On the other hands, baseline DAS28 for the 20 patients was 4.8±0.3 (2.5–6.8) in TCZ group. There were no differences between ADA and TCZ groups. RA patients with an insufficient response to ADA or TCZ showed highly significant improvement of DAS28 after 12 weeks (2.9±0.3 and 2.2±0.4, respectively), and 24 weeks (2.5±0.4 to 2.2±0.2, respectively). ADAM-10 highly correlates with CDAI, and fractalkine/CX3CL1. Serum ADAM-10 levels were no remarkable change after treatment with ADA despite decrease of disease activity of RA. On the other hand, serum ADAM-10 levels in patients who were treated with TCZ were significantly diminished following successful treatment and clinical improvement (baseline 408±88 pg/ml and 54 weeks 138±51 pg/ml, $p<0.05$). Univariate logistic regression analysis, baseline of DAS28 (ESR), baseline of CDAI, and ADAM-10 were selected as significant variables for improvement of DAS28 (ESR) at 24 weeks. Multiple regression analysis showed that ADAM-10 was only identified as independent predictive variable for improvement of DAS28 (ESR) at 24 weeks. ADAM-10 baseline in TCZ responder was significantly higher than TCZ nonresponders at 24 weeks (620±134 pg/ml and 109±25 pg/ml, respectively, $p<0.05$).

Conclusions: This study indicates that ADAM-10 is correlated with RA disease activity, and is higher in TCZ responders. These results suggest that ADAM-10 may be a predictor of treatment effectiveness for RA with TCZ.

Disclosure of Interest: None declared

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THU0065 CYTOKINES AND LIPOCALIN-2 IN PREGNANT WOMEN WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Rheumatoid arthritis (RA), and especially seronegative RA, is often ameliorated by pregnancy, while systemic lupus erythematosus (SLE) is prone to flare and associated with pregnancy complications. Cytokines and chemokines are of great importance for immune processes during pregnancy. The inflammatory marker Lipocalin-2 (LCN2) has become increasingly relevant as a potential clinical biomarker of rheumatic diseases (1). LCN2 is produced in the maternal-fetal interface during normal pregnancies and correlates with the presence and severity of preeclampsia (2).

Objectives: To obtain a better understanding of immune regulation and the disparate immune responses in pregnant women with RA and SLE. In this pilot study, we analyzed levels of multiple cytokines, chemokines and LCN2 in women with seropositive RA, seronegative RA, SLE and healthy controls during pregnancy and postpartum.

Methods: The Norwegian National Advisory Unit on Pregnancy and Rheumatic Diseases collect serum samples in a biobank from women with inflammatory rheumatic diseases before pregnancy, during pregnancy week 10–12, week 23–25, week 30–32 and 6 weeks, 6 months and 12 months postpartum. Control serum samples were collected from healthy pregnant women at matching time-points. We analyzed serum cytokine and chemokine levels using a multiplex assay. A sandwich ELISA was used to measure LCN2. In this pilot study we included pregnant women with SLE (n=4), seropositive RA (n=4), seronegative RA (n=2) and healthy pregnant controls (n=4). The total cohort consists so far of 18 pregnant women with SLE and 23 pregnant women with RA.

Results: We observed lower LCN2 levels during pregnancy in SLE patients, compared to controls and RA patients. LCN2 levels in seropositive RA patients and controls were found to be comparable during pregnancy, whereas pregnant women with seronegative RA showed higher LCN2 levels. Levels of IFNγ, IL-6 and IP-10 were higher in SLE than in RA patients during the course of pregnancy. IL-17 was slightly higher only in seropositive RA patients compared to controls. TNFα was slightly higher in both SLE and RA patients compared to controls, levels of anti-inflammatory IL-10 were very low or undetectable in all groups.

2. Trimester	Controls	SLE	Seropos RA	Seroneg RA
LCN2 (ng/ml)	285,5 (±74,7)	126,5 (±44,6)	232,6 (±67,4)	330,2 (±3,2)
IFNγ (pg/ml)	15,0 (±22,4)	40,4 (±65,1)	6,9 (±5,2)	26,1 (±9,9)
IL-6 (pg/ml)	3,4 (±1,9)	5,9 (±2,0)	3,8 (±1,5)	5,3 (±1,0)
IP-10 (pg/ml)	60,3 (±14,5)	138,3 (±92,1)	61,7 (±8,9)	64,9 (±7,3)
IL-17 (pg/ml)	1,3 (±1,3)	2,3 (±2,2)	4,8 (±9,0)	0,6 (±0,2)
TNFα (pg/ml)	2,2 (±2,5)	4,2 (±5,4)	3,3 (±3,5)	3,2 (±0,7)

Conclusions: We found interesting differences in cytokine, chemokine and LCN2 levels during pregnancy in women with SLE, seropositive RA and seronegative RA. The results need confirmation in the total cohort and will be further explored for a better understanding of the disparate immune modulation of RA and SLE during pregnancy.

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THU0066 OSTEOCLAST DIFFERENTIATION GENE EXPRESSION PROFILING REVEALS CCL4 MEDIATES RANKL-INDUCED OSTEOCLAST MIGRATION

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Background: The migration of osteoclast from circulation and bone marrow into bone surface has suggested as a novel therapeutic point for bone erosion in RA.

Objectives: We explored the mechanisms involved in osteoclast migration.

Methods: Gene expression profiling was identified by microarray analysis and validated by Real-time PCR during differentiation of bone marrow-derived macrophages (BMMs) into osteoclast (OCs). RANKL induced osteoclast precursor cell line RAW264.7 migration and invasion in the presence and absence of anti-CCL4 antibody was measured in vitro. Intracellular signaling pathway was assessed by Western blotting. Osteoclast formation was identified by TRAP staining.

Results: A panel of 11 chemokines signal was significant increase in osteoclastic differentiation of BMMs by Microarray. High expression of CCL4 was validated in primary BMMs and RAW264.7 cell line during differentiated into OCs. RANKL induced osteoclast precursor cell migration and invasion was decreased upon addition of anti-CCL4 antibody. OCs formation and OCs related genes expression were not affected by CCL4 inhibition. Neutralization of CCL4 promoted the PI13K phosphorylation at 45 to 60min after RANKL stimulation in RAW264.7.

Conclusions: CCL4 regulates RANKL-induced OCs migration, suggesting that CCL4 inhibition could be bone protective in RA

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Disclosure of Interest: None declared

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THU0067 NLRP3 INFLAMMASOME ACTIVITY IN MONOCYTES IS REGULATED BY 12/15-LIPOXYGENASE

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Background: Activation of the NLRP3 inflammasome is a major inflammatory pathway in monocytes in response to various exogenous and endogenous stimuli. However, negative regulation of inflammasome activity is not well understood. Glucocorticoids (GC) are drugs of choice for the treatment of many inflammatory diseases. Recently, we could show that treatment of monocytes with GC leads to re-programming towards a specific population involved in resolution of inflammation. Gene analysis has shown up-regulated expression of 12/15-lipoxygenase (12/15-LOX) in GC-and LPS/GC-treated monocytes. 12/15-LOX reacts with polyunsaturated-fatty-acids to generate anti-inflammatory lipid-mediators, which contribute to resolution of inflammation.

Objectives: The aim of our study was to determine the contribution of 12/15-LOX on the inflammatory response on murine monocytes.

Methods: Bone marrow-derived monocytes were isolated from wild-type (wt) C57BL/6 and 12/15-LOX$^{-/-}$ mice and stimulated with GC and/or LPS as well as various inhibitors or stimulants. Gene expression was analyzed using qRT-PCR. Protein expression was examined by Western-Blot, Flow-Cytometry and ELISA. T-cell response was analyzed by co-culture of stimulated monocytes with allogenic T-cells.

Results: 12/15-LOX$^{-/-}$ monocytes showed slightly higher secretion of IL-1β as compared to wt cells after LPS stimulation. The differences between wt and 12/15-LOX$^{-/-}$ were much more pronounced when monocytes were additionally exposed to ATP. LPS treatment markedly enhanced expression of pro-IL-1β in 12/15-LOX$^{-/-}$ monocytes. No differences could be observed between wt and 12/15-LOX$^{-/-}$ monocytes in secretion of other proinflammatory mediators as well as the expression of inflammasome components. However, expression of cleaved caspase-11 was up-regulated in 12/15-LOX$^{-/-}$ monocytes exposed to LPS. Additionally, inhibition of caspase-11, caspase-1 and 5-LOX significantly reduced the high secretion of IL-1β in 12/15 LOX$^{-/-}$ monocytes. Interestingly, 12/15-LOX$^{-/-}$ rather than wt monocytes stimulated with LPS led to enhanced T-cell proliferation.

Conclusions: Our results demonstrate that 12/15-LOX plays a regulatory role during inflammatory immune response by counteracting the NLRP3 inflammasome activity through down-regulation of caspase-11 and 5-LOX activity. Thus, we identified a novel negative regulatory pathway of inflammasome activity.

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Disclosure of Interest: None declared
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THURSDAY, 15 JUNE 2017

Rheumatoid arthritis - prognosis, predictors and outcome

THU0068 THE RISK OF INDIVIDUAL AUTOANTIBODIES, AUTOANTIBODY COMBINATIONS AND AUTOANTIBODY LEVELS FOR ARTHRITIS DEVELOPMENT IN CLINICALLY SUSPECT ARTHRALGIA

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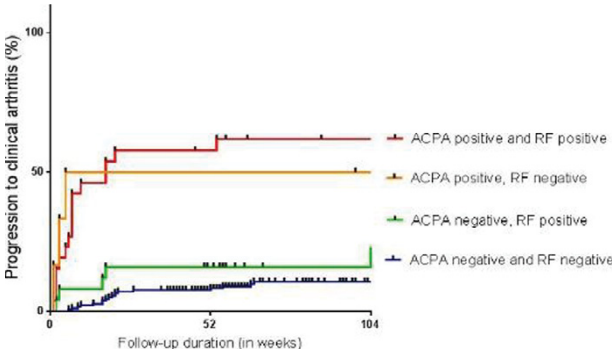
Background: Autoantibody testing is helpful to predict progression to arthritis in subjects at risk. Previous longitudinal studies mainly focussed on autoantibody-positive arthralgia patients. Consequently predictive values of autoantibodies were evaluated relative to each other. This study assessed risks of having anticitrullinated protein antibodies (ACPA), rheumatoid factor (RF) and/or anti-carbamylated protein antibodies (anti-CarP) for arthritis development in arthralgia patients considered at risk for RA by rheumatologists based on clinical characteristics (Clinically Suspect Arthralgia, CSA).
Objectives: To assess risks of having anticitrullinated protein antibodies (ACPA), rheumatoid factor (RF) and/or anti-carbamylated protein antibodies (anti-CarP) for arthritis development in arthralgia patients considered at risk for RA by rheumatologists based on clinical characteristics (CSA).
Methods: Baseline ACPA, RF and anti-CarP antibodies of 241 patients, consecutively included in the CSA-cohort, were studied in relation to development of clinical arthritis during a median follow-up of 103 (IQR 81–114) weeks.
Results: ACPA, RF and anti-CarP antibodies were all univariably associated with arthritis development, hazard ratios (95% CI) were 8.5 (4.7–15.5), 5.1 (2.8–9.3) and 3.9 (1.9–7.7). Only ACPA, and not RF or anti-CarP, was independently associated (HR 5.1, 2.0–13.2). Relative to autoantibody-negative CSA-patients, ACPA-negative/RF-positive patients had HRs of 2.6 (1.04–6.6), ACPA-positive/RF-negative patients 8.0 (2.4–27.4), and ACPA-positive/RF-positive patients 10.5 (5.4–20.6, Figure). PPVs for development of clinical arthritis within two years were: 38% for ACPA-negative/RF-positive, 50% for ACPA-positive/RF-negative, and 67% for ACPA-positive/RF-positive patients. Higher ACPA-levels were not significantly associated with increased progression to clinical arthritis, in contrast to higher RF-levels. Autoantibody levels were stable during follow-up.



Conclusions: ACPA conferred the highest risk for arthritis development and had an additive value to RF. However, >30% of ACPA-positive/RF-positive CSA-patients did not develop arthritis during two-year follow-up. Thus CSA and information on autoantibodies is insufficient to accurately identify imminent autoantibody-positive RA.

Disclosure of Interest: None declared
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THU0069 HOW MANY RHEUMATOID ARTHRITIS PATIENTS IN REMISSION EXPERIENCE PAIN? WHAT TYPES AND WITH WHAT FREQUENCY WERE PAINKILLERS RECEIVED? IS REACHING REMISSION A REALISTIC GOAL?

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Background: The primary treatment goal in rheumatoid arthritis (RA) patients is to reach remission. Earlier diagnosis, advancements in disease-modifying antirheumatic drugs, and improved treatment strategies have enabled increasing numbers of RA patients to achieve remission. However, the definition of remission involves the fulfillment of specific criteria, which include a number of swollen and tender joints, the erythrocyte sedimentation rate (ESR), and the visual analog scale of pain (VAS pain). Some patients with RA in remission wished to take painkillers because they experienced pain and physical limitations in their daily life or at work. Is reaching remission a realistic goal?
Objectives: To evaluate VAS pain and patient's global assessment (PGA) in those with RA in remission, and to determine the types and frequency of which painkillers were received.
Methods: In a study of 554 RA patients with a definite RA diagnosis according to 1987 ACR criteria, we enrolled 235 patients (82% females). All patients had DAS28-ESR <2.6, defined as clinical remission, and had no acute pain as a result of operation or trauma. The mean age and disease activity were 53.6 years and 2.67, respectively. Seventy-one percent of patients were treated with MTX, 30.2% with glucocorticoids, and 38.4% with a biological agent. We evaluated VAS pain and PGA and investigated why patients experienced dissatisfaction with VAS pain and PGA. Moreover, we elucidated how many patients used painkillers and what types of painkillers were used.
Results: The mean values of clinical and laboratory data were described as follows: 28 swollen joints, 0.69; 28 tender joints, 1.56; RF, 157 IU/mL; C-reactive protein, 0.14 mg/dL; ESR, 19 mm/h; and health assessment questionnaire disability index score, 0.618. Steinblocker stages (I/II/III/IV) were (166/51/18/0), respectively and Steinblocker classes (I/II/III/IV) were (155/68/12/0), respectively. The mean VAS pain was 1.81. Thirty-five (14.9%) of 235 patients had VAS pain >3 (Fig. 1). The mean PGA was 1.54. Seventeen patients (7.2%) reported PGA >3 (Fig. 2). Reasons for VAS pain or PGA of >3 were musculoskeletal pain (48.6%), neuropathic pain (23.1%), psychological reasons (9.3%), and other (19%). Thirty-one patients (13.2%) were treated with painkillers such as NSAIDs (46.2%), acetaminophen (22.5%), pregabalin (18.6%), tramadol (4.1%), and other (8.6%). The mean values for VAS pain and PGA were improved after using painkillers by 0.73 and 0.36, respectively. There was a significant difference in the improvement rate of VAS pain and PGA between pre-use and post-use of pain-killer (Fig. 3).

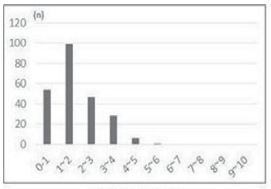

Fig.1 VAS pain

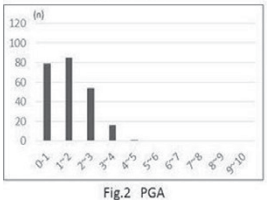

Fig.2 PGA

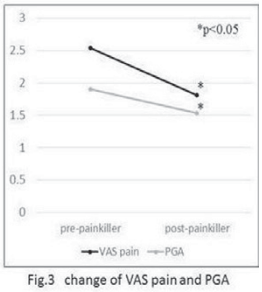

Fig.3 change of VAS pain and PGA

Conclusions: VAS pain and PGA are important for understanding the patients' functional disabilities and problems. We should attend to patients' demands and make an informed decision to form a realistic goal for RA treatment. Given that VAS pain and PGA were improved because of the use of painkillers in the current study, we suggest that the ability to appropriately prescribe painkillers is an important method with which to satisfy RA patients in remission.

Disclosure of Interest: None declared
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THU0070 TREAT-TO-TARGET IN RA: WHAT LEVEL OF TREATMENT RESPONSE IS NECESSARY BY 3 MONTHS IN ORDER TO ACHIEVE THE TREATMENT TARGET BY 6 MONTHS? RESULTS FROM A REAL LIFE STUDY

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Background: When initiating therapy with disease-modifying anti-rheumatic drugs