197 (92%) and 185 (88%) entered the OL period, of whom 165 (84%) and 162 (88%) completed. At W44, ACR responses at W24 were maintained for pts who continued ABA, and improved for those who switched from PBO to ABA (Figure). Continued improvements in DAS28 (CRP) and HAQ-DI after W24 were seen for ABA and PBO/ABA groups, with mean (SE) changes from BL to W44 of –1.81 (0.09) and –1.84 (0.10) in DAS28 (CRP) (changes to W24 were –1.35 [0.10] and –0.94 [0.11]) and –0.37 (0.04) and –0.38 (0.04) in HAQ-DI (changes to W24 were –0.33 [0.04] and –0.20 [0.05]), respectively. There was minimal progression based on mean (SE) change from BL in PsA-modified total SHS at W44/52 in the ABA and PBO/ABA groups: 0.18 (0.12) vs 0.30 (0.12). Complete resolution of BL enthesitis occurred in 48.6% and 43.9% and BL dactylitis in 68.9% and 60.0% of pts with ABA and ABA/PBO, respectively, at W44/52. At W44, for ABA and PBO/ABA, PASI 50 responses were 30.1% and 34.5%; PASI 75 responses were 19.9% and 16.9%. There were no new safety signals.

Conclusions: Responses were maintained across musculoskeletal endpoints up to 1 year in a relatively refractory population of pts continuing on SC abatacept. Abatacept was well tolerated.

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From classics to new: synthetic DMARDs in RA

OP0224 SIMILAR SHORT TERM CLINICAL RESPONSE TO INITIAL TREATMENT WITH HIGH VERSUS LOW DOSE METHOTREXATE IN MONO- AND COMBINATION THERAPY IN EARLY RHEUMATOID ARTHRITIS PATIENTS

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Background: Aiming at rapid decrease of disease activity, there has been a trend to start with higher doses of methotrexate (MTX) in newly diagnosed rheumatoid arthritis (RA) patients, both as monotherapy and in combination with other antirheumatic drugs (DMARDs). We hypothesized that in combination with other very effective medication, there might be no additional benefit of high over low doses of MTX.

Objectives: To compare early clinical response to high versus low doses of MTX in mono- and combination therapy in DMARD naive early RA patients.

Methods: RA patients included in the observational international METEOR cohort with symptom duration ≤5 years, time between diagnosis and first visit ≤2 months, MTX prescribed as (part of) first treatment, no medication change within 3 to 6 months after treatment start and available outcome data on disease activity, were selected. Patients were divided into 4 medication groups: MTX monotherapy, MTX + synthetic (cs)DMARDs, MTX + oral glucocorticoid (+ possibly csDMARDs) or MTX + biologic (b)DMARDs (+ possibly csDMARDs). Missing data were imputed using multivariate normal imputation. MTX dose was dichotomized: low dose ≤10 mg/week; high dose ≥15 mg/week. A propensity score (PS) was calculated to adjust the relationship between MTX dose and outcome for potential confounding by indication. Linear mixed model analyses for DAS, DAS28, and HAQ were performed for each medication group, with MTX-dose and time (days between assessment visit and baseline assessment) as co-variates. Associations were adjusted for the PS. Random intercept and slope were used to account for irregular time intervals between visits.

Results: Patients who started on MTX monotherapy had lower baseline disease activity and fewer were erosive and autoantibody positive; other baseline characteristics were comparable between medication groups. The number of patients on combination therapy with bDMARDs was too small to perform analyses (26 visits in 11 patients). For patients starting on MTX monotherapy, MTX+csDMARDs or MTX+glucocorticoids, the PS-adjusted effects of MTX-dose (high vs low) on DAS, DAS28 and HAQ were small and not clinically meaningful. The unadjusted main associations between MTX-dose and outcomes were often in opposite direction and/or much larger than the PS adjusted associations, suggesting that confounding by indication indeed plays a role and that (at least some) correction was achieved by adjusting for the PS (table 1).

Table 1: Unadjusted and propensity score adjusted results of the linear mixed model analyses to investigate the effectiveness of high versus low methotrexate dose on disease activity (DAS and DAS28) and physical functioning (HAQ), stratified per medication group.

	DAS		DAS28		HAQ	
Methotrexate monotherapy (n patients=449, n visits=975)						
	β	95% CI	β	95% CI	β	95% CI
MTX-dose group PS adjusted	0.052	-0.17; 0.28	0.085	-0.24; 0.41	0.043	-0.11; 0.20
MTX-dose group unadjusted	-0.55	-0.71; -0.39	-0.19	-0.45; 0.071	0.17	0.059; 0.28
Methotrexate + csDMARDs (n patients=265, n visits=574)						
	DAS		DAS28		HAQ	
	β	95% CI	β	95% CI	β	95% CI
MTX-dose group PS adjusted	0.036	-0.26; 0.33	0.0066	-0.39; 0.41	-0.014	-0.21; 0.18
MTX-dose group unadjusted	-0.19	-0.45; 0.071	-0.29	-0.65; 0.065	0.080	-0.094; 0.25
Methotrexate + oral glucocorticoid (+/-csDMARDs) (n patients=485, n visits=1075)						
	DAS		DAS28		HAQ	
	β	95% CI	β	95% CI	β	95% CI
MTX-dose group PS adjusted	-0.017	-0.26; 0.22	-0.14	-0.45; 0.17	-0.023	-0.17; 0.12
MTX-dose group unadjusted	-0.33	-0.50; -0.15	-0.64	-0.86; -0.41	0.14	0.040; 0.25

DAS=disease activity score, HAQ=health assessment questionnaire, PS=propensity score, 95% CI=95% confidence interval, MTX=methotrexate. MTX-dose group is a binary variable with low dose =10 mg/week and high dose =15 mg/week. Low dose is the reference category.

Conclusions: In a daily practice derived database in DMARD-naive early RA patients, we found no early clinical benefit of high over low initial MTX doses, neither for MTX monotherapy nor for combination therapy with MTX and csDMARDs or glucocorticoids. This seems to contradict a general trend over time to start higher MTX-doses.

Disclosure of Interest: None declared

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OP0225 THE EFFECT OF A LOW VERSUS HIGH FIRST PRESCRIBED DOSE OF METHOTREXATE ON EULAR RESPONSE AT SIX MONTHS USING DATA FROM THE RAMS STUDY

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Background: Methotrexate (MTX) is one of the most commonly used drugs for the treatment of rheumatoid arthritis (RA). Recommendations by an international panel state that oral MTX should be started at 10–15mg/week, with escalation of 5mg every 2–4 weeks up to 20–30mg/week (1). In the UK, practice varies in terms of the starting dose prescribed for MTX, likely because of a lack of published evidence on the importance of MTX dose on its efficacy and safety.

Objectives: To compare 6 month response to MTX in RA patients starting 7.5mg/wk versus those starting a 15mg/wk.

Methods: Patients were recruited to the national, UK, multi-centre (n=35) longitudinal observational Rheumatoid Arthritis Medication Study (RAMS), including patients starting MTX for the first time with complete DAS28 at baseline and six months were included in this analysis. Patients were categorized into EULAR non-responders, moderate responders or good responders. Patients were categorised into those starting a low dose of MTX (≤7.5mg/wk) (LM-group) or a high

Table 1

	LM-group (n=171)	HM-group (n=639)	P
Age, years	58 (47–69)	61 (51–69)	0.13
Gender, % female	70	60	0.03
Disease duration, months	6 (3–11)	6 (3–11)	0.65
Tender joint count	7 (3–13)	5 (2–11)	0.05
Swollen joint count	5 (2–9)	5 (2–10)	0.62
Physician VAS, mm	47 (27–67)	33 (18–50)	0.0001
Patient VAS, mm	50 (26–70)	35 (20–55)	0.0001
DAS28 score at baseline	4.2 (3.4–5.2)	4.1 (3.2–5.1)	0.24
DAS28 score at 6 months	3.5 (2.7, 4.1)	3.0 (2.2, 4.1)	0.004
HAQ score	1.3 (0.6–1.8)	0.9 (0.4–1.5)	0.001
Other nbDMARD use, n (%)	30 (17)	61 (10)	0.003
EULAR response at 6 months, n (%)			0.09
Non-responders	50 (45)	184 (42)	
Moderate responders	36 (32)	108 (25)	
Good responders	26 (23)	145 (33)	
Fully adjusted RRR (95% CI)*			
Non-responders	–	ref	
Moderate responders	–	1.01 (0.56, 1.82)	0.97
Good responders	–	2.65 (1.37, 5.14)	0.004

Scores are median [IQR].

dose of MTX (≥15mg/wk) (HM-group). A multinomial logistic regression model was used to test the association between MTX start dose and EULAR response at 6 months,with adjustments (see table) (relative risk ratio (RRR), 95% CI). The model was clustered by centre to account for the prescribing preferences of individual centres.
Results: 810 patients were included in this study: 171/810 (21%) starting low dose MTX and 639/810 (79%) starting high dose MTX. Patients in the HM-group had significantly lower physician and patient VAS scores and less functional disability compared to those in the LM-group (table). These patients were also less likely to be prescribed concomitant (nbDMARDs) (17% vs. 10%). DAS28 score at 6 months was significantly lower for patients in the HM-group.
A fully adjusted multinomial logistic regression model, clustered by centre, showed that being in the high dose MTX group does not affect the odds of having a moderate response rather than no response, but does increase the odds of having a good response (RRR: 2.65 (95% CI 1.37, 5.14)).
Conclusions: Patients with RA starting MTX on a higher dose have increased odds of having a good EULAR response compared to non-response at 6 months.
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OP0226 SUSTAINED EFFECTIVENESS OF METHOTREXATE WITH STEP-DOWN GLUCOCORTICOID REMISSION INDUCTION (COBRA SLIM) FOR EARLY RHEUMATOID ARTHRITIS IN A TREAT-TO- TARGET SETTING: 2-YEAR RESULTS OF THE CARERA TRIAL

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Background: The CareRA trial showed that remission induction with MTX and a moderate-dose of Glucocorticoids (GC) (COBRA Slim) in a treat-to-target setting is effective and safe in early Rheumatoid Arthritis (eRA) patients. This strategy showed equally high remission rates at 52 weeks (W), a favourable safety profile compared to DMARD combinations and GC and very few patients had to start biologicals.
Objectives: To compare the outcome of different intensive combination treatment strategies in high-risk patients of the CareRA trial at W104, focussing on persistent disease control.
Methods: CareRA is a two-year prospective investigator-initiated pragmatic multicentre RCT; csDMARD naïve eRA patients were stratified into a high- or low-risk group based on classical prognostic markers (presence of erosions, RF, anti-CCP and DAS28-CRP). High-risk patients (n=289) were randomized to 1/3 arms: 1) COBRA Classic (n=98): Methotrexate (MTX)+Sulphasalazine+60mg prednisone tapered weekly to 7.5mg daily from W7; 2) COBRA Slim (n=98): MTX+30mg prednisone tapered to 5 mg daily from W6; 3) COBRA Avant-Garde (n=93): MTX+Leflunomide+30mg prednisone tapered to 5 mg daily from W6. From W28, GCs were tapered in all patients and stopped at W34. A predefined treat-to-target approach was applied until W52 and afterwards treatment was at the discretion of the rheumatologist. From W40, DMARD monotherapy was aimed for. From W28 onwards patients were evaluated every 3 months till W104. Efficacy measures were proportions of DAS28-CRP remission, good EULAR response, clinically meaningful HAQ response, HAQ=0 (ITT analysis). Adverse events related to therapy (AEs) were registered. Missing data were imputed by last observation carried forward.
Results: Remission rates at W104 in high-risk patients were 65.3%, 73.5% and 73.1% in the Classic, Slim and Avant-Garde group respectively (p=0.369). Also, other efficacy outcomes did not differ between groups (see table). From the high-risk patients that were in remission at year 1, 54.7%, 67.8% and 70.2% in the Classic, Slim and Avant-Garde group respectively, stayed in remission at every three-monthly evaluation until w104. Also DAS28-CRP scores remained relatively stable during the second year in these groups. In high-risk patients, the total numbers of AEs reported as related to study therapy, were 209 in 72 Classic patients, 164 in 69 Slim patients and 208 in 74 Avant-Garde patients (p=0.029). Serious AEs were reported in 3 Classic, 4 Slim and 3 Avant-Garde patients. Biologicals were started in 44 high-risk patients (15.2%), of which 7 receiving 2 different biologicals and 2 receiving 3 different ones. Biologicals were administered in 18 Classic, 11 Slim and 15 Avant-Garde patients.

	COBRA classic N=98	COBRA slim (high-risk) N=98	COBRA Avant-Garde N=93	p-value
DAS28-CRP change BL-w104	2.6±1.4	2.6±1.3	2.6±1.6	0.966
DAS28-CRP change w52-w104	0.0±1.0	0.2±1.0	0.3±1.1	0.112
DAS28 Remission w52	65.3%	60.2%	61.3%	0.741
DAS28 Remission w104	65.3%	73.5%	73.1%	0.369
Good EULAR response	78.6%	81.6%	78.5%	0.826
Clinically meaningful HAQ change	70.4%	62.2%	70.7%	0.363
HAQ = 0	39.8%	37.8%	38.7%	0.958

DAS28-CRP= 28 Joint disease activity score calculated with C-reactive protein; remission = DAS28-CRP <2.6; low disease activity = DAS-CRP ≤3.2; good EULAR response = low disease activity with a DAS28-CRP change >1.2; HAQ= health assessment questionnaire; clinically meaningful HAQ change = HAQ change >0.22.

Conclusions: All groups showed persistently high remission rates 2 years after remission induction with csDMARDs and GCs in a treat to target setting. COBRA Slim showed comparable efficacy with less adverse events compared to DMARD combinations with moderate or high GC induction dosages. In almost 70% of COBRA Slim patients achieving remission at year 1, this was maintained throughout the second year.
Disclosure of Interest: None declared
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OP0227 REMISSION INDUCTION WITH METHOTREXATE STEP-UP THERAPY VERSUS COMBINATION OF HYDROXYCHLOROQUINE, METHOTREXATE AND TRIAMCINOLONE: 3 YEAR RESULTS

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Background: The effectiveness of treat to target (T2T) in RA is widely acccepted, but there is no consensus regarding the best initial treatment in early rheumatoid arthritis[1]. Therefore, it is important to evaluate the results of such strategies in real life cohorts[2,3].
Objectives: Compare the effectiveness of step-up methotrexate (MTX) monotherapy and combination of hydroxychloroquine (HCQ), methotrexate and intramuscular injection of triamcinolone 80–120mg as initial treatment in early RA.
Methods: Historical cohorts of patients treated with MTX monotherapy (disease onset 2006–2011, N=297) and combination therapy (2012–2016, N=156) were compared. In both cohorts a b-DMARD was advised when no remission was reached within 6 months or in case of sustained activity thereafter. Baseline characteristics and disease activity (DAS28) measurements (N=4956, average 4.1/year) in the first 3 years of follow-up were available. The primary outcome measure was the proportion of patients having reached at least one DAS28 <2.6 (remission) during follow-up. Secondary outcomes were sustained remission over 36 months and time to first b-DMARD.
Results: Three patients did not start MTX, and 11 and 2 patients in the step-up and combination cohorts respectively did not have complete follow-up (Table). Within 12 months, more patients on combination treatment reached remission (88,2% vs 72.2%). In the second year these changed to 86.5% and 82.0% respectively. Combination treatment resulted in a higher percentage of DAS measurements below 2.6 over 3 years, reflecting sustained remission (Figure). A b-DMARD was started within 24 months in 20.6% of patients on monotherapy versus 14.1% on combination treatment, with an equal mean time to first b-DMARD of 12 vs 11 months after start of initial treatment.

Table 1

Table	MTX monotherapy (N=297)	MTX with HCQ and steroids (N=156)
Female, N (%)	180 (60.6)	101 (64.7)
Age (y), mean (SD, range)	59.5 (14.3, 18–89)	58.8 (12.9, 19–86)
Rheumatoid factor (N, %)	183 (61.6)	112 (71.8)
ACPA (N, %)	157 (65.3)	111 (71.2)
Follow-up (months) (range)	81 (8–132)	42 (11–62)
End of follow-up <3 yrs		
Death	4 (1.3%)	1 (0.6%)
Remission	4 (1.3%)	1 (0.6%)
Did not start MTX/Other	5 (1.7%)	1 (0.6%)
Any remission (DAS28 <2.6)		
First year	72.2%	88.2%
Second year	82.0%	86.5%
Third year	85.9%	87.0%
Start b-DMARD therapy		
First year	32 (10.8%)	17 (10.9%)
Second year	29 (9.8%)	5 (3.2%)
Third year	8 (2.7%)	5/104 (4.8%)

Conclusions: Combination treatment results in more remissions in the first year of treatment. In the second and third year the remission percentage on monotherapy comes close to combination treatment, at the cost of a 6% higher proportion of patients stepping up to biologicals. Overall, the combination of MTX with HCQ and triamcinolone results in more sustained remissions.
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