Fig. 1a

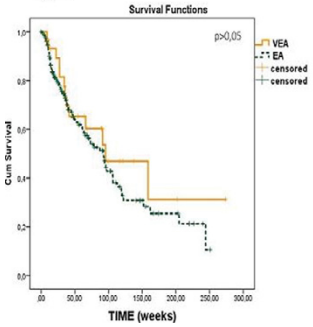
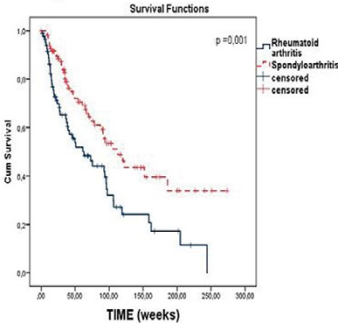


Fig. 1b



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:

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Disclosure of Interest: None declared

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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.

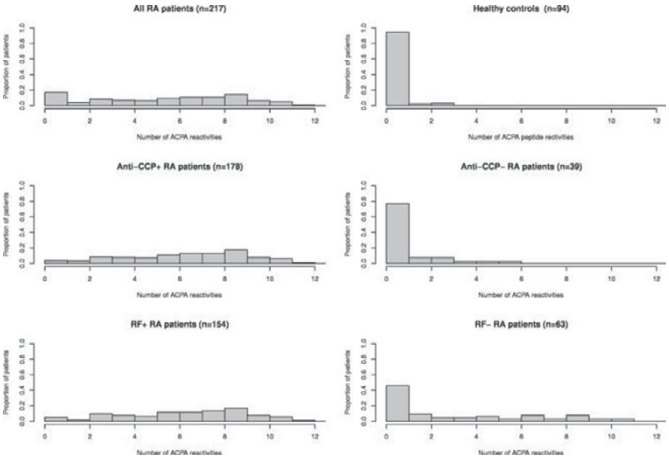
Objectives: To assess the prevalence of baseline ACPA reactivities in an inception cohort of early RA patients, including subgroups based on anti-CCP/RF status, and to compare the findings to healthy controls.

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.

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[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

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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]

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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5565

FRI0113 VALIDATION AND RESULTS OF THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS (SPARRA) QUESTIONNAIRE

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Background: A range of symptoms can be present in persons at risk of rheumatoid arthritis (RA). However, information on the nature, location, timing, severity and predictive value of these symptoms is largely lacking. The Symptoms in Persons At Risk of Rheumatoid Arthritis (SPARRA) questionnaire has been developed with support from EULAR, informed by data from a qualitative study[1] and with input from patient research partners.
Objectives: To test the psychometric properties of the SPARRA questionnaire in an international group of arthralgia patients at risk of RA and to quantify these symptoms.
Methods: The SPARRA questionnaire contains questions about presence, severity, impact and location of 13 symptoms. 240 individuals (69% rheumatoid factor and/or ACPA positive, 23% seronegative with clinically suspect arthralgia and 8% first degree family members of patients with RA) completed the questionnaire in the Netherlands (N=125), United Kingdom (N=70), Sweden (N=15), Austria (N=11) and Switzerland (N=19). Individuals had no history or presence of clinically diagnosed arthritis at the time of first physical examination. Reliability (test-retest) and validity (face, content and construct validity) were tested.
Results: Face validity was tested by a group of experts on the at-risk phase of RA and feedback on the questionnaire was asked and received from 30 arthralgia patients, leading to only minor comments. The test-retest within 7–14 days (N=51) showed moderate to good agreement (kappa mean 0.565, range 0.309–1; agreement mean 71%, range 59–100%). The content validity was high, in line with the fact that the items were derived from a qualitative study in seropositive arthralgia patients. In contrast, the construct validity (relation to visual analog scale scores (VAS) for pain and well-being) was low (R-square 0.040–0.199), suggesting that the questions measure different elements in different time frames and grasp symptom content not captured with regular VAS pain/well-being. Most symptoms were present in a high percentage of individuals, with pain, stiffness and fatigue as the most common ones. When a symptom was present, it was usually experienced as moderate to severe, and with moderate impact. ACPA positive individuals reported lower presence of symptoms then ACPA negative individuals (mean 47% for ACPA-positive (N=118), 41% for only RF positives (N=53) and 59% in seronegative individuals (N=69)), but functional impact was higher in ACPA positive individuals (51%, versus 42% in seronegatives, NS). Note that the inclusion criteria for the seronegative individuals was presence of symptoms.
Conclusions: This study provides evidence of good psychometric properties of the SPARRA questionnaire, except for low construct validity. This means the questionnaire adds information to currently available clinical measures in persons at risk of RA. Future studies are needed to evaluate whether SPARRA data can help to improve the prediction of RA.
References:
[1] Stack, Rheumatology 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2450

FRI0114 ALLOGRAFT INFLAMMATORY FACTOR 1 (AIF1) POLYMORPHISMS RS4711274 (G/A) AND RS2269475 (C/T) MAY PREDICT ETANERCEPT PLUS METHOTREXATE RESPONSE IN FRENCH CAUCASIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Several risk loci for Rheumatoid Arthritis (RA) have been identified by Genome Wide Association Studies (GWAS), but they do not include Allograft Inflammatory Factor 1 (AIF1). Nevertheless, a few studies have shown that AIF1 rs2269475 (C/T) is associated with RA[1,2].
Objectives: We propose 1) To examine associations in French Caucasian patients with RA, of the seven most described AIF1 SNPs; 2) To study their linkage disequilibrium with HLA-DRB1 alleles; 3) To evaluate whether AIF1 single nucleotide polymorphisms (SNPs) could predict first line treatment responses in RA.
Methods: We amplified the AIF1 gene region containing the 7 SNPs and sequenced PCR products on a total of 469 individuals, including 95 Anti-Citrullinated Protein Antibody (ACPA) positive RA patients, 146, patients with scleroderma, 132 healthy controls and 96 additional healthy controls selected from a large database of volunteer bone marrow donors (VBMD) for carrying at least one RA-associated allele. Patients and controls were HLA-DRB1 genotyped. Patients with RA were divided into 2 groups, a first group called "*non responders*" was defined as patients who did not respond to first-line methotrexate (MTX) combined with Etanercept and a second group called "*good responders*" was defined as patients who did respond to methotrexate combined with Etanercept.
Results: Two SNPs were associated with RA: *rs4711274 (G/A)* and *rs2269475 (C/T)*. The frequency of minor allele carriers was respectively 37% (A) and 36% (T) in patients with RA versus 18% among controls (p=0.0014 and p=0.001). Furthermore, patients with RA-associated HLA-DRB1 alleles carried more often minor alleles for both SNPs (p=0.0005). Preliminary clinical data show that 56% of non-responders (N=16) carried the minor alleles of both rs4711274 and rs2269475 compared to only 21% of good responders (N=24, p=0.02).
Conclusions: AIF is an inflammation-responsive protein encoded within the HLA class III region on chromosome 6 (6p21.3). As already described in British and Polish Caucasians, we found a significant AIF1 Rs2269475 association with RA. We also found an association with Rs4711274 in linkage disequilibrium with the former. The increased frequency of minor AIF1 alleles in RA was not associated with a particular HLA-DRB1 allele, but to any HLA-DRB1 allele carrying the shared epitope.
Finally, patients who failed to respond to Etanercept and MTX carried more often minor alleles of the 2 described AIF1 SNPs.
Further analysis on a larger groups of patients is required to confirm whether AIF1 SNPs can predict response to therapy with Etanercept and Methotrexate.
References:
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Disclosure of Interest: None declared
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FRI0115 EVER-SMOKING IS ASSOCIATED WITH DISEASE SEVERITY AND OPIOID USE IN RHEUMATOID ARTHRITIS

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Background: Cigarette smoking, both current and past, is a risk for incident rheumatoid arthritis (RA), even for those with low exposure rates of 1–10 pack years. Current smoking is also associated with severity of disease and poorer response to treatments. It is however not known whether any exposure to cigarettes impacts disease expression, especially for those who have discontinued smoking.
Objectives: To assess the disease severity in RA according to smoking status (ever-, past-, current-, non-smoker).
Methods: As part of a study to examine cigarette and marijuana smoking in rheumatic disease patients, consecutively attending rheumatology patients completed an anonymous self-administered questionnaire including: pain severity on visual analog scale (VAS), patient global assessment (PtGA) and cigarette or marijuana smoking status. Concomitant physician recorded information included: sociodemographics, co-morbidities, treatments for RA, physician global assessment (PGA). Patients were categorized according to smoking status. Categorical variables were compared between groups with the Chi-Square test and continuous variables with the Student's t-test. Variables showing a statistical trend ($p<0.15$) in univariate analysis were considered in multivariate logistic regression.