In those patients who progressed to RA, we only found a statistical association with the presence of high RF +and with the presence of doppler at the carpal level ($p=0.048$).

Conclusions: The results of our study suggest that the EULAR definition of CSA, although more useful when used by rheumatologists, does not reach sufficient accuracy for the diagnosis of RA, while the presence of subclinical synovitis detected by UsMD could be useful. The highest levels of RF were related to the presence of synovitis in our cohort, unlike ACPA. Further studies would be needed to recommend its introduction into clinical practice and, in our opinion should be considered in future sets of classification criteria.

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AB0246

GENETIC VARIABILITY WITH TOLL-LIKE RECEPTOR 10 AFFECTS SUSCEPTIBILITY TO RHEUMATOID ARTHRITIS AND MODULATES RESPONSE TO BIOLOGICAL TREATMENT

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Background: Genetic variability in Toll-like receptor 10 (TLR10) may change the balance between pro- and anti-inflammatory responses, and hence modulate the susceptibility to infection and to autoimmune disease including rheumatoid arthritis (RA).

Objectives: Therefore we aimed to assess the possible associations of the TLR10 genetic variants with RA susceptibility and/or response to treatment

Methods : TLR10 gene (rs 11096957, N241H, A>C) polymorphism was genotyped by LightSNIP assay in 303 RA patients (237F/66M) and in 140 healthy individuals from Polish population.

Results: RA patients with the AC genotype showed predisposition to disease development [OR 1.99 (1.32–3.01); $p=0.001$], while the AA homozygosity seemed to play a protective role [OR 0.63 (0.42–0.95); $p=0.034$]. Response to treatment with TNF-alpha inhibitors was more effective after 6 months as compared to 3 months ($p=0.001$), especially in female patients ($p=0.05$). Women carrying the A allele responded better to treatment after 6 months of anti-TNF treatment as compared to those with the CC genotype ($p=0.053$). Response to biological treatment was more effective in patients with low stage of disease ($p=0.01$), with rheumatoid factor (RF) positivity ($p=0.01$) and with double positivity against cytrulinated (CCP) protein and RF ($p=0.003$). RF-positive patients (especially women, $p=0.001$) characterised with a higher degree of the disease as compared to RF-negative cases ($p=0.01$). Men had a higher activity of the disease before anti-TNF treatment ($p=0.05$), therefore the remission of the disease was more common in women ($p=0.04$).

Conclusions: These results imply that the TLR10 polymorphism has an important role in RA and may potentially influence risk of the disease and effectiveness of biological treatment.

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AB0247

LACK OF AGEING WITH LONG TERM METHOTREXATE: OBJECTIVE MEASUREMENTS OF COGNITION, AUDIOMETRY, AND SLEEP

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Background: Methotrexate (MTX) has long been known to improve the cardiovascular system. Myocardial infarction, strokes, and mortality are significantly reduced in patients compliant with long term MTX.¹ Hearing loss at middle age is an independent major risk factor for dementia,² and sleep over 8 hours is associated with better health. MTX use may affect all of these risk factors.

Objectives: Our hypothesis is that the cardiovascular benefits of long term MTX treatment would translate into improved cognition, improved hearing, and better sleep patterns.

Methods: Cambridge Cognition (CamCog based in Cambridge) developed cognitive objective testing to study brain function. Camcog is widely used to assess cognitive function in atherosclerotic disease, dementia and ageing. The CamCog tests are computer based. Programs used in this trial included "PAL", paired associates learning for new learning memory and "SWM", spatial working memory along with new strategic thinking during the test. These tests provide 22 assessments per patient. In separate testing, each patient was scored on the mini-mental state examination, including serial 7's, WORLD spelled backward, memory retention of 3 items, and drawn forms such as clock faces.² Sleep patterns were assessed by questionnaire.

Results: There were 88 patients with RA between the ages of 80–101 years who had been treated with MTX a minimum of 20 years. The average PALFAM score for the group was 16.3 (sd 2.7) with a maximum score of 20. The SWMBE score for errors for the group was 2.2 (sd 4.4) with the best score 0 errors. In all 22 scoring categories of the CamCog tests, the 88 long term MTX users scored in the top quintile, and better than average for published results for healthy people at age 65. All scores were statistically significant ($p<0.01$) compared to healthy 65 year olds. It was not possible to compare age, sex matched normal individuals because the normative CamCog database only extends to age 90. All 88 subjects scored above 24 on the mini-mental testing (reflecting no cognitive impairment on that test). The audiometry testing was much better than expected for age, in the top tertile. Of the 88 patients on long term MTX, 3 had hearing aides. Sleep duration averaged 8.5 hours/pm which is considered excellent for maintaining cognition.³

Conclusions: This is a subset of people with cardiovascular risk due to age and RA. The CV risk assessment tool* for our subgroup predicted 10 year risk for MI or CVA at 54%. We did not see MI or CVA over 20 years, despite RA. Expanding on that physiology, we found 88 RA patients on long term MTX had above average cognitive testing, completed mini-mental test, drawings, audiometry close to the scores expected for people 3 decades younger. One reason these preliminary results cannot be generalised to other populations is that only RA patients were studied with long term MTX. Also our group were 80–101 years old and there may be a survival advantage in this subgroup since all were healthy at age 65. A study in a larger general population given MTX for several years would be needed to evaluate the benefit in cognition, hearing, and sleep.

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* ASCVD algorithm in the ACC/AHA Guidelines on the Cardiovascular Risk

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AB0248

EVALUATION OF SUBCUTANEOUSLY (SC) INJECTED TC 99M TILMANOCEPT LOCALIZATION IN ACTIVE RHEUMATOID ARTHRITIS (RA) SUBJECTS BY PLANAR AND SPECT/CT

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Background: In rheumatoid arthritis (RA), infiltrating macrophages play a critical role in the immunopathogenesis of the disease by generating pro-inflammatory cytokines and chemokines and by contributing directly to joint damage. Current imaging modalities do not directly assess activated macrophage-mediated disease processes in RA. Use of non-invasive imaging to detect macrophage infiltration of synovial joints may allow for more sensitive identification of synovitis and earlier recognition of RA, identify joints at risk for progressive inflammation and destruction, provide a better means of quantifying joint inflammation and disease activity, and measure or even predict response to macrophage-directed therapy. Tc 99 m tilmanocept is a synthetic radiopharmaceutical imaging agent that binds with high affinity to the mannose receptor (CD206) located on the cell surface of synovial macrophages. We investigated whether subcutaneous (SC) administration of tilmanocept labelled with Tc 99 m could specially image macrophage mediated inflammation in RA but not in healthy control (HC) subjects.

Objectives: To investigate whether subcutaneous (SC) administration of tilmanocept labelled with Tc 99 m could specially image macrophage mediated inflammation in RA but not in healthy control (HC) subjects.

Methods: Subjects received a SC injection of either 50 µg or 200 µg tilmanocept radiolabeled with 2mCi Tc99m in 0.4 mL. 18 subjects were enrolled as follows – Cohort 1: HC: 50 µg/2mCi; n=5; Cohort 2: HC: 200 µg/2mCi; n=4; Cohort 3: RA 50 µg/2mCi; n=4; Cohort 4: RA 200 µg/2mCi; n=5. Subjects were imaged with whole body planar scans at 2–3 hours and 4–6 hours post injection as well as separate 5 min planar images of both hands. If there were areas of increased localization, SPECT images were obtained.

Results: Tc 99 m tilmanocept localised most effectively at the 200 µg mass dose 2–3 hours post- administration in RA subjects (cohort 4). Localization was observed in 60% of the subjects in joints of the bilateral wrists, hands, and knees. No localization was observed in HCs receiving the same mass dose (cohort 2).

Abstract AB0248 – Figure 1. Contrast of wrist and elbow of SC RA subject

Conclusions: Our findings represent a potential advance in the imaging of RA using a novel immunodiagnostic imaging strategy to specifically visualise macrophage-mediated elements of the RA disease process. This study demonstrates the potential for Tc 99 m tilmanocept to be used as an imaging tool for macrophage-mediated synovial inflammation in RA patients. This strategy can be used to identify patients at risk for activated macrophage-mediated joint damage, to quantify synovitis and disease activity, to provide further insight into immune-mediated mechanisms of RA, and to enable future targeted delivery of immunomodulatory therapeutics.

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AB0249 INFLUENCE OF AUTOANTIBODIES PROFILE ON DISEASE ACTIVITY MEASUREMENT IN A COLOMBIAN COHORT OF RHEUMATOID ARTHRITIS PATIENTS

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Background: Traditionally, the role of Rheumatoid Factor (RF) and/or Anti-citrullinated antibodies (ACCP) presence have characterised for diagnosis and prognosis of Rheumatoid Arthritis (RA). However, Anti-nuclear antibodies (ANA) are not routinely measured for the diagnosis of the disease or RA prognosis establishment during first appointment. Recently, evidence showed that positive ANA titles could be considered as poor prognosis factor for RA, and also a higher probability of developing immunogenicity against biologic therapies.

Abstract AB0249 – Table 1. Auto-antibodies profile, disease activity by DAS-28 ESR (initial and follow-up to 3, 12, 24 and 36 months) and mean weekly MTX dose in a Colombian cohort of RA patients

PROFILE (RF/ACCP/ANA)	DAS-28 (INITIAL)	DAS-28 (3 MONTHS)	N	DAS-28 (12 MONTHS)	N	DAS-28 (24 MONTHS)	N	DAS-28 (36 MONTHS)	N	MEAN WEEKLY MTX DOSE (mg)
—	3.317	.3072603	73	0.1267188	64	0.9367073*	41	0.8593334*	30	9.26
+-	3.375	-.2905715	7	-.5806667	6	-.2648572	7	0.17	4	10.82
++	3.434	.263663	92	0.6267033*	91	0.7705405*	74	0.6138596*	57	14.01
→	3.201	.0314815	27	-.2926087	23	0.1705263	19	0.8038461	13	10.2
++-	4.123	.8346712**	73	1.048**	66	1.23**	51	0.53	38	16.19
++	3.542	.3822857	56	0.5656604*	53	0.71325*	40	0.8733333*	33	14.91
+++	4.695	1.57*	12	1.77*	14	3.359	6	2.03	2	15.69
+++	4.118	.6474576*	118	0.9343478**	115	1.196**	86	1.25**	66	15.83

*p<-0.05 **p<0.001

Objectives: To compare the disease activity measurement from a Colombian cohort of patients with RA, based on their auto-antibodies profile.

Methods: The study used a cohort of Colombian patients with RA. A database was developed using the information from the clinical records. The data included were: RF, ACCP, ANA, and the disease activity measured using DAS-28 ESR. Disease activity results were obtained in the following periods of time: 0, 3, 12, 24 and 36 months. Patients were classified based on the different autoantibody profiles (RF/ACCP/ANA:—, +-, ++, →, +++, ++, ++, +++). Mean DAS-28 ESR results from each period of time were calculated. Also mean weekly Methotrexate (MTX) dose was calculated for each profile. Mean differences between initial, and the follow-up period were calculated using Kruskal-Wallis test. Statistical analysis was made using STATA 12.0 software.

Results: 635 patients with RA were included. 32% of them were men, and 68% were women. Mean age was 54.3 years. The most prevalent profile was +++with 118 patients, and the less frequent was +-. Patients with +++profile had the best response to treatment over time, but also they required more MTX dose. Less response during time was observed with +- profile, however the amount of patients from these group was relatively low. As it was expected, —profile patients required less weekly MTX dose (9.26 mg). It was interesting that patients with —+profile present a worst outcome based on DAS-28 activity, and less response to the treatment.

Conclusions: Results from the study suggest the importance of including the measurement of ANA titles in the initial categorization and follow-up of patients with RA. The presence of ANA seems to have a worst prognosis. ANA co-existence with ACCP appear to have a worst outcome, compared to +- or ++-profile. Auto-antibody profile in RA could direct the best therapeutic strategy for each patient. Validation of these results are required based on other cohorts.

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AB0250 ENDOTYPING OF ARTHRITIC PATIENTS USING NOVEL SEROLOGICAL BIOMARKERS

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Background: Accurate patient stratification is critical if medical professionals are to adopt a precision medicine approach when planning clinical trials or prescribing medication. This approach results in a superior level of drug response in the target group, a reduction in adverse effects and reduced costs for payers. Best practice treatment recommendations and disease activity markers such as DAS28, as opposed to a treat to target approach, guide current treatment of arthritic disease. There is currently a lack of tools to enable patient stratification, in part due to traditional biomarkers reflecting systemic inflammation rather than the target tissue.

Objectives: In this paper, we explore the use of a combination of novel tissue specific biomarkers for patient clustering with the objective of identifying different disease profiles.

Methods: Four biomarker substudy cohorts were pooled for this study, including two RA studies; LITHE (n=574) and OSKIRA-1 (n=131) and two OA studies; SMC1 (n=447) and SMC2 (n=81) all of which have been described in detail before. Whilst the principle focus was to examine RA patient profiles, OA studies were included to enrich the cohort with a non-RA population. OSKIRA and LITHE both had measurements at 24 weeks with additional measurements at 52 week s in LITHE.