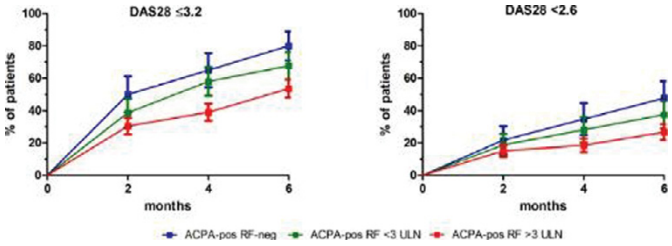
selected for outcome analyses. Among seropositive patients, both LDA and remission were less frequently achieved in case of RF-positivity. Relevantly, in ACPA-positive patients (n=273), the co-occurrence of RF dose-dependently influenced clinical outcomes. After 6 months of treatment, LDA and disease remission were achieved respectively by 69.6% and 47.8% of single ACPA-positive, 68.8% and 37.5% of ACPA-positive RF-low, and 57% and 27.6% of ACPA-positive RF-high patients (chi-square for trend p=0.18 for LDA, p=0.05 for remission). After adjusting for confounders (age, gender, symptoms' duration, baseline disease activity, use of prednisone, recruitment period), high levels of RF independently predicted failure to achieve LDA with an HR (95% CI) of 0.61 (0.39 to 0.95) and failure to achieve remission with an HR (95% CI) of 0.63 (0.35 to 0.99) (Figure 1). In contrast, ACPA levels did not show any significant predictive value, neither for thresholds of >3 ULN nor of >100 U.



Conclusions: Among ACPA-positive RA patients, disease characteristics may vary in association with the extent of overall humoral autoimmunity. In particular, the concomitant presence of high levels of IgM RF seems associated with lower response rates to csDMARDs. Collectively, these findings highlight the importance of further subclassifying patients with autoantibody-positive RA in order get deeper insights into disease mechanisms and clinical outcomes.

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SAT0061 HAQ SCORE IS AN INDEPENDENT PREDICTOR OF SUSTAINED REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objectives: We compared remission rates, according to different definitions of remission in rheumatoid arthritis (RA) and investigated the potential predictors of sustained remission at the 2-year follow-up.

Methods: We obtained data on 291 RA outpatients, seen from July 2009 to September 2012. Sociodemographic data and answers to questionnaires were collected in face-to-face interviews. Remission was defined according to the Disease Activity Score in 28 joints (DAS28)-ESR, DAS28-CRP, Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), and ACR/EULAR Boolean definition. Sustained remission was defined as when the patient continued in remission at two consecutive annual assessments. Predictors of sustained remission according to the DAS28-CRP were assessed by univariate and multivariate analyses.

Results: For the 291 RA patients, the remission rates of RA were 17.9% (DAS28-ESR), 54.3% (DAS28-CRP), 10.3% (SDAI), 10.0% (CDAI), and 5.8% (Boolean). On follow-up for 2 years, the sustained remission rates of RA were 46.5% (DAS28), 55.0% (DAS28-CRP), 37.5% (SDAI), 32.0% (CDAI), and 30.8% (Boolean). RA patients who achieve sustained remission according to the DAS28-CRP were younger, and had more education, higher monthly income, lower Health Assessment Questionnaire (HAQ) score, lower physician global assessment, lower patient global assessment, lower patient pain assessment, and higher EQ-5D. In multivariate analysis, only the HAQ score predicted sustained remission according to DAS28-CRP (OR=0.257, 95% CI 0.067–0.980, p =0.047).

Conclusions: The remission rates of RA patients differed according to the definition of remission, and the highest sustained remission rate was classified by the DAS28-CRP. A lower HAQ score was an independent predictor of sustained remission over 2 years, according to the DAS28-CRP.

Disclosure of Interest: None declared

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SAT0062 14-3-3ETA PREDICTS JOINT DAMAGE PROGRESSION AND FLARING AFTER ADALIMUMAB DISCONTINUATION

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Background: The HONOR (humira discontinuation without functional and radiographic damage following sustained remission) study was designed to investigate the possibility of patients discontinuing adalimumab (ADA) therapy for 1 year without flaring (DAS28-ESR ≥3.2). 14–3-3η is a mechanistic serum marker that is modifiable over the disease course, does not correlate with CRP and is a predictor of radiographic progression even in patients who achieve clinical remission. The uncoupling of inflammation and joint damage processes in RA underscores a risk of premature discontinuation of biologic treatment when aiming to achieve sustained remission. Serum markers that could indicate which patients are at risk of flare and continued joint damage despite clinical remission are highly desirable.

Objectives: In this study, serum 14–3-3η was investigated as a predictor of joint damage and flares in the HONOR cohort.

Methods: Serum 14–3-3η levels were measured in 62 Japanese patients, 51 of which were from the HONOR study at baseline, 1-year after treatment initiation, at discontinuation and at the time of flare. Of the 62 patients, 46 (74%) patients achieved sustained drug-free remission up to 1 year following ADA discontinuation. Sharp van der Heidje (SHS) scores were available at therapy initiation, discontinuation, and at 52 weeks following. Relationships between continuous variables were assessed using uni- and multi-variable Gaussian linear regression models and logistic regression.

Results: At baseline and discontinuation, median (QR) 14–3-3η levels were 0.28 ng/ml (0.07–2.11) and 0.22 ng/ml (0.04–1.28) respectively, with 26 (59%) of 44 and 29 (54%) of 54 patients being positive (≥0.19 ng/ml) at the corresponding time-points. Paired t-test revealed that levels of 14–3-3η were significantly different between baseline and discontinuation, p=0.030. Level of 14–3-3η at baseline was positively associated with SHS at 12 months and at the time of flare, p=0.038. Bivariable modeling revealed that baseline 14–3-3η together with the change in 14–3-3η had a significant interacting effect on SHS at 12 months and the time of flare, p=0.02. Higher baseline 14–3-3η levels together with an increase in levels at the time of discontinuation was strongly associated with an increased SHS. Adding CRP, flare, sustained remission through 12 months, MTX dose at initiation and at ADA discontinuation did not improve predictive effects of 14–3-3η with SHS. Baseline 14–3-3η levels alone was not associated with flares at 12 months (p=0.15) however when combined with CRP, a significant interaction was present (p=0.03). Specifically, patients with a low CRP, and a high 14–3-3η level had a higher likelihood of flaring versus those with a low 14–3-3η, 22% versus 12%.

Conclusions: Baseline 14–3-3η and increases in its levels are associated with worse radiographic outcomes in patients who achieve clinical remission and discontinue ADA. To reduce the risk of flare in patients who are candidates for discontinuation of ADA, CRP and 14–3-3η measurements should be considered in combination as markers of flare prediction.

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SAT0063 A PROSPECTIVE STUDY ON COMPARISON OF COMPOSITE INDICES WITH ULTRASOUND FOR DETECTING REMISSION AND PREDICTION OF FLARE IN 2 YEARS

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Background: Treat-to-target (T2T) approach suggests using a composite index when following patients with rheumatoid arthritis (RA) without identifying which one to use.

Objectives: In this prospective study we aimed to compare the accuracy of different indices for RA patients in remission taking Ultrasound Global Synovitis Score (GLOESS) as a gold standard and their predictive value for flares in 2 years.

Methods: RA patients who were considered to be in clinical remission according to the clinician were recruited. Disease activity was assessed using DAS28-CRP, CDAI, SDAI and RAPID-3 and 38 joints per patient were scanned by US and scored according to GLOESS. The total GLOESS scores were calculated for 38 joints and also for 28 joints by excluding the MTP joints. The number of joints with ≥2 GLOESS was calculated. Flare data was collected in 3 subsequent visits in the following 2 years, whenever available.

Results: Ninety-six consecutive patients (80.2% females) were recruited. Patients were more frequently categorized as being in remission using DAS28 (80%) compared to CDAI (50%), SDAI (45.2%) and RAPID 3 (37.5%). Patients that were in remission according to CDAI had lower GLOESS scores on 28 joints (p=0.05) and had less joints with ≥2 signals (p=0.04) (table). For SDAI patients in remission had significantly less number of joints with grade 3 signals (p=0.03) and tend to have lower GLOESS scores on 28 joints as well as lower number of joints with ≥2 signals (p=0.06). None of the US scores were able to differentiate different disease states according to DAS28-CRP or RAPID. Flare data was available in 76 patients, 22 of whom had flares. Patients that had flare had higher GLOESS scores on 28 joints at baseline (p=0.05) and tend to have higher number of joints with grade 3 signals (p=0.06). Although numerically higher, none of the clinical indices were able to predict flares based on remission status (remission vs non remission: CDAI: 22.5% vs 36.1, p=0.2; SDAI: 22.9 vs 36.8, p=0.2; DAS28: 25.4% vs 50%, p=0.1; RAPID3: 20% vs 34.8%, p=0.2).

Table 1. The distribution of US-GLOESS according to different categories by indices

	GLOESS 38 joints mean±SD	GLOESS 28 joints mean±SD	Joint counts ≥ score 2 mean±SD	Joint counts with score 3 mean±SD
DAS-28				
Remission (n=77)	10.9±7.5	7.8±7.2	3.5±3.1	0.7±1.3
LDA (n=11)	14.5±6.6	10.0±5.4	4.9±3.0	0.9±1.4
VMDA (n=5)	9.6±6.2	5.4±3.5	3.0±2.3	0.80±1.7
CDAI				
Remission (n=48)	10.0±6.9	6.9±6.2	3.02±2.7	0.60±1.0
LDA (n=48)	12.7±7.7	9.1±7.2	4.3±3.3	0.94±1.5
SDAI				
Remission (n=42)	9.9±6.6	6.6±5.9	2.9±2.6	0.5±0.9
LDA (n=50)	12.4±7.8	9.1±7.5	4.2±3.3	0.9±1.5
MDA (n=1)	13.0	4.0	5.0	0
RAPID				
Remission (n=36)	10.3±6.2	6.7±4.6	3.1±2.6	0.5±0.8
Low activity (n=28)	9.6±5.8	6.6±4.6	2.7±2.2	0.3±0.7
MDA (n=30)	14.0±9.4	10.7±9.7	5.1±3.9	1.4±1.9
HDA (n=2)	15±1.4	8.5±2.1	5±1.4	0

LDA: Low disease activity MDA: Moderate disease activity HDA: High Disease activity.

Conclusions: Our results show that CDAI is superior then other clinical indices to assess remission in RA. US has the superiority over clinical indices to predict flares and 28 joint GLOESS is superior to 38 joints.
Disclosure of Interest: None declared
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SAT0064 HIGH MMP3 SERUM LEVELS ARE ASSOCIATED WITH EXTENSIVE STRUCTURAL DAMAGE IN PATIENTS WITH EARLY, TREATMENT NAIVE RHEUMATOID ARTHRITIS (RA): TWO YEARS PROSPECTIVE CLINICAL AND ULTRASONOGRAPHIC STUDY

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Objectives: To investigate the association of high baseline MMP-3 serum levels with hands and feet joints structural damage progression, estimated by ultrasonography (US), in patients with early, treatment "naïve" RA without X-ray visible erosions.
Methods: Sixty-three pts. (9 males and 54 females; mean age 53.4 yrs 21–81±14.1) with early RA (EULAR/ACR 2010 criteria) and symptom duration of ≤12 months (mean duration of 3.8 months) had baseline serum MMP-3 levels tested. Patients had been DMARDs/glucocorticoid naïve, without visible X-ray erosions at the study entry. The subsequent structural joints damages, that were estimated by high frequency linear probe by ESAOTE My Lab 70 machine, as well as clinical markers of disease activity, in the first 2 years were followed. The presence of bone erosion was analyzed at the wrist, MCP2 and MCP5 joints of both hands, as well as at MTP5 joints according to OMERACT US group definition. In order to estimate progression of preexisting erosion the total volume (TV) of bone erosion were calculated by multiplying three diameters (mm): a-the length of erosion; diameter b- the width and diameter c-the depth of erosion. Anova statistical method was performed in data processing.
Results: 46 pts. had basal serum MMP-3 level higher than normal (MMP-3 positive). The 504 joints were assessed summary by US on each visit. The 122 bone erosions in total (1.9 per patient) were depicted at baseline and 213 bone erosions (4.3 per patient) at follow-up visit in whole group. After 24 months MMP3 positive pts. had significantly higher total number of US erosions than MMP-3 negative (3.8 vs. 2.4, p=0.039). The total volume of bone erosion (mm^3) was higher in MMP-3 positive than MMP-3 negative pts. after 24 months of treatment, but without statistical significance (18.6 vs. 8.9, p=0.07). MMP-3 positive pts. had a significantly higher value of ESR, CRP and DAS28 than MMP-3 negative pts. at the baseline visit (53.6 vs.25.9, p=0.002; 36.6 vs. 9.5, p=0.005; 6.0 vs. 4.8, p=0.002, respectively). All of those parameters were significantly decreased after 24 months in a group of MMP-3 positive compared to MMP-3 negative pts. (p=0.009, p=0.021, p=0.028, respectively).
Conclusions: After 2-year of follow-up, US assessment showed a significantly higher number of new bone erosions in patients with early, treatment "naïve" RA and baseline MMP3 levels higher than normal (MMP3 positive) compared to patients with normal baseline levels of MMP3, as well as a biger TV of bone erosions but not statistically significant. The parameters of RA activity (ESR, CRP, DAS28) significantly correlated with baseline MMP-3 levels of higher than normal.
Disclosure of Interest: None declared
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SAT0065 ACPA AGAINST DIFFERENT CITRULLINATED PEPTIDES IDENTIFY SPECIFIC PHENOTYPES OF RHEUMATOID ARTHRITIS

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Background: Anti-citrullinated protein/peptide antibodies (ACPA) have been suggested to identify a more severe phenotype of rheumatoid arthritis (RA).
Objectives: In this study in an inception cohort of early RA we have analysed a number of antibodies against different citrullinated and/or mutated peptides using a multiplex platform in relation to the patients disease inflammation and radiological destruction
Methods: Patients with early RA (≤12 m of symptoms) fulfilling the 1987 ARA criteria (n=1022, 692f/330m, mean age56.7±14.0 years) were sampled at the time of diagnosis and assessed using disease activity score (DAS28) at baseline, 6, 12, 18 and 24 months. Radiographs were graded using Larsen score (baseline and *at* 24 m). Plasma sampled at baseline was analysed for presence of antibody reactivities against 21 different citrullinated peptides/proteins; Fibrinogen (Fib) α36–50, Fibα573, Fibα591, Fibα621–635, Fibβ36–52, Fibβ60–74, Fibβ62–78 (72), Fibβ62–78 (74), Filaggrin (Fil307–324), α-Enolase peptide 5–21 (CEP-1), Vimentin (Vim) 2–17, Vim60–75, F4-R-Cit, F4-Cit-Cit, F4- Cit-R), or mutated proteins (Bla26, Pept1, Pept5, PeptZ1, PeptZ2) and type II Collagen citrullinated or not using a custom-made microarray assay based on the ImmunoCAP ISAC system (Phadia AB, Sweden). Cut-off levels were at the 98th percentile of controls (n=477). Anti-CCP2 was analysed using ELISA (Euro Diagnostica, Sweden).
Results: The most frequent appearing ACPA were; Fibβ60–74 (63%), Vim60–75 (56.6%), Fibβ36–52 (55.1%), Fil307–324 (54.9%), CEP-1 (53.7%) and Pept5 (52.0%) besides CCP2 (67.5%). Adding all ACPAs gave additional 13.1% of positivity in the anti-CCP2 negative group, yielding a positivity of 77.5%. The median (IQR) number of positive ACPA-peptide was 8 (11). There was a high degree of correlation between the antibodies, e.g., anti-Fibβ60–74 vs. -Vim60–75, -Fibβ36–52 or anti-CCP2 antibodies and also anti-Fil307–324 vs. -Fibβ36–52, -F4 R-Cit or anti-CCP2 antibodies (rs 0.692–0.79). Positivity for all antibodies was associated with higher ESR (baseline and AUC_{24}). A number of antibodies were associated with both high DAS28 (baseline and AUC_{24}) and radiological findings/progression (anti-CCP2, - Fil307–324, -Vim60–75 and Vim 2–17, and -CEP1 antibodies), whilst some others were more associated with inflammation (DAS28, baseline and AUC_{24}) (anti-Fibβ60–74, -Pept5 and -F4R-cit antibodies) and others more with radiological destruction/progression (anti-Fibβ36–52, -Fibβ74, -PeptZ1, -F4 Cit-R antibodies). Partial least squares regression analyses confirmed the results with significant correlation between radiological progression and antibodies against Vim2–17, Fibβ36–52, CEP1, Fibα621–635, and CCP2 and between DAS28AUC_{24} and Vim60–75, Vim2–17, Fibα621–635 and F4-R-Cit. Patients treated with biologics during the first 24 months (11.2%) were significantly more frequent positive for anti-CCP2, -Vim60-75, -Fibα36–50, -PeptZ1 and -PeptZ2 antibodies vs. being negative.
Conclusions: Analyses at baseline, of the ACPA specificity profiles allowed different patterns of disease activity and radiological progression during the first 24 months of the disease to be identified.
Disclosure of Interest: None declared
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SAT0066 HISTOLOGICAL AND ULTRASOUND SYNOVIAL PREDICTORS OF CLINICAL DIFFERENTIATION TO DEFINED ARTHRITIS IN PATIENTS WITH SERONEGATIVE UNDIFFERENTIATED PERIPHERAL INFLAMMATORY ARTHRITIS

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Background: Undifferentiated Peripheral Inflammatory Arthritis (UPIA) is a common diagnosis at the first clinical evaluation in rheumatological settings. However, the likelihood of developing a well-defined rheumatic disease in UPIA patients is still matter of debate.
Objectives: To examine the role of ultrasound (US) and histological parameters in the disease outcome of patients with seronegative UPIA.
Methods: Fourty-two patients with IgA/IgM-Rheumatoid Factor and anti-citrullinated peptide antibodies negative UPIA, naïve to any Disease-Modifying Anti-Rheumatic Drugs, underwent Gray Scale (GSUS) and power Doppler (PDUS) evaluation and US guided synovial tissue biopsy. Synovial expression of CD68, CD3, CD21, CD20 and CD31 was evaluated by immunohistochemistry. IL-6, VEGF-A and VEGF-D peripheral blood (PB) and synovial fluid (SF) levels were measured by ELISA. To exclude Reactive Arthritis, each patient underwent genital and throat swabs. Afterwards, each UPIA patient was treated with chloroquine 250 mg/daily and followed every 3 months for 1 year and classified as having