Abstract AB0269 – Table 2. Ankle and knee involvement in remission

	DAS28<2.6. 417 patients in total	DAS28<2.6. RF pos, anti- MCV pos: 131 patients	DAS28<2.6. RF neg, anti- MCV neg: 120 patients
Right knee synovitis	1,43%	2,29%	0
Left knee synovitis	0,95%	1,52%	0
Both knees synovitis	0	0	0
% of patients with knee involvement	2,39%	3,87%	0
Right ankle synovitis	6,71%	6,87%	6,66%
Left ankle synovitis	7,19%	7,63%	8,33%
Both ankles synovitis	0,23%	0,76%	0
% of patients with ankle involvement	13,66%	13,74%	15%

Conclusions: Our present data show that ankle synovitis is rather common in patients with serologically and clinically different forms of RA and highlight the importance of careful medical examination, even in case of clinical remission.

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AB0270

TREATMENT RESPONSE TO RITUXIMAB IN COMBINATION WITH LEFLUNOMIDE IS INFLUENCED BY ANTICCP STATUS IN ACTIVE RHEUMATOID ARTHRITIS: RESULTS FROM A MULTICENTER RANDOMISED PLACEBO-CONTROLLED INVESTIGATOR INITIATED CLINICAL TRIAL IN ACTIVE RHEUMATOID ARTHRITIS (AMARA-STUDY)

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Background: Use of biologicals such as Rituximab (RTX) in Rheumatoid Arthritis (RA) is effective and often only licensed in combination with Methotrexate (MTX). In cases of contraindications to or intolerances, other cDMARDs are frequently used in routine care without data from RCTs. Patients with positive antiCCP-status were identified in previous studies to better respond to RTX in combination with MTX.

Objectives: Here we present for the first-time data of the impact of antiCCP status on ACR response in the combinational therapy of RTX and Leflunomide (LEF).

Methods: A total of 189 patients with active RA (DAS28 >3.2 and at least 3 SJC and 3 TJC) despite stable LEF treatment were screened for a 52 weeks double-blind placebo controlled multicenter RCT. Patients were randomised to receive either two times 1000 mg RTX i.v. or PLA, followed by a second course of RTX of either two times 500 or 1000 mg at week 24. The primary endpoint of the study was superiority of RTX in ACR20 and 50 responses during 24 weeks treatment period. Adult patients who had inadequate response to more than one antiTNF or failed more than three cDMARDs were excluded. Disease activity was measured at each visit and compared according to antiCCP status. For safety evaluation, frequency and severity of adverse events were documented.

Results: Of 189 screened patients 148 were randomised. The mean age was 56 years; the mean body weight 76 kg and 74% were female. The disease activity (DAS28) at baseline was 5.57 for RTX and 5.54 for PLA. 57.1% of the patients were antiCCP-positive for RTX compared to 59.6% for PLA. In the RTX group, antiCCP-positive patients' disease duration was 8.8 years compared to 5.6 years in the antiCCP-negative group, DAS28 was 5.73 vs. 5.32 and CRP levels were

11.1 mg/L vs. 5.3 mg/L. RTX demonstrated significant superiority compared to PLA at week 16 in both, ACR 20 and ACR 50 response. AntiCCP-positive patients showed a higher probability to respond to the RTX/LEF treatment than antiCCP-negative patients (figure 1). 43 serious adverse events were reported, 27 of them in the RTX treatment group during the placebo-controlled period.

Abstract AB0270 – Figure 1

Conclusions: Here we report data of the first RCT investigating the combination of RTX with LEF in RA. The treatment with RTX in combination with LEF demonstrated significant efficacy compared to PLA for ACR20 and 50 responses with highest response level at week 16. AntiCCP-positive patients showed a higher probability for treatment response compared to antiCCP-negative ones. The combination of RTX and LEF demonstrated a reasonable safety profile.

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AB0271

RS12218 POLYMORPHISM IN SAA1 GENE IN THE RUSSIAN POPULATION OF RA PATIENTS IS ASSOCIATED WITH SECONDARY AMYLOIDOSIS. A PILOT STUDY

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Background: Secondary amyloidosis (SA) is a serious complication of rheumatoid arthritis (RA), which is often fatal. Identification of associated risk factors, including genetic ones, is an important task.

Objectives: To assess the role of SAA1 gene polymorphism, encoding serum amyloid-A, as a risk factor predisposing to SA in the sample of Russian RA patients.

Methods: The study included 60 patients with RA, fulfilled the American College of rheumatology criteria (ACR) 1987. Of these 35 (mean age 49.5±10.8 y, mean disease duration 18.5±8.9) developed SA manifestations, confirmed histologically: group SA (+). 25 patients (mean age 56.7±11.7 y, mean disease duration 16.3±7.5 y) did not have either clinical or histological SA signs: group SA (-). The control group (C) consisted of 65 healthy employees. SAA1 gene polymorphism rs12218 (-13 T/C), mapped in the 5' flanking region of the gene, was studied in 125 subjects by polymerase chain reaction in real time (RT-PCR) with subsequent melting curves analysis.

Results: Statistically significant differences in the rates of TT, TC and CC genotypes of rs12218 polymorphism were established between SA(+) group and the controls (17.1%, 64.0%, 48.6% and 38.5%, 46.1%, 15.4%, respectively, p=0.029). High rate (58.6%) of the mutant C allele in SA(+) group compared to the control group (38.5%) predetermines high risk of susceptibility to SA in RA patients [OR 2.26, 95% CI(1.20–4.28), p=0.010]. Significant differences in rs12218 polymorphism rates were found between SA(+) and SA(-) groups [p<0.001]. The frequency of TC + CC genotype was significantly higher in the SA (+) group compared to SA(-) group [82.9% vs 36.0%, p<0.001]. The risk of predisposition to SA development among RA patients was increased when C allele frequencies in the group with SA (58.6%) were compared with the group without SA (22.0%) [OR 5.01, 95% CI (2.07–12.58), p<0.001]. No significant differences were found in the frequencies of genotypes and rs12218 alleles between SA(-) pts and the controls (p>0.05).

Conclusions: Our data confirm that genetic polymorphism rs12218 in SAA1 gene, is associated with the development of secondary amyloidosis in RA patients and mutation in this gene is an important risk factor predisposing to the development of this severe complication in the Russian population.

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AB0272

MEAN PLATELET VOLUME AS A POTENTIAL BIOLOGICS THERAPY RESPONSE PREDICTOR AND DISEASE ACTIVITY INDICATOR IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease that primarily affects joints. Currently, the most widely used markers of acute phase response are C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). However, in recent years it has been suggested that platelet histogram indices, such as mean platelet volume (MPV) could be predictors of disease activity in patients with RA.

Objectives: The aim of this study was to assess whether MPV can be used as a disease activity marker by analysing a possible correlation between MPV and DAS-28, serum CRP levels, and ESR in patients starting with or switching between different biological DMARDs (tocilizumab, infliximab). Finally, we investigate whether MPV value at baseline can be a therapy outcome predictor by comparing two groups of patients (remission and active disease) at the 12 month time point based on DAS-28 value.

Methods: Fifteen patients (aged 56.5±9.3 years) fulfilling the American College of Rheumatology (ACR) criteria for RA were retrospectively enrolled in the study from the rheumatology outpatient clinic at the University Hospital Centre Zagreb, Croatia. DAS-28 has been used to evaluate disease activity at baseline, 3 months, 6 months, 9 months, and 12 months after starting biological DMARD therapy. Laboratory assessments included a complete blood count (including MPV), ESR, and CRP levels at each visit.

Results: We have observed a significant reduction in DAS-28 within the 12 month assessment period (from 5.33±1.24 to 2.25±1.23). MPV varied between 8.5±0.6 at baseline and 9.0±0.8 at the 12 month time point, with its peak being at the 9 month time point (9.3±0.8). Mean MPV had an inverse correlation with mean DAS-28 ($r=-0.94$, $p=0.02$), as well as mean ESR ($r=-0.91$, $p=0.03$). A weaker correlation was observed with mean CRP ($r=-0.56$, $p=0.3$).

When assessing whether MPV could be used as a therapy response predictor, patients were divided into two groups: those in remission at the 12 month time point ($n=10$) and those with significant disease activity ($n=5$), with remission being defined as a DAS-28 value of 2.8 or less. There was no significant difference in MPV values between those groups (8.5±0.56 for those in remission and 8.52±0.545 for those with active disease).

Abstract AB0272 – Figure 1

Conclusions: The results of this study provide additional evidence supporting the previously reported correlation between MPV and other disease activity markers (DAS-28, ESR) to treatment response in RA patients. It seems MPV isn't a viable therapy outcome predictor given that there is no significant difference in MPV value in patients in remission and those not in remission.

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AB0273

ASSESSMENT OF SERUM LEVELS OF 14-3-3H PROTEIN IN RHEUMATOID ARTHRITIS: IS IT A SPECIFIC MARKER FOR THE DISEASE?

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Background: 14-3-3η protein was suggested to be significantly higher in serum and synovial fluid of rheumatoid arthritis (RA) patients compared to healthy individuals and other diseases such as osteoarthritis (OA) and ankylosing spondylitis (AS).¹ Accordingly, 14-3-3η is now thought to be a diagnostic marker for early RA. Furthermore, some reports suggest that it correlates well with disease activity.²

Objectives: To assess the usefulness of serum levels of 14-3-3η protein in the diagnosis of RA in comparison with hands OA patients and healthy controls; furthermore, to correlate its levels with markers of inflammation in RA patients.

Methods: This study was carried out as a case control comparative study. Our sample consisted of three groups. Group 1 was made up of 30 RA patients fulfilling 2010 ACR-EULAR classification criteria for RA;³ Group 2 made up of 30 hands OA patients according to OA ACR criteria⁴ and group 3 of 30 healthy volunteers. Patients with other rheumatic and/or systemic diseases or infections were excluded.

Patients were assessed using detailed clinical history and examination. Laboratory investigations included complete blood picture, ESR, CRP, RF, ACPA and serum levels of 14-3-3η protein using manual enzyme-linked immunosorbent assay (ELISA).

Results: Mean (SD) age of RA group was 45.5 (9.5) years old; for OA group was 50.3 (8.8) years old, and the control group was 46.2 (6.9) years old. Females represented 96.7% of group 1; 83.3% of group 2, and 86.7% of group 3. RF was positive in 78% of RA group, 6.7% in OA group and 6.3% of control group. Mean (SD) of RF titer was 123 (10.3), 15.3 (5.4) and 14.4 (5.2) IU/ml respectively. ACPA was positive in 96.7% of group 1 and was negative in groups 2 and 3. Mean (SD) ACPA was 64.4 (6.6) U/ml in RA group.

Mean (SD) ESR was 32.5±8.2 in group 1, 22.0 (6.6) in group 2 and 16.1 (7.3) mm/hour in group 3. Mean (SD) CRP was 17.9 (5.04), 5.7 (2.8) in group 2 and 4.9 (2.4) mg/L in group 3.

Mean (SD) levels of 14-3-3η protein were significantly higher among RA compared to OA and control groups (3.63 (1.35), 0.23 (0.14) and 0.28 (0.08) ng/ml, respectively) ($p<0.0001$).

The optimal cutoff point of 14-3-3η protein to diagnose RA was >0.2 with a sensitivity of 80%, specificity of 87%, positive predicted value of 86% and negative predicted value of 81%. The eta protein also had high diagnostic odds ratio (26.1). No correlation was found between serum levels of 14-3-3 eta and CRP nor ESR ($p>0.05$).

Conclusions: 14-3-3η is a specific marker for RA that should be used in conjunction with RF and ACPA for diagnosis of the disease. However, no correlation was found between 14-3-3η and markers of inflammation.

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