Supplementary table S1: Comparison of radiographic and clinical efficacy responses to rituximab 2x500 mg +MTX versus rituximab 2x1000 mg +MTX at weeks 52 or 104

Outcome	Rituximab 2×500 mg + MTX	Rituximab 2×1000 mg + MTX	Ex-p value
Screening to week 52			
Radiographic (mITT)			
Change in mTSS	0.60	0.34	0.0762
Change in total erosion score	0.40	0.19	0.0832
Change in JSN score	0.19	0.14	0.4058
Disease activity (ITT)			
ACR20	76.7%	80.0%	0.3513
ACR50	59.4%	64.8%	0.1858
ACR70	42.2%	46.8%	0.2642
ACR90	17.3%	16.4%	0.8046
ACRn	41.49	45.05	0.3164
EULAR good response	39.8%	42.8%	0.4580
DAS28 LDA	40.2%	42.8%	0.4974
DAS28 remission	25.3%	30.4%	0.1867
Physical function (ITT)			
HAQ-DI decrease 0.22	86.7%	86.8%	0.9357
Screening to week 104			
Radiographic (mITT)			
Change in mTSS	0.76	0.41	0.1216
Change in total erosion score	0.50	0.23	0.1125
Change in JSN score	0.26	0.18	0.5156
Disease activity (ITT)			

ACR20	74.7%	74.0%	0.8480
ACR50	59.8%	62.4%	0.5481
ACR70	42.2%	46.4%	0.3279
ACR90	20.5%	23.2%	0.4611
ACRn	44.80	47.75	0.4486
EULAR good response	44.2%	47.6%	0.4490
DAS28 LDA	44.6%	47.6%	0.4831
DAS28 remission	33.7%	32.0%	0.6863
Physical function (ITT)			
HAQ-DI decrease ≥0.22	83.1%	85.2%	0.4819

p values are for comparison of 2×500 mg + MTX vs. 2×1000 mg + MTX . All p values are exploratory/descriptive. mTSS, total erosion score and joint space narrowing score were tested using the Van-Elteren test adjusted for the stratification factors (RF status, region) applied at randomisation. ACRn, DAS28 and HAQ-DI were tested using analysis of variance model adjusted for baseline stratification factors and baseline values for DAS28 and HAQ-DI; Cochran–Mantel–Haenszel test for categorical variables. Linear extrapolation has been used on radiographic endpoints, last observation carried forward or non-responder imputation has been used on other endpoints. ACRn, American College of Rheumatology index of improvement in rheumatoid arthritis; DAS28, Disease Activity Score in 28 joints; EULAR, European League Against Rheumatism; HAQ-DI, Health Assessment Questionnaire-Disability Index; JSN, joint space narrowing; LDA, low disease activity; MTX, methotrexate; mTSS, total Genant-modified Sharp score.

Supplementary table S2: Subgroup analysis in patients seropositive or seronegative for RF and/or ACPA

Outcome	**Placebo + MTX**	**Rituximab 2×500 mg + MTX**	**Rituximab 2×1000 mg + MTX**
Probability of no radiographic progression, OR (95% CI) (mITT)			

RF and/or ACPA seropositive		1.737	2.228
		(1.182–2.554)	(1.513–3.281)
RF and ACPA seronegative		0.900	1.833
		(0.263–3.075)	(0.558–6.027)
ACR50, % (ITT)			
RF and/or ACPA seropositive	38	61**	65**
RF and ACPA seronegative	64	46	42

****Ex-p<0.0001 vs placebo + MTX. All p values are exploratory/descriptive.**

RF and/or ACPA seropositive group mITT and ITT (rituximab 2×500 mg + MTX, 2×1000 mg + MTX, placebo): n=219, 218, 212 and 227, 224, 227, respectively (total number of patients in the rituximab 1000 mg autoantibody subgroups differed because two patients could not be classified [seronegative for RF but no ACPA data, so unable to assign to either group]). RF and ACPA seronegative group mITT and ITT (rituximab 2×500 mg + MTX, 2×1000mg + MTX, placebo): n=20, 24, 21 and 22, 24, 22, respectively. OR of probability of no radiographic progression for rituximab relative to placebo. ACPA, anti-citrullinated peptide antibody; ACR, American College of Rheumatology; CI, confidence interval; MTX, methotrexate; OR, odds ratio; RF, rheumatoid factor.