Table 1. Baseline characteristics

	UPA	UPA + MTX	Total
Age, years	57.7 (13.2) n=257	58.1 (11.4) n=276	57.9 (12.3) n=533
Disease duration, years	9.4 (8.3) n=253	8.5 (7.7) n=272	9.0 (8.0) n=525
CRP, mg/dL	1.3 (1.9) n=257	1.1 (1.7) n=276	1.2 (1.8) n=533
CRP >ULN, n (%)	137 (53.3) n=257	159 (57.6) n=276	296 (55.5) n=533
TJC28	7.4 (6.0) n=257	7.9 (6.4) n=276	7.7 (6.2) n=533
SJC28	5.5 (3.7) n=257	5.6 (4.1) n=276	5.6 (3.9) n=533
Patient's Global Assessment	6.2 (1.9) n=257	6.3 (1.8) n=276	6.3 (1.8) n=533
Physician's Global Assessment	5.8 (1.5) n=257	5.9 (1.6) n=276	5.9 (1.6) n=533
DAS28(CRP)	4.6 (1.0) n=257	4.6 (1.0) n=276	4.6 (1.0) n=533
DAS28(ESR)	4.8 (1.1) n=224	4.9 (1.2) n=239	4.9 (1.1) n=463
CDAI	24.9 (10.2) n=257	25.7 (10.8) n=276	25.4 (10.5) n=533
SDAI	26.2 (10.5) n=257	26.9 (11.3) n=276	26.6 (10.9) n=533
RAID	5.7 (2.0) n=255	5.7 (2.0) n=275	5.7 (2.0) n=530
Pain (RAID-1)	6.2 (2.2) n=255	6.1 (2.3) n=275	6.2 (2.2) n=530
SF-12 Physical Component Summary	32.6 (8.5) n=245	33.9 (8.6) n=262	33.3 (8.6) n=507
SF-12 Mental Component Summary	42.4 (11.6) n=245	42.6 (11.3) n=262	42.5 (11.5) n=507
HAQ-DI	1.3 (0.7) n=250	1.3 (0.6) n=270	1.3 (0.6) n=520
PHQ-9	8.9 (5.3) n=252	8.6 (5.3) n=272	8.7 (5.3) n=524
Erosions, n (%)	87 (33.9) n=257	95 (34.4) n=276	182 (34.1) n=533

Data are mean (SD), n unless otherwise stated

Figure Number of prior bDMARDs or tsDMARDs for rheumatoid arthritis

bDMARD, biologic DMARD; DMARD, disease-modifying antirheumatic drug; tsDMARD, targeted synthetic DMARD

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AB0256

BARICITINIB (BARI) VERSUS BIOLOGICS IMPACT ON STEROID TAPERING IN RHEUMATOID ARTHRITIS (RA)

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Background: Biologic and target synthetic disease modifying anti-rheumatic drugs (bDMARDs and tsDMARDs) are recommended to control RA disease activity, pain and steroid use. Following randomized clinical trials (RCTs) and their post-hoc analyses, the Janus Kinase Inhibitor tsDMARDs BARI was superior to reference bDMARD Adalimumab in reducing disease activity, pain and functional disability. In addition, BARI monotherapy also determined more significant pain reduction and functional improvement when compared to Tocilizumab monotherapy (3).

Objectives: to confirm RCT results in a real-life clinical setting, with focus on disease activity, pain, functional disability and steroid tapering, when comparing BARI to bDMARDs for the treatment of active RA.

Methods: RA patients starting BARI or a bDMARD for active RA were retrospectively evaluated from June 2019 to June 2020. Disease activity (DAS28CRP, SDAI, CDAI), pain visual analogic scale (pain_VAS), functional disability (HAQ) assessments and mean prednisone dosage (pred_dose) were collected at baseline (BL), 3 months (3M) and 6 months (6M) after BARI/bDMARD initiation. The changes of the outcome measures were evaluated between BL-3M, 3M-6M and BL-6M, as well as between BARI and bDMARDs groups. Finally, we assessed the variables associated with prednisone tapering in the whole population.

Results: 90 out of 100 RA patients evaluated (baseline: age 57±12 years, disease duration 131±100 months, DAS28PCR 4.8±1.0, pain_VAS 61±23 mm, prednisone dose 5.5±5.3 mg) were eligible for the study; 49 received BARI and 41 bDMARDs (17 abatacept, 12 TNF inhibitors, 11 tocilizumab, 1 rituximab). At BL, the two groups did not differ statistically in terms of age, sex, disease duration, disease activity, pain_VAS, previous bDMARD failure or ts/bDMARD naive, concomitant conventional synthetic DMARDs treatment, pred_dose. Both BARI and bDMARDs determined a significant reduction in activity scales and HAQ when comparing BL-3M and BL-6M, with only pain_VAS and pred_dose showing a significant decrease in the 3M-6M interval. When comparing the two groups, BARI showed a significantly higher reduction of pred_dose (-3.2±5.1 vs -1.7±3.7 mg at BL-3M, and -4.1±5.3 vs -1.9±4.6 mg at BL-6M), which was not significant after adjusting for BL pred_dose. No other difference was seen when the two groups, including the numerically higher reduction of pain_VAS in the BARI group (-29±28 vs -20±27 mm at BL-3M and -35±25 vs -30±28 mm at BL-6M comparison). The analysis of the predictors for steroid tapering (Δmean_pred) in the two intervals, showed that BL DAS28PCR, DAS28PCR BL-3M change and BL pred_dose were associated with BL-3M Δmean_pred, while 3M pain_VAS and 3M pred_dose were associated with 3M-6M Δmean_pred.

Conclusion: Although limited by the small samples and the retrospective nature, our real-life comparison shows similar efficacy of BARI and bDMARDs in terms of disease activity control, functional disability and pain. In addition, the treatment with BARI or bDMARD did not influence the steroid tapering, which was driven mostly by its initial dose, disease activity and pain. Larger real-life multi-center studies are warranted to confirm our results.

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AB0257

IMPACT OF CONVENTIONAL ANTIRHEUMATIC TREATMENT ON CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Cardiovascular diseases (CVD) are the most common and socially significant comorbidities and the main cause of premature mortality in rheumatoid arthritis (RA). Appropriate RA therapy should not only suppress RA activity, but also reduce CVD risk.

Objectives: To evaluate CVD risk and analyze its association with the use of conventional therapy in RA patients (pts).

Methods: The study included 100 pts with RA (92 women and 8 men) aged 30 to 60 without established CVD. The median age was 49.5 [44.5;53] years, duration of RA was 144 [60;240] months, DAS28 was 4.4 [3.3;5.3] points. Eighty six RA pts (86%) treated with disease-modifying antirheumatic drugs (DMARDs) (methotrexate, n=55; leflunomide, n=12; hydroxychloroquine, n=8; sulfasalazine, n=11), including 33 pts (33%) in combination with glucocorticoids (GCs). Fourteen pts (14%) received monotherapy with GCs. Pts were divided into three treatment groups: DMARDs group, n=53; GCs group, n=14; DMARDs+GCs group, n=33. CVD risk was calculated with ASSIGN, QRISK3, and ERS-RA scales.

Results: No differences were found between the groups when calculating CVD risk using ASSIGN (table 1). Estimated CVD risk by QRISK3 was lower in DMARDs group (4.9 [3.0; 7.7]) than in DMARDs+GCs group (7.1 [4.1; 13.6], p<0.05). High CVD risk on the ERS-RA scale was determined less frequently (13%) and median CVD risk was lower in DMARDs group (4.2 [2.2; 5.4]) than in GCs group (5.7%; 8.9 [4.8; 11.7], p<0.01) and DMARDs+GCs group (39%; 6.6 [3; 9.3], p<0.05, respectively). In DMARDs group, significant differences in CVD risk by ERS-RA were found in pts treated with hydroxychloroquine (2 [1.4; 5.8]) and leflunomide (6.2 [2.8; 12.3], p<0.05).

Conclusion: RA pts treated with DMARDs have a reduced risk for CVD than pts treated with GCs or a combination of DMARDs and GCs. GCs significantly increase CVD risk. To clarify the impact of hydroxychloroquine and leflunomide on CVD risk, a study on a larger number of pts is required.

Table 1. The impact of conventional antirheumatic therapy on CVD risk.

Treatment	ASSIGN		QRISK3		ERS-RA	
	High CVD risk, %	median [25-75 percentiles]	High CVD risk, %	median [25-75 percentiles]	High CVD risk, %	median [25-75 percentiles]
DMARDs, n=53	6	11 [6.5;14]	2	4.9 [3.7;7.7] *	13*	4.2 [2.2;5.4] *
GCs, n=14	7	9.5 [7;13]	7	6.6 [4.4;15.8]	57*	8.9 [4.8;11.7] *
DMARDs+GCs, n=33	15	10 [5;13.5]	9	7.1 [4.1;13.6] *	39*	6.6 [3.9;9.3] *

Note: * - p<0.01 between pts receiving DMARDs and GCs; * - p<0.05 between pts receiving DMARDs and DMARDs+GCs.

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AB0258

DMARD-TREATMENT OF UNDIFFERENTIATED ARTHRITIS INTENSIFIED DURING THE LAST DECADE, BUT DID NOT RESULT IN IMPROVED LONG TERM OUTCOMES

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Background: EULAR guidelines stress timely initiation of DMARD-treatment in early arthritis patients also when classification criteria are not yet fulfilled. Consequently, undifferentiated arthritis (UA) patients may be increasingly treated with disease modifying antirheumatic drugs (DMARDs), despite inadequate placebo-controlled evidence for its effectivity. Implementation of this guideline also hampers future placebo-controlled trials in UA. However, historical data, with inclusion period as instrumental variable, can provide insight whether long term

outcome is improved with increased DMARD-use, and thus serve to investigate if DMARD-treatment is effective in UA.

Objectives: With 25-years of observational data of newly referred UA-patients, we studied whether enhanced treatment strategies resulted in better long term outcomes for UA.

Methods: Between 1993 and 2019, 1132 consecutive UA-patients, not fulfilling the 1987/2010 criteria for RA or any other distinct diagnosis, were included in the Leiden Early Arthritis Cohort; patients were divided in 5 inclusion periods (1993-1998, 1999-2005, 2006-2010, 2011-2014, 2015-2019). Frequency of DMARD-initiation after diagnosis was compared. We studied the following outcomes: the course of disease activity scores (DAS28-CRP) and Health assessment questionnaires (HAQ), progression to RA after 1-year (according to the 1987 and/or 2010 criteria) and the frequency of prolonged DMARD-free status within 10-years of follow-up (this was defined as either spontaneous remission or sustained remission after discontinuation of DMARD-treatment).

Results: The current population of UA-patients, thus not fulfilling 1987 or 2010 criteria, had rather mild disease: the median SJC was 1, the median TJC 2, 95% was autoantibody-negative and the median HAQ was 0.6. These characteristics were similar in the different inclusion periods. Initiation of DMARD-treatment in UA increased over time: 18%, 35%, 38%, 43% up to 55% in respectively 1993-1998, 1999-2005, 2006-2010, 2011-2014 and 2015-2019, in which methotrexate became more common in the last decade. Frequency of progression to RA after 1-year did not decrease and was 14%, 21%, 26%, 19% and 28% in the respective inclusion periods. Long-term DAS28CRP-scores improved from 2011 onwards (range -0.18, -0.24; p<0.05). However HAQ-score over time did not improve compared to the 1993-1998 period (range -0.00, -0.08; p>0.05). Also the percentages of patients in DMARD-free status after 10-years of follow-up did not significantly improve over time: 57%, 58%, 59% (for 1993-1998, 1999-2005, 2006-2010 respectively, p=0.59).

Conclusion: Intensified DMARD-treatment of patients with UA did not result in improved outcomes. These data may indicate overtreatment of UA-patients. Yet, methods to stratify which UA-patients should be treated remains warranted.

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AB0259

EVALUATION OF THE EFFECT OF FILGOTINIB ON THE PHARMACOKINETICS OF ROSUVASTATIN, ATORVASTATIN, AND PRAVASTATIN

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Background: Filgotinib is an orally administered small molecule that preferentially inhibits Janus kinase 1 and is approved for use in Europe and Japan in adult patients with rheumatoid arthritis (RA) who have had an inadequate response to conventional therapies. Patients with RA are at a higher risk of cardiovascular morbidity and mortality relative to the general population¹. Thus, it is important to understand potential drug-drug interactions of filgotinib with lipid-lowering agents such as statins. Based on in vitro studies, filgotinib is not expected to significantly increase exposure of statins via inhibition of the organic anion transporting peptide (OATP) at clinically relevant exposures. Hence, in Phase 2 and Phase 3 clinical studies, statins were allowed for use with filgotinib. A post-hoc analysis showed no increase in statin-induced AEs such as muscle or liver toxicities when statins were coadministered with filgotinib ("Concomitant Use of Statins in Filgotinib-Treated Patients with Rheumatoid Arthritis: A Post Hoc Analysis", submitted to EULAR 2021).

Objectives: The objectives of this study (NCT04608344) were to evaluate the effect of filgotinib on the pharmacokinetics of atorvastatin, pravastatin, and rosuvastatin, which are sensitive substrates for the OATP-1B1/1B3, and the short-term safety of administering filgotinib with or without statins.

Methods: This was an open-label, randomized, two-way, crossover study in healthy adult volunteers (n = 27). Study participants received a single dose of atorvastatin (ATV 40mg) and a single dose of a cocktail of pravastatin (PRA 40mg)/rosuvastatin (ROS 10mg), on two different occasions with washout in between, alone or in combination with filgotinib (200mg QD for 11 days). Serial pharmacokinetic sampling was performed and pharmacokinetic parameters for each statin were calculated. Safety was assessed throughout the study. An analysis of variance using a mixed-effects model was applied to the natural logarithmic transformation of pharmacokinetic parameters (C_{max} and AUC_{inf}) for ATV, 2-OH-ATV (active metabolite of ATV), PRA, and ROS. Geometric-least squares means (GLSM) ratios and 90% confidence intervals (90% CI) of pharmacokinetic parameters were estimated for each analyte and were compared against pre-specified lack of pharmacokinetic alteration boundaries of 70 to 143%.

Results: Of the 27 enrolled participants, 25 participants completed all study treatments. Most AEs and laboratory abnormalities were Grade 1 or 2 in severity; 1 participant discontinued due to a Grade 3 increase in creatine kinase and 1 participant discontinued due to difficulty in blood draws. Following coadministration of filgotinib with ATV, relative to ATV alone, ATV AUC_{inf} was unaffected