Methods: Serum samples from patients enrolled in the Pathobiology of Early Arthritis Cohort (PEAC) were collected before treatment with MTX. Response to therapy was determined after 6 months by calculating the initial and final DAS28 of the patients. Their classification was performed following the EULAR response criteria. Sixty samples at baseline from this cohort (30 good responders and 30 non-responders) were depleted from the 14 most abundant proteins by affinity chromatography to remove background. Then, they were analysed by reversed-phase nanoliquid chromatography coupled to mass spectrometry using a SWATH strategy in a tripleTOF MS (Sciex). The quantitative data obtained in this proteomic analysis were processed using the ProteinPilot 5.0.1 and PeakView 2.1 software (Sciex). Machine learning analyses were performed on a train set of 30 samples (15 responders and 15 non-responders) via support vector machine (SVM) using the Classyfire, e1071 and caret R packages. Results were verified in an independent set of 24 samples by a two-stage support vector machine (TSSVM) with RBF kernel and 10 cross-fold validation for each meta-model.

Results: The proteomic analysis led to the identification and quantification of 229 proteins that were common between the screening and validation sets. Independent screening and validation data sets were preprocessed by PCA for dimension reduction and analysed by machine learning tools, leading to the definition of a panel of 8 proteins (one of them involved in MTX metabolism) differentiating the groups of responders and non-responders to MTX with strong agreement (Kappa >0.80), very high accuracy and good relevant metrics (table 1).

Abstract SAT0074 – Table 1. Metrics of the classification performance of the 8-protein panel identified in this work to predict response of the patient to MTX. Cut-off for significance was p-value <0.05.

Train set							
Accuracy	95% CI	p-value	Kappa	Sensitivity	Specificity	Pos pred value	Neg pred value
0.9333	(0.7793	1.108e-05	0.8667	0.8824	1.0000	1.0000	0.8667
	0.9918)						
Validation set							
Accuracy	95% CI	p-value	Kappa	Sensitivity	Specificity	Pos pred value	Neg pred value
0.9583	(0.7888	0.0007722	0.9091	1.0000	0.9375	0.8889	1.0000
	0.9989)						

Conclusions: We have defined a panel of circulating proteins useful to predict the response to MTX therapy in rheumatoid arthritis patients.

Disclosure of Interest: None declared

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SAT0075

ADDITIONAL TARGET OF NORMAL SERUM MATRIX METALLOPROTEINASE-3 IS A POTENTIAL BIOMARKER FOR LESS ONE-YEAR RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: Matrix metalloproteinase (MMP)-3 plays important roles in bone and cartilage destruction in rheumatoid arthritis (RA). Our previous study showed continuously elevated serum MMP-3 for 3–6 months predict one-year radiographic progression in RA (Arthritis Res Ther. 2015 17:289). However, whether serum MMP-3 normalisation is a biomarker for better outcome remains elusive.

Objectives: To explore the association of serum MMP-3 normalisation with clinical and radiographic outcome in RA.

Methods: RA patients with moderate to high disease activity (DAS28-CRP>3.2) were treated according to treat to target (T2T) strategy and followed up at regular intervals (0, 1 st, 3rd, 6th and 12th months). Demographic and clinical data were collected according to the 2017 EULAR recommendation and serum MMP-3 was detected by ELISA at each visit. X-ray assessment of hand/wrist was repeated at baseline and month 12 and radiographic progression was defined as a change of the Sharp/van der Heijde modified sharp score ≥ 0.5 units.

Results: (1) Among 200 RA patients recruited, there were 163 (81.5%) female, with median disease duration 24^(11–84) months, median DAS28-CRP 4.9 (4.2–5.7). There were 29% patients showed one-year radiographic progression.² The median MMP-3 was 209.7 (108.6–430.0) ng/ml. RA patients without radiographic progression had significant lower level of serum MMP-3 than those with radiographic progression at baseline and each visit (figure 1A, all p<0.001).³ There were 13.0%, 14.5%, 17.0%, 25.5% and 31.0% patients having normal MMP-3 at baseline and 1 st, 3rd, 6th and 12th months, respectively. There were significantly

lower percentage of RA patients with normal MMP-3 at baseline and each visit showed radiographic progression than those with elevated MMP-3 (figure 1B, all p<0.05).⁴ There were 8.5%, 13.0%, 20.0% and 25.5% patients who achieved therapeutic target and showed normal MMP-3 at 1 st, 3rd, 6th and 12th months, respectively. Among patients achieved therapeutic target, there were significantly lower percentage of normal MMP-3 patients showed radiographic progression than those with elevated MMP-3 (figure 1C, all p<0.05).⁵ There were 6.5%, 11.0%, 14.5%, 20.5% and 25.5% patients who had normal CRP and normal MMP-3 at baseline and 1 st, 3rd, 6th and 12th months, respectively. Among patients with normal CRP, there were significantly lower percentage of normal MMP-3 patients at 1 st, 3rd, 6th and 12th months showed radiographic progression than those with elevated MMP-3 (figure 1D, all p<0.05).

Abstract SAT0075 – Figure 1. Dynamic change of serum MMP-3 and indicators of disease activity and radiographic progression in RA. **A** Comparison of disease activity and radiographic progression indicators between RA patients with and without radiographic progression. **B** Comparison of T2T achieving and the percentage of RA patients showing radiographic progression between normal and elevated serum MMP-3 groups at each visit. **C** Comparison of the percentage of RA patients showing radiographic progression among groups with or without T2T achieving and normal serum MMP-3. **D** Comparison of the percentage of RA patients showing radiographic progression among groups with or without normal CRP and normal serum MMP-3.

Conclusions: Additional target of normal serum MMP-3 may be a potential biomarker for less one-year radiographic progression.

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SAT0076

SYNOVIAL MAST CELLS AND RESPONSES TO SYNTHETIC AND BIOLOGIC DMARDS IN EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS

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Background: Mast cells (MCs) are immune cells implicated in the pathogenesis of Rheumatoid Arthritis (RA), but their presence in synovia has not been assessed systematically and their association with disease progression and treatment response is unknown.

Objectives: To analyse MCs in the synovia of patients with early vs established RA in correlation with histological and clinical phenotype.

Methods: DMARDs-naïve patients with early (<12 months) RA (n=97) and patients with established RA failing synthetic DMARDs and candidate to biologic treatment (n=27) underwent ultrasound-guided synovial biopsy. Sections of paraffin embedded synovial tissue were stained with H and E to measure the degree of synovitis (Krenn Score). Sequentially cut sections were stained by immunohistochemistry to evaluate the presence of immune cells, including CD117 (c-kit) positive mast cells. Upon SQ scoring (0–4), patients were stratified into synovial pathotypes (Lymphoid, Fibroid, and Myeloid), as previously described

Results: In the cohort of DMARDs-naïve early RA (mean disease duration 6 months), MC+ve patients (67.7%) had significantly higher synovial inflammation (Krenn score), higher prevalence of the lymphoid pathotype, higher inflammatory markers and disease activity; however, they did not differ in terms of response to sDMARDs at 6 months (table 1, left). In established RA (mean disease duration 5 years), MC+ve patients (48.1%) had significantly higher synovial inflammatory scores and higher prevalence of the lymphoid pathotype, while systemic inflammatory markers or disease activity scores were not different. At 6 months follow-up, MC+ve patients had significantly higher rates of response to anti-TNF α (table 2, right).

Abstract SAT0076 – Table 1

	Early RA				Established RA			
	All (n=99)	MC- (n=32)	MC+ (n=67)	P value*	All (n=27)	MC- (n=14)	MC+ (n=13)	P value*
Disease duration, months (SD)	6 (3)	5 (3)	6 (3)	0.664	62.6 (56.2)	68.5 (62.1)	56.3 (50.77)	0.616
ESR, mean (SD)	38 (30)	28 (24)	44 (31)	0.008	33 (26)	31 (31)	36 (22)	0.231
CRP, mean (SD)	17 (25)	8 (14)	21 (29)	0.007	11 (23)	13 (32)	10 (5)	0.025
ACPA+, %	75.8%	75%	76.1%	0.839	63%	64.3%	61.5%	0.883
DAS28, mean (SD)	5.65 (1.41)	5.55 (1.41)	5.95 (1.00)	0.405	6.53 (0.88)	6.54 (0.94)	6.52 (0.86)	0.905
Lymphoid pathotype, %	45.9%	9.4%	63.6%	<0.001	53.8%	30.8%	76.9%	0.018
High synovitis, %	48.4%	12%	62.1%	<0.001	46.2%	23.1%	69.2%	0.018
6 months DAS28, mean (SD)	3.48 (1.95)	3.13 (1.79)	3.67 (2.02)	0.248	3.87 (1.3)	4.44 (1.23)	2.89 (0.71)	0.004
6 months DAS28<3.2, %	52.4%	62.1%	47.2%	0.196	36.8%	8.3%	85.7%	0.001

*Mann-Whitney or Chi square as appropriate

Conclusions: We here show that early RA patients with MC+ve synovitis and high levels of local and systemic inflammation do not respond differently to synthetic DMARDs. In the context of established RA after sDMARDs failure, patients with MC+ve synovitis, despite having similar levels of systemic inflammatory markers and disease activity, had higher chances of responding to anti-TNF- α . Although the latter observation will need validation on larger cohorts, our data suggests that the analysis of synovial MCs might help defining synovial histopathology and possibly contribute to the prediction of treatment response.

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SAT0077 CHANGE IN FREQUENCY OF ARTHROPLASTY SURGERY IN RHEUMATOID ARTHRITIS: A 13 YEAR POPULATION HEALTH STUDY

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Background: Improvement in the medical management of rheumatoid arthritis (RA) over the past two decades may have reduced the need for arthroplasty surgery but the literature to date has reported inconsistent findings.

Objectives: To compare the annual frequency of hip, knee and other arthroplasty surgery in a prevalent cohort of RA cases and matched controls over 13 years.

Methods: A retrospective cohort study was performed utilising administrative healthcare data from approximately 1 million people with access to universal

healthcare between 1997 and 2010. RA cases were identified using a previously validated RA case definition in the same dataset.¹ Each case was matched by age and sex to 4 randomly selected controls. The annual frequency of arthroplasties in cases and controls was compared. In addition the frequency of coronary artery interventions (bypass grafting, angioplasty and stenting) was compared. Data included physician billings, hospital discharges and patient registry information using ICD-9 and ICD-10. Statistical analysis used least squares regression t-tests and 2-proportion z-tests.

Results: The number (prevalence) of RA cases increased from 3913 (0.42%) to 4911 (0.52%) over the study. The mean (SD) age changed from 56.7 (15.9) to 60.1 (14.9) years and the proportion of females from 70.8% to 73.9%. In both the first and last years of the study the frequency of all arthroplasty procedures was higher in cases than controls (p<0.001) (Table). Over time there was a gradual and significant reduction in arthroplasty surgery in RA cases by 51.9% (p<0.001). This was in contrast to controls in whom the frequency of procedures increased by 31.9% (p=0.002) with the exception of hip arthroplasty. For the latter procedure, the frequency decreased by 63% in RA cases (p<0.001) and 35% in controls (p=0.617). In contrast to arthroplasty procedures the frequency of cardiac procedures, which were higher in RA cases in both the first (p=0.013) and final (p=0.003) years of observation, increased in both cases and controls over time although did not reach statistical significance in either.

Abstract SAT0077 – Table 1. Demographics and surgical procedures in RA patients and controls

Demographics	1997		2010	
	RA cases	Controls	RA cases	Controls
Age (SD) in years	56.7 (15.9)	56.7 (15.9)	60.1 (14.9)	60.1 (14.9)
Female (%)	70.8	70.8	73.9	73.9
% population undergoing procedure in 1997		% population undergoing procedure in 2010		
Surgical procedures		RA cases		Controls
Total arthroplasties	4.78	0.47	2.30	0.62
Hip arthroplasty	1.43	0.20	0.53	0.13
Knee arthroplasty	1.74	0.13	0.81	0.27
Other arthroplasty	1.76	0.13	0.98	0.22
Cardiac procedures	0.36	0.16	0.57	0.29

Conclusions: There was a striking reduction in arthroplasty surgery in RA cases over 13 years of observation. Lack of similar changes in controls and sustained rates of cardiac procedures over the same time suggests that this was not due to limited surgical access for RA patients. Improvement in medical treatment of RA is likely responsible.

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SAT0078 WHICH CDMAID STRATEGY IS MOST EFFECTIVE IN NEWLY DIAGNOSED SERONEGATIVE RHEUMATOID ARTHRITIS PATIENTS; POST-HOC ANALYSIS OF THE TREACH STUDY

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Background: The disease spectrum of rheumatoid arthritis (RA) is heterogeneous. Literature suggests that these different disease subsets could be treated differently, with less aggressive treatment for rheumatoid factor and anti-citrullinated protein antibody negative RA patients ("seronegative RA"). Current treatment guidelines, however, do not take this into account since evidence is lacking. Especially, data about standardised treatment strategies in seronegative patients are needed.

Objectives: To compare 1 year clinical efficacy of 4 different initial treatment strategies in newly diagnosed, seronegative RA patients, according to the 2010 criteria.

Methods: For this post-hoc analysis data of the tREACH trial (stratified, single-blinded, randomised clinical trial) were used. Eligible patients, for the tREACH, were stratified into 3 probability tertiles (low, intermediate and high) according to their likelihood of progressing to persistent arthritis based upon the prediction model of Visser. For this analysis we selected all seronegative RA patients, of whom respectively 81% and 19% were in the intermediate and high stratum. Patients received 1 of the following 4 initial treatment strategies, which were