SUPPLEMENTARY MATERIALS

Supplementary Table 1 Summary of phase 3 studies included in the post hoc analysis

Study	ClinicalTrials.gov identifier	Patient population	Number of patients randomised and treated	Treatment arms	Background therapy	Study duration
ORAL Solo [1]	NCT00814307	Active RA; DMARD-IR	610	Tofacitinib 5 mg BID Tofacitinib 10 mg BID Placebo*	-	6 months
ORAL Start [2]	NCT01039688	Active RA; MTX-naïve	956	Tofacitinib 5 mg BID Tofacitinib 10 mg BID MTX†	-	24 months
ORAL Step [3]	NCT00960440	Active RA; TNFi-IR	399	Tofacitinib 5 mg BID Tofacitinib 10 mg BID Placebo*	MTX	6 months
ORAL Scan [4]	NCT00847613	Active RA; MTX-IR	797	Tofacitinib 5 mg BID Tofacitinib 10 mg BID Placebo‡	MTX	24 months
ORAL Sync [5]	NCT00856544	Active RA; DMARD-IR	792	Tofacitinib 5 mg BID Tofacitinib 10 mg BID Placebo‡	csDMARD	12 months
ORAL Standard [6]	NCT00853385	Active RA; MTX-IR	717	Tofacitinib 5 mg BID Tofacitinib 10 mg BID Placebo‡	MTX	12 months

	Adalimumab 40 mg Q2W

*Patients receiving placebo advanced blindly to tofacitinib 5 or 10 mg BID at Month 3.

†Starting dose of 10 mg/week, followed by increments of 5 mg/week every 4 weeks to 20 mg/week by Week 8.

‡Patients receiving placebo who did not respond (ie, those not achieving ≥20% improvement in swollen and tender joint counts) at Month 3 were blindly advanced to tofacitinib 5 or 10 mg BID; at Month 6, all remaining placebo patients were advanced to tofacitinib.

BID, twice daily; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DMARD, disease-modifying antirheumatic drug; IR, inadequate responder; MTX, methotrexate; Q2W, once every 2 weeks; RA, rheumatoid arthritis; TNFi, tumour necrosis factor inhibitors.

Supplementary Table 2 Additional baseline characteristics

BMI category, kg/m^2	Tofacitinib 5 mg BID (N=1589)			Tofacitinib 10 mg BID (N=1611)			Placebo (N=680)		
	<25 (N1=686)	25 to <30 (N1=515)	≥30 (N1=388)	<25 (N1=696)	25 to <30 (N1=472)	≥30 (N1=443)	<25 (N1=308)	25 to <30 (N1=186)	≥30 (N1=186)
Females, n (%)	581 (84.7)	409 (79.4)	323 (83.3)	608 (87.4)	374 (79.2)	375 (84.7)	252 (81.8)	142 (76.3)	158 (85.0)
RA duration in years, mean (SD)	7.1 (7.3)	7.9 (8.7)	7.3 (7.7)	7.9 (8.3)	7.5 (8.1)	7.5 (7.6)	8.6 (8.4)	10.0 (8.6)	9.6 (8.3)
Prior MTX, n (%)	515 (75.1)	378 (73.4)	293 (75.5)	508 (73.0)	340 (72.0)	335 (75.6)	293 (95.1)	177 (95.2)	178 (95.7)
Baseline csDMARD* use, n (%)	395 (57.6)	274 (53.2)	228 (58.8)	390 (56.0)	256 (54.2)	249 (56.2)	236 (76.6)	140 (75.3)	136 (73.1)
Prior non-TNFi bDMARDs, n (%)	24 (3.5)	27 (5.2)	24 (6.2)	26 (3.7)	20 (4.2)	26 (5.9)	10 (3.3)	13 (7.0)	23 (12.4)
Baseline GC use, n (%)	397 (57.9)	292 (56.7)	215 (55.4)	384 (55.2)	259 (54.9)	220 (49.7)	183 (59.4)	108 (58.1)	103 (55.4)
Baseline GC dose, mg/day,† mean (SD)	6.2 (2.6)	6.8 (3.0)	7.3 (5.9)	6.1 (2.7)	7.3 (12.4)	7.5 (7.2)	6.5 (2.9)	7.1 (2.8)	6.9 (2.6)

N1 values may vary for each outcome based on the number of patients assessed.

*Including MTX.

†Among patients receiving GC at baseline.

bDMARD, biologic disease-modifying antirheumatic drug; BID, twice daily; BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; GC, glucocorticoids; MTX, methotrexate; n, number of patients with characteristic; N, number of patients in each treatment group with a baseline BMI value; N1, number of patients in each BMI category; RA, rheumatoid arthritis; SD, standard deviation; TNFi, tumour necrosis factor inhibitors.

Supplementary Table 3. Univariate model results summarising odds ratio (95% CI) for ACR50 response and estimates* (95% CI) for continuous outcomes at Month 6, for BMI as a categorical or continuous variable

Tofacitinib	**ACR50 response**		**ΔDAS28-4(ESR)**		**ΔDAS28-4(CRP)**		**ΔCDAI**		**ΔHAQ-DI**	
dose (BID)	**5 mg**	**10 mg**	**5 mg**	**10 mg**	**5 mg**	**10 mg**	**5 mg**	**10 mg**	**5 mg**	**10 mg**
BMI category, kg/m^2										
25 to <30 vs <25	0.83 (0.65 to 1.06)	0.88 (0.69 to 1.13)	0.08 (-0.09 to 0.26)	0.10 (-0.08 to 0.28)	0.06 (-0.10 to 0.23)	0.07 (-0.11 to 0.24)	-0.44 (-2.13 to 1.24)	-0.75 (-2.43 to 0.93)	0.03 (-0.05 to 0.11)	0.04 (-0.04 to 0.12)
≥30 vs <25	0.82 (0.63 to 1.08)	0.72 (0.56 to 0.92)	0.13 (-0.06 to 0.32)	0.24 (0.06 to 0.42)	0.14 (-0.05 to 0.32)	0.20 (0.03 to 0.37)	-0.67 (-2.54 to 1.20)	-0.26 (-1.97 to 1.45)	0.10 (0.02 to 0.19)	0.06 (-0.02 to 0.15)
BMI	0.98 (0.97 to 1.00)	0.97 (0.95 to 0.99)	0.01 (0.00 to 0.02)	0.02 (0.01 to 0.03)	0.01 (0.00 to 0.02)	0.02 (0.01 to 0.03)	0.00 (-0.12 to 0.11)	0.00 (-0.11 to 0.11)	0.01 (0.00 to 0.01)	0.00 (0.00 to 0.01)

Red text indicates statistical significance at p<0.05. For categorical variables with more than two levels, the pairwise comparisons are considered significant if both the overall and pairwise p values are <0.05.

*For categorical BMI vs continuous outcomes, the estimate reflects the least squares mean difference between categories. For continuous BMI vs continuous outcomes, the estimate is the slope of the relationship.

Δ, change from baseline; ACR, American College of Rheumatology; BID, twice daily; BMI, body mass index; CDAI, Clinical Disease Activity Index; CI, confidence interval; DAS28-4(CRP), Disease Activity Score in 28 joints, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index.

Supplementary Table 4. Comparison of stepwise and Lasso/1se* analyses (with no forced variables) for selection of BMI in the multivariable final models

		Stepwise		Lasso	
		Tofacitinib 5 mg BID	**Tofacitinib 10 mg BID**	**Tofacitinib 5 mg BID**	**Tofacitinib 10 mg BID**
Disease activity measure	**BMI†**	**Estimate (95% CI)**	**Estimate (95% CI)**	**Estimate (95% CI)**	**Estimate (95% CI)**
ACR50 response‡	25 to <30 vs <25 kg/m^2				
	≥30 vs <25 kg/m^2				
	Continuous		0.98 (0.96 to 1.00)		0.98 (0.96 to 1.00)
ΔDAS28-4(ESR)	25 to <30 vs <25 kg/m^2	0.09 (-0.07 to 0.26)	0.13 (-0.03 to 0.29)		0.15 (-0.01 to 0.31)
	≥30 vs <25 kg/m^2	0.07 (-0.11 to 0.25)	0.21 (0.05 to 0.38)		0.25 (0.09 to 0.41)
	Continuous		0.02 (0.01 to 0.03)		0.02 (0.01 to 0.03)
ΔDAS28-4(CRP)	25 to <30 vs <25 kg/m^2		0.10 (-0.04 to 0.24)		0.10 (-0.05 to 0.25)
	≥30 vs <25 kg/m^2		0.21 (0.06 to 0.36)		0.20 (0.04 to 0.36)
	Continuous		0.02 (0.01 to 0.03)	0.01 (0.00 to 0.02)	0.02 (0.01 to 0.03)
ΔCDAI	25 to <30 vs <25 kg/m^2				
	≥30 vs <25 kg/m^2				
	Continuous				
ΔHAQ-DI	25 to <30 vs <25 kg/m^2	0.01 (-0.06 to 0.08)			

≥30 vs <25 kg/m^2	0.10 (0.03 to 0.18)	
Continuous	0.01 (0.00 to 0.01)	0.01 (0.00 to 0.01)

Red text indicates statistical significance at p<0.05. For categorical variables with more than two levels, the pairwise comparisons are considered significant if both the overall and pairwise p values are <0.05.

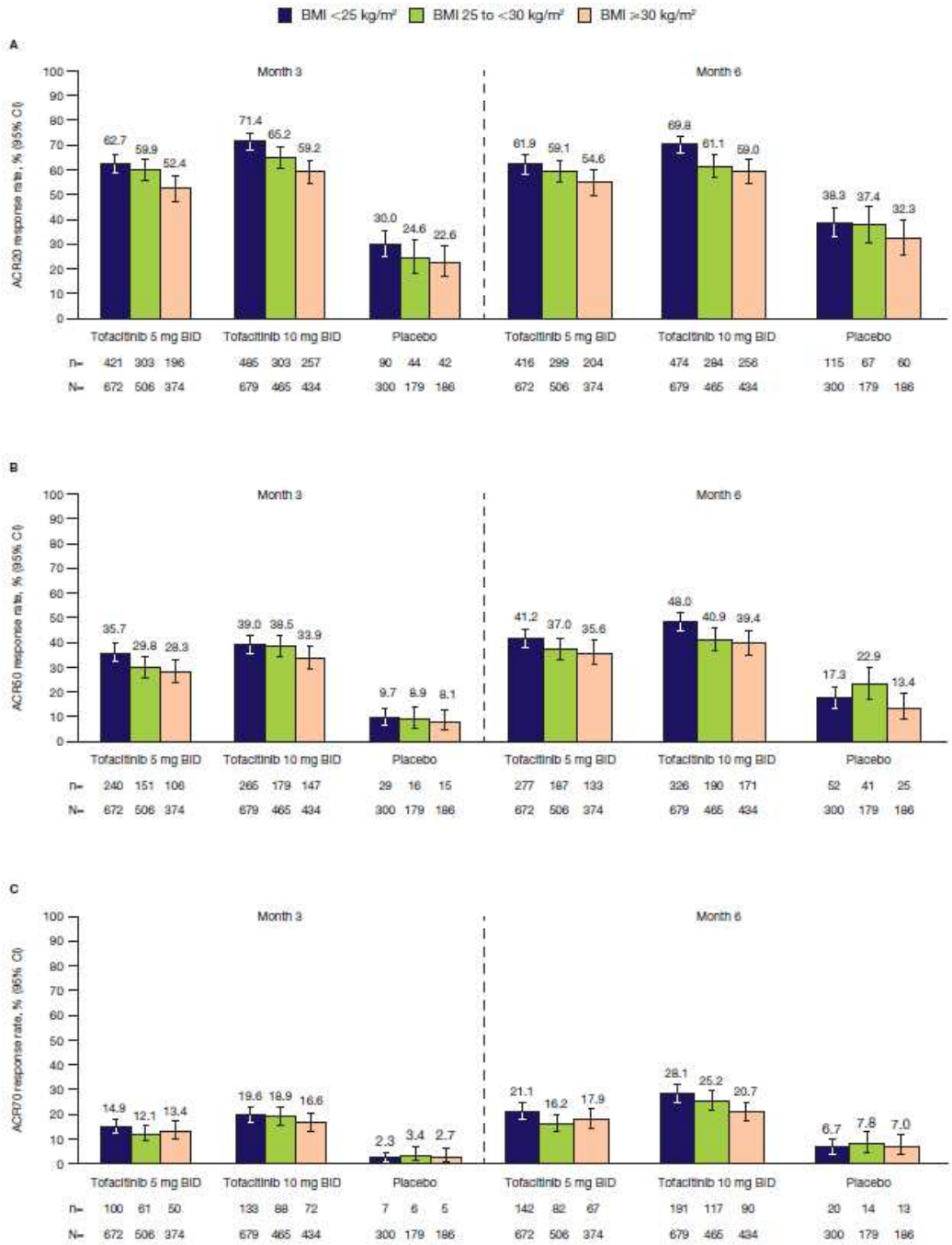
*Final model includes all selected covariates using the lambda 1se criterion (the largest value of lambda such that the error is within 1 standard error of the minimum) in the Lasso selection procedure.

†For categorical BMI vs continuous outcomes, the estimate reflects the least squares mean difference between categories. For continuous BMI vs continuous outcomes, the estimate is the slope of the relationship.

‡For ACR50 response, the estimate is the odds ratio.

Δ, change from baseline; ACR, American College of Rheumatology; BID, twice daily; BMI, body mass index; CDAI, Clinical Disease Activity Index; CI, confidence interval; DAS28-4(CRP), Disease Activity Score in 28 joints, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; Lasso, least absolute shrinkage and selection operator; VAS, visual analogue scale.

Supplementary Figure 1 Proportion of patients achieving A) ACR20, B) ACR50, and C) ACR70 response at Months 3 and 6, stratified by baseline BMI (FAS, NRI).



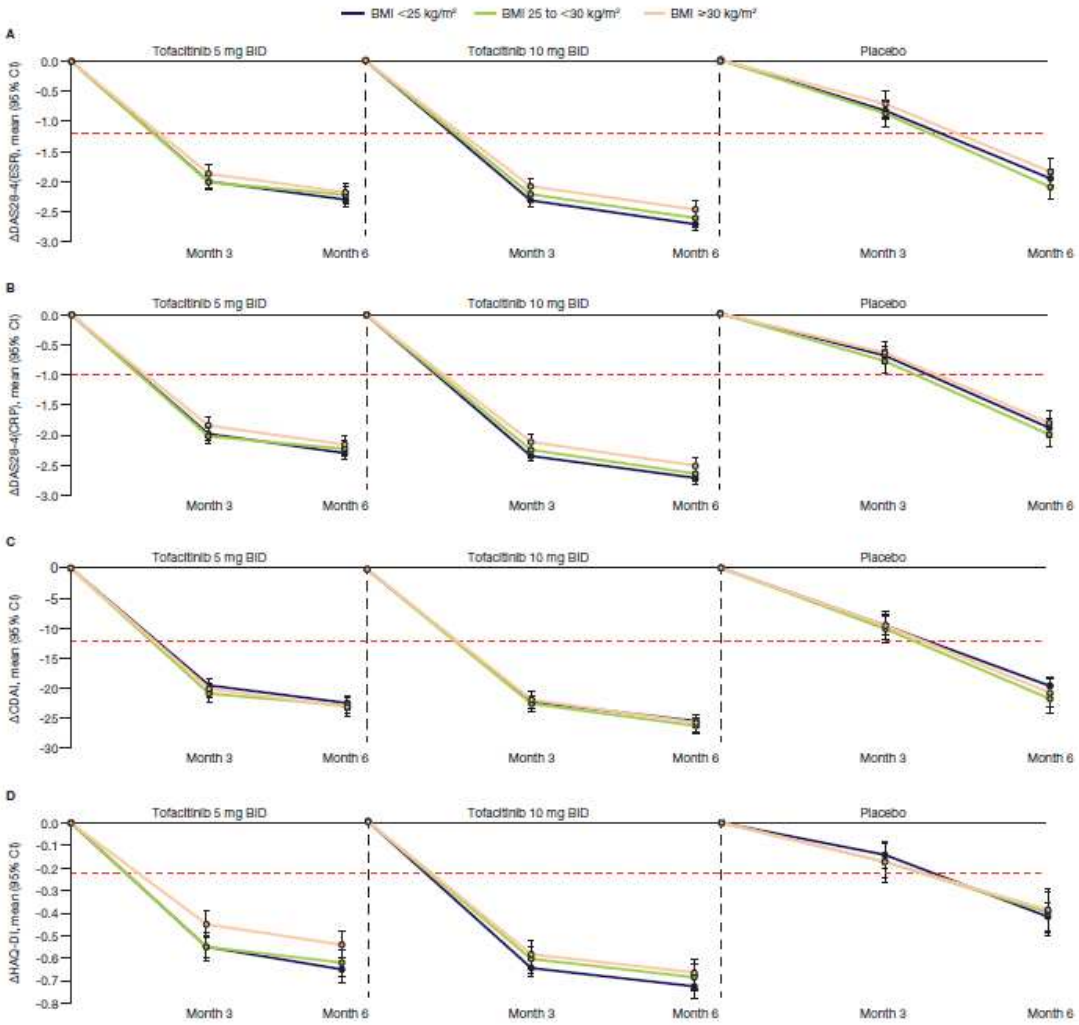
Across all BMI categories, ACR20/50/70 response rates were statistically significant ($p<0.05$) with tofacitinib 5 or 10 mg BID vs placebo, at Month 3 and Month 6.

For this analysis, a difference between BMI categories of ≥10% was considered clinically meaningful.

The placebo group at Month 6 includes patients who received placebo through to Month 3 and advanced to tofacitinib from Month 3 to Month 6 per protocol.

ACR, American College of Rheumatology; BID, twice daily; BMI, body mass index; CI, confidence interval; FAS, full analysis set; n, number of patients with response; N, number of evaluable patients; NRI, non-responder imputation.

Supplementary Figure 2 Change from baseline in A) DAS28-4(ESR), B) DAS28-4(CRP), C) CDAI, and D) HAQ-DI through to Month 6 in patients receiving tofacitinib 5 mg BID, tofacitinib 10 mg BID, or placebo, stratified by baseline BMI (FAS, no imputation).

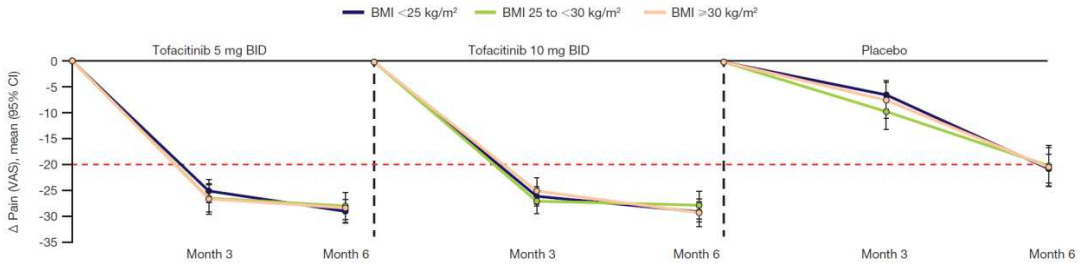


The placebo group at Month 6 includes patients who received placebo through to Month 3 and advanced to tofacitinib from Month 3 to Month 6 per protocol.

For this analysis, differences of ≥1.2 (DAS28-4[ESR]), ≥1.0 (DAS28-4[CRP]), ≥12 (CDAI) [7], and ≥0.22 (HAQ-DI) [8] between BMI categories were considered clinically meaningful (red dashed lines in each panel).

Δ, change from baseline; BID, twice daily; BMI, body mass index; CDAI, Clinical Disease Activity Index; CI, confidence interval; DAS28-4(CRP), Disease Activity Score in 28 joints, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; FAS, full analysis set; HAQ-DI, Health Assessment Questionnaire-Disability Index.

Supplementary Figure 3 Change from baseline in pain (VAS) through to Month 6 in patients receiving tofacitinib 5 mg BID, tofacitinib 10 mg BID, or placebo, stratified by baseline BMI (FAS, no imputation).

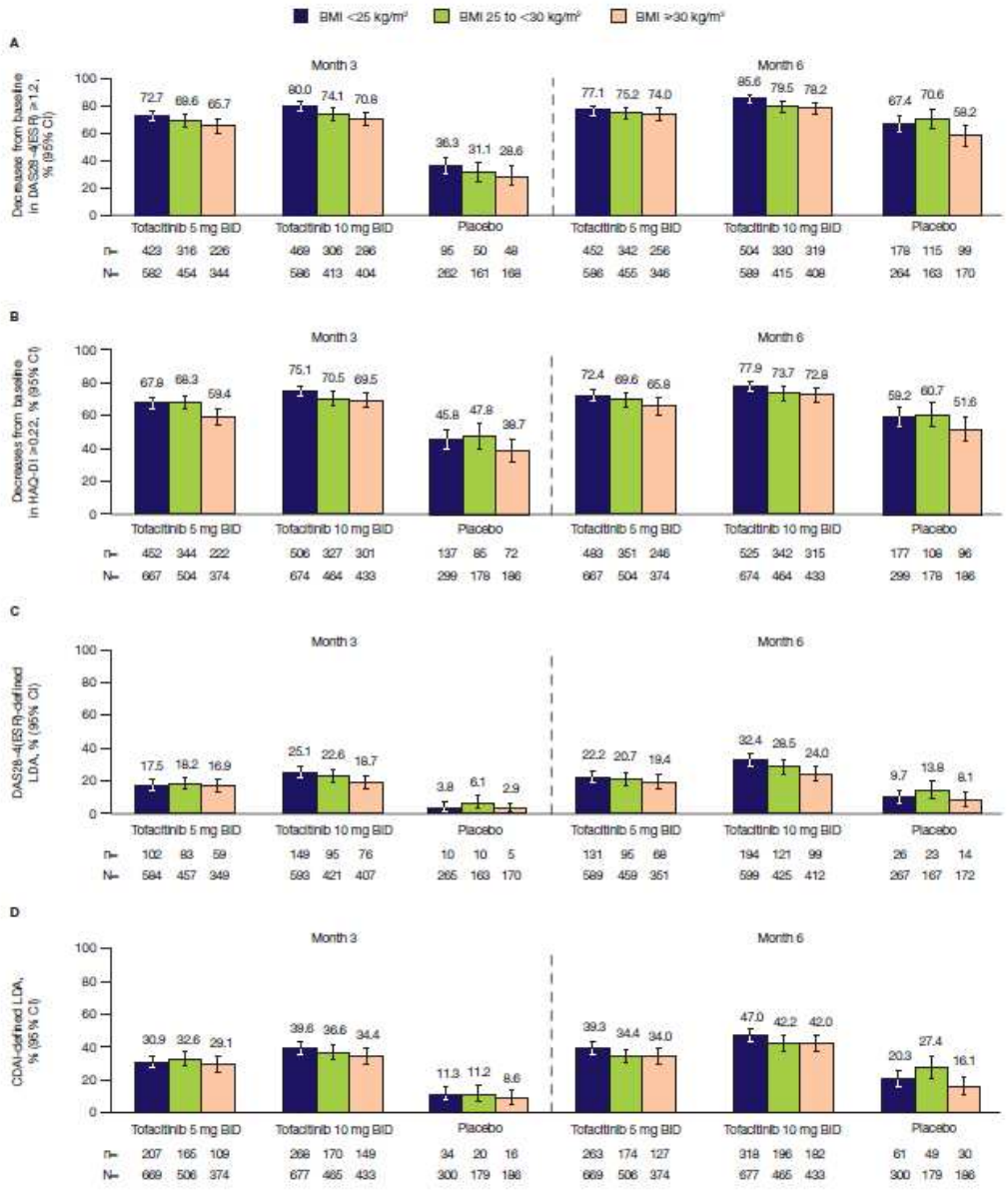


The placebo group at Month 6 includes patients who received placebo through to Month 3 and advanced to tofacitinib from Month 3 to Month 6 per protocol.

For this analysis, a difference of ≥20 in pain (VAS) between BMI categories was considered clinically meaningful (red dashed line) [7].

Δ, change from baseline; BID, twice daily; BMI, body mass index; CI, confidence interval; FAS, full analysis set; VAS, visual analogue scale.

Supplementary Figure 4 The proportion of patients reporting improvements ≥MCID defined by decreases from baseline in A) DAS28-4(ESR) ≥1.2 and B) HAQ-DI ≥0.22, and LDA defined by C) DAS28-4(ESR) ≤3.2 and D) CDAI ≤10 at Months 3 and 6 (FAS, NRI), stratified by baseline BMI category.

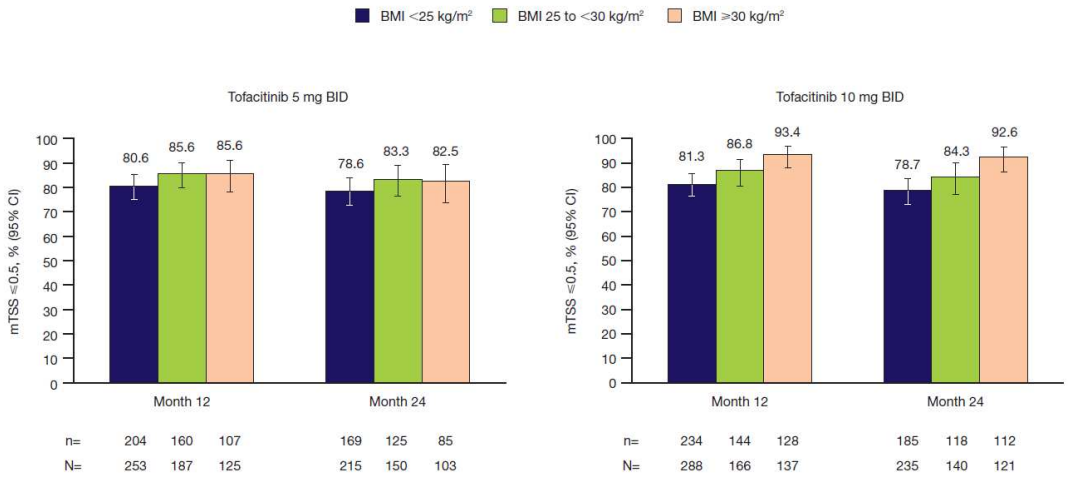


The placebo group at Month 6 includes patients who received placebo through to Month 3 and advanced to tofacitinib from Month 3 to Month 6 per protocol.

For this analysis, a difference between BMI categories of ≥10% was considered clinically meaningful.

BID, twice daily; BMI, body mass index; CDAI, Clinical Disease Activity Index; CI, confidence interval; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; FAS, full analysis set; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDA, low disease activity; MCID, minimum clinically important difference; n, number of patients meeting criteria for improvement ≥MCID; N, number of evaluable patients; NRI, non-responder imputation.

Supplementary Figure 5 The proportion of patients with changes from baseline in mTSS ≤0.5 (radiographic non-progressors) at Months 12 and 24 (FAS, no imputation).



For this analysis, a difference between BMI categories of ≥10% was considered clinically meaningful.

BID, twice daily; BMI, body mass index; CI, confidence interval; FAS, full analysis set; mTSS, modified Total Sharp Score; n, number of patients meeting criteria for radiographic non-progression (change from baseline in mTSS ≤0.5); N, number of evaluable patients.

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