

Supplementary Table 2a: Clinical outcomes at week 52 per treatment arm in the high-risk and low-risk group by Per Protocol Analysis

	COBRA Classic	COBRA Slim	COBRA Avant-Garde	p-value
Number of patients	62	75	60	
DAS28 (CRP) Change	2.7±1.3	2.5±1.4	2.7±1.5	0.547
Remission	79.0%	69.3%	75.0%	0.427
Low Disease Activity	88.7%	86.7%	88.3%	0.926
Good EULAR Response	82.3%	78.7%	80.0%	0.870
Moderate EULAR Response	90.3%	89.3%	95.0%	0.476
HAQ Change	0.7±0.6	0.5±0.6	0.7±0.7	0.088
Clinically Meaningful HAQ Change	69.3%	68.0%	80.0%	0.257
HAQ = 0	46.8%	40.0%	53.3%	0.302

	MTX-TSU	COBRA Slim	p-value
Number of patients	36	30	
DAS28 (CRP) Change	2.2±1.8	2.6±1.5	0.318
Remission	66.7%	83.3%	0.123
Low Disease Activity	88.9%	96.7%	0.234
Good EULAR Response	66.7%	76.7%	0.372
Moderate EULAR Response	80.6%	93.3%	0.132
HAQ Change	0.5±0.6	0.7±0.7	0.358
Clinically Meaningful HAQ Change	58.3%	66.7%	0.487
HAQ = 0	30.6%	56.7%	0.033

DAS28(CRP)= 28 Joint disease activity score calculated with C-reactive protein; DAS28(CRP) change= DAS score on baseline minus DAS score on week 52; Remission was defined as DAS28(CRP) <2.6; Low Disease Activity was defined as DAS(CRP) ≤3.2; Good EULAR Response was defined as low disease activity with a DAS28(CRP) change >1.2. Moderate EULAR Response was defined as DAS28(CRP) change >1.2 or a DAS28(CRP) ≤5.1 and a DAS28(CRP) change between 0.6 and 1.2; HAQ = Health Assessment Questionnaire; HAQ change = Baseline HAQ minus week 52 HAQ; clinically meaningful HAQ change was defined as a HAQ change >0.22. Data are presented as mean ± standard deviation or as percentages. Statistical analysis was performed by χ^2 or Kruskal-Wallis test. A p-value <0.05 was considered statistically significant. Δ= difference; C.I. = Confidence Intervals (calculated by the Newcombe method for differences between proportions).

Supplementary Table 2b: Different measures of remission (ITT analysis)

	COBRA Classic	COBRA Slim (High Risk)	COBRA Avant-Garde	p-value	MTX-TSU	COBRA Slim (Low Risk)	p-value
Number of patients	98	98	93		47	43	
SDAI remission	37.8%	30.6%	45.2%	0.116	29.8%	44.2%	0.157
Boolean Remission	26.5%	17.3%	30.1%	0.105	21.3%	37.2%	0.096
DAS28(ESR) Remission	58.2%	52.0%	54.8%	0.689	55.3%	62.8%	0.472

SDAI= Simplified Disease Activity Index; SDAI= TJC28+SJC28+CRP (mg/dl)+PGA(0-10)+PhGA(0-10); SDAI remission= SDAI≤3.3, Boolean Remission= TJC28≤1 AND SJC28≤1 AND PGA≤1 AND CRP≤1. DAS28 (ESR) remission= DAS28(ESR)≤2.6