was not. These findings suggest that the data obtained with disease-specific scales are closely related to performance-based physical function in patients with knee osteoarthritis. Studies in larger groups of patients with knee osteoarthritis are needed to clarify the data obtained in our study.

**References**


**PP09**

**E74-like factor-3 is synergistically regulated by interleukin-17A and tumour necrosis factor and controls the production of inflammatory cytokines and matrix metalloproteinases in synovial fibroblasts**

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**Objectives:** Tumour necrosis factor (TNF) and interleukin-17A (IL-17A) contribute to the pathogenesis of rheumatoid arthritis (RA). The interplay of their signalling leads to remarkable synergistic effects in induction of many inflammatory cytokines and extracellular matrix-degrading enzymes in synovial fibroblasts, but the mechanisms of synergy are poorly known. Transcription factor E74-like factor-3 (ELF3) is expressed in inflamed synovial membrane in RA and has been shown to regulate the expression of inflammatory genes in response to IL-17B. The aim of this study was to analyse the possible involvement of ELF3 in the synergistic induction of inflammatory mediators by IL-17A and TNF in synovial fibroblasts.

**Methods:** Human fibroblasts isolated from synovial membranes were treated with IL-17A and/or TNF and analysed for ELF3 expression using quantitative reverse transcription–polymerase chain reaction (qRT-PCR) and immunofluorescence. The regulation of ELF3 expression and the impact of ELF3 for the signalling mediated by IL-17A and TNF were studied using transient overexpression in HEK293 cells and in synovial fibroblasts, transient knockdown using siRNAs in synovial fibroblasts, signalling inhibitors, enzyme-linked immunosorbent assay, immunofluorescence, and qRT-PCR.

**Results:** ELF3 was only marginally induced by IL-17A or TNF alone, but the combination of IL-17A and TNF resulted in high and prolonged induction of ELF3. Depletion of ELF3 with siRNA reduced the production of several cytokines, chemokines, and matrix metalloproteinases in response to stimulation by IL-17A and TNF. Overexpression of ELF3 in HEK293 cells and in synovial fibroblasts resulted in increased responses to TNF. Induction of ELF3 expression was mediated by nuclear factor-kB pathway and C/EBPβ but was sensitive to cycloheximide treatment, indicating a requirement for de novo protein synthesis.

**Conclusions:** Transcription factor ELF3 is a key regulator of the signalling mediating the synergy between IL-17A and TNF in the production of inflammatory mediators in synovial fibroblasts.

**PP10**

**Prostacyclin: a potential novel therapeutic target to treat tendon pain and inflammation**

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**Objectives:** Prostacyclin has been proposed as a potential therapeutic target for the treatment of chronic inflammatory pain. However, recent studies have shown that prostacyclin might also play a role in the pathogenesis of chronic inflammatory diseases, including rheumatoid arthritis (RA) and osteoarthritis (OA). The aim of this study was to investigate the potential of prostacyclin as a therapeutic target for the treatment of chronic inflammatory pain.

**Methods:** The effects of prostacyclin on neuronal and glial cells were investigated using in vitro experiments. Neurons and glial cells were treated with prostacyclin and the effects on cell viability, migration, and survival were measured using a cell viability assay and a migration assay. The results were compared with those obtained using control cells.

**Results:** Prostacyclin was found to have a significant effect on the viability and migration of neuronal and glial cells. The effect of prostacyclin on cell viability and migration was dose-dependent and the results were statistically significant compared with control cells.

**Conclusions:** Prostacyclin has a significant effect on the viability and migration of neuronal and glial cells. These findings suggest that prostacyclin might be a potential therapeutic target for the treatment of chronic inflammatory pain.
Increased expression of PGIS and IP tandem abstracts α–production in diseased compared to healthy polymerase chain reaction. Eased tendon tissues by diseased tendon cells sug- clin synthase (PGIS), induced prostaglandin E2 (PGE2) in both fl +−. Immunostaining of dis receptor in diseased tendons and increased produc- from these cells. Inhibited both PGE2 and 6-keto PGF1 blockade with either NS-398 or naproxen completely healthy and diseased tendon cells. Conversely, COX pathogenesis of tendon in gest that prostacyclin may contribute to the reduced PGE2 and increased 6-keto PGF1 with the selective mPGES-1 inhibitor Compound III potential role in pain associated with disease. Target- tendon cells. Incubation of IL-1 bolite 6-keto PGF1 ment potently induced the prostacyclin (PGI2) meta- healthy and diseased tendon cells. The same treat- with IL-1 NMDAR-1. Stimulation of cultures of tendon cells show increased numbers of macrophages (CD68+ cells), and increased expression of cyclooxygenases COX-1 and COX-2, prostacyclin synthase (PGIS), the prostacyclin receptor (IP receptor), and microso- mal prostaglandin E synthase-1 (mPGES-1). PGIS co-localized with podoplanin, a marker of stromal fibroblast activation, and nociceptive neuromodulator NMDAR-1. Stimulation of cultures of tendon cells with IL-1β induced prostaglandin E2 (PGE2) in both healthy and diseased tendon cells. The same treatment potently induced the prostacyclin (PGI2) meta- 6-keto PGF1α in diseased compared to healthy tendon cells. Incubation of IL-1β-treated tendon cells with the selective mPGES-1 inhibitor Compound III reduced PGE2 and increased 6-keto PGF1α in both healthy and diseased tendon cells. Conversely, COX blockade with either NS-398 or naproxen completely inhibited both PGE2 and 6-keto PGF1α production from these cells.

Conclusions: Increased expression of PGIS and IP receptor in diseased tendons and increased production of 6-keto PGF1α by diseased tendon cells suggest that prostacyclin may contribute to the pathogenesis of tendon inflammation, and play a potential role in pain associated with disease. Targeting the prostacyclin pathway presents a novel potential therapeutic strategy to modulate inflammation and pain in tendon disease.

PP11

Novel adipokine associated with osteoarthritis: retinol binding protein-4 (RBP-4) is a member of the lipocalin family, and it is a vitamin A (retinol) carrier in the blood. RBP-4 binds to vitamin A receptor (also called stimulated by retinoic acid 6, STRA6) and acts also as an endogenous ligand for Toll-like receptor-4 (TLR-4). RBP-4 has been described as an adipokine that contributes to insulin resistance and metabolic syndrome (MetS). As obesity, MetS, and adipo- kines are associated with osteoarthritis (OA), we investigated whether RBP-4 is related to OA.

Methods: Cartilage, synovial fluid and blood samples were collected from 100 OA patients [62 females; body mass index 29.7 (8.3) kg/m², age 72 (14) years, median (IQR)] undergoing knee replacement surgery. Adipokines and other biomarkers were measured by immunoassay. Genome-wide expression analysis was carried out with the Illumina HiSeq2500 RNA-sequencing sys- tem, and confirmed with quantitative reverse transcription–polymerase chain reaction.

Results: According to the RNA-Seq analysis, RBP-4 was the most prominently expressed adipokine in chondrocytes from OA patients. Cartilage samples from OA patients released RBP-4 protein into the culture medium (11.9 ± 0.5 ng/10 mg cartilage, mean ± sem) and these levels correlated positively with the cartilage-released adipin (r = 0.27, p = 0.007), leptin (r = 0.29, p = 0.004), and especially adiponectin (r = 0.54, p < 0.0001). RBP-4 showed also a positive correlation with MMP-1 (r = 0.26, p = 0.010) and MMP-3 (r = 0.24, p = 0.017) within the culture medium. RBP-4 was present in the synovial fluid (SF) samples from OA patients (20.4 ± 1.2 µg/mL) and correlated with levels measured in cartilage culture medium from the same patients (r = 0.27, p = 0.025). Plasma RBP-4 levels (49.2 ± 1.8 µg/mL) were higher than those in SF and there was a positive correlation between those two (r = 0.45, p < 0.0001). Plasma RBP-4 correlated positively also with the adipokine adipin (r = 0.39, p < 0.0001) and the OA biomarker MMP-3 (r = 0.25, p = 0.012).

Conclusions: We show here for the first time that RBP-4 is produced within OA joints, and it is associated with increased levels of adipokines and MMPs 1 and 3. The results suggest a role for RBP-4 in the pathogenesis of OA and as a possible target for disease-modifying drugs for the treatment of OA.

PP12

Transient receptor potential ankyrin-1 is an inflamma- tion-induced factor in human keratinocytes and pro- motes the expression of inflammatory genes in vitro

S Luostarinen, M Hämäläinen, E Moilanen

Novel adipokine associated with osteoarthritis: retinol binding protein-4 is produced by cartilage and corre- lates with matrix metalloproteinases in osteoarthritis patients

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Objectives: Transient receptor potential ankyrin-1 (TRPA1) is a cation channel expressed in sensory neurons, and mediates pain, itch, and neurogenic inflammation. We and others have shown that TRPA1 is also expressed in some non-neuronal cells and supports inflammatory responses. To address the pathogenesis of inflammatory skin conditions in rheumatic diseases, we aimed to investigate TRPA1 expression and its function under inflammatory stimuli in human keratinocytes.

Methods: Human HaCaT keratinocyte cell line and skin biopsies from wild-type (WT) and TRPA1-deficient (knockout, KO) mice were used in the studies. TRPA1 expression was determined by quantitative reverse transcription–polymerase chain reaction and Western blotting, and secretion of inflammatory mediators was assessed by immunoassay. Pharmacological inhibitors MG132/PDTC, cyclosporine/tacrolimus, SB203580, and JNK inhibitor VIII were used to investigate the regulatory role of nuclear factor-κB (NF-κB), calcineurin-nuclear factor of activated T cells (NFAT), and mitogen-activated protein (MAP) kinases p38 and JNK, respectively. A967079 and HC-030031 were used as TRPA1 antagonists and dexamethasone as a standard anti-inflammatory compound.

Results: TRPA1 expression was very low in non-stimulated keratinocytes, but highly inducible by the pro-inflammatory cytokine tumour necrosis factor (TNF) in a time- and dose-dependent manner. TNF-induced TRPA1 expression was mediated through NF-κB, and p38 and JNK MAP kinase pathways as judged by studies with pharmacological inhibitors. The glucocorticoid dexamethasone and the calcineurin inhibitors cyclosporine and tacrolimus (which are widely used in the treatment of inflammatory skin diseases) significantly inhibited TRPA1 expression in human keratinocytes. Furthermore, pharmacological inhibition and/or genetic deletion of TRPA1 suppressed the production of TNF-induced inflammatory factors monocyte chemoattractant protein-1, interleukin-6, and matrix metalloproteinase-9 in keratinocytes and/or skin biopsies ex vivo.

Conclusions: In the present study, TRPA1 was found to be expressed in human keratinocytes under inflammatory conditions in an NF-κB, p38 and JNK MAP kinase, and calcineurin-NFAT-dependent manner, and to promote the synthesis of inflammatory factors. The results reveal TRPA1 as a potential mediator and drug target in inflammatory skin conditions.

PP13

Interleukin-6 in osteoarthritis: effects of pinosylvin and monomethyl pinosylvin

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Objectives: Interleukin-6 (IL-6) is a pro-inflammatory mediator contributing to the pathogenesis of rheumatoid arthritis, but the role of IL-6 in osteoarthritis (OA) remains less clear. In the present study, we report the levels of IL-6 in OA patients and the effects of stilbenoid compounds pinosylvin and monomethyl pinosylvin on the expression of the inflammatory cytokine IL-6 and the major cartilage matrix components aggrecan and collagen II in human OA chondrocytes.

Methods: Plasma and synovial fluid (SF) samples were collected from 100 OA patients [body mass index 29.7 (8.3) kg/m², age 72 (14) years, median (IQR); 62/38 females/males] undergoing total knee replacement surgery in Coxa Hospital for Joint Replacement, Tampere, Finland. Concentrations of IL-6 and matrix metalloproteinases (MMPs) were determined by immunoassay. For pharmacological studies in primary chondrocyte cultures, the OA cartilage was processed and chondrocytes were isolated by enzymic digestion using collagenase enzyme blend. Isolated chondrocytes were stimulated with IL-1β (100 pg/mL) or IL-17 (50 ng/mL) in the presence and absence of the tested compounds, and expression of IL-6, aggrecan, and collagen II was determined by quantitative reverse transcriptase–polymerase chain reaction and enzyme-linked immunosorbent assay (IL-6).

Results: Synovial fluid levels of IL-6 [119.8 (193.5) pg/mL, median (IQR)] were considerably higher than its plasma levels [3.1 (2.7) pg/mL]. SF IL-6 correlated positively with the levels of the catabolic enzymes MMP-1 (r = 0.446, p < 0.001) and MMP-3 (r = 0.486, p < 0.001) in SF, as well as with the radiographic disease severity assessed by Ahlbäck classification criteria. Pinosylvin and monomethyl pinosylvin inhibited IL-6 production and increased aggrecan mRNA expression in primary human OA chondrocytes in a dose-dependent manner, and based on reporter-gene experiments, through inhibition of the inflammatory transcription factor nuclear factor-κB.

Conclusions: The results suggest that IL-6 is produced within the OA joint and contributes to the pathogenesis of OA. Scots pine-derived pinosylvin and monomethyl pinosylvin were discovered to have promising disease-modifying effects in OA chondrocytes through reduced IL-6 and enhanced aggrecan expression.

Inflammatory arthritides

PP14

Relationships between pain on functionality, quality of life, and kinesiophobia in patients with ankylosing spondylitis

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Objectives: Ankylosing spondylitis (AS) is an inflammatory rheumatic disease and primarily affects the axial skeleton, manifesting in a common symptom of chronic pain (1, 2). Musculoskeletal pain inhibits physical performance and limits mobilization, and thus functionality. One of the most focused targets of AS treatment for physical therapists is to improve functionality. So, it is significant to identify the role of contributory factors to the functionality of patients to be able to design effective physiotherapy interventions (3). The aim of the study was to investigate relationships between pain intensity, physical activity, kinesiophobia, functional status, and disease activity in AS patients.

Methods: Thirty AS patients (mean age 32.6 ± 5.041 years) participated voluntarily in the study. Pain intensity was evaluated using the McGill Pain Questionnaire. Disease activity was assessed by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and the Bath Ankylosing Spondylitis Functional Index (BASFI) was used to measure functional status. Kinesiophobia was assessed by the Tampa Kinesiophobia Index. Physical activity was measured using an accelerometer. The relation between pain and the aforementioned parameters was analysed by Spearman’s rank correlation test.

Results: Significant correlations were found between pain intensity and BASDAI and BASFI total scores (p < 0.05). On the other hand, there was no significant correlation between pain intensity, kinesiophobia, and data obtained from the accelerometer (p > 0.05).

Conclusions: The results indicate that pain affects the disease activity and functionality of AS patients. The higher the pain intensity of AS, the higher the disease activity and lower the functional level. Since pain intensity had no relation to kinesiophobia scores, it could be caused by mobility limitations arising from spinal stiffness, so that people with AS might feel more confident against fear of pain and injury resulting from movement. The existence of kinesiophobia and having physical activity measures independent of pain are positive outcomes for the success of physiotherapy treatments. AS patients can be encouraged to perform exercise and increase their level of physical activity during their daily life, even when they experience pain.

References

PP15
Increased progression of atherosclerosis in patients with rheumatoid arthritis is partially reflected by disease severity at the time of diagnosis: 11-year prospective follow-up

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Objectives: Patients with rheumatoid arthritis (RA) have increased mortality and morbidity due to cardiovascular disease (CVD) compared to the general population. While it has been established that atherosclerosis is increased, there is much yet to be revealed about the underlying cause. Contributory factors, such as inflammation, traditional CVD risk factors, and metabolic disease, have been suggested, but no full explanation has yet been proposed. In this prospective case–control study, we investigated how the progression of subclinical atherosclerosis is associated with CVD risk factors and parameters of inflammation in patients with RA compared with matched controls.

Methods: By the time of diagnosis, patients from northern Sweden diagnosed with early RA are consecutively recruited into an ongoing prospective study. From these patients, a subgroup aged ≤ 60 years was consecutively included for ultrasound measurements of intima–media thickness (IMT) of the common carotid artery at inclusion (T0) (n = 79), after 5 years (T5) (n = 71) and after 11 years (T11) (n = 55). 44 age- and gender-matched controls were included and 31 could be re-evaluated after 11 years of follow-up as the dependent variable.

Table PP15. Simple regression models among 55 patients with rheumatoid arthritis, with intima media thickness (IMT) after 11 years of follow-up as the dependent variable.

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, T0</td>
<td>0.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Systolic BP, T0</td>
<td>0.03</td>
<td>0.009</td>
</tr>
<tr>
<td>SCORE, T0</td>
<td>0.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Reynolds risk score, T0</td>
<td>0.2</td>
<td>0.009</td>
</tr>
<tr>
<td>Larsen score, T0</td>
<td>0.1</td>
<td>0.043</td>
</tr>
<tr>
<td>DAS28, T0</td>
<td>-0.236</td>
<td>0.4</td>
</tr>
<tr>
<td>Cholesterol, T0</td>
<td>0.1</td>
<td>0.7</td>
</tr>
</tbody>
</table>

T0, at study inclusion; BP, blood pressure; SCORE, European Systematic COronary Risk Evaluation; DAS28, 28-joint Disease Activity Score.
T11. Clinical evaluation, including Larsen score (of hands and feet), CVD risk factors, and risk scores, was carried out.

**Results**: IMT increased significantly between T0 and T11 among patients with RA [IMT T0: 0.51 (0.12); T11: 0.68 (0.16); p < 0.0001] and controls [IMT T0: 0.54 (0.12); T11: 0.63 (0.13); p < 0.0001]. Results from conditional logistic regression showed a higher progression rate between T0 and T11 in the RA group compared with the controls (p < 0.05). In simple regression models, IMT T11 was significantly associated with several traditional CVD risk factors as well as Larsen score at T0 among RA patients (Table PP15).

**Conclusions**: In this prospective study, we found that there was an increased progression of atherosclerosis among RA patients, compared with controls, 11 years after diagnosis, and that this increase was associated with Larsen score and age at baseline.

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**PP16**

**Automated cell-phone monitoring of disease activity and medication problems in early rheumatoid arthritis**

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Table PP16. Baseline characteristics of the patients.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Control (n = 80)</th>
<th>Intervention (n = 82)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, female</td>
<td>56 (70)</td>
<td>58 (71)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59 ± 14</td>
<td>54 ± 13*</td>
</tr>
<tr>
<td>Seropositive (RF and/or anti-CCP)</td>
<td>69 (86)</td>
<td>70 (85)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>11.3 ± 3.5</td>
<td>12.6 ± 3.6†</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.5 ± 5.1</td>
<td>26.7 ± 5.2</td>
</tr>
<tr>
<td>Measures of disease activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAS28</td>
<td>4.4 ± 1.3</td>
<td>4.1 ± 3.8</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (mm/h)</td>
<td>28 ± 18</td>
<td>24 ± 22</td>
</tr>
<tr>
<td>Serum C-reactive protein (mg/L)</td>
<td>20 ± 22</td>
<td>16 ± 22</td>
</tr>
<tr>
<td>Number of swollen joints</td>
<td>6.5 ± 5.4</td>
<td>6.4 ± 5.1</td>
</tr>
<tr>
<td>Number of tender joints</td>
<td>9.0 ± 7.4</td>
<td>7.7 ± 7.0</td>
</tr>
<tr>
<td>Patient’s global assessment (VAS)</td>
<td>46 ± 28</td>
<td>45 ± 28</td>
</tr>
<tr>
<td>Physician’s global assessment (VAS)</td>
<td>41 ± 19</td>
<td>37 ± 20</td>
</tr>
<tr>
<td>Physical function (HAQ)</td>
<td>1.0 ± 0.7</td>
<td>0.9 ± 0.6</td>
</tr>
<tr>
<td>Radiography</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosions in hand or foot radiographs</td>
<td>14 (18)</td>
<td>17 (21)</td>
</tr>
</tbody>
</table>

*Data are shown as n (%) or mean ± sd.
RF, rheumatoid factor; CCP, cyclic citrullinated protein antibodies; DAS28, 28-joint Disease Activity Score; VAS, Visual Analogue Scale; HAQ, Health Assessment Questionnaire.

*p = 0.021; †p = 0.026.

**Objectives**: Frequent monitoring of early rheumatoid arthritis (RA) patients is required to achieve good outcomes. We studied the influence of text message (SMS)-enhanced monitoring on early RA outcomes. Here, we present the results of a randomized study comparing SMS-based follow-up to routine care.

**Methods**: We randomized 166 early, drug-naïve RA patients, who fulfilled the EULAR 2010 RA classification criteria, to SMS-enhanced follow-up or to routine care. All patients attended visits at 0, 3, and 6 months, and had a follow-up visit at 12 months. Treatment was at the physicians’ discretion. The 6 month intervention
included 13 SMSs at 1–2 week intervals between weeks 0 and 24. Questions concerned medication problems (yes/no) and disease activity [patient global assessment (PGA) on a scale of 0–10]. If response SMSs indicated medication problems or PGA exceeded predefined thresholds, the patients were contacted and arranged an extra visit if needed. Primary outcome was 6 month Boolean remission, defined as no tender or swollen joints (46 joint count), and normal C-reactive protein. Quality of life (QoL, 36-item Short Form Health Survey) and 28-joint Disease Activity Scores (DAS28) were assessed.

**Results:** Six- and 12-month follow-up data were available for 162 and 157 patients, respectively. Patients’ baseline characteristics are shown in Table PP16. All patients started intensive therapy; 96% started methotrexate, and 89% started a combination of two or three conventional disease-modifying anti-rheumatic drugs. In the intervention group, 47% (38/82) of the patients reported medication problems and 49% (40/82) of the patients reported SMS-PGAs above the alarm limit (Figure PP16). Remission rates in the intervention and control groups were, respectively, 51% and 42% at 6 months (p = 0.34) and 57% and 43% at 12 months (p = 0.17). The respective DAS28 scores were 1.92 ± 1.12 and 2.22 ± 1.11 at 6 months (p = 0.09) and 1.79 ± 0.91 and 2.08 ± 1.22 at 12 months (p = 0.28). No differences in QoL were observed.

**Conclusions:** Remission rates were remarkably high in both groups. Our study failed the primary outcome despite a trend favouring the intervention group. Studies conducted in less well-resourced settings might reveal whether SMS-enhanced follow-up provides additional value.

**PP17**

Marginal jawbone loss is associated with onset of rheumatoid arthritis and is related to plasma level of receptor activator of nuclear factor kappa-B ligand

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**Objectives:** The association between two chronic inflammatory diseases, periodontal disease (PD) and rheumatoid arthritis (RA), has been addressed in recent years. These diseases share several risk factors (smoking and shared epitope) and features besides inflammation, e.g. presence of bone destruction and the link between rheumatic and dental pathology via citrullination. The aim of this study was to investigate whether periodontitis, presenting as marginal jawbone loss, preceded the onset of symptoms of RA. Furthermore, the plasma levels of receptor activator of nuclear factor kappa-B (RANKL), a cytokine crucial for bone resorption, and anti-citrullinated peptide antibodies (ACPAs) were analysed in relation to RA development and jawbone loss.

**Methods:** Dental radiographs from the premolar/molar region of the jaws of 176 individuals, of whom 93 had subsequently developed RA, and 83 controls were used for measuring the levels of marginal jawbone loss. Of the 93 individuals who developed RA, 46 had radiographs before symptom onset of RA. Forty-five of these pre-symptomatic individuals were matched with controls, based on gender, age, and smoking status. Plasma RANKL concentration and ACPAs (as anti-cyclic citrullinated peptide-2 antibodies) were analysed using enzyme-linked immunosorbent assay (BioVendor, Karasek, Czech Republic).

**Results:** Jawbone loss was significantly higher in never-smoking, pre-symptomatic individuals compared with controls, and increasing levels of bone loss were also associated with a higher risk of developing RA later in life (hazard ratio = 1.06, 95% CI 1.01, 1.11). The jawbone loss increased significantly during the predating time. Among smokers, no association was found. RANKL-positive pre-symptomatic individuals had significantly higher levels of jawbone loss, particularly in individuals positive for both RANKL and ACPA compared with those positive for one factor or double negative.

**Conclusions:** Higher levels of marginal jawbone loss were found to precede the onset of symptoms in non-smokers. Pre-symptomatic individuals who were RANKL positive, and particularly also ACPA-positive individuals, had significantly increased levels of jawbone loss.

**PP18**

A mass cytometry insight into synovial fluid of rheumatoid arthritis

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**Objectives:** For the past decade, disease outcome and preservation of functional state in rheumatoid arthritis (RA) have dramatically improved alongside the development of biological therapies targeting different sites of the inflammation. There is currently no way of predicting response to therapies, resulting in only 60–70% of patients being primary responders to first line treatment, tumour necrosis factor-α (TNF-α) antagonists. Through neutralization processes, some primary responders subsequently develop secondary non-response. Through the study of immune cell signatures in peripheral blood
Algorithm-based visualization of 11 cell subsets in a rheumatoid arthritis synovial fluid sample. One dot represents one cell, and the closer these dots lie, the more similarities they share. tSNE, t-distributed stochastic neighbour embedding.

**Methods:** Mass cytometry allows for the simultaneous detection of up to 40 surface and functional markers, enabling identification of cell populations based on phenotype and activation state. Patient and control samples were stimulated with the pro-inflammatory cytokines TNF-α and interleukin-6. For each patient and control, clinical data were registered, enabling investigation of correlations through comparison of findings in immune cells from PB and SF.

**Results:** Unsorted patient material has been analysed to optimize the protocol for both PB and SF. A TNF-α marker panel has been tested, with a focus on different fixation methods and approaches to reducing the viscosity of SF. Seven OA controls and 14 RA patients have been included for biobanking.

**Conclusions:** The lack of reliable and specific biomarkers in this patient group is evident. By detecting such markers at a single-cell level, clinicians will be better armed to predict responses to therapies and identify secondary non-responders. Once a small and definite number of such has been detected, it is hoped that the findings can be translated to clinical flow cytometry.

**References**


**PP19**

**Vitamin D in individuals before onset of rheumatoid arthritis: relation to vitamin D binding protein and its associated genetic variants**

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**Objectives:** Vitamin D has been implicated as being involved in the aetiopathogenesis of several autoimmune diseases including rheumatoid arthritis (RA). Previous studies present contradictory results. Vitamin D binding protein (DBP), the major transport protein, is also involved in various inflammatory processes. The aim of this study was to investigate the relationship between circulating levels of 25-hydroxyvitamin D [25(OH)D], DBP, and polymorphisms in group-specific component (GC) in pre-symptomatic individuals and matched controls within prospective cohorts in northern Sweden.

**Methods:** Blood samples donated to the Medical Biobank before the onset of symptoms of RA (n = 515, mean ± sd time before the onset of symptoms 6.2 ± 9.3 years) and from matched (2:1) population-based controls (n = 267) were used. Plasma 25(OH)D levels were analysed using liquid chromatography–tandem mass spectrometry and DBP levels were analysed using enzyme-linked immunosorbent assay. GC polymorphisms (rs4588 and rs7041) were analysed with TaqMan assays (Applied Biosystems).

**Results:** Levels of 25(OH)D or DBP were not statistically different between pre-symptomatic individuals and controls in a crude or a multiple-adjusted logistic regression model. However, an increased risk for future RA was found in females of DBP (odds ratio 1.0001, 95% CI 1.000–1.0003), adjusted for carriage of the minor allele of rs4588, in a multiple-adjusted model (p < 0.05).

**Conclusions:** This study indicated that vitamin D is not associated with the future risk of RA, although increasing levels of DBP were associated with an increased risk
of disease in females carrying the minor allele of a DBP encoding SNP.

### PP20

**Intensive treatment of rheumatoid arthritis patients prevents myocardial abnormalities: a cardiac magnetic resonance follow-up study**

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**Objectives:** Rheumatoid arthritis (RA) patients have twice the risk, compared with those without RA, of developing congestive heart failure not explained by common cardiovascular risk factors or coronary heart disease (1). Pro-inflammatory cytokines have been suggested to play an important role in the development of myocardial dysfunction (2). In the present study, we examined whether patients with active RA have myocardial abnormalities and whether progression of myocardial involvement can be prevented through the use of disease-modifying anti-rheumatic drugs (DMARDs).

**Methods:** Cardiac magnetic resonance (cMR; 1.5 T or 3.0 T) including late gadolinium enhancement (LGE), T1 relaxation time, and ventricular functions, was performed in (i) 30 patients with untreated active early RA starting first DMARDs and (ii) 28 patients with chronic RA with inadequate response to conventional synthetic DMARDs starting biological DMARDs. The RA patients were re-examined after 1 year. cMR was conducted once in 22 fibromyalgia (FM) subjects with LGE images and 35 healthy volunteers serving as controls.

**Results:** At baseline, RA patients had impaired ventricular functions and longer T1 time compared with controls. None of the FM subjects had LGE, but it was a very frequent finding in RA patients at baseline (67%). In parallel with DMARD treatment targeting to remission, Disease Activity Score based on 28-joint count—C-reactive protein (DAS28-CRP) declined over the study period. Although the number of RA patients with LGE remained unchanged over time, the number of LGE-positive segments of the heart stayed either at the same level or improved in 91% of RA patients. Over time, ventricular functions of RA patients showed improvement (Table PP20). Classical cardiovascular risk factors were worse in FM subjects compared with RA patients.

**Conclusions:** In parallel with decreasing RA activity during intensive DMARD therapy, myocardial function improved and progression of LGE was prevented. Treatment targeting to remission from the early stages of RA is important to prevent not only joint damage but also myocardial involvement.

### Table PP20. Ventricular functions in 58 rheumatoid arthritis patients over the 1 year period.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (%)</th>
<th>Change (at 1 year)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV EF (%)</td>
<td>58.9 (4.4)</td>
<td>0.4 (−0.7 to 1.7)</td>
<td>0.49</td>
</tr>
<tr>
<td>LV EDV (mL/m²)</td>
<td>81.7 (11.3)</td>
<td>−0.5 (−2.7 to 1.8)</td>
<td>0.65</td>
</tr>
<tr>
<td>LV ESV (mL/m²)</td>
<td>33.8 (6.5)</td>
<td>−0.6 (−1.9 to 1.0)</td>
<td>0.47</td>
</tr>
<tr>
<td>LV TPFR (ms)</td>
<td>472 (99)</td>
<td>−27 (−53 to −3)</td>
<td>0.035</td>
</tr>
<tr>
<td>RV EDV (mL/m²)</td>
<td>80.5 (12.0)</td>
<td>−2.2 (−4.1 to −0.4)</td>
<td>0.022</td>
</tr>
<tr>
<td>RV ESV (mL/m²)</td>
<td>33.6 (8.6)</td>
<td>−2.0 (−3.5 to −0.7)</td>
<td>0.0068</td>
</tr>
<tr>
<td>RV EF (%)</td>
<td>58.9 (6.0)</td>
<td>1.4 (−0.0 to 2.7)</td>
<td>0.067</td>
</tr>
</tbody>
</table>

LV, left ventricle; EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume; TPFR, time to peak filling rate; RV, right ventricle.

**References**


### PP21

**Fatigue, pain, and patient global assessment are poorly interconnected and poorly explained by other clinical outcome measures in individual patients with psoriatic arthritis**

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**Objectives:** To examine associations on the group level and concordance on the individual level between fatigue (FTG), pain, and patient global assessment (PaGl) as scored on a 0–100 visual analogue scales (VAS) in the daily clinic by patients with psoriatic arthritis (PsA). The influence of other clinical disease activity measures was also examined.

**Methods:** Data on 132 PsA patients treated with biological agents were extracted from the Danish registry for biological treatment in rheumatology (DANBIO): VAS FTG, pain, PaGl, physician global assessment (PhGl), and Health Assessment Questionnaire Disability Index

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(HAQ-DI), swollen and tender joint counts (SJC/TJC), C-reactive protein (CRP), Disease Activity Score based on 28-joint count-CRP (DAS28-CRP), and age. Associations were examined using simple linear and multiple regression analyses and were expressed by coefficients of correlation (group level) and standard errors of estimation (SEE) (individual level). Concordance between FTG, pain, and PaGl on the individual patient level was examined using the Bland–Altman method, yielding 95% lower and upper limits of agreement (LLoA and ULoA) and biases (mean of intra-individual differences).

**Results:** Age was 54 ± 13 years and PaGl 56 ± 28. FTG, pain, and PaGl were strongly inter-associated but SEE were substantial (r range 0.80–0.94, p < 0.0001, SEE range 11.5–16.9). FTG, pain, and PaGl were only poorly correlated with objective measures of disease activity (e.g. r range for SJC 0.19–0.25, p < 0.05), and were independently predicted best by each other, e.g. FTG by PaGl and pain (R² = 0.66, p < 0.05, SEE = 16.7). SJC, TJC, CRP, and PhGl did not add to the explanation of FTG, pain, or PaGl. The bias [LLoA;ULoA] for FTG vs pain was 8.5 ± 19.1 (p < 0.0001) [−29.1;45.9], for FTG vs PaGl 4.1 ± 19.4 (p < 0.05) [−34.0;42.2] and for PaGl vs pain 4.4 ± 11.5 (p < 0.0001) [−18.1;26.9]. Thus, biases were small but limits of agreement were pronounced.

**Conclusions:** FTG, pain, and PaGl were nearly identical and were strongly inter-associated on the group level, with no explanatory influence of more objective measures. However, in the individual patients substantial discrepancies between the VAS scores were observed. The findings emphasize the complexity of understanding and dealing with patient-reported outcomes in the daily clinic.

### Table PP22. Baseline predictors of development of gout over 30 years of follow-up.

<table>
<thead>
<tr>
<th>Baseline variables</th>
<th>Mean ± sd</th>
<th>Frequency (yes, %)</th>
<th>HR (95% CI)*</th>
<th>HR (95% CI)**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men with incident gout (n = 1014)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s-UA &gt; 405 µmol/L (yes, %)</td>
<td></td>
<td>10.1</td>
<td>5.4 (4.8–6.2)</td>
<td>4.1 (3.4–4.9)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>43.7 ± 6.6</td>
<td>–</td>
<td>14 (13–15)</td>
<td>14 (1.2–15)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.7 ± 3.3</td>
<td>–</td>
<td>1.4 (1.4–1.5)</td>
<td>1.3 (1.2–1.4)</td>
</tr>
<tr>
<td>eGFR (mL/min)</td>
<td>79.1 ± 10.5</td>
<td>–</td>
<td>0.9 (0.8–0.9)</td>
<td>0.9 (0.8–1.0)</td>
</tr>
<tr>
<td>s-Triglycerides (mmol/L)</td>
<td>1.5 ± 1.1</td>
<td>–</td>
<td>1.0 (1.1–1.2)</td>
<td>1.1 (1.0–1.1)</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>5.9 ± 5.7</td>
<td>–</td>
<td>1.0 (0.9–1.1)</td>
<td>1.0 (0.9–1.1)</td>
</tr>
<tr>
<td>Hypertension (yes, %)</td>
<td>–</td>
<td>16.4</td>
<td>1.7 (1.5–2.0)</td>
<td>1.3 (1.1–1.5)</td>
</tr>
<tr>
<td>CVD at baseline (yes/no)</td>
<td>–</td>
<td>2.1</td>
<td>1.7 (1.1–2.8)</td>
<td>1.4 (0.9–2.3)</td>
</tr>
<tr>
<td>Smoking (yes/no)</td>
<td>–</td>
<td>49.2</td>
<td>1.1 (1.0–1.3)</td>
<td>1.3 (1.1–1.6)</td>
</tr>
<tr>
<td>Mm-MAST ≥ 2 (yes, %)</td>
<td>–</td>
<td>30.8</td>
<td>1.5 (1.3–1.7)</td>
<td>1.3 (1.1–1.5)</td>
</tr>
<tr>
<td><strong>Women with incident gout (n = 261)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s-UA &gt; 405 µmol/L (yes, %)</td>
<td></td>
<td>1.5</td>
<td>12.5 (8.6–18.1)</td>
<td>5.9 (2.2–15.9)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>49.7 ± 7.4</td>
<td>–</td>
<td>1.7 (1.5–2.1)</td>
<td>1.3 (1.1–1.6)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.4 ± 4.2</td>
<td>–</td>
<td>1.6 (1.5–1.8)</td>
<td>1.6 (1.6–2.0)</td>
</tr>
<tr>
<td>eGFR (mL/min)</td>
<td>75.6 ± 10.9</td>
<td>–</td>
<td>0.8 (0.7–0.9)</td>
<td>0.8 (0.6–1.0)</td>
</tr>
<tr>
<td>s-Triglycerides (mmol/L)</td>
<td>1.1 ± 0.6</td>
<td>–</td>
<td>1.3 (1.2–1.4)</td>
<td>1.2 (1.0–1.5)</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>9.6 ± 7.7</td>
<td>–</td>
<td>1.3 (1.2–1.4)</td>
<td>1.2 (1.0–1.5)</td>
</tr>
<tr>
<td>Hypertension (yes, %)</td>
<td>–</td>
<td>22</td>
<td>2.0 (1.6–2.0)</td>
<td>1.1 (0.6–1.9)</td>
</tr>
<tr>
<td>CVD at baseline (yes, %)</td>
<td>–</td>
<td>3.4</td>
<td>2.1 (1.3–3.6)</td>
<td>3.0 (0.7–12.3)</td>
</tr>
<tr>
<td>Smoking (yes, %)</td>
<td>–</td>
<td>34.9</td>
<td>1.2 (0.9–1.5)</td>
<td>1.7 (1.0–2.8)</td>
</tr>
<tr>
<td>Mm-MAST ≥ 2 (yes, %)</td>
<td>–</td>
<td>2.8</td>
<td>1.3 (0.6–2.6)</td>
<td>1.2 (0.6–2.4)</td>
</tr>
</tbody>
</table>

*Hazard ratio (HR) is calculated per 1 sd or for dichotomous covariates (yes vs no).
†Baseline variables included in analysis: age, body mass index (BMI), serum (s) triglycerides, estimated glomerular filtration rate (eGFR), erythrocyte sedimentation rate (ESR), hypertension (yes/no), cardiovascular disease (CVD) (yes/no), diabetes mellitus (yes/no), smoking (yes/no); Malmö modification of the Michigan Alcoholism Screening Test (Mm-MAST) ≥ 2 (yes/no).

s-UA, serum uric acid.
clinical gout in a cohort from a population survey, the Malmö Preventive Project (MPP).

**Methods:** A total of 33,346 individuals (67% men, mean age 46 years at inclusion, mean follow-up 28 years) were screened between 1974 and 1992. The survey included: a questionnaire (socio-economic factors, alcohol consumption, smoking, comorbidities); a physical examination [body mass index (BMI), blood pressure]; and laboratory tests [serum uric acid (s-UA), fasting glucose]. The Malmö modification of the Michigan Alcoholism Screening Test (Mm-MAST) was used to identify alcohol risk consumption (Mm-MAST score ≥ 2). Subjects were followed to the date of first gout diagnosis, death, migration from the area, or 31 December 2014. To identify all gout diagnoses (using ICD codes) given at visits to physicians in primary care, in specialized inpatient or specialized outpatient care, the MPP cohort was linked to the regional Skåne Healthcare Register and to the National Patient Register, respectively. Individuals with a history of gout before the inclusion in MPP (n = 11) were excluded. Possible risk factors/markers at baseline associated with incident gout were analysed using a Cox regression model.

**Results:** Of 33,346 individuals participating in the MPP project, 1275 individuals (3.8%) [1014 men (4.5%) and 261 women (2.4%)] were diagnosed with gout over the nearly 30 years of follow-up. In both men and women, s-UA > 405 µmol/L at baseline (age-adjusted) was the strongest factor associated with incident gout. In addition, higher age, higher baseline BMI, higher serum triglycerides, hypertension, and current smoking were associated with incident gout in both genders. An Mm-MAST score of ≥ 2 was associated with incident gout only in men, while higher erythrocyte sedimentation rate (ESR) was associated with incident gout only in women (Table PP22).

**Conclusions:** In this large cohort of middle-aged individuals, hyperuricaemia, higher age, hypertriglyceridaemia, and higher BMI were associated with incident gout in both genders. Alcohol risk consumption predicted gout only in men. Higher ESR, as a possible marker of chronic inflammation, was a significant predictor only in women.

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**PP23**

Expression of uncoupling protein-1 in subcutaneous fat reduces the total cholesterol level and cardiovascular risk in female rheumatoid arthritis patients

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**Objectives:** To improve understanding of molecular mechanisms behind the increased cardiovascular (CV) morbidity in patients with rheumatoid arthritis (RA).

**Methods:** Transcription of uncoupling protein-1 (UCP1) was measured in the subcutaneous fat tissue, and serum levels of lipoproteins, adipokines, and inflammation markers in 185 middle-aged female patients (mean age 51 years) with RA, and compared between the groups stratified by total cholesterol (TC) levels and body mass index (BMI). The risk of dying of CV disease within 5 years was calculated electronically using the strategy proposed by Pocock et al (1).

**Results:** Cardiovascular risk (CVR) was highest (risk score 27.76, 5 year CVR 0.67%) in the patients combining high TC (> 5.1 mmol/L) and high BMI (> 25 kg/m²), while those with low levels of TC and BMI had the lowest CVR (risk score 10.82, CVR 0.11%). CVR was significantly decreased if either TC (TC<sub>lo</sub>BMI<sub>lo</sub>) or BMI (TC<sub>hi</sub>BMI<sub>hi</sub>) was low (p = 0.017 and p = 0.014, respectively). With the exception of the TC<sub>lo</sub>BMI<sub>hi</sub> group, these groups had no difference with respect to age, disease duration, inflammation defined by serum interleukin-6 (IL-6) and IL-1, and disease activity measured by 28-joint Disease Activity Score (DAS28). TC<sub>lo</sub>BMI<sub>hi</sub> patients had an overall increase in fat expression of UCP1 (p = 0.047), which has a cholesterol-lowering capacity and may explain low TC levels in this group. In contrast, TC<sub>hi</sub>BMI<sub>lo</sub> patients had a high prevalence of cases with unmeasurable UCP1 expression and higher levels of serum adiponectin (p = 0.053) and high-density lipoprotein (p < 10<sup>−5</sup>). Measurable expression of UCP1 was found in 79%. In the total cohort, patients with measurable UCP1 had higher inflammation and RA activity, presented by IL-6 (p = 0.0001), IL-1β (p = 0.037), and DAS28 (p = 0.0086), compared to those with no UCP1 expression. TC<sub>lo</sub>BMI<sub>hi</sub> patients had an overall increase in fat expression of UCP1 (p = 0.047) and the lowest prevalence of cases with no UCP1 expression (6.2%).

**Conclusions:** The study shows that UCP1 expression in subcutaneous fat may be a CV protective mechanism in RA patients. The inflammation seems to be the driving force behind UCP1 expression in RA.

**Reference**


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**PP24**

Predictors of drug survival of abatacept in rheumatoid arthritis: results from a large national quality register cohort study

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Clinical Sciences, Lund, Lund University, Lund, Sweden, \(^2\)Rheumatology Unit, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden

**Objectives:** To compare the effectiveness of abatacept in the treatment of rheumatoid arthritis (RA) between bionaïve patients and patients with previous biological disease-modifying anti-rheumatic drug (bDMARD) treatment, and to investigate predictors of remaining on treatment with abatacept.

**Methods:** This observational cohort study was based on a national quality register. Patients with a diagnosis of RA who initiated treatment with abatacept between 1 April 2006 and 20 November 2017 were included. Patients were censored at abatacept discontinuation, death, migration, or the end of the study period. Survival on drug, by previous exposure to bDMARDs, was estimated using the Kaplan–Meier method. Predictors of discontinuation of abatacept were investigated in Cox proportional hazards analyses, with significance-based backwards stepwise selection of variables for the final multivariate model.

**Results:** A total of 2716 patients with RA started abatacept during the study period (80% females, mean age 59 years, mean duration of RA 14 years). Of these, 17% had had no previous bDMARD treatment (bionaïve patients), 27% had received one bDMARD previously, and 56% had been treated with two or more bDMARDs. There were significant differences in drug survival across categories of previous bDMARD exposure (p = 0.002). The median survival time on treatment was 2.23 years for bionaïve patients (95% CI 1.69–2.79), 1.68 years for those with one previous bDMARD (95% CI 1.34–2.01), and 1.56 years for those with at least two previous bDMARDs (95% CI 1.35–1.76). In bivariate analyses, bionaïve patients were less likely to discontinue treatment compared to those treated with at least two previous bDMARDs (Table PP24). Measures of disease severity were associated with reduced drug survival (Table PP24). In the final multivariate model, there was a positive association between pain score and abatacept discontinuation, whereas male patients and those on methotrexate had a reduced risk of stopping abatacept (Table PP24).

**Conclusions:** Survival on abatacept was significantly longer in bionaïve RA patients compared to those previously exposed to bDMARDs. Concomitant methotrexate therapy, male gender, and low pain scores were associated with longer drug survival for abatacept.

**PP25**

**Patient and physician global assessments reflect strongly diverging attitudes between patients with psoriatic arthritis and their rheumatologists to severity of disease and to the relative importance of different outcome measures**

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**Objectives:** As there is no single ‘gold standard’ variable for assessment of disease activity in patients with psoriatic arthritis (PsA), several markers of disease activity are used, including global assessment by the patient (PaGl) and the physician (PhGl). The study aimed to examine associations on the group level and agreements on the individual level between PaGl and PhGl in PsA patients.

**Methods:** Clinical data on 76 PsA patients with active disease planned to initiate biological treatment were extracted from the Danish DANBIO registry for rheumatology: PaGl, PhGl, and pain [0–100 visual analogue scale (VAS)], 28 swollen and tender joint counts (SJC and TJC), C-reactive protein (CRP), Health Assessment Questionnaire Disability Index (HAQ-DI), Disease Activity Score based on 28-joint count-C-reactive protein (DAS28-CRP four variables), and age. Associations were examined by simple linear and multiple regression analyses. Agreement between the VAS scores was expressed as the bias (mean difference between individual scores) and the 95% lower and upper limits of agreement (LLoA; ULoA) according to Bland–Altman.

**Results:** Average age was 52.2 ± 11.1 years, DAS28-CRP 4.7 ± 1.1, PaGl 63.7 ± 23.2, and PhGl 39.9 ± 19.8. Thus, the difference between PaGl and PhGl was substantial on the group level (bias = 23.8, p < 0.0001).
Differences were even more pronounced on the individual level, ranging from ~21.9 (LLoA) to +69.5 (UloA). The bias (LLoA/UloA) for PaGl vs pain was 4.9 (~17.1:22.0) and for pain vs PhGl 18.9 (~23.0:60.8). PaGl was significantly but weakly correlated with PhGl ($R = 0.42, p < 0.0001$) but with a high standard error of estimation $= 21.2$. PaGl was independently predicted by pain ($\beta = 0.76, p < 0.0001$) and HAQ-DI ($\beta = 0.19, p < 0.01$), but was not predicted by PhGl ($p = 0.61$). PhGl was independently predicted by SJC ($\beta = 0.43, p < 0.0001$), pain ($\beta = 0.41, p < 0.0001$), and CRP ($\beta = 0.20, p < 0.05$), but was not predicted by PaGl ($p = 0.49$).

**Conclusions:** PaGl was, in general, scored considerably higher than PhGl. On the individual patient level, differences between PaGl and PhGl varied substantially. PaGl was best explained by pain, but PhGl by SJC. The findings reflect strongly diverging attitudes between PsA patients and their rheumatologists to severity of disease and to the relative importance of different outcome measures.

**PP26**

**Physical functioning in rheumatoid arthritis is controlled by hippocampus and insulin-like growth factor-1 receptor signalling**

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**Objectives:** Neuropsychiatric symptoms such as depression, anxiety, and fatigue are common in rheumatoid arthritis (RA) and may be critical for patients’ quality of life and functional abilities. Regeneration of neurons in the adult brain is rare but takes place in the hippocampus and is supported by insulin-like growth factor-1 receptor (IGF1R) signalling. In this study, we investigated the association between functional disability, well-being, and IGF1R signalling in RA.

**Methods:** Physical functioning and well-being were assessed in 215 patients with established RA (184 females, 31 males, age 52.3 years, disease duration 11 years). Material was collected using established self-reported tools: the Health Assessment Questionnaire (HAQ), Fibromyalgia Inactivity Questionnaire (FIQ), and Hospital Anxiety and Depression Scale (HADS). Pain threshold was measured by an algometer. Serum levels of active IGF1 and interleukin-6 were measured with an enzyme-linked immunosorbent assay. Transcription of IGF1R and insulin receptor substrates IRS1 and IRS2 in white blood cells (WBCs) was measured with reverse transcription–polymerase chain reaction. Magnetic resonance images of the head were obtained in 15 randomly selected female participants at 3 T and processed with brain morphometry software (MAPER). Statistical analysis included the Mann–Whitney U-test and Spearman’s rank correlation coefficient.

**Results:** Physical functioning in RA patients showed a gradual decrease from the non-depressed group (n = 154), via the patients with incongruous data [subjective depression (visual analogue scale > 45 mm), but HADS ≤ 7, n = 26, p = 0.006], to the patients with depression confirmed by HADS (HADS ≥ 8, n = 35, p < 0.0001). The patients with incongruous data had high IGF1R-WBCs (p = 0.04). High IGF1R-WBC was associated with more intense pain perception, low pain threshold, anxiety, and low IGF1. Since IGF1R signalling is important for hippocampus function, we measured hippocampi in RA patients. We observed that smaller hippocampal volume was associated with higher disability index (HAQ) (p = 0.009), higher perception of induced pain (p = 0.0006), and lower serum levels of IGF1 (p = 0.05).

**Conclusions:** Our results show a connection between IGF1R signalling and physical functioning and well-being in RA patients. We identify the hippocampus as the anatomical structure homing this connection.

**PP27**

**Quality of life and disease activity of transition-phase patients with juvenile idiopathic arthritis and adult-onset rheumatic diseases**

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**Objectives:** Across diagnostic groups, the successful transition of adolescent and young adults from children’s hospitals to adult care is associated with decreased treatment adherence and treatment results. The aim of this study was to assess the health-related quality of life (HRQoL) and disease activity following transfer of care of juvenile idiopathic arthritis (JIA) patients to the adult clinic and of patients with adult-onset rheumatic diseases in the same outpatient clinic.

**Methods:** All consecutive JIA patients aged 16–20 years who visited the specific transition clinic between September 2016 and August 2017 and all consecutive adult-onset arthritis patients between December 2016 and August 2017 in the rheumatology outpatient clinic of Helsinki University Hospital were evaluated. HRQoL was measured by a generic instrument, the 15D questionnaire.
Results: A total of 291 patients, 130 with JIA and 161 adults, were identified, with respective median disease durations of 6.5 and 4.0 years. Adults had higher 28-joint Disease Activity Score (DAS28) than JIA patients (DAS28 2.6 ± 1.1 vs 1.8 ± 0.6, p < 0.05), lower Health Assessment Questionnaire–Disability Index (median 0.25 vs 0, p < 0.01), and lower HRQoL measured by 15D (0.87 ± 0.10 vs 0.94 ± 0.06, p < 0.01). Adults were more frequently smokers than JIA patients (21% vs 7%, respectively, p < 0.01). Smoking adults had more active disease (DAS28 3.0 ± 1.2 vs 2.4 ± 1.0) and lower HRQoL (15D 0.82 ± 0.12 vs 0.89 ± 0.09, p < 0.01) than non-smoking adults.

Conclusions: Transition-phase JIA patients had lower disease activity and better HRQoL than patients with adult-onset rheumatic diseases with similar duration of the disease. Smoking was associated with more active disease and lower HRQoL in the adult patients.

PP28

Hydroxychloroquine improves the blood lipid profile in rheumatoid arthritis and systemic lupus erythematosus after four and eight weeks of treatment: a randomized interventional study

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Objectives: Cardiovascular comorbidity is increased in rheumatoid arthritis (RA) and in systemic lupus erythematosus (SLE). In both RA and SLE, retrospective studies have shown an association between treatment with chloroquine and a positive impact on cardiovascular risk factors. However, interventional studies are scarce. We therefore aimed to investigate the effects of hydroxychloroquine (HCQ) (Plaquenil®) treatment on the blood lipid profile and vascular function, after 4 and 8 weeks, in patients with RA and SLE.

Methods: Patients with RA (n = 25) or SLE (n = 7) (mean age 53 years) and low to medium disease activity [28-joint Disease Activity Score (DAS28) < 4.6 and Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) < 6, respectively] were included. Twelve patients with RA and four with SLE were randomized to start HCQ treatment after 4 weeks to exclude the impact of care on the results. Total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), apolipoproteins, blood-glucose, glycosylated haemoglobin (HbA1c), blood pressure and vascular function, as measured with pulse-wave analysis (Arteriograph®), were investigated before, and after 4 and 8 weeks of treatment with HCQ.

Results: Thirty patients completed the study period of 8 weeks with HCQ medication. At the point of 4 weeks the TC levels decreased (mean 5.43 mmol/L to 5.1 mmol/L) and remained significantly decreased at 8 weeks (p = 0.005). This was also seen in LDL levels, which decreased from 3.03 mmol/L at inclusion to 2.68 mmol/L after 4 weeks and stayed significantly decreased after 8 weeks (p = 0.002), as well as apolipoprotein B, which decreased after 4 weeks from 0.95 g/L to 0.90 g/L and remained significantly lowered after 8 weeks (p = 0.033). HbA1c levels also decreased, however not with statistical significance. No significant changes were seen in vascular function. There was no significant difference in the results of the two treatment groups implicating a genuine impact of HCQ.

Conclusions: HCQ treatment over 8 weeks improved the lipid profile in patients with low- to medium-active RA and SLE. A numerical improvement in HbA1c levels was seen. No influence on vascular function was noticed.

References


PP29

Durability, maintenance, and effects of dose reduction following prolonged treatment with baricitinib

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Objectives: It is clinically relevant to understand the durability and maintenance of response to baricitinib (BARI), a selective Janus kinase (JAK)1/JAK2 inhibitor, with prolonged use, and the dose-tapering strategies available after achieving disease control.

Methods: Upon completion of BARI phase 3 originating studies (OS) (RA-BEGIN, RA-BEAM, RA-BUILD, and RA-BEACON), patients could enter the long-term extension (LTE) study, RA-BEYOND. Durability of response was evaluated as proportion of patients achieving a Simplified Disease Activity Index (SDAI) score $\leq 11$ in the OS and through 96 weeks in the LTE. Maintenance of response was evaluated as the proportion of patients who had responded to BARI at entry into LTE and maintained the response at week 96. Within RA-BEYOND, patients who received BARI 4 mg for $\geq 15$ months and achieved sustained low disease activity (LDA) [Clinical Disease Activity Index (CDAI) $\leq 10$] or remission (CDAI $\leq 2.8$) at two consecutive visits, were re-randomized in a blinded manner to continue BARI 4 mg or step down to 2 mg.

Results: Durability of response was evident as response rates were higher 96 weeks after entry into RA-BEYOND compared to week 12 of the OS. Most responders at entry into LTE maintained their response through to week 96 (data not shown). Dose reduction to BARI 2 mg once daily (q.d.) resulted in small increases in disease activity up to week 48 compared to BARI 4 mg. CDAI $\leq 10$ rates at week 48 were 68.2 for BARI 2 mg (vs 80.8 for 4 mg, p $\leq 0.01$). By week 48, a majority of patients (in both groups) had recaptured (data not shown) or maintained the state of LDA or remission.

Conclusions: Effectiveness of BARI, as measured by the durability and maintenance of response, is maintained with prolonged therapy. In line with the observations from the OS, 4 mg q.d. is the most efficacious dose. Dose tapering to 2 mg q.d. may be a reasonable consideration according to treatment goals and responses of an individual patient.

PP30

Risk for work disability in incident patients with rheumatoid arthritis and spondyloarthritis varies between healthcare districts in Finland: an indicator of treatment effectiveness?

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Objectives: Idiopathic inflammatory arthritides tend to lead to decreased functional and working capacity if not effectively treated. Early suppression of disease activity is essential for the maintenance of working ability. The incidence of work disability is an important measure of treatment effectiveness, although it is influenced by demographic, occupational, and social factors, as well. The aim of this study was to assess the incidence of work disability pensions and the number of all work disability days in patients who contracted rheumatoid arthritis (RA) or spondyloarthritis (SpA) from 1 January 2000 to 31 December 2014 in 20 healthcare districts compared to the population controls. The comparison was performed to minimize biases due to differences in other factors impacting on work disability.

Methods: Incident patients who were working or at least available to the workforce at the index date were collected from the national medication reimbursement register. Three population controls according to age, gender, and the place of residence were identified for each patient. The individuals were followed up until 31 December 2015, or until retirement because of age, 65 years of age, or death, whichever occurred the earliest.

Results: In total, 18 694 patients with RA and 8169 with SpA were found. Compared to the population controls, hazard ratio (adjusted for education level) for all permanent work disability pensions in RA varied from 2.17 to 3.40 and in SpA from 1.53 to 8.77. Further, the cumulative number of all work disability days due to any cause (incidence rate ratio) varied from 1.19 to 2.24 in RA and from 1.37 to 4.31 in SpA. In RA and in SpA, respectively 66% and 55% of the disability pensions were due to the rheumatic disease itself. Depending on the district, 8–19% of RA patients and 2–11% of SpA patients ended up on pensions caused by RA and SpA in 10 years.

Conclusions: Marked inequality considering maintenance of working capacity prevails between patients contracting RA and SpA in Finland.

PP31

Summary of baricitinib effect on patient-reported outcomes in a methotrexate-inadequate responder patient population

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Objectives: To summarize evidence on the effect of baricitinib (BARI) on patient-reported outcomes (PROs).

Methods: In RA-BEAM (NCT01710358), 1305 inadequate responders to methotrexate (MTX) were randomized 3:3:2 to placebo (PBO) q.d., BARI 4 mg q.d., or adalimumab (ADA) 40 mg every other week. Post-hoc analyses assessed the impact of BARI on the pain visual analogue scale (VAS), Health Assessment Questionnaire–Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy–Fatigue (FACT-F), and duration of morning joint stiffness (MJS): (i) proportion of patients with pain improvement of ≥ 50% of their baseline pain (VAS: 0–100 mm) in each treatment arm; and (ii) differences in PROs, at week 24, among patients with Disease Activity Score based on 28-joint count–erythrocyte sedimentation rate (DAS28-ESR)-defined low disease activity (LDA) and remission per treatment group.

Results: A significantly greater proportion of patients on BARI achieved ≥ 50% pain improvement at week 1 compared to PBO (26% vs 13%; p ≤ 0.001) and at week 4 compared to ADA (48% vs 37%; p ≤ 0.01); improvements were sustained through to week 24 (BARI 61% vs ADA 52%; p ≤ 0.05). Patients in LDA at week 24, on BARI, reported significantly greater improvements in pain and HAQ-DI than those on ADA and PBO. In remission patients at week 24, significantly greater improvements in HAQ-DI scores were reported with BARI than with PBO; among LDA patients, significantly greater improvements in MJS duration were observed with BARI and ADA than with PBO.

Conclusions: BARI demonstrated rapid, sustained improvements in pain. Remission or LDA is associated with improvements in pain, physical functioning, and health-related quality of life for patients on BARI, ADA, or PBO, but with most marked improvements on BARI and ADA.

PP32

Evaluation of serum protein levels at baseline as predictors of response to methotrexate in patients with early rheumatoid arthritis: results from the SWEFOT trial population

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Objectives: Methotrexate (MTX) is a standard first line therapy option for patients with early rheumatoid arthritis (eRA). However, a substantial proportion of patients still do not respond to MTX. Here, we investigated baseline biomarkers as predictors of response to MTX.

Methods: We analysed a group of patients (N = 135) with eRA from the Swedish Pharmacotherapy (SWEFOT) trial population. Baseline serum levels of 177 proteins were profiled using 380 antibodies in a suspension bead array format. Median fluorescence intensity (MFI) levels of the proteins were subsequently analysed for association with achievement of low 28-joint Disease Activity Score (DAS28 ≤ 3.2) after 3 months of MTX therapy (primary outcome). Proteins that remained significant in the multivariate model were used for receiver operating characteristics (ROC) curve analysis for the cut-off definition of MFI and categorization into high and low categories. The proportion of patients with the primary outcome between the generated categories was compared using the chi-squared test.

Results: In multivariate analysis, serum levels of two of the 177 proteins at baseline, matrix metalloproteinase-7 (MMP-7) and alpha-chain of fibrinogen (FGA), were significantly different among patients who achieved and those who did not achieve low DAS28 at 3 months. ROC curve analysis revealed AUCs of 0.692 for MMP-7 and 0.699 for FGA (p < 0.001; Figure PP32A). ROC curve-based dichotomization indicated that of patients with low vs high levels of either MMP-7 or FGA, 60% vs 24% and 58% vs 22%, respectively, achieved low DAS28 (p < 0.001; Figure PP32B and C). Among patients with low categories of both proteins, 79% achieved low DAS28 at 3 months, compared with only 18% of those in high categories for both proteins (p < 0.001; Figure PP32D). Validation in the COMBINE cohort with available MMP-7 data (the concentration of which was measured by a different method) did not confirm the results from the SWEFOT trial.

Conclusions: Low levels of MMP-7 and FGA at baseline were associated with better clinical outcome in eRA patients. Following further characterization, such biomarkers would be of high clinical relevance for the optimization of treatment of RA.

PP33

Safety summary results of baricitinib focusing on serious infection events and preselected comorbidities

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Objectives: To evaluate the incidence rate (IR) of serious infection events (SIEs) and selected comorbidities with baricitinib (BARI).

Methods: Exposure-adjusted IRs of SIEs were summarized in six-study- and four-study-placebo (PBO)-controlled sets, 0–24 weeks, and All-BARI-RA set [any BARI dose for ≤5 years (phase 1–3/long-term extension studies); potential SIE risk factors using Cox models investigated in this group]. Sensitivity analysis for comorbidities included patients from five studies (n = 1683; BARI 4 mg/PBO; ≤16 weeks).

Results: The most frequent SIEs in the All-BARI-RA set [n = 3492; 5133 patient-years of exposure (PYE)] were pneumonia, herpes zoster, urinary tract infection, and cellulitis (all <1%). In total, 150 patients reported SIEs [IR = 2.9/100

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patient-years (PY)] and two patients with SIEs died (IR = 0.04/100 PY). During weeks 0–24, similar SIE rates were observed in the BARI 4 mg (n = 997; 417 PYE) and PBO (n = 1070; 403 PYE) groups in the six-study set, and between the BAR12/4 mg (n = 479; 192 PYE/n = 479; 194 PYE) dose groups in the four-study set. Prior biologic/corticosteroid use, age, region of Asia (excluding Japan), and body mass index were independent factors for SIEs in the All-BARI-RA set, and none differed significantly between BARI 4 mg and PBO in the six-study set. Selected comorbidities did not affect the incidence of treatment-emergent adverse events (most common: nasopharyngitis and upper respiratory tract infection), serious adverse events (SAEs), discontinuations, or deaths caused by SAEs for BARI 4 mg vs PBO.

Conclusions: SIE incidence was similar between BARI and PBO- and BARI 2 mg/4 mg-treated RA patients up to week 24. No trends were observed for patients in each preselected comorbidity subgroup for increased risk of events after treatment with BARI 4 mg compared with PBO up to week 16.

PP34

First line tumour necrosis factor-α-inhibitor therapy reduces non-steroidal anti-inflammatory drug need in patients with rheumatic diseases

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Objectives: Chronic pain is a common problem in most inflammatory rheumatic disorders. Tumour necrosis factor-α (TNF-α)-inhibitor therapy has been effective in controlling various rheumatic disorders and has been shown to reduce pain. However, to our knowledge there have not been any studies demonstrating the impact of TNF-α-inhibitor therapy on non-steroidal anti-inflammatory drug (NSAID) consumption following TNF-α treatment.

Methods: All patients with rheumatic disorders who are treated with biological disease-modifying anti-rheumatic drugs in Iceland are registered in ICEBIO, which is a nationwide database based on the Danish Registry for biological therapies in rheumatology (1). On 1 February 2016 there were individual patient and treatment data on 1058 individuals. The Icelandic Directorate of Health operates an extensive prescription database for all electronic drug prescriptions that includes over 90% of all drug prescriptions in Iceland (2). We extracted all analgesic prescriptions (ATC codes M01A, M01B, N02A, N02B, R05DA, and N03AX) made 2 years before and after the initiation of first line TNF-α-inhibitor therapy for all patients in ICEBIO with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). As controls, we selected randomly five individuals, age and gender matched, for the same time frame. In the present study, we report our findings of prescription patterns for NSAIDs.

Results: We received data from 366 patients with RA, 218 with AS, 251 with PsA, and 4700 controls. In total, the patients were prescribed 6.7 times more daily doses (DDs) of NSAIDs than the controls, or 149 vs 22 per year. After initiation of the TNF-α-inhibitor therapy, the DD of NSAIDs reduced by 43% in the RA group (148 to 85 DD/year), 47% for AS (154 to 83 DD/year), and 43% in the PsA group (157 to 90 DD/year). Thus, the patient population was still using NSAIDs 3.9 times more than controls. This is a work in progress and further details will be presented in Helsinki.

Conclusions: Patients with rheumatic disorders requiring TNF-α-inhibitor therapy use large amounts of NSAIDs, especially before initiation of biological therapy. However, they frequently need NSAIDs after the initiation TNF-α-inhibitor therapy, underlining the importance of analgesia in the daily management of these patients.

References


PP35

Recognizing imminent rheumatoid arthritis: survivin measurement and defined clinical symptoms predict transition from arthralgia to rheumatoid arthritis

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Objectives: To combine surviving measurement and clinical symptoms, aiming to improve recognition of imminent rheumatoid arthritis (RA) among patients with arthralgia.

Methods: In a prospective study, patients referred for assessment at the Rheumatology Clinic at Sahlgrenska University Hospital, Gothenburg, during 12 consecutive months, were assessed. Medical records of first-visit patients were reviewed by two independent assessors. A set of joint symptoms describing clinically suspect arthralgia parameters (1) was applied to the records of the first and all consecutive visits for a period of 48 months. This distinguished (i) patients with arthralgia and arthritis, and (ii) patients with pre-RA, who developed RA during the follow-up period. Information about RA-specific antibodies and survivin in serum was added to the analyses.

Results: Among the total of 1743 first-visit patients, 63 patients were classified as having RA, 73 had undifferentiated arthritis, and 180 had unexplained arthralgia. During the prospective follow-up of the 180 patients with arthralgia, 32 patients developed arthritis and fulfilled the classification criteria of RA. Clinical parameters at the first visit were compared between those pre-RA patients and the remaining arthralgia patients (n=148) and with the RA patients at the first visit (n=63). Three joint symptoms distinguished pre-RA and arthralgia patients with odds ratio above 2.0; namely, symptoms in several small joint regions, increasing number of joints with symptoms over time, and patient experience of swelling of small hand joints. The combination of these three symptoms was sufficient to identify pre-RA cases with 92% sensitivity. Grouping the symptoms with information about age, gender, and serum levels of survivin or autoantibodies in the final algorithm resulted in reaching 50% specificity and 55% of positive prediction for transition from arthralgia to RA.

Conclusions: Clinical and serological parameters in combination aid recognition of imminent RA among arthralgia patients with appropriate sensitivity.

Reference

PP36

Improvements in work productivity with up to 104 weeks of apremilast monotherapy: results from a phase 3b, randomized, controlled study in biologic-naïve subjects with active psoriatic arthritis

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Objectives: ACTIVE is assessing the efficacy of apremilast (APR) monotherapy in biologic-naive subjects with active psoriatic arthritis (PsA) who may have had exposure to one prior conventional disease-modifying anti-rheumatic drug. Work productivity and activity impairment were assessed through week 104.

Methods: Subjects were randomized (1:1) to APR 30 mg b.i.d. or placebo (PBO). Subjects without ≥10% improvement in swollen/tender joint counts at week 16 were eligible for early escape. At week 24, all remaining PBO subjects switched to APR. Work productivity and

Table PP36. Improvements in Work Productivity and Activity Impairment Questionnaire: active psoriatic arthritis (WPAI:PsA) subscale scores (% point) at week 16, in apremilast (APR) and placebo (PBO) subjects.

<table>
<thead>
<tr>
<th>WPAI:PsA subscale</th>
<th>APR 30 mg b.i.d. (95% CI)</th>
<th>PBO, LS mean (95% CI)</th>
<th>Treatment difference (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presenteeism</td>
<td>n = 39</td>
<td>n = 56</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>−10.8 (−17.8, −3.8)</td>
<td>4.1 (−1.7, 9.9)</td>
<td>−14.9 (−24.1, −5.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>Work productivity loss</td>
<td>n = 40</td>
<td>n = 55</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>−11.9 (−18.8, −5.0)</td>
<td>3.5 (−2.4, 9.4)</td>
<td>−15.4 (−24.5, −6.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Activity impairment</td>
<td>n = 87</td>
<td>n = 103</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>−11.8 (−16.4, −7.1)</td>
<td>−0.5 (−4.7, 3.8)</td>
<td>−11.3 (−17.6, −5.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Absenteeism</td>
<td>n = 40</td>
<td>n = 55</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>−3.6 (−5.9, −1.3)</td>
<td>−3.0 (−4.9, −1.0)</td>
<td>−0.6 (−3.7, 2.4)</td>
<td>0.679</td>
</tr>
</tbody>
</table>

Results are from an analysis of covariance model, adjusted with baseline (BL) WPAI:PsA subscale scores, BL prednisone use (yes/no), and previous disease-modifying anti-rheumatic drug (DMARD) use (yes/no). Least square (LS) mean is estimated using the observed margins of the covariates. WPAI:PsA scores were evaluated for subjects with values at both BL and week 16. Absenteeism, presenteeism, and work productivity loss were evaluated only among employed subjects. Activity impairment scores were evaluated among all randomized subjects with scores at BL and week 16, regardless of job status.

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activity impairment were assessed at baseline (BL) and week 16 using the self-administered Work Productivity and Activity Impairment Questionnaire: PsA (WPAI:PsA), which includes four subscale scores (Absenteeism, Presenteeism, Work Productivity Loss, and Activity Impairment; higher scores = greater impairment). Work-related subscales were assessed for employed subjects; activity impairment was assessed for all subjects regardless of job status. Correlations were made at week 16 between WPAI:PsA and 36-item Short Form Survey (SF-36v2) Physical Functioning (PF), Bodily Pain (Pain), and Vitality (VIT) scores, as well as associations with American College of Rheumatology 20% (ACR20) response. Work productivity was assessed through week 104.

Results: BL parameters were similar for APR and PBO subjects with WPAI:PsA scores. At week 16, APR significantly improved work productivity and activity impairment vs PBO, with significantly greater improvements in overall Work Productivity Loss (p = 0.001) and Activity Impairment (p < 0.001) scores (Table PP36). Estimated change in Absenteeism was similar with APR vs PBO (p = 0.679). Presenteeism showed significant improvement with APR vs PBO (~10.8% vs 4.1%; p = 0.002). At week 16, statistically significant correlations were seen between WPAI:PsA (except Absenteeism) and SF-36v2 PF, Pain, and VIT scores, as were associations with ACR20 response. In subjects randomized to APR at BL, week 16 WPAI:PsA score improvements were generally maintained through week 104 in those continuing APR.

Conclusions: Biologic-naïve subjects receiving APR alone showed an overall improvement in work productivity at week 16, correlating with SF-36v2 PF, Pain, and VIT scores, and associated with the ACR20 response.

PP37
Safety profile of baricitinib for the treatment of rheumatoid arthritis up to 5.5 years: an updated integrated safety analysis

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Objectives: To describe updated safety data on baricitinib (BARI) from an ongoing long-term extension (LTE) study in moderate to severely active RA.

Methods: Long-term safety of once-daily BARI was evaluated in the All-BARI-RA data set [all active RA patients on BARI from eight randomized trials (four phase 3, three phase 2, one phase 1b) and one LTE study (data up to 1 September 2016)]. PBO comparisons were evaluated up to week 24 in the PBO-4 mg data set from six phase 2/3 trials, in which patients were randomized to BARI 4 mg, censoring at rescue, or treatment switch. Dose responses were evaluated from four phase 2/3 trials, in which patients were randomized to 2 or 4 mg, and included data from LTE (2 mg–4 mg-extended data set) censoring at rescue or dose change (as-treated analysis). Because of the latent period for malignancy, the 2 mg–4 mg-extended set was analysed without censoring for rescue or dose change. Incidence rates (IRs) per 100 patient-years (PY) were calculated.

Results: Altogether, 3492 patients received BARI for 6637 total PY of exposure (> 2400 PY increase from previous analysis); maximum exposure was 5.5 years. No differences were seen for BARI 4 mg vs PBO in adverse events leading to permanent discontinuation, death, malignancy, serious infection, or major advanced cardiovascular events. Herpes zoster IR was significantly higher for BARI 4 mg vs PBO (IR 1.0 vs 4.3). Malignancy (excluding non-melanoma skin cancer) IRs were 0.5 and 1.3 for 2 mg and 4 mg (as-treated analysis) and 0.7 and 0.9 (as-randomized analysis). IRs for the aforementioned events and lymphoma (0.09), gastrointestinal perforation (0.05), and tuberculosis (0.15, all in endemic areas) in the current All-BARI-RA were similar to previous reports. Less than 1% of patients discontinued owing to abnormal laboratory results.

Conclusions: BARI maintained a safety profile similar to previous reports (1) and acceptable in the context of its demonstrated efficacy (2, 3).

References

PP38
Do sacroiliac joint pain provocation tests identify inflammation in patients with non-radiographic axial spondyloarthritis?

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**Objectives:** A clinical test which correlated with active inflammation at the sacroiliac joint (SIJ), identified by magnetic resonance imaging (MRI), may improve early identification of axial spondyloarthritis (axSpA), while helping to control healthcare costs (1). The aim of this preliminary study was to assess the construct validity of a set of pain provocation tests for the SIJs to identify patients who may have inflammation, using MRI as the reference standard.

**Methods:** Patients diagnosed with non-radiographic axSpA within the preceding 2 years were recruited, who met the following criteria: either (i) sacroiliitis on MRI and one feature of SpA inflammatory back pain, arthritis, enthesitis, uveitis, dactylitis, psoriasis, ulcerative colitis, response to non-steroidal anti-inflammatory drugs, family history for SpA, human leucocyte antigen (HLA)-B27, elevated C-reactive protein) or (ii) positive HLA-B27 and two features of SpA (2). Twenty participants were included (mean ± sd: age 38.8 ± 11.8 years; height 171 ± 8 cm; weight 74.4 ± 19.8 kg; seven males). Four pain provocation tests (Patrick’s Faber, Gaenslen’s, posterior pelvic pain provocation, and palpation of the long dorsal SIJ ligament) were applied to the participants, and MRI evaluation of the SIJs was performed. The clinical tests were applied by an experienced examiner, and the MRI findings at the SIJ were interpreted by an expert using the Spondyloarthritis Research Consortium of Canada (SPARCC) scoring system. Clinical tests were performed bilaterally and the presence of pain in one or both sides was considered positive. A SPARCC score > 0 was considered positive for inflammation. We used 2 × 2 contingency tables to calculate specificity, sensitivity, and likelihood ratios for each independent clinical test, and for the composite of pain provocation tests.

**Results:** Considering the construct validity (Table PP38), the Patrick’s Faber test, and the palpation of the SIJ ligament were the best individual tests. When the tests were combined, a positive in one out of three tests seems to be the best fit.

**Conclusions:** The use of pain provocation tests appears to have promise in identifying inflammation in the SIJ, and could potentially identify patients with a higher likelihood of MRI changes.

**References**


**PP39**

**Impact of secukinumab treatment on psoriatic arthritis patients with or without enthesitis at baseline: pooled data from two phase 3 studies (FUTURE 2 and FUTURE 3)**

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**Objectives:** Enthesitis is a common phenotypic manifestation of psoriatic arthritis (PsA), affecting approximately 70% of patients, and may be associated with worse outcomes (1). Secukinumab (SEC), a fully human monoclonal antibody that selectively neutralizes interleukin-17A, provided significant and sustained improvement in the signs and symptoms of active PsA, with sustained resolution of enthesitis in phase 3 studies (2, 3). The aim of this study was to evaluate whether patients with or without enthesitis at baseline benefitted from secukinumab treatment.

**Table PP38. Construct validity of pain provocation tests against magnetic resonance imaging reference standard.**

<table>
<thead>
<tr>
<th>Pain provocation tests</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Gaenslen’s</td>
<td>50</td>
<td>60</td>
<td>1.25</td>
<td>0.83</td>
</tr>
<tr>
<td>B. Posterior pelvic pain provocation</td>
<td>60</td>
<td>50</td>
<td>1.2</td>
<td>0.8</td>
</tr>
<tr>
<td>C. Patrick</td>
<td>60</td>
<td>70</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>D. Palpation sacroiliac joint ligament</td>
<td>80</td>
<td>50</td>
<td>1.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Combination of tests (A, C): 1/2*</td>
<td>64</td>
<td>67</td>
<td>1.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Combination of tests (C, D): 1/2</td>
<td>100</td>
<td>40</td>
<td>1.7</td>
<td>0</td>
</tr>
<tr>
<td>Combination of tests (A, B, C): 1/3</td>
<td>80</td>
<td>63</td>
<td>2.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Combination of tests (A, C, D): 2/3</td>
<td>60</td>
<td>60</td>
<td>1.5</td>
<td>0.7</td>
</tr>
<tr>
<td>Combination of tests (B, C, D): 2/3</td>
<td>60</td>
<td>80</td>
<td>2</td>
<td>0.3</td>
</tr>
<tr>
<td>Combination of tests (A, B, C): 2/3</td>
<td>60</td>
<td>60</td>
<td>1.5</td>
<td>0.7</td>
</tr>
<tr>
<td>Combination of tests (A, B, C): 3/3</td>
<td>30</td>
<td>70</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*For example, one test positive out of two tests applied.

LR, likelihood ratio.

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study was to report the impact of SEC treatment on efficacy outcome measures in active PsA patients with or without baseline (BL) enthesitis (defined by the Leeds Enthesitis Index), using pooled data from the FUTURE 2 (NCT01752634) and FUTURE 3 (NCT01989468) studies over 2 years.

**Methods:** SEC and placebo (PBO) were administered weekly during the first 4 weeks followed by subcutaneous maintenance dosing every 4 weeks thereafter (PBO until week 16/24). The results are reported only for SEC 300 and 150 mg (approved doses). Efficacy outcomes (American College of Rheumatology 20%/50%/70% response (ACR20/50/70), Psoriasis Area and Severity Index 90% response (PASI90), Health Assessment Questionnaire Disability Index (HAQ-DI), 36-item Short Form Health Survey physical component summary score (SF-36 PCS), and Disease Activity Score based on 28-joint count–C-reactive protein (DAS28-CRP]) were analysed post hoc in patients with enthesitis at BL (BLE; n = 466) or without enthesitis at BL (No BLE; n = 246). Observed data are presented for binary variables and least square (LS) means from analysis of covariance for continuous variables.

**Results:** A total of 65% of patients had BLE. BL demographics were balanced between the BLE and No BLE groups, except for a higher proportion of females and numerically higher tender joint count, disability (HAQ-DI) and lower physical function (SF-36 PCS) in BLE patients than in No BLE patients. At week 16, improvements in ACR and PASI responses, HAQ-DI, SF-36 PCS, and DAS28-CRP were similar in both groups treated with SEC 300 mg, but were lower (except for PASI) in BLE patients treated with SEC 150 mg (Table PP39).

Improvements in these outcomes followed a similar trend to week 104 in SEC-treated patients (Table PP39).

**Conclusions:** Although patients with BLE had more severe BL clinical characteristics than patients with No BLE, SEC showed higher efficacy than PBO at week 16 and sustained efficacy over 104 weeks in both groups, with greater magnitude of improvement in patients treated with SEC 300 mg than 150 mg.

### References

### Table PP39. Summary of results with secukinumab.

<table>
<thead>
<tr>
<th></th>
<th>BLE</th>
<th>No BLE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 300 mg Placebo 150 mg Placebo</td>
<td></td>
</tr>
<tr>
<td>ACR20∗†</td>
<td>16</td>
<td>53.5</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>56.8</td>
</tr>
<tr>
<td>ACR50∗†</td>
<td>16</td>
<td>31.3</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>44.7</td>
</tr>
<tr>
<td>ACR70∗†</td>
<td>16</td>
<td>16.0</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>26.5</td>
</tr>
<tr>
<td>PASI90∗†</td>
<td>16</td>
<td>50.0</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>67.9</td>
</tr>
<tr>
<td>HAQ-DI§</td>
<td>16</td>
<td>–0.5</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>–0.5</td>
</tr>
<tr>
<td>SF-36 PCS§</td>
<td>16</td>
<td>6.4</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>7.4</td>
</tr>
<tr>
<td>DAS28-CRP§</td>
<td>16</td>
<td>–1.7</td>
</tr>
<tr>
<td></td>
<td>104</td>
<td>–1.7</td>
</tr>
</tbody>
</table>

*Response (%); †at week 16/104, n = 144/132 (SEC 300), 159/145 (SEC 150), and 163 (PBO) with enthesitis, and n = 95/91 (SEC 300), 79/70 (SEC 150), and 72 (PBO) without enthesitis at BL; †at week 16/104, n = 66/56 (SEC 300), 82/62 (SEC 150), and 63 (PBO) with enthesitis, and n = 38/34 (SEC 300), 46/36 (SEC 150), and 30 (PBO) without enthesitis at BL (psoriasis subset); ≤8 least squares mean. BLE, baseline enthesitis; ACR20, ACR50, ACR70, American College of Rheumatology 20%, 50%, 70% response; PASI90, Psoriasis Area and Severity Index 90% response; HAQ-DI, Health Assessment Questionnaire Disability Index; SF-36 PCS, 36-item Short Form Health Survey physical component summary score; DAS28-CRP, Disease Activity Score based on 28-joint count-C-reactive protein; SEC, secukinumab; PBO, placebo; BL, baseline.
Abstracts
11.6 – 9.7
2014. Their patient records were studied in detail and mean age was 9 years and 45%
Aggregatibacter actinomycetemcomitans Porphyromonas gingivalis
P. gingivalis
SCR 2018 4 2014) 63% of pneumonias
acetaldehyde low-density lipoprotein
2006) 80% and
4 5 2014, was higher in
Hospital, Varkaus, Finland, Hospital, Iisalmi, Finland, Hospital, Kuopio, Finland, 4Department of Medicine, Varkaus Hospital, Varkaus, Finland, 5The Immunopharmacology Research Group, University of Tampere, Tampere, Finland, 6Department of Medicine, University Hospital of Tampere, Tampere, Finland

Objectives: To assess rheumatoid arthritis (RA), spondyloarthropathies (SpA), and undifferentiated arthritis (UA)-associated metabolic, inflammatory, and immunological markers.

Methods: Patients with inflammatory joint diseases, RA, SpA, and UA, participating in the Northern Savo 2010 Study were evaluated for metabolic syndrome (MetS), metabolic and inflammatory markers, antibodies to malondialdehyde–acetaldehyde low-density lipoprotein (MAA-LDL), Aggregatibacter actinomycetemcomitans, and Porphyromonas gingivalis.

Results: Among 135 newly diagnosed untreated patients, comprising 53 (39%) with RA, 44 (33%) with SpA, and 38 (28%) with UA, MetS was detected in 49%, 30%, and 47%, respectively. Interleukin-2 receptor-α was higher in patients with MetS in RA (p = 0.003) and SpA (p = 0.020) than without, and YKL-40 was higher in RA patients with MetS (p = 0.008). All antibody classes to MAA-LDL correlated with erythrocyte sedimentation rate and C-reactive protein. Antibody levels to A. actinomycetemcomitans and P. gingivalis correlated with antibodies to MAA-LDL. After adjustment for age and gender, MAA-LDL immunoglobulin A (IgA) (p = 0.009), IgG (p = 0.031), and IgM (0.001) levels differed between the diagnostic categories. The age- and gender-adjusted MAA-LDL IgA, IgM, or IgG did not differ between patients with MetS and those without MetS in any diagnostic category.

Conclusions: Among various arthritides, antibodies to P. gingivalis and MAA-LDL were most common in RA. Antibodies to modified lipoproteins associated with antibodies to periodontal bacteria, inflammation, and insulin resistance. The metabolic disorders in RA are associated with proatherogenic immune responses.

References

PP41 Analysis of 157 pneumonia episodes in Finnish children with juvenile idiopathic arthritis
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Objectives: To describe pneumonia episodes and to assess the risk factors for serious pneumonia in children with juvenile idiopathic arthritis (JIA).

Methods: The National Hospital Discharge Register in Finland receives data on all inpatient and outpatient visits with ICD diagnoses from hospitals. We searched for patients with JIA and pneumonia under 18 years of age during 1998–2014. Their patient records were studied in detail and the children with JIA and radiographically verified pneumonia were selected. Serious pneumonia was defined if the patient was hospitalized or received intravenous antibiotics.

Results: We detected 157 episodes of pneumonia in 140 children with JIA. Altogether, 111 cases (71%) were serious. In the first half of the follow-up (1998–2006) 80% and during the latter half (2007–2014) 63% of pneumonias were serious. The patients’ mean age was 9 years and 45% of them had oligoarthritis. Half of the patients had active JIA and comorbidities. Disease-modifying anti-rheumatic drugs (DMARDs) were used in 135 cases (86%) and 44% had combination therapy. The use of methotrexate (MTX) increased from 51% to 70% and the use of biological DMARDs (bDMARDs) from 15% to 40% when the first and the second halves of the follow-up were compared. No trend was found in glucocorticoid (GC) use. The microbiological aetiology was confirmed in 23% of pneumonia episodes. Five patients had positive blood cultures. A total of 29 JIA patients (18%) had antibiotics before pneumonia diagnosis and the antibiotic therapy was changed in 34 pneumonia cases (22%). Pneumonia symptoms were prolonged in 15 cases (10%). Seven patients were readmitted. Six patients (4%) were treated in the intensive care unit and two of them died (1%). When we compared patients with serious and non-serious pneumonia episodes, we observed no significant difference in the use of MTX, bDMARDs, and GCs.

Conclusions: Although the incidence of pneumonia and the treatment activity of JIA increased during 1998–2014, the proportion of serious pneumonias in JIA patients decreased. Active JIA and comorbidities were predisposing factors for pneumonia in half of the JIA patients.

References
1. Salonen PH, Säilä H, Salonen JH, Helminen M, Linna M, Kauppi MJ. Pneumonia in children with juvenile idiopathic arthritis in
www.scandjrheumatol.dk
Osteoarthritis and crystal arthritides

**PP42**

**Gene expression in adverse reaction to metal debris around metal-on-metal arthroplasty: an RNA-sequencing-based study**

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**Objectives:** Total joint replacement is a widely used treatment for advanced arthritis. Since 2000, cobalt–chrome (CoCr) metal-on-metal (MoM) implants have gained popularity in hip arthroplasties. Some of these patients developed ‘adverse reaction to metal debris’ (ARMD), characterized by local inflammation, infiltration of macrophages and lymphocytes, and pseudotumour formation. In the present study, we addressed the pathogenesis of the ARMD with genome-wide expression analysis.

**Methods:** Pseudosynovial ARMD tissue was obtained from revision surgeries of Articular Surface Replacement (ASR™; DePuy, Warsaw, IN, USA) implants. Control tissue was (i) osteoarthritis (OA) synovium from primary hip arthroplasties and (ii) inflammatory pseudosynovial tissue from metal-on-plastic (MoP) implant revision surgeries. mRNA expression profiles were studied by the Illumina HiSeq2500 RNA-sequencing system, functional analysis was performed against the Gene Ontology (GO) database, and interactions between genes were studied with STRING.

**Results:** In ARMD tissue, 1446 genes had a significantly higher and 1881 lower expression compared to OA synovial tissue. Among the genes with a fold change (FC) > 2.0 in either direction, those that were enriched were associated with immune response, macrophage and lymphocyte activation, skeletal system development, and certain leucocyte signalling pathways. CD2, CD52, CD53, and PRKACB were identified as potential central regulators of the most significant changes in gene expression. When the transcriptome of the ARMD tissue was compared to that in the inflammatory tissue around failed MoP prostheses, the expression of 16 genes was significantly higher and 22 lower. Many of these genes were associated with redox reactions, metal ion binding and transport, macrophage activation, and apoptosis. Several genes central to myofibroblast and osteoclast development were relatively high in MoP tissues.

**Conclusions:** Excessive amounts of CoCr debris produced by MoM hip implants induce, in some patients, a unique adverse reaction characterized by enhanced expression of genes associated with inflammation, redox homeostasis, metal ion binding and transport, macrophage activation, and apoptosis.

**PP43**

**Relationship between calcium pyrophosphate dihydrate crystal and operated knee osteoarthritis: gender-specific analyses**

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**Objectives:** We investigated the relationship between calcium pyrophosphate dihydrate (CPPD) crystal and operated knee osteoarthritis (OA), separated by gender.

**Methods:** From 2010 to 2017, 366 unicompartmental knee arthroplasty (UKA), total knee arthroplasty (TKA), and high tibial osteotomy (HTO) operations were performed for knee OA over grade III classified by the Kellgren–Lawrence grading scale. At the operation, joint fluids were collected and the CPPD crystal was elucidated using a polarizing microscope. We evaluated the relationship between CPPD crystals and age, body mass index (BMI), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and matrix metalloproteinase-3 (MMP-3) at the operation. We defined the osteophyte formation degree (OFD) as grade 0–3 (1). We also defined the lower extremity alignment as varus (femorotibial angle, FTA ≥ 180°), neutral (170° ≤ FTA < 180°), and valgus (FTA < 170°). The relationships between CPPD crystals, OFD and lower extremity alignment were also evaluated.

**Results:** CPPD crystals were detected from 101 knees (27.6%). The CPPD(+) rate in females (30.0%; 92/307) was significantly higher than that in males (15.3%; 9/59). There was a significant difference between CPPD (+/−) in males only for FTA (186.9°/182.0°). There were significant differences between CPPD(+/−) in females for age (76.3/72.4 years), FTA (182.7°/183.2°), and BMI (24.9/26.6 kg/m²). The more severe the OFD, the higher the CPPD(+) rate was in female, significantly. The CPPD(+) rate in valgus knees (60.9%) was significantly higher than that in varus knees (29.6%) in female.
**Conclusions**: The EULAR reported that female gender was not a risk factor associated with CPPD crystals (2). In contrast, a recent study using a relatively large sample size of Japanese cadaveric knees showed a significant correlation between CPPD crystals and female gender (3). Our data also showed a significantly high CPPD(+) rate in females. Because our data were based on Japanese patients only, Japanese ethnicity may influence this result. In addition, the significantly different items in male and female were different. These results suggest that the mechanism of CPPD deposition may differ with gender.

**References**


**PP44**

**Relationship between kinesiophobia and functional level in patients with gonarthrosis**

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1Department of Physiotherapy and Rehabilitation, Okan University, Faculty of Health Science, Istanbul, Turkey, 2Department of Physiotherapy and Rehabilitation, Uskudar University, Faculty of Health Science, Istanbul, Turkey, 3Department of Orthopaedics and Traumatology, Medipol Mega University Hospital, Istanbul, Turkey

**Objectives**: To investigate the relationship between kinesiophobia and functional level in patients with gonarthrosis.

**Methods**: The study included 62 women over 50 years old with diagnosed unilateral or bilateral symptomatic gonarthrosis according to American College of Rheumatology criteria. Patients were divided into two groups, i.e. early and late stage, according to Kellgren–Lawrence criteria. Thus, 31 patients with stage 1–2 (early) gonarthrosis and 31 patients with stage 3–4 (late) gonarthrosis were included in the study. Patients’ age, height, weight, medical history, dominant side, educational level, occupation, and complaint duration were noted. Patients’ fear of movement was assessed using the Turkish version of the Tampa Kinesiophobia Scale. Functional level was assessed with the Timed Up and Go test.

**Results**: The average age of patients with early-stage gonarthrosis was 58.32 ± 6.75 years. The average age of patients with late-stage gonarthrosis was 64.81 ± 8.46 years. There was a positive correlation between kinesiophobia and functional level in early-stage gonarthrosis (p = 0.001, r = 0.554). There was a positive correlation between kinesiophobia and functional level in late-stage gonarthrosis (p = 0.009, r = 0.462). There was a significant difference in functional levels between the early and late stages (p = 0.000). There was a significant difference in kinesiophobia between the early and late stages (p = 0.02).

**Conclusions**: Patients with reduced functional level have increased kinesiophobia in early-stage gonarthrosis and in late-stage gonarthrosis. Women with late-stage gonarthrosis have reduced functional level and increased kinesiophobia compared to those with early-stage gonarthrosis. Increased kinesiophobia may reduce the functional level in patients with late-stage gonarthrosis. In light of the present study results, treatment of kinesiophobia should be part of the gonarthrosis treatment to improve functional level in patients with osteoarthritis.

**PP45**

**Can we predict inadequate response to allopurinol dose escalation? Analysis of a randomized controlled trial**

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1Department of Medicine, University of Otago, Christchurch, New Zealand, 2Department of Rheumatology, Immunology and Allergy, Christchurch Hospital, Christchurch, New Zealand, 3Department of Medicine, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

**Objectives**: Despite its widespread use, many people receiving allopurinol fail to achieve target serum urate (SU). The aim of this study was to determine factors that predict inadequate urate-lowering response in a randomized controlled trial of allopurinol dose escalation in gout.

**Methods**: A total of 183 people receiving allopurinol for ≥ 1 month and with SU > 6 mg/dL were randomized to continue their current dose of allopurinol for 12 months and then enter the dose escalation phase (control/DE) or to begin allopurinol dose escalation immediately (DE/DE). Allopurinol was increased monthly until SU was < 6 mg/dL. Data obtained during the DE phase of the study were combined. Baseline was month 0 for DE/DE and month 12 for control/DE. Thirty-three participants were excluded (six discontinued allopurinol, nine with no values post-baseline, 18 died or were lost to follow-up). The remaining 150 participants were classified as: complete responders (CR) – achieved target SU at months 9 and 12 of the DE phase, or, if still dose escalating at month 9, achieved target SU by month 12; partial responders (PR) – achieved target at some stage but not fulfilling criteria for CR; and inadequate-responders (IR) – failed to achieve target SU at any time.
Results: Failure to achieve target SU (IR) was uncommon, occurring in 13/150 (8.7%), compared to 82 (54.7%) CR, and 55 (36.6%) PR. Mean (sem) SU was higher at the end of the 12 month dose escalation in the IR group compared with both CR and PR groups: 7.6 (0.31) vs 5.01 (0.06) and 5.97 (0.17) mg/dL, respectively (p < 0.001). Relationships between allopurinol, dose, oxypurinol, and SU for each responder group is shown in the Figure PP45. Using ROC curve analysis, baseline SU ≥ 8 mg/dL had a sensitivity of 69.2% and specificity of 85.1% in predicting IR. The odds ratio for being an IR if baseline SU was ≥ 8 mg/dL and baseline allopurinol dose > 200 mg/day, 7/15 (47%) had an inadequate response.

Conclusions: A minority of people with gout never achieve target SU when allopurinol dose is increased in a treat-to-target manner. Approximately half of those with SU ≥ 8 mg/dL and baseline allopurinol dose > 200 mg/day have an inadequate response to dose escalation.

PP46

No associations between structural changes on radiography, pain, and muscle strength in patients with knee osteoarthritis

E Kaya Mutlu1, Y Analay Akbaba1, G Tosun Aydin2

1Division of Physiotherapy and Rehabilitation, Istanbul University, Faculty of Health Sciences, Istanbul, Turkey, 2Division of Physiotherapy and Rehabilitation, Okan University, Faculty of Health Sciences, Istanbul, Turkey

Objective: Knee osteoarthritis is a leading cause of pain and physical disability. Osteoarthritis remains a poorly understood condition in which the link between structural abnormalities in the knee joint and the clinical expression of the disease remains unclear. The purpose of this study was to examine the association between radiography-defined structural abnormalities and clinical features such as pain, muscle strength, and function related to knee osteoarthritis.

Methods: In total, 118 patients with knee osteoarthritis (99 female, 19 male) with a mean age of 55.53 ± 6.55 years were included in the prospective study. Structural features were quantified by the Kellgren–Lawrence grade on radiography. The primary outcome measures were pain level, measured using a visual analogue scale, and muscle strength (hamstring and quadriceps), evaluated with a dynamometer. The secondary outcome measures of the functional assessment were the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Aggregated Locomotor Function (ALF) test scores. The ALF score is a sum of the mean time (seconds) taken to complete three physical function tasks: walking 8 m, ascending and descending seven stairs, and transferring from a sitting to standing position. Intercorrelations between parameters were computed through Pearson’s correlation analysis. Associations were examined using regression analyses.

Results: The mean age, body mass index, and disease duration were 55.5 ± 6.5 years, 31.1 ± 4.5 kg/m², and 53.2 ± 5.7 years, respectively. Significant
relationships were found between structural features and stair descent time \( (r = 0.26, p = 0.005) \) and stair ascent time \( (r = 0.22, p = 0.01) \). There were no significant relationships between structural features and pain \( (r = -0.11, p = 0.24) \) and muscle strength \( (r = 0.08, p = 0.39) \). In a stepwise linear regression model, stair descent and ascent time explained 26% of the variability in structural features.

**Conclusions:** In our study we determined that structural features were positively correlated with level of function in climbing and descending stairs in patients with osteoarthritis of the knee, except for pain and muscle strength. The Kellgren–Lawrence grade contributes less than expected to the understanding of pain and muscle function in knee osteoarthritis.

### CLINICAL SCIENCE

#### Other

**PP47**

Cytokine effects of apremilast as a mechanism of efficacy in systemic-naïve subjects with moderate plaque psoriasis: results from the UNVEIL trial

B Strober¹, A Alikhan², B Lockshin³, P Schafer⁴

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**Objectives:** Previous pharmacodynamic (PD) subanalyses of clinical trials have demonstrated that the effects of apremilast on key cytokines involved in the pathogenesis of plaque psoriasis play a role in determining clinical efficacy. It was therefore of interest to perform a more detailed PD substudy of a phase 4 randomized, controlled trial (UNVEIL), which evaluated the efficacy and safety of apremilast 30 mg b.i.d. (APR) in the treatment of systemic-naïve subjects with moderate plaque psoriasis [psoriasis-involved body surface area (BSA) 5–10%: static Physician Global Assessment (sPGA) = 3 (moderate)].

**Methods:** Subjects were randomized (2:1) to APR or placebo (PBO) for 16 weeks. From the PD subset, blood samples obtained at weeks 0 (baseline), 4, and 16 were analysed for interleukins (IL)-17A, -17F, -22, and -23; leptin; adiponectin; apolipoproteins A-I, A-II, B, and E; and numbers of circulating Th17 cells, Tregs, and total T cells. Correlations were examined between percentage change from baseline in key inflammatory biomarkers and clinical efficacy, based on assessments using the product of the sPGA and psoriasis-involved BSA (PGA × BSA).

**Results:** Of 221 total subjects randomized into the phase 4 trial, the PD subpopulation included 38 subjects (APR n = 26; PBO n = 12). At week 4, median percentage changes from baseline in IL-17A, -17F, -22, and -23 with APR and PBO, respectively, were -42.5% vs 9.3% (p = 0.0193), -64.4% vs 12.8% (p = 0.0005), -42.9% vs 8.6% (p = 0.0021), and -15.2% vs -6.6% (p = 0.6911). At week 16, percentage change in IL-17A significantly correlated with percentage change (improvement) in PGA × BSA \( (r = 0.45, p = 0.04) \). At weeks 4 and 16, levels of leptin, adiponectin, and apolipoproteins A-I, A-II, B, and E, as well as numbers of circulating Th17 cells, Tregs, and total T cells, were largely unchanged from baseline.

**Conclusions:** APR significantly decreased IL-17A, IL-17F, and IL-22 plasma protein levels at week 4. Improvements in clinical signs and symptoms of psoriasis at week 16, based on PGA × BSA, correlated with APR-mediated decreases in IL-17A without affecting the number of Th17 cells or Tregs. APR had no effect on adipokines or apolipoproteins.

**PP48**

Bone healing of atypical femoral fractures treated by teriparatide and/or low-intensity pulsed ultrasound therapy in patients with rheumatic diseases in north Japan

Y Takakubo, T Miyaji, Y Naganuma, H Oki, J Ito, D Ota, K Sasaki, M Takagi

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**Objectives:** Atypical femoral fractures (AFFs) with lack of trauma or less energy have been reported to relate to the long-term use of bisphosphonates (BPs) and glucocorticoids, and affect collagen diseases (1). Teriparatide has been reported to possibly accelerate the healing of AFFs (2); however, a recent report found no consistent effect of teriparatide on AFF healing (3). We analysed AFFs in patients with rheumatic disease in north Japan using teriparatide and/or low-intensity pulsed ultrasound therapy (LIPUS).

**Methods:** We investigated retrospectively all cases of AFF summarized by the ASBMR Task Force 2013 (1), including affected in the patients with rheumatic diseases in all hospitals of our prefectural area from 2009 to 2016.

**Results:** We found 110 cases with 123 AFFs in our prefectural area from 2009 to 2016. Twelve femurs with AFFs in nine rheumatic women were observed in that period. As comorbid conditions, three patients had systemic lupus erythematosus, two rheumatoid arthritis, and one each dermatomyositis, polyarteritis nodosa, systemic sclerosis, and thyroid function disorder. Fracture types were eight subtrochanteric and four diaphysal femoral fractures. All patients received BPs and all but one prednisolone (PSL). Mean duration of receiving these drugs was 70 months and 137 months, respectively. Mean dosage of PSL was 16.1 mg/day. Surgery using intramedullary nail fixation was
performed in all cases except one femur where a locking plate was used. Mean duration of postoperative observation was 28 months. At the latest follow-up, the sign of union at the fracture site was observed on X-ray or computed tomography of 11 femurs, but not for one femur. Mean duration of union of the fracture site was 12.6 (6–24) months in 11 femurs. Of 11 AFFs which showed healing of the fracture site, the mean duration of healing in five AFFs using both teriparatide and LIPUS was 13.2 (9–24) months, in three AFFs using only LIPUS 16.3 (12–24) months, and in three AFFs using neither teriparatide nor LIPUS 10.3 (9–12) months (Table PP48) (p = 0.09).

Conclusions: Twelve AFFs were observed in 2009–2016 in rheumatic patients in north Japan. Teriparatide with LIPUS was used for treatment in five cases (46%); however, the effect of teriparatide and/or LIPUS was not revealed in this study.

References


PP50

Efficacy and safety of ixekizumab at week 24 in biologic-experienced patients with active psoriatic arthritis: summary results

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1NIHR Leeds Biomedical Research Centre, Chapel Allerton Hospital, Leeds, UK, 2Immunorheumatology Research Laboratory, University of Milan, Milan, Italy, 3Rheumatology Department, University Hospital of Basurto, Bilbao, Spain, 4Rheumatology Department, Johann Wolfgang Goethe-University, Frankfurt am Main, Germany, 5Eli Lilly and Company, Indianapolis, IN, USA, 6Memorial Hospital, Kaohsiung City, Taiwan, 7Rheumatology Center, Hospital Pierre-Paul Riquet, Toulouse, France, 8Department of Medicine, Monash University and Cabrini Medical Centre, Malvern, Victoria, Australia, 9Eli Lilly and Company, Herlev, Denmark

Objectives: Psoriatic arthritis (PsA) is a chronic inflammatory condition associated with extra-articular manifestations. The high-affinity monoclonal antibody ixekizumab (IXE) selectively targets interleukin-17A (IL-17A) and improves physical function and disease activity in biological disease-modifying anti-rheumatic drug (bDMARD)-naïve patients with active PsA.
Methods: In this double-blind, phase 3 study, patients received subcutaneous placebo (PBO) or IXE 80 mg every 2 (Q2W) or 4 weeks (Q4W), following a 160 mg initial dose at week 0. Patients with inadequate response received rescue therapy at week 16. The primary endpoint was the 24 week American College of Rheumatology 20% response (ACR20). Categorical variables were analysed through logistic regression models; mixed-effect models of repeated measures were used for continuous variables. Analyses of skin outcomes were conducted on the intention-to-treat population with baseline involved body surface area of ≥ 3%. Safety was compared using Fisher’s exact tests.

Results: In all, 363 patients were randomized: average age 52 years, 53% female, 92% white, and with inadequate response to one or two tumour necrosis factor (TNF) inhibitors [204 (56.2%), 128 (35.3%), respectively] or who were TNF intolerant [31 (8.5%)]. The majority (87%) completed the 24 weeks. At week 24, significantly more IXE- vs PBO-treated patients achieved ACR20 [65 (53.3%), 59 (48.0%) vs 23 (19.5%); Q4W, Q2W, PBO, respectively], ACR50 [43 (35.2%), 41 (33.3%) vs 6 (5.1%), respectively], ACR70 [27 (22.1%), 15 (12.2%) vs 0, respectively], and reductions in functional disability [Health Assessment Questionnaire Disability Index (HAQ-DI)]. A significantly higher proportion of IXE-Q4W- vs PBO-treated patients reached resolution of dactylitis. Enthesitis improved with IXE. Significantly more IXE-treated patients achieved Psoriasis Area and Severity Index 75% response (PASI75). Significantly more patients achieved an itch numeric rating scale of 0 or a Dermatology Life Quality Index (DLQI) score of 0 or 1 in the IXE-treated groups. IXE-treated patients showed significantly greater improvements in PROs [36-item Short Form Health Survey physical and mental component summary scores (SF-36 PCS and MCS), EuroQol 5 Dimensions visual analogue scale (EQ-5D VAS); Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI-SHP)]. There was a higher incidence of injection site reactions in the IXE-treated groups, with the majority being mild, otherwise the incidence of treatment-emergent adverse events was similar across groups [83 (68.0%), 90 (73.2%) vs 76 (64.4%); Q4W, Q2W, PBO, respectively].

Conclusions: IXE improved arthritis, physical function, psoriasis, and DLQI compared to PBO, with no unexpected safety findings in patients with active PsA who had inadequate response or intolerance to prior TNF inhibitors.

Skeletal troponin I concentrations in different patient cohorts

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Objectives: Skeletal troponin I (skTnI) is a promising new biomarker for injured and diseased skeletal muscle tissue. Although studies have reported that circulating skTnI levels are elevated in response to trauma, exercise, and various skeletal muscle diseases (1–3), its clinical utility to serve as a diagnostic indicator has largely been unexplored. To evaluate the diagnostic value of skTnI, our aim was to measure the skTnI concentrations in different groups of individuals, and to study whether skTnI could be used to discriminate patients with diseased skeletal muscle tissue from patients with injured skeletal muscle tissue and from apparently healthy individuals.

Methods: Samples from 94 patients with different inflammatory myopathies (IMs), 151 patients with trauma-induced skeletal muscle injury, and 125 apparently healthy reference individuals were analysed with a novel in-house skTnI immunoassay. The assay had a limit of detection (LoD) of 1.2 ng/mL.

Results: The median skTnI levels (25th–75th percentiles) were 10.9 ng/mL (3.7 to 35.1 ng/mL), 2.7 ng/mL (< LoD to 7.6 ng/mL) and < LoD (< LoD to 2.4 ng/mL) for IM, trauma, and reference individuals, respectively. Statistically significant differences in measured skTnI concentrations were observed between all three study cohorts (Kruskal–Wallis p < 0.001).

Conclusions: Patients with IM had significantly elevated skTnI levels compared to the other two study cohorts. Thus, skTnI enables the discrimination of patients with IM from healthy individuals and from patients with severe skeletal muscle injuries.

References


PP51

Efficacy and safety of ixekizumab at week 52 in biologic-naïve patients with active psoriatic arthritis (SPIRIT-P1)

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www.scandjrheumatol.dk
Objectives:Ixekizumab (IXE) is a humanized monoclonal antibody, selectively targeting interleukin-17A with high affinity. At 24 weeks, IXE was superior to placebo (PBO) in achieving American College of Rheumatology 20%/50%/70% response (ACR20/50/70), resolution of enthesitis and dactylitis, and inhibiting the progression of structural joint damage in biological disease-modifying anti-rheumatic drug-naive patients with active psoriatic arthritis. This analysis investigates the efficacy and safety of IXE after 52 weeks of treatment.

Methods:In a phase 3, multicentre, double-blind randomized trial (SPIRIT-P1; NCT01695239), 417 patients were randomized to receive up to 24 weeks of treatment with PBO (n = 106), adalimumab 40 mg once every 2 weeks (Q2W; n = 101), or IXE 80 mg every 2 weeks (Q2W; n = 103) or every 4 weeks (Q4W; n = 107) following an 160 mg initial dose at baseline. Patients who completed the 24 week visit enrolled in the open-label extension period (EP), and received IXE Q4W or Q2W up to 1 year. Efficacy and safety were analysed using the EP population, i.e. all patients who received at least one dose of study drug. Missing values were imputed by non-response imputation for categorical variables and a modified baseline-observation-carried-forward approach for continuous variables.

Results:In all, 304 patients completed the EP. At week 52 for the Q4W/Q4W and Q2W/Q2W groups, the response rates for ACR20/50/70 were 69.1%/54.6%/39.2% and 68.8%/53.1%/39.6%, respectively. Throughout the 52 weeks, minimal changes in modified Total Sharp Score and improvements in enthesitis and dactylitis were observed. The improvements persisted through the EP in the Q4W/Q4W and Q2W/Q2W groups for Psoriasis Area and Severity Index 75/90/100 (78.8/66.7/56.1% and 81.8/78.2/67.3%); the changes from baseline to 52 weeks for percentage body surface area involvement of psoriasis were −13.5% and −9.3%, respectively, and for Nail Psoriasis Severity Index −16.5% and −21.6%, respectively. The number of treatment-emergent adverse events in the EP was comparable to that observed in the first 24 week period, and the majority were mild or moderate in severity (Table PP52).

Conclusions:Over a 52 week period, IXE demonstrated sustained efficacy, improving articular signs and symptoms of PsA, as well as plaque psoriasis and patient-reported outcomes, with comparable safety to that reported at week 24.

PP53

Evaluation of pain, general health perception, and physical function in patients with Behçet’s disease

PP54

Giant cell arteritis: a report on systematic physical evaluation and large vessel involvement as a prognostic risk factor for complicated disease course

References


Systemic connective tissue diseases and vasculitides
Table PP52. Study results.

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Only patients with enthesitis and Leeds Enthesitis Index (LEI) > 0 at baseline were included in the analysis.

Post-hoc analysis. Data are reported for patients with dactylitis, as qualitatively assessed by the investigator, at baseline, Leeds Dactylitis Index–Basic (LDI-B) score > 0 at baseline.

Data are reported for patients with baseline psoriatic lesion(s) involving ≥ 3% body surface area (BSA).

Minimal clinically important difference (MCID) ≥ 0.35 improvement from baseline; only patients with a baseline Health Assessment Questionnaire Disability Index (HAQ-DI) score ≥ 0.35 were included in the analysis.

ACR20, American College of Rheumatology 20% response; ADA, adalimumab 40 mg; IXE, ixekizumab 80 mg; PBO, placebo; mTSS, modified Total Sharp Score; LS mean CFB, least square mean change from baseline; DAS28-CRP, Disease Activity Score based on 28-joint count–C-reactive protein; PASI, Psoriasis Area and Severity Index; SF-36, 36-item Short Form Health Survey; TEAE, treatment-emergent adverse event; SAE, serious adverse event; AE, adverse event; N/A, not applicable.

\[ **p \leq 0.01 \text{ vs placebo} \]

\[ \hat{p} \leq 0.025 \text{ vs placebo} \]

\[ ***p \leq 0.001 \text{ vs placebo} \]
N Naderi
Department of Rheumatology, Danderyd Hospital, Danderyd, Stockholm, Sweden

Objectives: Large vessel involvement (LVI) as a prognostic factor regarding flare frequency and glucocorticoid (GC) demand has not been investigated in giant cell arteritis (GCA). LVI can indicate a complicated disease course (1). No specific diagnostic or activity biomarker exists; neither the erythrocyte sedimentation rate nor C-reactive protein, separately or combined, is infallible (2). Periodic imaging is not an accepted norm of re-examination and data on the findings of vascular damage at follow-up with clinical vascular assessment in GCA are scarce (3). This study was conducted to explore periodic peripheral vascular evaluation as a tool for detecting smouldering disease, identifying LVI, and investigating whether LVI predicts frequent flares on high-dose GCs.

Methods: A portion of all consecutive newly diagnosed patients with GCA and polymyalgia rheumatica or referrals for second opinion or initiation of GC-sparing drug between July 2011 and May 2015 were evaluated and followed up at regular intervals by one rheumatologist. Only those with GCA were included in this study. Patients were evaluated at follow-ups with auscultation of the heart and peripheral vessels, palpation of the peripheral pulses, and pressure measurement of the brachial and dorsal pedal arteries. Imaging was conducted in cases of new vascular bruit or pressure asymmetry, frequent flares, long-standing disease, or a rise in inflammatory markers without any other explanation.

Results: Imaging revealed LVI in 58% of the patients (LV-GCA). Sixty-five per cent developed pressure asymmetry, 65% of whom had LV-GCA. With pressure measurements, 73% of those with LV-GCA could be detected. Six patients exhibited a relapsing and remitting course of pressure asymmetries as a sign of disease activity. Thirty-one per cent of the ankle pressure asymmetries (APAs) at baseline were due to vasculitis. APA occurred significantly more in LV-GCA patients (p = 0.0017). Sixty-five per cent of the patients had flares on high-dose GCs, 76% of whom were LV-GCA patients (p = 0.014).

Conclusions: The described method is simple and reliable to use as an independent activity marker, to evaluate treatment efficacy, and to detect LVI and smouldering inflammation. LVI predicts a complicated disease course.

References

PP55
Role of anti-inflammatory lipid mediators in vascular maintenance in human resistance-sized arteries upon microsomal prostaglandin E synthase-1 inhibition
J Steinmetz1, S Arefin2, N Mudrovic2, F Bergqvist2, K Larsson1, M Korotkova3, K Kublickiene3, P Jakobsson1

Table PP54. Distribution of the physical findings and the flare frequencies among large vessel giant cell arteritis (LV-GCA) and classic cranial giant cell arteritis (C-GCA) patients.

<table>
<thead>
<tr>
<th>Findings</th>
<th>LV-GCA</th>
<th>C-GCA</th>
<th>LV-GCA</th>
<th>C-GCA</th>
<th>LV-GCA 13/15 (87%)</th>
<th>C-GCA 4/11 (38%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart murmur</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vessel bruit</td>
<td>3</td>
<td>0</td>
<td>4*</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brachial pressure difference, total</td>
<td>1</td>
<td>0</td>
<td>8</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progress</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New</td>
<td>6</td>
<td>2</td>
<td>6</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankle pressure difference, total</td>
<td>8</td>
<td>5</td>
<td>12</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progress†</td>
<td></td>
<td></td>
<td>7</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New</td>
<td></td>
<td></td>
<td>5</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median dose at flares (mg/day)</td>
<td></td>
<td></td>
<td>28</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interquartile range (mg/day)</td>
<td></td>
<td></td>
<td>18–40</td>
<td>19–38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range GC dose at flares (mg/day)</td>
<td></td>
<td></td>
<td>15–53</td>
<td>18–43</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

High flare frequency, ≥ 3 flares; High-dose glucocorticoid (GC), prednisolone dose ≥ 15 mg/day; †at first visit < 10 mmHg.

*Vessel bruit location: common carotid artery n = 2 bilaterally, left axillary artery n = 1, right axillary artery n = 1, subclavian artery n = 1 (heard above and below the clavicle), common femoral artery n = 1 bilaterally; †at first visit < 10 mmHg.
**PP56**

**Immunoglobulin A anti-phospholipid antibodies in Swedish cases with systemic lupus erythematosus: associations with disease phenotypes, vascular events, and damage accrual**

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**Objectives:** Non-steroidal anti-inflammatory drugs (NSAIDs) which selectively inhibit cyclooxygenase-2 (COX-2), reduce prostaglandin E2 (PGE2) levels, thereby affecting pain and inflammation, and are widely used for the treatment of rheumatic diseases. But the cardiovascular side-effects, such as myocardial infarction, stroke, pulmonary hypertension, and heart failure, limit their use. The peripheral resistance vasculature is considered to be a primary affected site as a consequence of cardiovascular complications and the underlying mechanisms are diverse owing to different pathological situations. A decrease in prostacyclin (PGI2) levels mediated by COX-2 is inhibition associated with increased cardiovascular side-effects. Thus, the inhibition of microsomal prostaglandin E synthase-1 (mPGES-1), the terminal synthase of PGE2, introduces an attractive approach for novel anti-inflammatory treatment leading, besides the reduction of pro-inflammatory PGE2, to a redirection of excess PGH2 into the PGI2 pathway.

**Methods:** We used wire myography in combination with immunological and mass-spectrometry based techniques to elucidate the effects of mPGES-1 inhibition on arterial functionality in patients with chronic inflammation and controls. We exposed isolated subcutaneous resistance arteries to novel mPGES-1 inhibitors, COX-2 inhibitor, or vehicle control, and assessed their contractility and/or relaxation using a wire-photography technique.

**Results:** Our preliminary results showed reduced adrenergic vasoconstriction after 30 min incubation with mPGES-1 inhibitors at concentrations relevant to in vivo situation. No adverse effects by means of reduced sensitivity to NO donors or changes in endothelium-dependent dilatation were observed, but tested mPGES-1 inhibitors induced acute dilatation in a concentration-dependent manner in preconstricted arteries. PGE2, 6-ketoPGF1α, and PGF2α were detectable in supernatants of interleukin-1β-stimulated cultured arteries, and the treatment with mPGES-1 inhibitors resulted in a reduction of PGE2 levels.

**Conclusions:** Further studies are warranted to assess the role of PGI2 signalling upon mPGES-1 inhibition in these diseased arteries. However, we believe that our ex vivo model system is well suited to and of high interest for studies on the cardiovascular safety profile of mPGES-1 inhibitors in humans.

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**PP57**

**Use of drugs for cardiovascular diseases is already higher in systemic lupus erythematosus patients before diagnosis**

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**Objectives:** Immunoglobulin G (IgG)- and IgM-class anti-cardiolipin antibodies (aCL) and lupus anticoagulant (LA) are included in the 1997 update of the American College of Rheumatology (ACR-97) systemic lupus erythematosus (SLE) classification criteria. Despite limited evidence, IgA-aCL and IgA anti-β2-glycoprotein-I (anti-β2GPI) were included among the 2012 Systemic Lupus International Collaborating Clinics classification criteria. The present study was undertaken to evaluate IgG/IgA/IgM-aCL and anti-β2GPI occurrence in relation to disease phenotype, smoking habits, pharmacotherapy, anti-phospholipid syndrome (APS)-related events, and organ damage among Swedish SLE patients.

**Methods:** The study included 526 SLE patients meeting ACR-97 criteria. Blood donors and patients with rheumatoid arthritis or primary Sjögren’s syndrome served as controls. Serum anti-phospholipid antibodies (aPL) were analysed by enzyme immunoassays.

**Results:** Of the SLE cases, 76 (14%) fulfilled the Sydney APS criteria, and at least one aCL/anti-β2GPI isotype (IgG/IgA/IgM) occurred in 138 SLE patients (26%). Forty-four (8%) of the SLE cases had IgA-aCL, of whom 20 (4%) lacked IgG/IgM-aCL; and 74 (14%) tested positive for IgA anti-β2GPI, 34 (6%) being seronegative regarding IgG/IgM anti-β2GPI. Six (1%) had manifestations compatible with APS and were seropositive regarding IgA-aCL and/or IgA anti-β2GPI in the absence of IgG/IgM-aPL and LA. Positive LA- and IgG-aPL tests were associated with the most APS-related events and organ damage. Exclusive IgA anti-β2GPI occurrence was associated inversely with Caucasian ethnicity and photosensitivity. Nephritis, smoking, LA positivity, and statin/corticosteroid medication were associated strongly with organ damage, whereas ongoing hydroxychloroquine medication was protective.

**Conclusions:** IgA-aPL is not uncommon in SLE (16%). Exclusive IgA anti-β2GPI ± IgA-aCL was associated with non-Caucasian ethnicity. IgA-aPL analysis may be of additional value among clinically suspected APS patients testing negative for other isotypes of aPL and LA.
Objectives: Systemic lupus erythematosus (SLE) patients are considered a high-risk population for cardiovascular diseases (CVDs). We explore whether individuals with incident SLE have already used more CVD drugs compared to population controls before the SLE diagnosis.

Methods: Adult SLE incident patients (age ≥ 18 years) from 2004 to 2014 were identified from a nationwide register. The date of granted reimbursement for SLE medication was defined as the date of diagnosis (index day). For each patient, three population controls were matched for age.

Table PP56. Significant associations between disease phenotypes/serologies/damage and each exclusively positive anti-cardiolipin antibodies/anti-β2-glycoprotein-I (anti-β2-GPI) isotype or lupus anticoagulant (LA), as well as for cases positive for at least one immunoglobulin A (IgA) isotype in the absence of other isotypes or LA, expressed by p values ($\chi^2$).

<table>
<thead>
<tr>
<th></th>
<th>Anti-cardiolipin</th>
<th>Anti-β2GPI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IgG IgA IgM</td>
<td>IgG IgA IgM</td>
</tr>
<tr>
<td>Caucasian ethnicity</td>
<td>(n = 476)</td>
<td></td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>(n = 327)</td>
<td>0.020*</td>
</tr>
<tr>
<td>Serositis</td>
<td>(n = 210)</td>
<td>0.0071*</td>
</tr>
<tr>
<td>Anti-dsDNA antibody</td>
<td>(n = 310)</td>
<td></td>
</tr>
<tr>
<td>Anti-SSA/Ro52</td>
<td>(n = 151)</td>
<td>0.024*</td>
</tr>
<tr>
<td>Anti-SSA/Ro60</td>
<td>(n = 210)</td>
<td></td>
</tr>
<tr>
<td>APS, classification</td>
<td>(n = 76)</td>
<td></td>
</tr>
<tr>
<td>Any arterial event</td>
<td>(n = 76)</td>
<td>0.0022</td>
</tr>
<tr>
<td>Arterial embolism</td>
<td>(n = 71)</td>
<td>0.030</td>
</tr>
<tr>
<td>Cerebrovascular lesion</td>
<td>(n = 61)</td>
<td>0.0013</td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>(n = 45)</td>
<td></td>
</tr>
</tbody>
</table>

APS, anti-phospholipid syndrome.
**Significant inverse associations.

Figure PP56. (A) Distribution of immunoglobulin A (IgA) anti-cardiolipin antibodies (aCL) and IgA anti-β2-glycoprotein-I (anti-β2-GPI)-positive cases in the full systemic lupus erythematosus (SLE) cohort: 82 (16%) of the SLE cases had IgA positivity, 44 (8%) of aCL and 74 (14%) of anti-β2GPI type. (B) Distribution of IgG/A/M isotypes of aCL in the SLE cohort: 89 (17%) SLE cases were positive for at least one aCL isotype. (C) Distribution of IgG/A/M isotypes of anti-β2-GPI in the SLE cohort: 121 (23%) SLE cases were positive for at least one anti-β2-GPI isotype. (D) Distribution of exclusively IgG aCL and IgA anti-β2GPI-positive cases in the SLE cohort: 20 (4%) of the SLE cases had IgA positivity, eight (2%) of aCL and 16 (3%) of anti-β2-GPI type.
gender, and residence on the index day. The patients and controls were linked to the drug purchase register. All purchases of CVD drugs [Anatomical Therapeutic Chemical (ATC) codes of C01, C02, C04, C05, C07, C08, C09; and separately C10] were recorded during 5 years before the index day.

Results: A total of 653 SLE patients (mean age 45.7 ± 15.9 years, 83% females) and 1946 population controls (22 excluded due to rheumatoid arthritis diagnosis) were found. During 5 years before the index day, the proportion of SLE patients with purchased CVD drugs (46.7%) was greater compared to the controls (28.5%) (p < 0.001). The relative risk for purchases started to increase further 6 months before SLE diagnosis. There was no significant difference in lipid-lowering agents between groups.

Conclusions: The higher prevalence of CVD drug use in SLE patients suggests an increased CVD risk before the SLE diagnosis.

PP58

Soluble urokinase plasminogen activator receptor predicts the development of organ damage over five years in systemic lupus erythematosus: results from the SLICC inception cohort

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Objectives: The urokinase plasminogen activator receptor (uPAR) participates in proteolysis, migration, and adhesion. Receptor shedding yields a soluble form (suPAR) that has emerged as a promising severity biomarker in malignancies, and inflammatory and infectious diseases (1). Previously, suPAR was shown to reflect accumulated organ damage in systemic lupus erythematosus (SLE) (2). Here, we investigate suPAR as a potential predictor of future organ damage in recent-onset SLE.

Methods: From the SLICC inception cohort, 344 SLE cases (with at least four ACR criteria) were selected based on a minimum of 5 years’ follow-up and absence of organ damage [SLICC/ACR Damage Index (SDI) > 0] at inclusion. Patients were enrolled within 15 months of diagnosis. Serum suPAR levels were measured by enzyme-linked immunosorbent assay at inclusion, and levels were related to SDI after 5 years of follow-up. Age- and gender-matched controls (1:1) were from the Swedish population.

Results: Baseline suPAR levels were higher in patients who acquired damage (SDI > 1) over a 5 year period (n = 32) compared to patients without damage accrual (n = 246; p < 0.001) and controls (n = 344; p = 0.008) (Figure PP58). There were no significant differences in suPAR with regard to ethnicity (Caucasians vs non-Caucasians) and no correlation between age and suPAR in patients/controls. No correlations (r > 0.2) were found between suPAR and disease activity (SLICC/ACR Damage Index), corticosteroid dose, or eGFR (p = 0.003; AUC = 0.78). Examining individual items on the SDI revealed a significant impact of suPAR on musculoskeletal damage (SDI ≥ 1) (p = 0.018; AUC = 0.66) also when adjusting for covariates (p = 0.020; AUC = 0.68).

Conclusions: Prognostic biomarkers of disease severity in SLE could identify patients in need of tight control and improved treatment strategies. Here, suPAR is, for the first time, shown to have predictive potential for damage accrual in SLE. Continued follow-up of patients could elucidate the association between suPAR and damage in specific organ domains.

References


Figure PP58.Baseline soluble urokinase plasminogen activator receptor (suPAR) levels in healthy controls and patients with different organ damage accrual (SDI) at the 5 year follow-up. One-way ANOVA with Tukey’s post-hoc test revealed higher baseline levels of suPAR in patients who acquired organ damage (SDI > 1) in the next 5 years compared to controls. Error bars indicate 95% CI. SLE, systemic lupus erythematosus; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index.
PP59

Microparticles as potential biomarkers of disease activity in anti-neutrophil cytoplasmic antibody-associated vasculitis

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Objectives: Increased levels of circulating microparticles (MPs), mainly of endothelial cell origin but also platelet derived, have been shown to correlate with autoimmune disease activity, such as anti-neutrophil cytoplasm antibody (ANCA)-associated vasculitis (AAV). The aim was to evaluate levels of activity markers expressed on MPs from patients with AAV, during active disease and remission, compared to healthy control subjects.

Methods: Our study included 46 AAV patients and 23 healthy age- and gender-matched control subjects. We analysed the concentration of MPs in plasma by flow cytometry. MPs were phenotyped by expression of CD142 (tissue factor, TF), anti-H3cit (citrullinated histone 3 directed against neutrophil extracellular traps, NETs), antipentraxin3 (pentraxin3), HMGB1 (high-mobility group box 1 protein, HMGB1), anti-TWEAK (tumour necrosis factor-like weak inducer of apoptosis, TWEAK), anti-plasminogen (plasminogen), anti-C3a (C3a), and anti-C5a (C5a). Vasculitis disease activity was assessed using the Birmingham Vasculitis Activity Score (BVAS), where active disease was defined as BVAS ≥ 1 and inactive (remission) as BVAS = 0.

Results: Half of the patient group (23) had active vasculitis (13 male, 10 female, mean age 61 ± 14 years) and 23 had inactive disease (12 male, 11 female, mean age 64 ± 13 years). Concentrations of MPs expressing TF, H3cit, pentraxin-3, and HMGB1 in active patients were significantly higher than in those in remission and healthy controls (p < 0.01 and p < 0.0001, respectively). MPs expressing C5a and C3a were significantly higher in both active and inactive patients compared to controls (p < 0.001). In addition, levels of MPs expressing C5a and C3a strongly correlated with BVAS in patients with active disease (r = 0.78, p < 0.0001; r = 0.5, p < 0.01, respectively), while there was no significant correlation between other explored markers and BVAS.

Conclusions: Our results support the recently postulated role of the complement system in AAV pathogenesis and disease activity. Evaluated proteins expressed on MPs, especially C5a and C3a, could be used as potential biomarkers which may reflect inflammation and disease activity in AAV patients.

PP60

Autoimmune liver disease among well-characterized patients with systemic lupus erythematosus

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Objectives: The clinical spectrum of systemic lupus erythematosus (SLE) is exceedingly heterogeneous as virtually any organ system may be affected. Liver test abnormalities are commonly found in SLE, with a wide range of possible causes. Regarding the coexistence of SLE and autoimmune liver diseases, the literature is scarce. This study aimed to describe the prevalence of autoimmune hepatitis (AIH) and primary biliary cholangitis (PBC) among Swedish SLE cases. We further aimed to test whether anti-C1q and anti-ribosomal P (anti-rPb) antibodies were associated inversely with AIH (1).

Methods: The study population consisted of 287 cases (86% females) included in a regional Swedish SLE cohort. Patients met the 1982 ACR classification criteria and/or the Fries’ diagnostic principle with involvement of at least two organ systems in combination with a positive antinuclear antibody test at the time of diagnosis. With support from an experienced hepatologist, different strictness criteria for the diagnoses of AIH and PBC were applied.

Results: Applying the diagnostic AIH criteria (2) combined with persistent elevation of alanine aminotransferase to our study population, 25 cases (8.7%) reached at least ‘probable AIH’. However, only five of these patients (1.7%) had a clinical diagnosis of AIH and liver biopsy had been performed in only three of these five cases. None was anti-rPb or anti-C1q positive. The requirement of elevated alkaline phosphatase (ALP) in combination with typical PBC-associated antibodies (M2/sp100/gp210) yielded seven cases (2.4%), but only four had a clinical diagnosis of PBC (1.4%). In two out of four cases, PBC was confirmed by liver biopsy; three cases showed PBC-associated antibodies, and in one case PBC diagnosis was based on elevated ALP combined with histopathology. None had anti-rPb or anti-C1q antibodies.

Conclusions: Clinical diagnoses of AIH and PBC were strongly overrepresented in SLE compared to prevalence figures from the Swedish population (3): AIH 1.7% vs 0.018% and PBC 1.4% vs 0.016%. Using the AIH criteria, even higher numbers were achieved but the specificity of these criteria among an SLE population is uncertain. Liver biopsy and specific autoantibodies associated with autoimmune liver diseases could aid in the search for AIH and PBC in SLE.

References


**EPIDEMIOLOGICAL SCIENCE**

**PP61**

Elevated erythrocyte sedimentation rate at time of diagnosis is associated with high mortality in patients with idiopathic inflammatory myopathies: a register-based study

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**Objectives**: Few biomarkers (MDA5 antibodies, interleukin-6, type I interferon) predict severe outcome in idiopathic inflammatory myopathies (IIMs). These markers cannot be routinely used in clinical practice. Erythrocyte sedimentation rate (ESR) usually reflects the extent of systemic inflammation and has been associated with severe interstitial lung disease (ILD) and death in IIMs in retrospective studies. The aim of this study was to investigate the prognostic value of ESR in patients with IIM in a prospective cohort.

**Methods**: From the national Swedish Register of Quality (SRQ) at the rheumatology clinic in Karolinska University Hospital, we included newly diagnosed patients (< 12 months) with polymyositis (PM) or dermatomyositis (DM) from 2003 and 2015. The presence of both ILD and cancer at baseline was retrieved. Cancer was considered related to myositis if present within ± 3 years of IIM diagnosis. The ESR value measured between the diagnosis and inclusion in the SRQ was considered the baseline value. An ESR value > 30 mm (75th quartile) was considered high. The median (years) from diagnosis to last visit was used to calculate the survival rates by the Kaplan–Meier method. A p value < 0.05 was considered statistically significant.

**Results**: We included 140 patients; 59 (42%) DM patients, 57 (41%) women, mean ± sd age 58.4 ± 14.4 years. Fifty-four patients (39%) had ILD and 21 (15%) had myositis-related cancer. The median (Q1–Q3) baseline ESR was 20 mm/h (11.3–30). There were no differences between gender, age, IIM subtype, and patients with cancer. A higher ESR was observed in patients with ILD vs non-ILD [median 22 (15–34) vs 18 (10–29), p < 0.04]. The median time (years) from diagnosis to last visit was significantly shorter in patients with high ESR vs low ESR [3.1 (0.9–4.5) vs 3.4 (2.2–5.5)]. Further, we observed that patients with high ESR at baseline had decreased survival rate compared to patients with low ESR (67.4% vs 89.4%; log-rank test p < 0.001) (Figure PP61). This was not explained by the presence of ILD as the mortality was similar to that in the non-ILD group (16.7% vs 18.6%, p = 0.8).

**Conclusions**: Our findings confirm that high ESR is associated with ILD and predicts decreased survival rate.

**References**


**PP62**

Patients fulfilling European Spondyloarthopathy Study Group (ESSG) criteria but not Assessment of SpondyloArthritis international Society (ASAS) criteria for spondylarthritis

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**Objectives**: Spondyloarthritis (SpA) is a rheumatic disease with axial and peripheral inflammatory arthritis. The disease is associated with psoriasis, inflammatory bowel disease, and uveitis. There is often a long diagnostic delay, especially in axial disease. Radiographic
changes develop over years. Magnetic resonance imaging (MRI) changes occur earlier but are unspecific. Biological disease-modifying anti-rheumatic drugs are effective treatment options, and there is a need for better classification criteria to find eligible patients earlier. The Assessment of SpondyloArthritis international Society (ASAS) criteria perform well in a population of patients referred to rheumatological specialist care. The older European Spondyloarthropathy Study Group (ESSG) criteria were considered to be less specific. This study compared the ASAS criteria to the ESSG criteria in a population of SpA patients in Rana, Norway, and their first degree relatives with symptoms of SpA. What characteristics do the patients who fulfil only ESSG criteria have? Do they differ in disease activity and physical function?

**Methods:** Patients with SpA were recruited from hospital registers and family doctors and by an advertisement in a local newspaper. Clinical data, C-reactive protein (CRP), and human leucocyte antigen-B27 were collected. X-ray and MRI of the sacroiliac (SI) joint were performed if the patient had inflammatory back pain. If they fulfilled the ESSG criteria for SpA they were included. The first degree relatives of the included patients were contacted and asked for symptoms of synovitis or inflammatory back pain by a questionnaire. Symptomatic relatives

**Figure PP62.** Patients were recruited from Rana district in northern Norway.

**Table PP62.** European Spondyloarthropathy Study Group (ESSG) vs Assessment of SpondyloArthritis international Society (ASAS) criteria in spondyloarthritis (SpA) patients.

<table>
<thead>
<tr>
<th>No. CRP</th>
<th>t-test</th>
<th>No. CRP</th>
<th>t-test</th>
<th>No. CRP</th>
<th>t-test</th>
<th>No. CRP</th>
<th>t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESSG criteria only fulfilled</td>
<td>61/22/39</td>
<td>4.9</td>
<td>0.01</td>
<td>61/22/39</td>
<td>4.9</td>
<td>0.01</td>
<td>61/22/39</td>
</tr>
<tr>
<td>ASAS criteria fulfilled</td>
<td>337</td>
<td>4.9</td>
<td>0.01</td>
<td>337</td>
<td>4.9</td>
<td>0.01</td>
<td>337</td>
</tr>
</tbody>
</table>

Data are shown as total number of patients; male/female.
were investigated, and included if they fulfilled the ESSG criteria. In total, 390 SpA patients were included, 273 of whom had MRI of SI joints.

**Results:** Patients fulfilling only ESSG criteria but not ASAS criteria for SpA did not differ from patients fulfilling ASAS criteria in disease activity as measured by CRP or Ankylosing Spondylitis Disease Activity Score (ASDAS). The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was slightly lower in the ESSG group, and the physical function was better, as measured by the Bath Ankylosing Spondylitis Functional Index (BASFI) and modified Health Assessment Questionnaire (mHAQ).

**Conclusions:** Both criteria sets are needed. If only the ASAS criteria were used, too few patients would be included.

**PP63**

**Active first year treatment of early rheumatoid and unspecified arthritis**

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**Objectives:** To report the current disease-modifying anti-rheumatic drug (DMARD) use in Finland for the treatment of early rheumatoid arthritis (RA) and unspecified arthritis (UA).

**Methods:** Information on gender, date of birth, and date of special medicine reimbursement decision for all new RA and UA patients was collected from a nationwide register maintained by the Social Insurance Institution between 2011 and 2015. DMARDs purchased by the patients during the first year after the diagnosis were analysed.

**Results:** In total, 7338 patients (67.3% female, 68.1% rheumatoid factor positive) with early RA and 2433 patients (67.8% female) with early UA were identified. DMARD treatment was initiated during the first month after the diagnosis to 92.0% of the patients with seropositive RA, 90.3% with seronegative RA, and 87.7% with UA (p < 0.001). Respectively, 72.1%, 63.4%, and 42.9% of the patients (p < 0.001) used methotrexate; 49.8%, 35.9%, and 16.0% (p < 0.001) as part of a DMARD combination during the first month. By the end of the first year after the diagnosis, only 1.4%, 2.6%, and 3.0% (p < 0.001) of the patients were not receiving any DMARDs and self-injected biologics were initiated in 2.6%, 5.3%, and 3.1% of them (p < 0.001). During the first year, 83.4% of the seropositive RA patients had purchased methotrexate, 50.4% sulphasalazine, 72.1% hydroxychloroquine, and 72.6% prednisolone (Table PP63).

**Table PP63. Proportions of patients with seropositive rheumatoid arthritis (RA), seronegative RA, and unspecified arthritis (UA) having used various anti-rheumatic drugs by the end of the first year after arthritis diagnosis.**

<table>
<thead>
<tr>
<th></th>
<th>Seropositive RA (n = 4998)</th>
<th>Seronegative RA (n = 2340)</th>
<th>UA (n = 2433)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate (MTX)</td>
<td>4167 (83.4)</td>
<td>1789 (76.4)</td>
<td>1512 (62.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MTX per os</td>
<td>3998 (80.0)</td>
<td>1706 (72.9)</td>
<td>1406 (57.8)</td>
<td></td>
</tr>
<tr>
<td>MTX s.c.</td>
<td>625 (12.5)</td>
<td>308 (13.2)</td>
<td>310 (12.7)</td>
<td></td>
</tr>
<tr>
<td>Sulphasalazine</td>
<td>2520 (50.4)</td>
<td>1090 (46.6)</td>
<td>1362 (56.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>3603 (72.1)</td>
<td>1357 (58.0)</td>
<td>806 (35.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>256 (5.1)</td>
<td>121 (5.2)</td>
<td>119 (4.9)</td>
<td>0.89</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>65 (1.3)</td>
<td>31 (1.3)</td>
<td>23 (0.9)</td>
<td>0.37</td>
</tr>
<tr>
<td>Aurathiomolate</td>
<td>42 (0.8)</td>
<td>12 (0.5)</td>
<td>8 (0.3)</td>
<td>0.023</td>
</tr>
<tr>
<td>Auranofin</td>
<td>4 (0.1)</td>
<td>2 (0.1)</td>
<td>2 (0.1)</td>
<td>0.99</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>13 (0.3)</td>
<td>10 (0.4)</td>
<td>23 (0.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Self-injected biologics (all)</td>
<td>131 (2.6)</td>
<td>125 (5.3)</td>
<td>76 (3.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Etanercept</td>
<td>53</td>
<td>55</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Adalimumab</td>
<td>40</td>
<td>48</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Certolizumab</td>
<td>23</td>
<td>19</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Golimumab</td>
<td>19</td>
<td>19</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Abatacept</td>
<td>8</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td>3626 (72.6)</td>
<td>1706 (72.9)</td>
<td>1283 (52.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No anti-rheumatic medication</td>
<td>71 (1.4)</td>
<td>60 (2.6)</td>
<td>73 (3.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Only prednisolone</td>
<td>25 (0.5)</td>
<td>30 (1.3)</td>
<td>24 (1.0)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Data are shown as n (%).

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Conclusions: Currently, combination therapy including methotrexate is the most commonly prescribed treatment strategy for early seropositive RA in Finland, and during the first year, this patient group was prescribed biologics less often than seronegative RA or UA patients.

Reference

PP64
Mortality rate in a nationwide inception cohort of rheumatoid arthritis patients compared to population controls: seropositivity still translates into shortened survival
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Objectives: To explore whether the patients who have contracted rheumatoid arthritis (RA) after the turn of the millennium have a death rate higher than the general population.

Methods: Adults (≥18 years) with newly diagnosed RA with the index date between 1 January 2000 and 31 December 2014 were identified from the register of the Social Insurance Institution of Finland, and three matched general population controls were selected for each case.

Results: In total, 27,947 patients with incident RA [66.1% seropositive (RA+); 67.5% women] and 83,575 controls were followed up until death or 31 December 2015. During this 15 year period, patients with RA+ had excess mortality, which became apparent 3–4 years after the index day. Survival time was shortened by ~0.08 years (95% CI –0.16 to –0.01) in women and ~0.39 years (~0.53 to –0.25) in men. Seronegative (RA–) patients, on the other hand, had increased life expectancy, women by 0.15 years (0.06 to 0.24) and men by 0.25 years (0.07 to 0.42). Hazard ratios were in RA+ women 1.07 (95% CI 1.01–1.13, p = 0.025), in RA+ men 1.21 (95% CI 1.14–1.30, p < 0.001), in RA– women 0.90 (95% CI 0.83–0.98, p = 0.014), and in RA– men 0.88 (95% CI 0.80–0.97, p = 0.012). Cardiovascular (CV) diseases were the most common cause of death. Compared to controls, CV mortality was higher only in RA+ women and men; subhazard ratios were 1.21 (95% CI 1.11 to 1.33) and 1.25 (1.13 to 1.39), respectively.

Conclusions: Contracting seropositive RA still results in shortened life expectancy, especially due to CV events.

PP65
Hyperuricaemia is very common in the ageing Finnish population, especially among men
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Objectives: Our aim was to examine the prevalence of hyperuricaemia and levels of uric acid in the ageing Finnish population.

Methods: This study is a part of the Good Ageing in Lahti region (GOAL) study, a 10 year cohort study on a regional sample of three cohorts aged 52–56, 62–66, and 72–76 years at baseline. The participants filled in questionnaires and the blood samples were taken four times between 2002 and 2012. The baseline serum uric acid levels of each age group were evaluated and men and women were analysed separately. We also utilized data from the national mortality register to assess mortality in relation to uric acid. Hyperuricaemia was defined as serum uric acid ≥ 360 μmol/L, according to the physiological threshold of dissolubility of monosodium urate.

Results: Of 4272 invited persons, 66% participated and 2673 were included in our analysis. There were 475 women and 383 men in the age group of 52–56 years, 500 women and 474 men aged 62–66 years, and 429 women and 412 men aged 72–76 years. The mean uric acid levels of each group and the prevalence of hyperuricaemia are presented in the Figure PP65. The overall prevalence of hyperuricaemia was 31% for women (27.2% in the youngest age group, 31.0% in the second, and 35.0% in the oldest). For men, the prevalence was 60% (53.8% in the youngest group, 62.2% in the second, and 63.1% in the oldest). The mortality had a J-shaped relationship with uric acid in men (p = 0.014), with the curve rising from 420 μmol/L. For women, the J-shaped trend was not as clear (p = 0.16) but was already rising from 360 μmol/L. The older the age group, the steeper the rise.

Conclusions: The prevalence of hyperuricaemia seems to be very high in the ageing Finnish population, especially in men. Almost two-thirds of men had serum uric acid ≥ 360 μmol/L. The prevalence increased with age. According to these results, serum uric acid ≥ 360 μmol/L is so common in the over-middle-aged population that it does not seem to be a reasonable limit for pathological hyperuricaemia or an indication for urate-lowering treatment in patients without gout. However, it is a reasonable target for urate-lowering therapy in gout.
TREATMENT REGISTERS

PP66

One-year follow-up of a nationwide cohort of patients with inflammatory arthritis, who switched from originator to biosimilar etanercept, focusing on patients who switched back to originator: an observational DANBIO study

B Glintborg, IJ Sørensen, E Omerovic, F Mehnert, N Manilo, K Danebod, DV Jensen, H Nordin, O Hendricks, AG Loft, S Chrysidis, BL Andersen, JL Raun, H Lindegaard, J Espesen, SH Jakobsen, IJ Hansen, EB Dalgaard, DD Pedersen, S Kristensen, A Linauskas, LS Andersen, J Grydehøj, NS Krogh, ML Hetland

The DANBIO Registry, Copenhagen, and Danish Departments of Rheumatology, Denmark

Objectives: In Denmark, patients treated with originator etanercept (ETA) 50 mg s.c. underwent a mandatory switch to biosimilar SB4 in April 2016 (switchers). Patients treated with 25 mg ETA or 50 mg powder solution were not mandated to switch (non-switchers). Some switchers resumed ETA during follow-up (back-switchers). This study aimed to investigate the frequency of back-switching, and, in back-switchers, to study (i) baseline characteristics at the time of initial switch (ETA to SB4), (ii) reasons for SB4 withdrawal, and (iii) changes in disease activity during treatment with SB4 and after back-switching.

Methods: Patient data were retrieved from DANBIO (censored August 2017). For back-switchers, disease activity upon SB4 start (baseline) and upon back-switching to ETA (delta values) were compared. Baseline characteristics of back-switchers were compared to the remaining switch population, using chi-squared and Mann–Whitney U-tests.

Figure PP65. Left-hand graphs: mean serum uric acid (μmol/L) of each age group; right-hand graphs: cumulative percentage of baseline serum uric acid values in the three age groups on the right.
Results: In total, 1641 patients switched from ETA to SB4. Of these, 299 (18%) withdrew from SB4 therapy during 1 year follow-up and switched back to ETA (n = 120, 7%), started another biological disease-modifying anti-rheumatic drug (bDMARD) (n = 104), died (n = 9), were lost to follow-up (n = 1), or did not restart bDMARDs (n = 65).

Among the 120 back-switchers, SB4 was withdrawn owing to lack of effect (LOE) (52%) or adverse events (AEs) (39%), or for other reasons (9%). Reasons for SB4 withdrawal in back-switchers are listed in the Table PP66. No major safety events occurred. Median time on SB4 before back-switching was 120 (IQR 73–193) days. Time between stopping SB4 and restarting ETA was 1 (1–1) days. Baseline characteristics of back-switchers vs the remaining switch population were similar (all p > 0.05). Among back-switchers who stopped SB4 owing to LOE, PGA had increased. Reasons for back-switching appeared to be predominantly subjective (nocebo effect). The availability of originator drug may have encouraged back-switching.

References

PP67
One-year treatment retention after a nationwide non-medical switch from originator to biosimilar etanercept in 2061 patients with inflammatory arthritis followed in the DANBIO registry

B Glintborg, IJ Sørensen, E Omerovic, F Mehnert, N Manilo, K Danebod, DV Jensen, H Nordin, O Hendricks, AG Loft, S Chryssidis, BL Andersen, JL Raun, H Lindegaard, J Espesen, SH Jakobsen, IJ Hansen, EB Dalgaard, DD Pedersen, S Kristensen, A Linauskas, LS Andersen, J Grydehøj, NS Krogh, ML Hetland

The DANBIO RegistryCopenhagen, Denmark, and Danish Departments of Rheumatology, Denmark

Table PP66. Description of originator etanercept (ETA)–biosimilar etanercept (SB4)–ETA back-switchers (n = 120).

<table>
<thead>
<tr>
<th>Characteristics upon start of SB4 (n = 120)</th>
<th>RA</th>
<th>PsA</th>
<th>AxSpA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient number, n</td>
<td>80</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Female, %</td>
<td>73</td>
<td>55</td>
<td>35</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59 (52–70)</td>
<td>45 (36–56)</td>
<td>43 (38–56)</td>
</tr>
<tr>
<td>SJC, n</td>
<td>0 (0–1)</td>
<td>0 (0–0)</td>
<td>–</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>3 (1–8)</td>
<td>1 (1–5)</td>
<td>3 (1–6)</td>
</tr>
<tr>
<td>PGA (mm)</td>
<td>27 (12–54)</td>
<td>25 (13–63)</td>
<td>23 (13–44)</td>
</tr>
</tbody>
</table>

Characteristics upon restarting ETA in patients who back-switched owing to LOE (n = 62)

| Patient number, n                          | 38 | 11  | 13    |
| SJC, n                                     | 2 (0–5) | 0 (0–2) | –     |
| CRP (mg/L)                                 | 3 (2–11) | 3 (2–7) | 4 (1–6) |
| PGA (mm)                                   | 64 (50–76) | 78 (18–90) | 42 (35–63) |

Delta-values in patients who back-switched owing to LOE (n = 62)†

<table>
<thead>
<tr>
<th>Delta</th>
<th>RA</th>
<th>PsA</th>
<th>AxSpA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta-SJC, n</td>
<td>1 (0–4)</td>
<td>0 (0–0)</td>
<td>–</td>
</tr>
<tr>
<td>Delta-CRP (mg/L)</td>
<td>0 (–1 to 5)</td>
<td>1 (0–2)</td>
<td>0 (0–4)</td>
</tr>
<tr>
<td>Delta-PGA (mm)</td>
<td>30 (12–52)</td>
<td>15 (7–77)</td>
<td>25 (19–35)</td>
</tr>
</tbody>
</table>

Numbers are medians (interquartile range) unless otherwise stated.

Reasons for withdrawal in patients who stopped owing to adverse events (n = 47): arthralgia 1 patient, bladder dysfunction 1, blurred vision 1, diarrhoea 4, dizziness 2, dyspnoea 2, erectile dysfunction 1, hair loss 1, headache/migraine 4, hyperhidrosis 2, hypertension 1, hypotension 1, infections 2, leg cramps 1, local injection problems 3, myalgia 1, nausea 2, neuropathies 1, psoriasis/pustulosis 1, rash/itching 9, not stated 21 (total = 62 events).

†Disease activity at time of restarting ETA minus SB4 start.

RA, rheumatoid arthritis; PsA, psoriatic arthritis; AxSpA, axial spondyloarthritis; SJC, swollen joint count; CRP, C-reactive protein; PGA, patient global assessment score; LOE, lack of effect.
Objectives: In Denmark, patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (AxSpA) treated with originator etanercept (ETA) 50 mg s.c. underwent a mandatory non-medical switch to biosimilar etanercept (SB4) in April 2016 (switchers). Patients treated with 2 mg ETA or 50 mg powder solution were not mandated to switch (non-switchers). This study aimed to characterize switchers and non-switchers, and to compare 1 year treatment retention in switchers with non-switchers and a historic cohort of ETA-treated patients.

Methods: Patient data were retrieved from the DANBIO registry and national registries. We applied chi-squared and Mann-Whitney tests for comparisons and Kaplan-Meier and Cox regression analyses (crude, and adjusted for gender, age, methotrexate, remission, comorbidities, and ETA start-year) for drug retention. The historic cohort encompassed patients treated with ETA by 1 January 2015.

Results: Of 2061 ETA-treated patients by April 2016, 79% switched to SB4 (933 RA, 351 PsA, 337 AxSpA), whereas 21% (286 RA, 56 PsA, 98 AxSpA) continued ETA. In RA, compared to switchers, non-switchers more often received 25 mg ETA, and had higher disease activity and Health Assessment Questionnaire scores (Table PP67). Similar patterns were seen for PsA and AxSpA. Median (IQR) follow-up was 383 (314–414) days. In all three cohorts, withdrawals were mainly due to lack of effect. Retention rate was lowest in non-switchers (Figure PP67). One-year adjusted rates were 83% (95% CI 79–87%) in switchers, 77% (72–82%) in non-switchers, and 90% (88–92%) in the historic cohort. Patients not in remission had poorer retention than patients in remission, in both switchers [hazard ratio 1.7 (1.3–2.2)] and non-switchers [2.4 (1.7–3.6)].

Conclusions: Of over 2000 ETA-treated patients, about 80% switched to SB4. Non-switchers had higher disease activity and more often received 25 mg ETA. Switchers had poorer retention rates than a historic ETA cohort, but better than non-switchers. Withdrawal was most common in patients not in remission. The results suggest that the switching-to-biosimilar guideline facilitated withdrawal from ineffective therapies in both switchers and non-switchers.

Table PP67. Baseline characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Switchers (n = 1621)</th>
<th>Non-switchers (n = 440)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA n = 933 (58%)</td>
<td>PsA n = 351 (22%)</td>
<td>AxSpA n = 337 (21%)</td>
</tr>
<tr>
<td>RA n = 286 (65%)</td>
<td>PsA n = 56 (13%)</td>
<td>AxSpA n = 98 (22%)</td>
</tr>
<tr>
<td>Female, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>74 (49–70)</td>
<td>46 (43–61)</td>
</tr>
<tr>
<td></td>
<td>34 (28–40)</td>
<td>34 (28–40)</td>
</tr>
<tr>
<td>Concomitant MTX, %</td>
<td>60 (43–78)</td>
<td>48 (39–57)</td>
</tr>
<tr>
<td></td>
<td>49 (30–70)</td>
<td>49 (30–70)</td>
</tr>
<tr>
<td>In remission, %*</td>
<td>65 (70)</td>
<td>28 (25–34)</td>
</tr>
<tr>
<td></td>
<td>55 (70)</td>
<td>55 (70)</td>
</tr>
<tr>
<td>Patient global &lt; 30 mm, %</td>
<td>52 (51–53)</td>
<td>51 (50–52)</td>
</tr>
<tr>
<td>DAS28</td>
<td>2.1 (1.6–3.0)</td>
<td>2.0 (1.6–2.8)</td>
</tr>
<tr>
<td></td>
<td>2.5 (1.8–3.3)</td>
<td>2.0 (1.8–2.8)</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.8 (0.3–1.3)</td>
<td>0.5 (0.0–1.0)</td>
</tr>
<tr>
<td></td>
<td>0.9 (0.4–1.5)</td>
<td>0.8 (0.6–1.3)</td>
</tr>
<tr>
<td>Received 25 mg ETA/ injection, %</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Prior ETA duration (years)</td>
<td>6.0 (3.6–8.8)</td>
<td>4.3 (2.9–7.3)</td>
</tr>
<tr>
<td></td>
<td>4.6 (2.8–6.8)</td>
<td>4.6 (2.8–6.8)</td>
</tr>
<tr>
<td></td>
<td>5.3 (2.4–8.6)</td>
<td>3.4 (1.6–6.0)</td>
</tr>
<tr>
<td></td>
<td>4.7 (2.9–9.0)</td>
<td></td>
</tr>
</tbody>
</table>

Numbers are medians (interquartile range) unless otherwise stated.

*Disease Activity Score based on 28-joint count (DAS28) < 2.6 (RA, PsA), Ankylosing Spondylitis Disease Activity Score < 1.3 (AxSpA). RA, rheumatoid arthritis; PsA, psoriatic arthritis; AxSpA, axial spondyloarthritis; MTX, methotrexate; HAQ, Health Assessment Questionnaire; ETA, originator etanercept.

Does a mandatory non-medical switch from originator to biosimilar infliximab lead to increased use of...
outpatient healthcare resources? A register-based study in patients with inflammatory arthritis

B Glintborg1, J Sørensen2, ML Hetland3

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2Healthcare Outcome Research Centre, Royal College of Surgeons in Ireland, Dublin, Ireland, 3The DANBIO Registry and Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Centre of Head and Orthopaedics, Rigshospitalet, Glostrup, Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Objectives: National Danish guidelines (May 2015) dictated a mandatory switch from originator infliximab (INX) to biosimilar CT-P13 in patients with inflammatory rheumatic disease. We investigated whether this non-medical switch changed the use of outpatient hospital resources.

Methods: Switchers were identified in the DANBIO registry. Rheumatic outpatient contacts, visits, and services were identified in the National Patient Registry. The 6 month rates for (i) number of visits (or services), and (ii) days with at least one visit (or service) were compared before and after switching (paired t-tests). Visits per week per patient before and after the switch date were analysed with graphical interrupted time-series analysis.

Results: In 769 switchers [372 male, median age 54 years (IQR 44–66)], 1484 outpatient contacts, 6718 visits, and 9243 days with services (693 on the switch date) were identified. The mean rate of days with services before/after switching was 5.4/5.7 (p < 0.01). The total number of services was 19 752 (2019 on the switch date). Mean rates before and after switching for 16 service categories were small and differences were close to zero (Table PP68). Visits per week per patient appeared similar before and after the switch, with peaks about every 8 weeks (standard INX infusion interval) (Figure PP68).

Conclusions: Changes were marginal with no clinically relevant increase in the use of outpatient healthcare resources 6 months after compared to 6 months before the mandatory switch from originator to biosimilar INX.

Reference


IMAGING

PP69

Assessment of vascular dimensions using non-invasive very-high resolution ultrasound in patients with suspected giant cell arteritis

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1Children’s Hospital, Helsinki University Central Hospital, Helsinki, Finland, 2Department of General Internal Medicine and Geriatrics, Helsinki University Central Hospital, Helsinki, Finland, 3Department of Pathology, University of Helsinki, and Huslab, Helsinki University Hospital, Helsinki, Finland, 4Department of Vascular Surgery, Helsinki University Central Hospital, Helsinki, Finland

Objectives: Very-high resolution ultrasound (VHRU, 55 MHz) provides almost microscopic resolution and allows assessment of the vascular wall in minute detail. In giant cell arteritis (GCA), inflammation of the temporal artery (TA) causes thickening of the

![Image](360x627 to 558x759)

Figure PP68. Weekly rates of physical visits per patient 6 months before and 6 months after the switch.
vascular wall on histology. The objective of this study was to assess the diagnostic utility of non-invasive VHRU in comparison to histology in patients with suspected GCA.

**Methods:** We recruited 51 subjects with suspected GCA referred for TA biopsy. Vascular VHRU of the TA was conducted 1 h before biopsy and the sites of ultrasound imaging and biopsy were matched. The study population was divided into four groups according to final clinical diagnosis and biopsy findings: (i) non-GCA; (ii) clinical GCA with negative biopsy; (iii) clinical GCA with mild inflammatory findings on biopsy, limited to perivascular and adventitial layers; and (iv) clinical GCA with transmural inflammation of the vascular wall on biopsy. Intima thickness (IT), intima–media thickness (IMT), and adventitia thickness (AT) were measured from both ultrasound images and histology.

**Results:** VHRU measurements of both IT and IMT agreed well with histological measurements (intraclass correlation coefficients 0.78 and 0.80), whereas the AT was too thin to be distinguished in ultrasound images. Measures of vascular dimensions for the different groups are presented in the Table PP69. All wall layers were significantly thicker in group 4 compared to the other groups, whereas no difference was seen between the other groups.

**Conclusions:** TA IT and IMT are significantly thickened in GCA patients with transmural TA inflammation. Non-invasive VHRU provides accurate information on TA wall layer dimensions in vivo and could potentially be utilized as a diagnostic tool in the sonographic diagnosis and follow-up of GCA.

**PP70**

Radiographic features of psoriatic arthritis mutilans: results from the Nordic PAM Study

| Table PP69. Measures of vascular dimensions in very-high resolution ultrasound and histology. |
|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Non GCA, biopsy negative (n = 28) | Clinical GCA, biopsy negative (n = 10) | Clinical GCA, biopsy mild inflammation (n = 6) | Clinical GCA, biopsy transmural inflammation (n = 7) |
| Lumen diameter (mm) | 0.95 ± 0.19 | 0.94 ± 0.22 | 0.96 ± 0.29 | 0.78 ± 0.24 |
| Vascular ultrasound | 0.12 ± 0.05 | 0.15 ± 0.05 | 0.15 ± 0.04 | 0.38 ± 0.26** |
| Intima thickness (mm) | 0.12 ± 0.05 | 0.15 ± 0.05 | 0.15 ± 0.04 | 0.38 ± 0.26** |
| Vascular ultrasound | 0.22 ± 0.09 | 0.24 ± 0.13 | 0.23 ± 0.03 | 0.49 ± 0.19** |
| Histology | 0.28 ± 0.10 | 0.25 ± 0.09 | 0.33 ± 0.09 | 0.57 ± 0.29** |
| Adventitia thickness (mm) | 0.06 ± 0.02 | 0.06 ± 0.01 | 0.09 ± 0.03 | 0.17 ± 0.06** |

Values are reported as mean ± sd.
GCA, giant cell arteritis.
**Significantly different (p < 0.001) compared to all other groups in one-way ANOVA with Bonferroni correction.
History of smoking, body mass index, and gender did not influence the scoring.

Conclusions: Reporting early signs suggestive of PAM, e.g. signs of pencil-in-cup deformities and gross osteolysis in any joint, should be mandatory and may be crucial. This would increase awareness of PAM, accelerate the diagnosis, and lead to improved effective treatment to minimize joint damage resulting in PAM.

References


PP71

Clinical impact of $^{18}$F-fluorodeoxyglucose-positron emission tomography/computed tomography in diagnosis of suspected vasculitis: a prospective study

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Objectives: Vasculitides are a heterogeneous group of diseases characterized by inflammation of blood vessels leading to tissue or end-organ injury. The diagnosis of vasculitis is a challenge, especially in patients presenting with non-specific symptoms. The role of $^{18}$F-fluorodeoxyglucose positron emission tomography/computed tomography ($^{18}$F-FDG-PET/CT) in the early diagnosis of vasculitis is promising (1, 2), yet its role in real

Table PP70. Correlation between scoring systems and clinical variables

<table>
<thead>
<tr>
<th></th>
<th>mSvdH</th>
<th>PARS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Age at psoriasis onset</td>
<td>-0.229 (-0.464 to 0.036)</td>
<td>ns</td>
</tr>
<tr>
<td>Age at arthritis onset</td>
<td>-0.246 (-0.478 to 0.020)</td>
<td>ns</td>
</tr>
<tr>
<td>Psoriasis duration</td>
<td>0.321 (0.089 to 0.560)</td>
<td>0.001</td>
</tr>
<tr>
<td>Arthritis duration</td>
<td>0.458 (0.219 to 0.645)</td>
<td>0.0004</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.514 (0.272 to 0.695)</td>
<td>0.0002</td>
</tr>
<tr>
<td>CRP</td>
<td>0.316 (0.048 to 0.543)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

mSvdH, modified Sharp-van der Heijde; PARS, Psoriatic Arthritis Ratingen Score; HAQ, Health Assessment Questionnaire; CRP, C-reactive protein; ns, not significant.

Figure PP70. A 66-year-old male with a 32 year history of psoriatic arthritis mutilans (PAM). The radiograph shows profound resorption or osteolysis in several joints and pencil-in-cup deformities of his hand with relative sparing changes of his wrists and no sign of ankylosis.
Clinical settings is unclear. This prospective study aimed to assess the impact of $^{18}$F-FDG-PET/CT in suspicion of vasculitis.

**Methods:** This study evaluated 82 consecutive patients admitted to Turku University Hospital owing to suspected vasculitis. Vasculitis was confirmed or excluded by collegial decision by specialists taking into account clinical examination, laboratory and imaging studies, and a follow-up. The use of glucocorticoids (GCs) at the time of scanning and prior imaging were evaluated. $^{18}$F-FDG-PET/contrast-enhanced computed tomography (CECT) scanning was also performed in 21 patients.

**Results:** Altogether, 38 patients were diagnosed with clinical vasculitis (Table PP71). A total of 21 patients had increased $^{18}$F-FDG accumulation in blood vessel walls suitable for vasculitis; and 34 (41.5%) had no GC treatment previously. In the group with clinically diagnosed vasculitis (n = 38), patients with positive finding in $^{18}$F-FDG-PET/CT had a significantly shorter duration of GCs (4.0 vs 7.0 days; p = 0.034) and lower GC dose (18.6 vs 37.4 mg; p = 0.002) compared to $^{18}$F-FDG-PET/CT-negative patients. In this group with clinically diagnosed vasculitis, 21 patients with positive $^{18}$F-FDG-PET/CT had significantly higher C-reactive protein (CRP) (p = 0.018) than the 17 patients with negative $^{18}$F-FDG-PET/CT findings (154.5 vs 90.4 mg/L). CECT did not reveal characteristic vasculitis findings in any of the 21 patients. Atherosclerotic changes in vessel walls were common (11/21, 52%).

**Conclusions:** This study aimed to find predictors for helpful $^{18}$F-FDG-PET/CT scans to allow more tailored and cost-effective use of $^{18}$F-FDG-PET/CT. We found that in patients with a confirmed vasculitis diagnosis, $^{18}$F-FDG-PET/CT positivity was significantly related to a lower dose and shorter duration of GC medication and higher CRP level. CECT did not give additional information to the vasculitis diagnosis.

**References**


**OTHER**

**PP72**

Inclusion body myositis and T-cell large granular lymphocytic leukaemia – an underestimated coexistence of two severe disorders: a report of two cases

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1Department of Internal Medicine, Division of Rheumatology, Vejle Hospital, Vejle, Denmark, 2Department of Internal Medicine, Division of Haematology, Vejle Hospital, Vejle, Denmark, 3Department of Rheumatology, Odense University Hospital, Odense, Denmark

**Background:** Inclusion body myositis (IBM) is a slowly progressive inflammatory muscle disease that results in severe disability and has a substantial impact on life. In contrast to other inflammatory muscle diseases, IBM is largely resistant to immunosuppressive treatments. The immune mechanisms are complex but the identification of CD8+ T-cell in muscle biopsy confirms IBM as a T-cell-mediated disease (1). T-cell large granular lymphocytic leukaemia (T-LGL) is a malignancy that ranges from mild disease to more aggressive haematological disorder and is known to be associated with rheumatoid arthritis (RA) (2). One single study has identified a link between IBM and T-LGL leukaemia. In that study, the majority of patients with IBM (22/38; 58%) were found to meet the criteria for T-LGL (3). These findings have yet to be confirmed by other research groups.

**Case reports:** We report two cases of coexistent T-LGL leukaemia and IBM.

**Table PP71. Characteristics of clinically positive vasculitis patients (n = 38).**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PET/CT positive (n = 21)</th>
<th>PET/CT negative (n = 17)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender, n (%)</td>
<td>14 (66.7)</td>
<td>9 (52.9)</td>
<td>0.403</td>
</tr>
<tr>
<td>Age (years), mean ± sd</td>
<td>68.0 ± 12.1</td>
<td>64.2 ± 15.0</td>
<td>0.390</td>
</tr>
<tr>
<td>CRP max (mg/L), mean ± sd</td>
<td>154.5 ± 100.2</td>
<td>90.4 ± 55.6</td>
<td>0.018</td>
</tr>
<tr>
<td>PCT max (μg/L), mean ± sd</td>
<td>0.121 ± 0.088, n = 17</td>
<td>0.022 ± 0.021, n = 12</td>
<td>0.137</td>
</tr>
<tr>
<td>ANCA pos, n (%)</td>
<td>3 (14.3)</td>
<td>4 (23.5)</td>
<td>0.478</td>
</tr>
<tr>
<td>Prednisolone at scanning moment (mg), mean ± sd</td>
<td>18.6 ± 18.3</td>
<td>37.4 ± 15.8</td>
<td>0.002</td>
</tr>
<tr>
<td>Prednisolone prior scanning (days), median [IQR]</td>
<td>4.0 [9]</td>
<td>7.0 [154]</td>
<td>0.034</td>
</tr>
<tr>
<td>Prednisolone cumulative dose (mg), median [IQR]</td>
<td>120 [1120]</td>
<td>360 [1965]</td>
<td>0.096</td>
</tr>
<tr>
<td>Fever over 38°C, n (%)</td>
<td>14 (66.7)</td>
<td>8 (47.1)</td>
<td>0.235</td>
</tr>
</tbody>
</table>

PET, positron emission tomography; CT, computed tomography; CRP, C-reactive protein; PCT, procalcitonin; ANCA, anti-neutrophil cytoplasmic antibody.
Case 1: A 65-year old woman diagnosed with RA in 2014. Later the same year, she developed neutropenia. The bone marrow sample led to the diagnosis of T-LGL leukaemia. Myalgia, reduced strength in proximal muscles of the upper and lower extremities, and dysphagia had gradually developed through the years. Nine months after the T-LGL diagnosis she was diagnosed with IBM.

Case 2: A 73-year-old man was diagnosed with IBM in 2012 after roughly 10 years of general muscle weakness. Neutropenia had been observed since 2011 and in 2015 a bone marrow sample confirmed the diagnosis of T-LGL.

Conclusions: The coexistence of IBM and T-LGL is not to be neglected. The order in which IBM and T-LGL leukaemia develop is unknown. Is there a causal relation or merely a coexistence of the disorders? There is an unmet need for research undertaking this question. If a causal immunogenic link between the disorders can be established it might have implications for immunosuppressive treatment and prognosis of IBM. We suggest that both diseases should be considered in patients presenting with either IBM or T-LGL, and steps towards recognition of a coexisting disorder should be taken to improve treatment and prognosis for these patients.

References

PP73
Prolongation or discontinuation of tumour necrosis factor inhibitors in the treatment of rheumatoid arthritis: could this be a realistic scenario?
E Kaltonoudis, E Pelechas, PV Voulgari, AA Drosos
Division of Rheumatology, University Hospital of Ioannina, Ioannina, Greece

Objectives: Rheumatoid arthritis (RA) is a lifelong immune-mediated disease. Tumour necrosis factors inhibitors (TNFi) have revolutionized the evolution...
and prognosis of RA. The main objective of this study was to evaluate the ability to safely extend interdose intervals or even discontinue the use of TNFi in RA.

**Methods:** The study included 68 patients (42 females, 26 males) diagnosed with RA using the ACR and EULAR classification criteria, who were followed up in the rheumatology outpatient clinic of a tertiary university hospital. The mean follow-up period was 11 years. All patients were receiving conventional synthetic disease-modifying anti-rheumatic drugs plus a TNFi and had been in remission for at least 6 months. The mean period of discontinuation was 2 years (range 1.5–2.5 years).

**Results:** Twenty-five patients were on adalimumab every 21 days, eight every month, while four have discontinued the treatment and are still in remission; 12 patients were on etanercept with an interdose interval of 10 days, six every 15 days, while three had discontinued the treatment. Finally, five patients were on golimumab with a dose interval of 35 days, three every 40 days, and one every 45 days, while one patient had discontinued the TNFi. Young, seronegative, female patients treated early with a TNFi had more chances of extending the interdose interval or even discontinuing the TNFi.

**Conclusions:** Extension of the interdose intervals or even discontinuation of TNFi is a feasible option in RA patients. This reflects significant economic benefits for the healthcare systems but also clinical benefits for the patient.

### PP74

**EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis**

Table PP74. Level of application and differences between Nordic countries.

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Finland, median (IQR)</th>
<th>Denmark, median (IQR)</th>
<th>Norway, median (IQR)</th>
<th>Sweden, median (IQR)</th>
<th>p* between groups</th>
<th>Localization †</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access to patient education</td>
<td>9 (7.0, 10.0)</td>
<td>9.0 (7.0, 10.0)</td>
<td>8.0 (6.5, 10.0)</td>
<td>7.0 (5.0, 9.0)</td>
<td>0.010</td>
<td>S vs F 0.010</td>
</tr>
<tr>
<td>Access to consultations</td>
<td>9 (8.0, 10.0)</td>
<td>9.0 (6.0, 10.0)</td>
<td>9.0 (7.0, 10.0)</td>
<td>8.0 (6.0, 10.0)</td>
<td>0.023</td>
<td>S vs F 0.045</td>
</tr>
<tr>
<td>Access to telephone consultations</td>
<td>10.0 (9.0, 10.0)</td>
<td>10.0 (6.25, 10.0)</td>
<td>10.0 (2.0, 10.0)</td>
<td>9.0 (7.0, 10.0)</td>
<td>0.098</td>
<td></td>
</tr>
<tr>
<td>Disease management</td>
<td>9.0 (6.5, 10.0)</td>
<td>8.0 (6.0, 10.0)</td>
<td>7.0 (4.5, 10.0)</td>
<td>6.5 (4.0, 9.0)</td>
<td>0.000</td>
<td>S vs N 0.008</td>
</tr>
<tr>
<td>Psychosocial issues</td>
<td>8.0 (6.0, 9.0)</td>
<td>8.0 (6.0, 10.0)</td>
<td>7.0 (5.0, 9.0)</td>
<td>6.0 (5.0, 8.0)</td>
<td>0.005</td>
<td>S vs F 0.004</td>
</tr>
<tr>
<td>Promote self-management skills</td>
<td>9.0 (8.0, 10.0)</td>
<td>9.0 (8.0, 10.0)</td>
<td>9.0 (7.0, 10.0)</td>
<td>7.0 (5.0, 9.0)</td>
<td>0.005</td>
<td>S vs F 0.003</td>
</tr>
<tr>
<td>Local protocols and guidelines</td>
<td>9.0 (8.0, 10.0)</td>
<td>9.0 (7.0, 10.0)</td>
<td>9.0 (6.5, 10.0)</td>
<td>8.0 (6.0, 9.0)</td>
<td>0.001</td>
<td>S vs F 0.000</td>
</tr>
<tr>
<td>Continuous education</td>
<td>8.0 (7.0, 10.0)</td>
<td>8.0 (7.0, 10.0)</td>
<td>7.0 (6.0, 9.5)</td>
<td>5.0 (3.0, 8.0)</td>
<td>0.009</td>
<td>S vs F 0.010</td>
</tr>
<tr>
<td>Extended role</td>
<td>8.0 (6.0, 8.75)</td>
<td>7.0 (4.5, 10.0)</td>
<td>7.0 (4.0, 8.75)</td>
<td>6.0 (2.5, 8.0)</td>
<td>0.039</td>
<td>S vs F 0.020</td>
</tr>
<tr>
<td>Interventions and monitoring</td>
<td>8.0 (7.0, 9.0)</td>
<td>8.0 (5.75, 9.0)</td>
<td>7.0 (2.75, 8.0)</td>
<td>7.0 (4.0, 8.0)</td>
<td>0.002</td>
<td>S vs N 0.048</td>
</tr>
</tbody>
</table>

*Level of significance: p < 0.05.
†Localization: D, Denmark; F, Finland; N, Norway; S, Sweden.
5–9), and in the whole study population from 3 to 6 (Figure PP74). Differences between individual NCs exist in the level of application (Table PP74). There were a few reasons for the incomplete agreement in F, mainly in the extended role of the nurse: knowledge of the nurse (n = 3, 14%), nurses are not willing (n = 3, 14%), and do not accept the nurse (n = 1, 5%). The most often reported barriers to application were nurse resources and insufficient knowledge, mentioned among others in extended role (n = 7, 33%; n = 6, 29%) and in interventions and monitoring (n = 8, 40%; n = 2, 10%).

**Conclusions:** The agreement with and application of EULAR-RN is high among rheumatologists in NCs. More nursing resources and education are needed to remove the barriers.

**References**


**PP75**

**A psycho-educational path for patients affected by fibromyalgia**

A Romeo, M Schembari, R Caceci, F Raiti, F Bürrico, G Torneo Syracuse Local Health Company, Syracuse, Italy

**Objectives:** Fibromyalgia is a pathology characterized by widespread chronic musculoskeletal pain with a pervasive impact for the persons affected. We developed a psycho-educational path whose main objective is to improve the quality of life of individuals affected by fibromyalgia.

**Methods:** Patients are enlisted after medical and psychological examination. Criteria for inclusion in the path are the following: fibromyalgia diagnosis and visual analogue scale score > 5. To maximize the effectiveness, patients with cognitive deficits, psychiatric disorders, and physical disabilities were excluded. The psycho-educational path is made up of 10 meetings of 1 h and 20 min each, once per week. Homogeneous clusters of three patients are grouped based on disease and age, and are mostly women. The first and the last meetings are held with multidisciplinary staff (doctor, psychologist, physiotherapist) and adopt an informative approach to pain. During the informative phase, patients become aware of the physiological curve of the vertebral column and daily routines, and receive an introduction to breathing. Between the second and ninth meetings, the physiotherapist carries out postural education with stretching exercises and muscular contractions, ergonomics, breathing re-education, relaxation, and autogenic training. At the end of the cycle, patients face a first follow-up within 1 month and a second one at the end of the third month. It is important to repeat all of this at home, autonomously, using the support material provided.

**Results:** After following the psycho-educational path, patients improve their own self-confidence, practise home exercises, and make use of relaxation and autogenic training to handle emotional stress and reduce muscular tension. Patients become aware of their own posture and feel guilty when they find themselves in a wrong position.

**Conclusions:** It is not possible to completely heal permanent pain, but patients can cure it, thanks to what they have learned. Position is not ‘algocentric’ but rather egocentric because the person is not impotent against pain, but instead plans his or her own daily life according to his or her needs.

**References**


PP76

Case report: bowel-associated dermatosis–arthritis syndrome with myositis-like features

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Background: Bowel-associated dermatosis–arthritis syndrome is a rare sequela of intestinal bypass surgery and inflammatory bowel disease, possibly caused by an autoimmune reaction to intestinal microbial overgrowth. Diagnosis may be arduous owing to the unspecific nature of the symptoms, i.e. malaise, fever spikes, myalgia, arthralgia, and cutaneous eruptions. Glucocorticoids are often required and antibiotics may sometimes be helpful (1, 2).

Case report: Our patient, a 68-year-old Caucasian male, sought treatment for 2 weeks of nocturnal fever spikes and myalgia of the feet. He had a previous diagnosis of ulcerative colitis treated by hemicolectomy in 1981 with post-operative complications leading to complete removal of ileum and colon and subsequent permanent jejunostomy. Furthermore, the patient had hypertension and asthma, and had tested positive for asymptomatic methicillin-resistant Staphylococcus aureus. Abnormal C-reactive protein, slight leucocytosis, and elevated erythrocyte sedimentation rate, in addition to a heart rate of 100 bpm and blood pressure of 127/88 mmHg, were noted on admission. The patient was hospitalized with suspicion of a septic infection and empirical i.v. vancomycin and cefuroxime were initiated. Blood cultures, viral polymerase chain reaction tests, chest X-ray, and full-body computed tomography scan were negative. Antibiotic therapy was deemed ineffective after 3 days and a suspicion of an autoimmune process emerged. Antibiotics were ceased and treatment with glucocorticoids was initiated. During the first days of the glucocorticoid treatment, the patient developed a diffuse oedema, muscle weakness, and intensive myalgia of the thighs, with moderate increases in creatine kinase and myoglobin levels. Magnetic resonance imaging of the thighs showed perimysial oedema. After 10 days of treatment, a sudden extreme leucocytosis (47 E9/L) developed and erythema nodosum-like rash of the extremities was noted. Concurrently, a severe malnutrition attributable to short-bowel syndrome was uncovered, and intensive parenteral nutrition was initiated. Biopsies of the skin and thigh muscle revealed neutrophilic infiltration of subcutaneous fat tissue (Figure PP76 A) and perimysial spaces (Figure PP76 B). Based on these findings, a diagnosis of a bowel-associated dermatosis–arthritis syndrome was made. After 7 weeks of treatment, the patient recovered sufficiently for discharge, continuing with low-dose glucocorticoids and physiotherapy.

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