randomized trials (5 Ph3, 3 Ph2, 1 Ph 1b) and 1 LTE (data to 13-Feb-2018). Placebo (PBO) comparisons were evaluated to Week 24 from 7 Ph2/3 trials: pts randomized to PBO, bari 2-mg or 4-mg, with censoring at rescue/treatment switch. Dose responses were evaluated in the 2-mg/4-mg extended dataset from 4 Ph2/3 trials: pts randomized to 2- or 4-mg, LTE data included; data censored at rescue/dose change (as-treated analysis) and, due to latent period for malignancy, analyzed without censoring (as-randomized analysis). Incidence rates (IR) per 100 patient-years (PY) were calculated.

Results: 3770 pts received bari (10127 PYs); maximum exposure was 7 yrs (Table). No significant differences were seen for bari 4-mg vs PBO in adverse events leading to permanent drug discontinuation, death, malignancy, serious infection, or major adverse cardiovascular events. Herpes zoster IR was significantly higher for bari 4-mg vs PBO (3.8 vs 0.9) and numerically higher for bari 2-mg (3.1). IRs for deep vein thrombosis/pulmonary embolism were numerically higher in bari 4-mg vs PBO; IRs were similar by dose in 2-mg/4-mg-extended dataset. Malignancy (excluding non-melanoma skin cancer) IRs were 0.8 (2-mg) and 1.0 (4-mg; as-randomized analysis). Fewer than 1% of pts discontinued due to abnormal laboratory results.

Conclusion: In this updated integrated analysis of pts with active RA exposed to bari for up to 7 yrs, across safety topics, bari maintained a safety profile similar to that previously reported¹ and acceptable in the context of demonstrated efficacy.

Abstract THU0078—Table 1. demographics

Table	Placebo-controlled (to Week 24)			2-mg – 4-mg extended		All-Bari-RA
	Placebo (N=1215)	Bari 2-mg (N=479)	Bari 4-mg (N=1142)	Bari 2-mg (N=479)	Bari 4-mg (N=479)	All Bari RA (N=3770)
Exposure						
Total patient-years	450.8	185.8	471.8	675.6	698.6	10127
Median duration, days	166	168	169	257	342	1115
Longest exposure, days	235	197	211	1805	2520	2520
≥1 AE, n (EAIR)						
TEAE	748 (165.9)	316 (170.1)	803 (170.2)	378 (55.9)	417 (59.7)	3332 (32.9)
Serious adverse event including death	54 (12.0)	18 (9.7)	58 (12.3)	62 (9.2)	84 (12.0)	786 (7.8)
Temporary interruption due to AE	98 (21.7)	50 (26.9)	117 (24.8)	108 (16.0)	118 (16.9)	1111 (11.02)
Permanent discontinuation due to AE	37 (8.2)	20 (10.8)	50 (10.6)	39 (5.7)	59 (8.3)	426 (4.2)
Death, n (IR)	2 (0.4)	0	3 (0.6)	1 (0.2)	4 (0.6)	44 (0.4)
Malignancy, n (IR)						
Malignancy excluding NMSC						
As treated	2 (0.4)	1 (0.5)	2 (0.4)	3 (0.4)	10 (1.4)	85 (0.8)
As randomized	0	0	0	12 (0.8)	14 (1.0)	14 (1.0)
Lymphoma	0	0	0	0	1 (0.1)	8 (0.1)
NMSC	1 (0.2)	0	3 (0.6)	2 (0.3)	8 (1.1)	37 (0.4)
Infections, n (IR)						
Serious infection	19 (4.1)	8 (4.2)	19 (4.0)	21 (3.1)	32 (4.6)	283 (2.8)
Herpes zoster	4 (0.9)	6 (3.1)	18 (3.8)*	18 (2.7)	27 (3.9)	323 (3.3)
Tuberculosis	0	0	1 (0.2)	0	7 (0.5)	15 (0.2)
Opportunistic infection including MD HZ ^a	2 (0.5)	0	4 (0.9)	2 (0.3)	3 (0.4)	52 (0.5)
Adverse cardiovascular events of special interest, n (IR)						
Major adverse cardiovascular events	2 (0.5)	0	3 (0.7)	2 (0.3)	2 (0.3)	51 (0.5)
DVT/PE	0	0	6 (1.3)	4 (0.6)	4 (0.6)	49 (0.5)
DVT	0	0	3 (0.6)	4 (0.6)	2 (0.3)	35 (0.4)
PE	0	0	3 (0.6)	1 (0.2)	2 (0.3)	24 (0.2)
Gastrointestinal perforations, n (EAIR)	0	0	0	0	1 (0.1)	4 (0.04)

*P<0.05 Bari 4-mg vs PBO

^aNo statistical comparisons were performed.

AE=adverse event; Bari=baricitinib; DVT=deep vein thrombosis; EAIR = exposure adjusted incidence rate;

IR=incidence rate; NMSC=non-melanoma skin cancer; PE=pulmonary embolism; TE=treatment-emergent

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THU0079

AUTOANTIBODY-NEGATIVE PATIENTS, THE CUT-OFF OF SIX POINTS ACCORDING TO THE 2010 ACR/EULAR CRITERIA FOR RHEUMATOID ARTHRITIS MAY MISS A POPULATION OF SEVERE, PERSISTENT POLYARTHRITIS

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Background: At the group level, the classification criteria for rheumatoid arthritis (RA) developed in 2010 identify patients earlier than the 1987 criteria. However, performance of the new criteria in subjects negative for rheumatoid factor (RF) and anti-citrullinated protein autoantibodies (ACPA) is object of debate [1, 2]. In these patients, classification may be missed despite severe joint and systemic inflammation.

Objectives: To evaluate disease characteristics and arthritis persistence in autoantibody-negative patients with early polyarthritis fulfilling only 5 of the 10 points of the 2010 classification criteria for RA.

Methods: We included early arthritis patients from our Early Arthritis Cohort with at least one clinically swollen joint, symptoms for less than 12 months, no other explanation of arthritis and naïve to glucocorticoids and disease modifying anti-rheumatic drugs (DMARDs) at presentation. At baseline, fulfillment of each specific domain of the 1987 and the 2010 criteria was recorded. RF and ACPA were centrally determined on baseline sera. RF- and ACPA-negative patients achieving a total score of 5 in the 2010 criteria were compared to patients fulfilling RA criteria for baseline characteristics and for arthritis persistence (28-joints disease activity score [DAS28] >3.2) after 2 months of follow-up.

Results: Of the total population of 882 patients with new-onset inflammatory arthritis, comprehensive evaluation of the fulfillment of the 1987 and the 2010 criteria was available in 771 cases (87.4%). Of these, 476

(61.7%) were negative for both RF and ACPA. Among autoantibody-negative patients, 193 (40.5%) scored less than 6 points according to the 2010 criteria, with 82 (42.4%) scoring 5 points. 35.4% of these patients were captured by the 1987 criteria at baseline. Reasons for not fulfilling 1987 criteria in the remaining were morning stiffness <60 min in the majority of the cases (62.3%). As expected, autoantibody-negative patients scoring 5 points had lower disease activity with respect to autoantibody-negative patients fulfilling RA criteria (Table 1). Rather, disease activity, pain and loss of function were comparable to those of autoantibody-positive early RA patients (Table 1). After 2 months of follow-up, 58.1% of autoantibody-negative patients scoring 5 points remained in moderate disease activity (DAS28 >3.2).

Conclusion: In autoantibody-negative patients with new-onset arthritis scoring 5 of the 10 points of the 2010 criteria for RA classification, arthritis is equally severe and disabling compared to autoantibody-positive patients classified as RA from baseline. In the majority of these patients, arthritis persists in the short term. Prospective data are thus awaited in order to assess whether the cut point of the 2010 criteria needs to be lowered in autoantibody-negative inflammatory polyarthritis.

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Abstract Table 1. Baseline characteristics of the study cohort

	autoantibody-negative 2010 ACR/ EULAR score=5	autoantibody-negative 2010 ACR/ EULAR score ≥6	p	autoantibody-positive 2010 ACR/ EULAR score ≥6	p
symptoms' duration, median (IQR), weeks	30.6 (10.7 to 37.1)	15.6 (9.9-26.3)	0.04	15.3 (8.5 to 28.8)	0.04
DAS28, mean (SD)	4.53 (0.83)	5.25 (1.08)	<0.001	4.72 (1.15)	0.05
VAS pain, median (IQR)	51.5 (32.5- 70.5)	62 (50-80)	0.01	50 (31-77.5)	0.76
HAQ, median (IQR)	1 (0.47-1.5)	1.25 (0.75- 1.88)	0.003	1 (0.5-1.5)	0.44

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THU0080

DEVELOPMENT OF ULTRASOUND DETECTABLE ARTHRITIS AMONG ACPA POSITIVE SUBJECTS WITH MUSCULOSKELETAL SYMPTOMS: THE RISK RA PROSPECTIVE STUDY

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Background: Retrospective studies have shown that anti-citrullinated protein antibodies (ACPA) are a risk factor for the development of clinical arthritis.

Objectives: We aimed to investigate in a prospective setting if ACPA and other biomarkers could predict development of ultrasound detected arthritis.

Methods: Subjects with positive ACPA-test referred from primary care to the Rheumatology clinic that lacked arthritis in hands, feet and any other symptomatic joints by clinical and ultrasound examination (according to EULAR-OMERACT definition), were recruited into the Risk-RA research program during 2015-2016 and were followed up to the end of 2017. At inclusion a detailed clinical examination was performed and blood samples were analyzed for 13 specific ACPA reactivities (using a custom made peptide microarray) as well as 92 inflammation-associated protein biomarkers (using a multiplex immunoassay with Olink proximity extension technology). Presence of HLA-SE was analyzed using DR low-resolution kit. Univariate and multivariate analysis were used to investigate the

association between clinical and laboratory parameters and development of ultrasound detected arthritis adjusting for the follow-up time.

Results: 42% (27 out of 65) of the Risk RA subjects developed ultrasound detectable arthritis during a median follow up of 8 months. The remaining 58% (38 out of 65) were followed for a median of 25 months (range 12-44) without any signs of ultrasound detectable arthritis. Subjects developing arthritis had higher prevalence of HLA-SE (89% vs 56%) and increased occurrence of ultrasound detected tenosynovitis (44% vs 5%), as compared to those not developing arthritis. ACPA reactivities to citrullinated vimentin peptides (cit vim 2-17: 22% vs 6%; and cit vim 60-75: 70% vs 43%) and citrullinated histone peptides (cit H4 31-50: 89% vs 49%; and cit H3 21-44: 48% vs 23%) were a more common occurrence in subjects developing ultrasound detectable arthritis. Backward selection in a Cox regression model showed that ultrasound detectable arthritis could be predicted in a model including HLA-SE, tenosynovitis and ACPA reactivity to cit H4 31-50. Hazard ratio (HR) for arthritis development were 3.4 (95% CI 1.0-12, p 0.06) for HLA-SE carriers, 2.9 (95% CI 1.3-6.7, p 0.01) for tenosynovitis and 4.1 (95% CI 1.2-14, p 0.02) for Anti-citrullinated H4 31-50 positivity. Only modest differences were observed for few of the tested inflammatory markers in those developing as compared to those not developing ultrasound detectable arthritis: Interleukin-6 (3.9 vs 3.3 AU/ML), Programmed death-ligand 1 (4.9 vs 5.2 AU/ML) and Chemokine (C-X-C motif) ligand 6 (9.2 vs 9.5 AU/ML).

Conclusion: Certain ACPA fine specificities, HLA-SE and tenosynovitis predict the development of ultrasound detectable arthritis in seropositive individuals with musculoskeletal symptom who are at risk for RA.

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THU0081

ELEVATED SERUM TREM-1 LEVELS ARE ASSOCIATED WITH DAS28 AND PERIODONTITIS IN RHEUMATOID ARTHRITIS

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Background: The Triggering Receptor Expressed on Myeloid cells 1 (TREM-1) along with its putative ligand peptidoglycan recognition protein 1 (PGLYRP1) are involved in the propagation of the inflammatory response to microbial exposure(1). Periodontal disease (PD) has been suggested as an environmental risk factor for rheumatoid arthritis (RA), yet further studies are required to dissect the mechanisms underlying the association between the two(2).

Objectives: The present study aimed to investigate whether serum levels of TREM-1 and PGLYRP1 in patients with RA correlate with the presence and severity of PD, as well as bacterial load in saliva.

Methods: Serum and saliva samples were collected from 65 individuals with RA (F/M: 48/17), under sDMARD treatment for more than 6 months and never used biologic treatment), with Behcet syndrome (BS, n= 45, F/M: 31/12) and with systemic health (HC, n= 59, F/M: 40/19). RA disease activity was assessed by using 28-joint disease activity score (DAS-28). Oral health was evaluated by dental and periodontal indices. TREM-1 and PGLYRP1 were measured by ELISA, while total oral bacteria in saliva was assessed by quantitative real-time polymerase chain reaction and normalized against tooth number. For statistical analysis, non-parametric Kruskal Wallis, Mann-Whitney U and Spearman correlation tests were used.

Results: Patients with RA presented with a smaller number of teeth than the BS and HC groups (18.67±8.45; 24.02±3.7; 25.36±3.83, respectively) (p<0.001). Prevalence of severe periodontitis was higher in the RA group (33.8%) compared to BS (20.9%) and HC (5.1%). Total bacterial load was significantly higher in saliva of RA than HC (p<0.05). Serum TREM-1 and PGLYRP1 levels were significantly higher in RA (167,1±95,0 pg/ml; 157,5±228,8 pg/ml) than BS (102,8±44,4 pg/ml; 52,4±26,01pg/ml) and HC