Objectives: To examine the effect of age and education on the components of the 28-joint Disease Activity Score (DAS28-ESR) in patients with rheumatoid arthritis (RA).

Methods: Baseline data of Disease Modifying Anti-Rheumatic Drug (DMARD)-naïve patients with RA from the Norwegian Register of DMARDs (NOR-DMARD) were used. Linear regression models, adjusted for gender and education (low, intermediate and high level), were used to investigate the strength of the association between age (<45, 45–65 and >65 years) and each DAS28-component (Erythrocyte Sedimentation Rate (ESR), 28-tender joint count (28-TJC), 28-swollen joint count (28-SJC), and patient global assessment of disease activity (PGA)). Adjusted scores for components of DAS28 and total DAS28-ESR were computed and relative change across age categories was explored. Interactions between age and gender and age and education were also tested.

Results: Baseline data from 2037 patients (mean (SD) age 55.2 (14.0) years, 68% female) were available. Regression models were stratified for gender (p – interaction <0.05); education was a significant covariate in all regression analyses. Older males (>65 years) with an intermediate level of education would have a 21% higher ESR and 14% higher 28-SJC, as compared to their younger counterparts (<45 years). For females in the intermediate education category, the corresponding differences were 16% and 15%, respectively. Conversely, differences in 28-TJC and the PGA between the highest and lowest age group were negligible in both males and females (table 1). In absolute effects on DAS28, this means that in male patients the adjusted DAS28 for those >65 years was 4.8 compared to 4.3 in patients<45 years (females 5.0 compared to 4.6). For low and high levels of education, the results were comparable in terms of relative contribution to each DAS28-component.

Abstract FRI0024 – Table 1. Effect of age on DAS28 (ESR) for patients with an intermediate educational level.

Component	< 45 years (reference)	45 – 65 years	> 65 years	Difference between
Predicted values	n = 181 (25%)	n = 419 (58%)	n = 123 (17%)	highest and lowest age group (%)
Males				
28-TJC	1.32	1.33	1.34	2%
28-SJC	0.62	0.66	0.71	14%*
PGA	0.57	0.59	0.58	2%
ESR	1.83	2.00	2.22	21%*
DAS28-ESR	4.34	4.58	4.83	11%
Females				
28-TJC	1.32	1.39	1.33	1%
28-SJC	0.59	0.63	0.68	15%*
PGA	0.67	0.68	0.68	1%
ESR	1.99	2.14	2.31	16%*
DAS28-ESR	4.57	4.84	5.00	9%

Abbreviations: TJC, tender joint count; SJC, swollen joint count; PGA, patient global assessment; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; DAS28, 28-joint Disease Activity Score.
 *Difference in scores is significant (p < 0.05).

Conclusions: As expected, DAS28 increases with age. However, the components of DAS28 increase at different rates. The age-related increase in ESR and 28-SJC without a simultaneous increase in 28-TJC and PGA might imply that age-related processes (e.g. osteoarthritis and physiological increase in ESR) drive the DAS28 in older patients. The observed patterns were largely comparable between males and females. The age effect on DAS28 is relevant in a treat-to-target strategy and may be considered when identifying a defined target in individual patients.

Disclosure of Interest: None declared

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FRI0025 SERUM MEDIATED PEPTIDYLARGININE DEIMINASE (PAD) ACTIVATION IN EARLY RHEUMATOID ARTHRITIS

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Background: Peptidylarginine deiminases (PADs) are a family of enzymes catalysing the conversion of arginine residues to citrulline, a post translational modification which has been recognised in the generation of neo-epitopes due to anti-citrullinated protein antibodies (ACPAs) in rheumatoid arthritis (RA). ACPAs are

included in the classification criteria for RA, and may be present before disease onset and predictive of disease progression.

Objectives: To investigate whether serum of patients with early RA have the capacity to significantly increase the citrullination performed by PAD enzymes, and the possible role of increased enzyme activation as a mechanism preceding the production of ACPAs.

Methods: Serum from DMARD-naïve, early RA patients from the ARCTIC trial¹ classified according to the 2010 ACR/EULAR criteria were analysed for PAD4 activating capacities using HPLC fluorometric method. A sample was defined as positive if above mean +2 SD of the healthy controls. Patient characteristics and subgroups with PAD activity were assessed using Mann-Whitney U-test and chi-square test as appropriate.

Results: A total of 225 patients and 63 controls were included in the study. Patient characteristics and measures of disease activity and radiographic damage are presented in the table 1. Median PAD activity levels were higher in patients than in healthy controls (8768 [7491,11393] vs. 7046 [6347,7905], p<0.0001; figure 1). ACPA and rheumatoid factor (RF) positive patients had higher PAD activity than ACPA and RF negative patients (9104 [7739,13213] vs. 7281 [6764,9010], p<0.0001, and 8871 [7715,12259] vs. 8407 [6867,10062], p=0.048, respectively). PAD positivity occurred in 42% (n=95) of the patients and was more prevalent in ACPA positive compared to ACPA negative patients (47 vs. 20%, p=0.002), but not in RF positive vs. RF negative patients (44 vs. 38%, p=0.49). Disease Activity Score was numerically higher in patients positive for PAD than patients who were PAD negative (3.6 (1.1) vs. 3.3 (1.2), p=0.08).

Abstract FRI0025 – Table 1. Baseline characteristics in subgroups of RA patients and healthy controls

	All patients (n=225)	PAD4+ (n=95)	PAD4- (n=130)	Healthy controls (n=63)
Age ¹ , years	51.3 (13.8)	48.7 (13.5)	53.2 (13.7)	53.7 (9.0)
Female ²	137(61)	56(59)	81(62)	30 (48)
ACPA positivity ²	184(82)	87(92)	97(75)	0
RF positivity ²	160(71)	70(74)	90(69)	NA
Disease duration ¹ , months	7.1 (5.4)	8.3 (6.1)	6.2 (4.7)	NA
Ever-smoker ²	149(66)	63(66)	86(66)	NA
ESR ³	19 [11,32]	18 [11,30]	21 [11,32]	NA
SJC4 ³	9 [4,14]	10 [5,15]	8 [4,14]	NA
Ultrasound grey scale	18 [10,28]	20 [11,28]	17 [10,26]	NA
Ultrasound power Doppler ³	7 [3,14]	7 [3,14]	6 [2,13]	NA
Disease Activity Score ¹	3.4 (1.2)	3.6 (1.1)	3.3 (1.2)	NA
vdHS total score ³	4 [1.5,8.5]	4 [1.5,7.5]	4.5 [2,9]	NA
PAD activity level ³	8768 [7491,11393]	13175 [10370,19374]	7659 [6865–8316]	7046 [6347,7906]

¹Mean(SD), ²n(%), ³Median[25,75 percentile] Abbreviations: PAD, peptidylarginine deiminase; ACPA, anti-citrullinated protein antibody; RF, rheumatoid factor; ESR, erythrocyte sedimentation rate; SJC, swollen joint count; vdHS, van der Heijde modified Sharp

Abstract FRI0025 – Figure 1. PAD4 activity in patients and controls. Centre bar indicates median PAD4 activity level and error bars 25 and 75 percentile. The dashed line represents the cut-off value for increased PAD4 activity, defined as the mean plus two times the SD of the healthy controls.

Conclusions: Serum capacity to activate PAD4 was associated with ACPA and RF positivity in patients with early RA, but no distinct relationship was seen for Disease Activity Score.

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FRI0026

U-ACT-EARLY TRIAL 3 YEARS FOLLOW-UP. THE LONGER EFFECTIVENESS OF TREAT-TO-TARGET STRATEGIES IN EARLY RA WITH TOCILIZUMAB, METHOTREXATE, OR THEIR COMBINATION

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Background: The U-Act-Early trial was a 2 year placebo controlled, double-blind randomised controlled trial in early (DMARD-naïve) RA patients treated to the target of sustained remission (SR), starting with tocilizumab (TCZ), methotrexate (MTX) or their combination (TCZ +MTX)¹. When the treatment target was achieved, medication was tapered and stopped, if patients remained in remission. During the trial period, the strategies starting with TCZ were more effective than the strategy initiating MTX only. Subsequently, patients were followed for 3 years, during which treatment was open and according to usual care.

Objectives: To establish the effectiveness of step-up strategies starting with MTX, TCZ or their combination in early RA over a 5 year period.

Methods: 226 of the 317 patients starting in the U-Act-Early trial (initial strategy: 75 TCZ +MTX, 79 TCZ, 72 MTX) participated in the 3 year follow-up phase.

DAS28 was collected every 3 months during the first year and every 6 months thereafter.

The primary endpoint, was SR, defined as DAS28 <2.6 AND 28 joint count ≤4 for >24 weeks. Secondary endpoints were sustained drug free remission (sDFR), defined as remission for ≥3 months after tapering and stopping all medication during SR, and DAS28 over 5 years.

Differences between the randomised strategies in proportions of patients achieving SR and sDFR and durations of SR and sDFR were tested with Cochran-Mantel-Haenszel and Kruskal-Wallis tests, respectively.

A mixed model analysis was used to compare DAS28 over time, with a random intercept and fixed effects for: treatment, visit-week, the interaction visit-week* treatment, and it was corrected for gender, age, and for DAS28, RA-duration, CRP and RF-positivity at baseline.

Results: Baseline characteristics at the start of U-Act-Early of the patients included in this 3 year follow-up study were not significantly different from those of all patients included in U-Act-Early trial. Over 5 years, SR was achieved in 224/226 (99%) patients without significant differences (p=0.15) between the initial treatment strategies in proportions of patients achieving it, nor in durations (p=0.96) of these endpoints (table 1). Neither between-group significant differences were found for sDFR (proportion; p=0.10, duration; p=0.27), only a tendency for longer duration in TCZ +MTX. The mean DAS28 over 5 years was not significantly different between initial strategy groups (figure 1), but it was on average 0.15 (95% CI -0.12 to 0.42) units higher in the TCZ(+MTX) groups, compared to MTX initiation group.

Abstract FRI0026 – Table 1. Outcome for sustained (drug free) remission over 5 years

	Initial treatment strategy group			p-value
	TCZ+MTX	TCZ+placebo	MTX+placebo	
Sustained remission				
Proportion achieving, n/N (%)	75/75 (100)	77/79 (97.5)	72/72 (100)	0.15 ¹
Duration weeks, Median (IQR)	49 (37 - 81)	52 (40 - 71)	46 (36 - 114)	0.96 ²
Sustained drug free remission				
Proportion achieving, n/N (%)	26/75 (34.7)	19/79 (24.1)	14/72 (19.4)	0.10 ¹
Duration weeks, Median (IQR)	106 (72 - 157)	83 (31 - 156)	71 (30 - 147)	0.27 ²

¹= Cochran-Mantel-Haenszel test, ²=Kruskal-Wallis test

Abstract FRI0026 – Figure 1. DAS28 over time stratified for initial treatment strategy

Conclusions: On the short term, initiation of TCZ-based strategies yields the most benefit, but on longer term, no difference in important clinical outcomes was found anymore between initial strategy groups, probably due to continuation of the treat-to-target principle². Almost all patients achieved SR over 5 years, with a tendency for longer duration of sDFR in the TCZ+MTX strategy.

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FRI0027

PATIENT-BASED DISEASE ACTIVITY SCORE PREDICTS FLARE BETTER THAN IMPROVEMENT – BLOOD TEST PROVIDES INSIGNIFICANT CONTRIBUTION

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Background: Patient-derived Disease Activity Score (PDAS) was developed to allow rheumatoid arthritis (RA) patients to self-assess without the need of evaluator. Two versions, PDAS1 with ESR (erythrocyte sedimentation rate) and PDAS2 without, had been validated and shown to correlate well with DAS28 and display responsiveness to change in patients put on disease-modifying drugs. PDAS has the potential to inform disease activity change between evaluator's assessments and/or blood tests. This would be a useful monitoring tool to deliver treat-to-target tight RA control.

PDAS1=0.019×(PGA out of 100)+0.842×ln(ESR +2)+0.432×ln(patient 50 TJC +2)+0.271×HAQ