logistic regression analysis to assess the effects of different characteristics at baseline, including disease duration, on becoming refractory.

Results: By comparing patient characteristics (Table 1), more of the patients, who later will become refractory, are female (94.2% Vs 73.4%, p>0.001), have higher baseline disease activity (SDAI of 25.5 vs 17.7, p<0.001), and longer delay of the initial treatment from symptom onset (3.17 Vs 1.34 years, p=0.001).

The multivariable logistic regression model confirmed that a longer delay of first treatment is independently afflicted with a higher probability of a refractory disease course at a later stage. This model was adjusted for disease activity at baseline and gender (p<0.001, Figure 1). With increasing treatment delay, the chance of a dire disease course rises by approximately 1% every 6 months.

Table 1. Baseline characteristics in refractory and non-refractory patients

Baseline Descriptive	ReRA (n=69)	non-ReRA (n=282)	Sig.
% Female	94.2	73.4	<0.001
% RF +	56.5	62.1	0.398
% ACPA +	60.9	61.0	0.985
Time to Treatment*	3.17 (4.10)	1.34 (2.70)	0.001
SDAI	25.54 (12.24)	17.70 (12.17)	<0.001
CRP†	2.02 (2.30)	1.80 (2.02)	0.435
SJC 28	6.42 (5.35)	4.64 (4.72)	0.009
TJC 28	9.22 (6.98)	4.35 (5.40)	<0.001
EGA‡	37.78 (20.49)	28.77 (21.40)	0.002
PGA‡	55.19 (26.67)	41.42 (26.67)	<0.001

*years; †mg/dl; ‡100mm VAS scale.

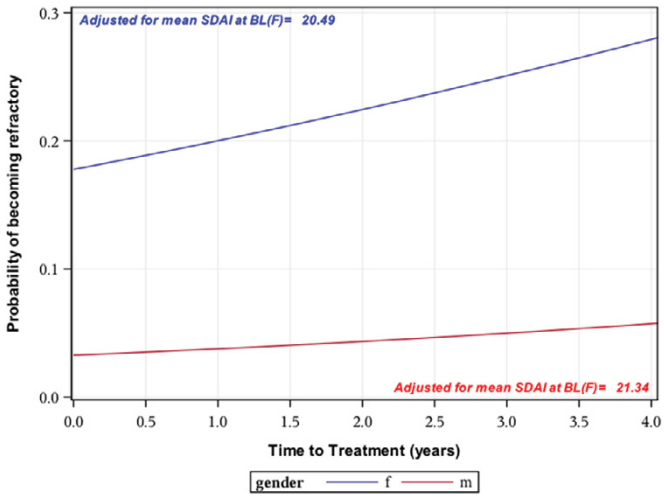

Figure 1: Predicted probabilities for becoming refractory depending on time to first treatment adjusted for baseline disease activity levels and gender.

Conclusions: Our data suggest that delay to initial treatment in RA affects the long-term course of RA. Earlier treatment initiation thus may change the severity of RA.

References:

[1] van Nies, J.A., et al., What is the evidence for the presence of a therapeutic window of opportunity in rheumatoid arthritis? A systematic literature review. Ann Rheum Dis, 2014. 73(5): p. 861–70.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3946

FRI0109 SHORT-TERM MONITORING OF SONOGRAPHIC CHANGES INDUCED BY A CORTICOSTEROID INJECTION IN METACARPOPHALANGEAL JOINT OF RHEUMATOID ARTHRITIS PATIENTS: A PILOT STUDY

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Background: Intra-articular corticosteroid injection is a well-established procedure in the daily practice since many decades [1]. High-resolution ultrasound (US), considered as *in vivo* microscopy, has the potential to help to understand how drugs develop their anti-inflammatory properties inside the articular space [2].

Objectives: To provide a very tight sonographic monitoring of the changes in a single metacarpophalangeal (MCP) joint in rheumatoid arthritis (RA) patients after the administration of intra-articular corticosteroid.

Methods: In this study we consecutively enrolled RA patients with active disease (Composite Disease Activity Index - CDAI >10), at least one tender and swollen MCP joint, and without contraindication to intra-articular corticosteroid injection (e.g. poor controlled diabetes). After the clinical evaluation that established the most clinically involved MCP joint to inject, patients underwent an US examination of the joint by an experienced sonographer. Synovitis was scored in grey scale (GS) in terms of joint space enlargement (measured at the level where the distance between the bone diaphysis and the joint capsule was greater), and power Doppler (PD) signal (scored by a semiquantitative method: 0 = no intra-articular flow, 1 = single vessel signal, 2 = confluent vessels, and 3 = vessel signal in more than 50% of the intra-articular area). After the baseline US assessment (T0), the MCP joints were injected with 20 mg triamcinolone acetonide under sonographic guidance. Sonographic follow-up was performed in five timepoints: two hours (T1) after the injection, four hours (T2), eight hours (T3), 24 hours (T4), and 48 hours after the injection (T5).

Results: Fifteen patients (13 women), with a mean age of 62.5 years, completed the follow-up. The mean CDAI was 28.9, anti-citrullinated protein antibodies were present in 9 patients. At T5, in all the patients was detectable a global reduction of joint space enlargement, of intra-articular PD signal, and of the numerical rating scale (NRS) of pain at the joint injected (Table). However, in majority of the patients (n: 13), the joint space enlargement showed an increase in the T1 and T2 US examinations, and in four patients PD signal, compared to T0, increased within the eight hours after the injection. No major adverse events were registered.

	Power Doppler grade (0–3)			Joint space enlargement (mm)			NRS pain (0–10)		
Case ID	First	Last	Maximum	First	Last	Maximum	First	Last	Maximum
1	2	1	3	3,4	2,4	4,2	3	1	5
2	2	0	2	4,4	3,7	5,7	8	1	8
3	2	0	2	2,1	1,3	3	7	2	7
4	3	1	3	2,1	1,8	2,9	9	0	9
5	3	2	3	4	4	4,9	10	0	10
6	3	1	3	6,5	2,7	6,5	2	1	2
7	2	0	2	3,5	1,2	3,6	6	0	6
8	1	1	3	4,6	3,3	4,6	3	0	3
9	3	0	3	2,5	2,1	3,6	2	0	2
10	2	1	3	4,3	3,9	5,6	7	3	7
11	3	1	3	5,3	3,3	5,7	8	3	8
12	3	1	3	3,3	2,6	3,3	7	3	7
13	2	1	2	2,6	2,3	3	7	2	7
14	3	1	3	3,1	2,2	4	7	2	7
15	2	1	3	4,5	3,7	4,5	7	0	7

Conclusions: A single intra-articular corticosteroid injection, performed under US guidance, is a very fast treatment to reduce synovitis of the injected joint. In the hours next to the injection is common to reveal a rise of joint space enlargement together with that of PD signal score.

References:

[1] Courtney P, Doherty M. Joint aspiration and injection and synovial fluid analysis. Best Pract Res Clin Rheumatol 2013;27:137–69.
[2] Filippucci E, Iagnocco A, Salaffi F, et al. Power Doppler sonography monitoring of synovial perfusion at the wrist joints in patients with rheumatoid arthritis starting adalimumab treatment. Ann Rheum Dis 2006; 65:1433–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5357

FRI0110 METHOTREXATE MONOTHERAPY IN REAL LIFE: A DRUG SURVIVAL ANALYSIS. COMPARISON BETWEEN VERY EARLY ARTHRITIS AND EARLY ARTHRITIS COHORTS

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Background: Methotrexate (MTX) is the first line drug suggested in the ACR/EULAR guidelines to treat the rheumatoid arthritis (RA) (1) and spondylarthritis (SpA). Although MTX efficacy is demonstrated by high levels of evidences, maximum benefit might require interventions even earlier. For this reason, it is suggested to identify the patients (pts) with symptom onset of less than 12 weeks, that is very early arthritis, to obtain better outcomes. Few data are available by the clinical practice on MTX monotherapy (MTXm) survival in very early or early arthritis pts.

Objectives: We aim to evaluate the presence of different outcomes in MTXm drug survival and MTX efficacy between Very Early arthritis (VEA) pts (less than 12 weeks from symptom onset) and Early arthritis (EA) pts (12–52 weeks from symptom onset), and between early RA pts and early SpA pts.

Methods: On 305 pts, we selected 219 pts (30 pts diagnosed as VEA (4,2 (4) weeks from symptom onset) and 155 pts as EA (25,7 (25) wks from symptom onset) in which MTXm could be started. The RA pts were 93 and SpA pts were 126. To assess the MTXm persistency the Kaplan-Meier survival curves analysis was performed and Cox regression analysis was used to assess clinical predictors of MTXm suspension. The results are expressed as mean±standard deviation or median (interquartile range). A p≤0.05 was set for statistically significant.

Results: No difference in MTXm survival was found between VEA pts 95,5 (36) wks and EA 92,5 (10) wks (p=0,38) (Fig.1a). We observed a significant difference in drug survival between early RA pts 63 (16) wks) and early SpA pts 112,7 (15,8) wks (p=0,001) (Fig.1b). In 55% early RA pts and in 45% early SpA pts the biotechnology drug needs to be added because of disease flare. In the remaining pts a low disease activity (DAS≤3,2) was observed. No adverse events were recorded in follow-up period. In early RA pts predictors of shorter MTXm survival were younger age at diagnosis (p=0,004), lower dose of MTX (p=0,032),

Fig. 1a

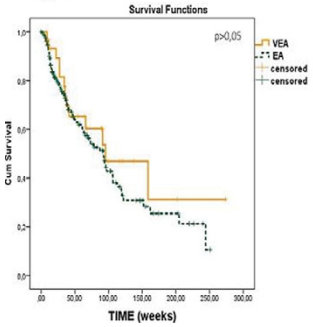
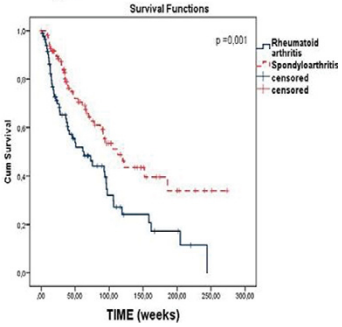


Fig. 1b



earlier diagnosis from symptom onset (p=0,0001), higher titer of rheumatoid factor (p=0,037) and female gender (p=0,019). In early SpA pts the only predictor of shorter MTXm survival was younger age at diagnosis (p=0,0,37). Smoking, disease activity at diagnosis and BMI were not predictors of MTXm survival.

Conclusions: The MTXm survival is not influenced by VEA or EA diagnosis. The RA seems to be less responder to MTXm than SpA. It might be due to the difficult to capture the earliest phase of disease, as circulating antibodies might appear years before the onset of symptoms in RA, and biomarkers reflecting bone destruction are elevated before arthritis is present, as described in previous studies. In particular, might be pay attention to younger pts, female gender and pts with higher titer of rheumatoid factor as they seem to present a more resistant RA disease. A high dose of MTX and earlier interventions are suggested in RA to improve the clinical outcome of patients and the MTXm survival.

References:

[1] Smolen JS et. Al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis 2014;73:492–509.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4237

FRI0111 ANTI-CITRULLINATED PROTEIN ANTIBODY REACTIVITIES IN TREATMENT NAÏVE EARLY RHEUMATOID ARTHRITIS

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Background: An increase in the number of anti-citrullinated protein antibodies (ACPA) reactivities precede RA onset, and may be involved in the pathogenesis of the disease. The presence of ACPA is associated with radiographic progression in RA, and it has been suggested that ACPAs with different reactivities may be associated with different phenotypes of RA.

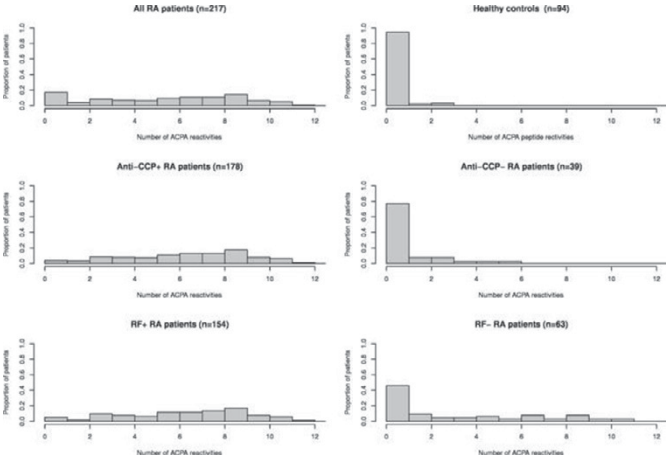
Objectives: To assess the prevalence of baseline ACPA reactivities in an inception cohort of early RA patients, including subgroups based on anti-CCP/RF status, and to compare the findings to healthy controls.

Methods: 217 DMARD-naïve early RA patients from the ARCTIC trial (1) were analysed. Radiographs were scored according to van der Heijde Sharp (vdHS) score. Anti-CCP status was analysed by FEIA (pos. if ≥10 IU/mL) and RF by ELISA (pos. if ≥25 IU/mL). ACPA titres (AU/ml) were considered pos. if above the 98-perc. of values in 619 non-RA subjects. Analysis of 13 ACPA reactivities targeting citrullinated peptides from fibrinogen, alpha-1 enolase, vimentin, fillagrin and histone was performed at baseline in patients and 94 controls (blood donors matched for age/gender/smoking), using a multiplex chip-based assay (2).

	anti-CCP+, n=178	anti-CCP-, n=39	RF+, n=154	RF-, n=63	All RA, n=217	Controls, n=94
Age, years[1]	50.8 (13.2)	55.0 (14.9)	51.9 (13.3)	50.8 (14.2)	51 (14)	52 (9.4)
Female[2]	109 (61)	22 (56)	91 (59)	40 (64)	131 (60)	63 (59)
Ever-smoker[2]	122 (69)	26 (67)	109 (71)	39 (62)	148 (68)	81 (64)
DAS[1]	3.4 (1.1)	4.0 (1.3)	3.5 (1.2)	3.5 (1.2)	3.5 (1.2)	NA
vdHS score[3]	4.0 [1.5–8.0]	4.5 [2.0–10.0]	4.5 [2.0–8.0]	3.5 [1.5–10.0]	4.0 [1.5–8.0]	NA
Vim60–75 cit[4]	152 (85)	7 (18)	130 (84)	29 (46)	159 (73)	5 (5)
H4 31–50 cit[4]	142 (80)	3 (8)	119 (77)	26 (41)	145 (67)	1 (1)
CEP1[4]	137 (77)	3 (8)	117 (76)	23 (37)	140 (65)	1 (1)
Fil307–324 cit[4]	134 (75)	2 (5)	113 (73)	23 (37)	136 (63)	0 (0)
Fib573 cit[4]	121 (68)	2 (5)	99 (64)	24 (38)	123 (57)	0 (0)
Fib36–52 cit[4]	116 (65)	1 (3)	96 (62)	21 (33)	117 (54)	2 (2)
H3 1–30 cit[4]	106 (60)	1 (3)	93 (60)	14 (22)	107 (49)	0 (0)
H4 14–34 cit[4]	103 (58)	2 (5)	90 (58)	15 (24)	105 (48)	3 (3)
H3 21–44 cit[4]	94 (53)	2 (5)	80 (52)	16 (25)	96 (44)	1 (1)
Vim2–17 cit[4]	87 (49)	1 (3)	80 (52)	8 (13)	88 (41)	0 (0)
Fib591 cit[4]	66 (37)	3 (8)	56 (36)	13 (21)	69 (32)	1 (1)
Fib74 cit[4]	60 (34)	6 (15)	54 (35)	12 (19)	66 (30)	3 (3)
Fib72 cit[4]	24 (14)	3 (8)	21 (14)	6 (10)	27 (12)	2 (2)

[1]Mean (SD), [2]n (%), [3]Median [IQR], [4]ACPA reactivity, n positive (%).

Results: Baseline characteristics are presented in the table. The figure shows the prevalence of ACPA reactivities in the subgroups, with median [IQR] number of antibody reactivities in all patients 7 [3,10], compared to 0 [0,0] in controls (p<0.001). The corresponding numbers were 8 [5,10] and 0 [0,1] for the anti-CCP+ vs. anti-CCP- patients (p<0.001), and 8 [5,10] and 2 [0,7.5] for the RF+ vs. RF- patients (p<0.001). Positivity for ACPA reactivities was seen mainly in the anti-CCP+ and RF+ patients, but also occurred more frequently in RF- and anti-CCP- patients (table) than in controls (anti-CCP- vs controls p=0.037, RF- vs controls p<0.001).



Conclusions: Prevalence of ACPA reactivities differed in subgroups of DMARD-naïve early RA patients according to anti-CCP and RF status. All RA subgroups, including RF- and anti-CCP- patients, had higher prevalence of ACPA reactivities compared to healthy controls.

References:

[1] Haavardsholm et al BMJ 2016.
[2] Hansson et al Arthr Res Ther 2012.

Disclosure of Interest: M. Jonsson: None declared, A. Hensvold: None declared, M. Hansson: None declared, L. Mathsson-Alm Employee of: Thermo Fisher Scientific, A.-B. Aga: None declared, J. Sexton: None declared, B.-T. Fevang Grant/research support from: Novartis, S. Lillegraven: None declared, A. Catrina: None declared, E. Haavardsholm Grant/research support from: AbbVie, MSD, Pfizer, Roche, UCB

DOI: 10.1136/annrheumdis-2017-eular.2915

FRI0112 SERUM LEVELS OF IL-33 AND SST2 ARE ASSOCIATED WITH FUNCTIONAL DISABILITY IN RHEUMATOID ARTHRITIS

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Background: Interleukin 33 (IL-33) is a cytokine related to amplification of the articular inflammation in rheumatoid arthritis (RA) animal models. Elevated IL-33 serum levels have been described in RA patients, suggesting a possible participation of this cytokine in the physiopathology of the disease.[1,2] IL-33 soluble receptor (sST2) is a decoy receptor that functions as an inhibitor of the interaction of the transmembrane receptor with IL-33.[3]

Objectives: To identify the association between serum levels of IL-33 and its soluble receptor (sST2) with clinical and laboratory characteristics of RA.

Methods: Cross-sectional observational study in which RA patients were submitted to clinical and laboratorial evaluation. IL-33 and sST2 serum levels were measured by ELISA (R&D System Inc, Minneapolis, MN, USA).

Results: 102 RA patients were included, 92,5% women, mean age of 55,5±10 years and mean disease duration of 17,6±9,5 years. Eighty-four (82,4%) patients had seropositive RA. The median (interquartile range) IL-33 serum level was 69.1 pg/ml (31.6 - 114.5). Higher scores on the visual analogue scale (VAS) of disease activity assessed by the examiner were associated with higher IL-33 values (CI95%: 0.01–0.05). In the group of patients with high titres of rheumatoid factor (RF), IL-33 levels were higher, compared to the group with negative RF (95% CI: 0.55 - 2.34). In 34 (33.3%) patients, IL-33 was undetectable and the presence of metabolic syndrome[4] represented a 63% lower chance (OR =0.37, 95% CI: 0.15–0.90) of having IL-33 detected. In addition, 1-unit increase in HAQ-DI increased by 2.43 times the chance of detecting IL-33 (95% CI: 1.23 - 4.80). The median sST2 serum level was 469.8 pg/ml (336.3–651). sST2 was associated with worse functional capacity by the classification of Steinbroker[5] (IC95%: 0.09 - 0.5), use (current or in the past) of tobacco (95% CI: 0.02 - 0.53) and use of leflunomide (95% CI: 0.05 - 0.53). There was no correlation between IL-33 and sST2 levels.

Conclusions: These findings may suggest that both IL-33 and its soluble receptor play a role as a marker of RA severity and functional disability. The negative association of IL-33 with metabolic syndrome is in agreement with the possible protective role of this cytokine in relation to lipid metabolism.[6]