Supplementary section

Online Supplementary Table 1. Efficacy responses at Month 3 for bDMARD-naïve vs 1 TNFi vs multiple TNFi patients in the P2/P3 cohort

Parameter, % (95% CI)	bDMARD-naïve			1 previous TNFi			≥2 previous TNFi		
	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
	N=638	N=1043	N=1066	N=113	N=145	N=154	N=58	N=77	N=62
ACR20	26.5 (23.1, 30.1)	60.3* (57.3, 63.3)	66.1* (63.2, 69.0)	27.4 (19.5, 36.6)	46.2* (37.9, 54.7)	50.0* (41.8, 58.2)	17.2 (8.6, 29.4)	39.0* (28.0, 50.8)	50.0* (37.0, 63.0)
ACR50	9.7 (7.5, 12.3)	32.7* (29.9, 35.6)	36.6* (33.7, 39.6)	10.6 (5.6, 17.8)	29.0* (21.7, 37.1)	27.3* (20.4, 35.0)	6.9 (1.9, 16.7)	20.8* (12.4, 31.5)	25.8* (15.5, 38.5)
ACR70	2.8 (1.7, 4.4)	12.9* (11.0, 15.1)	18.4* (16.1, 20.8)	2.7 (0.6, 7.6)	11.7* (7.0, 18.1)	12.3* (7.6, 18.6)	3.4 (0.4, 11.9)	9.1 (3.7, 17.8)	8.1 (2.7, 17.8)
CDAI≤10[a]	14.3 (11.5, 17.4)	32.4* (29.5, 35.4)	39.8* (36.8, 42.9)	14.4 (8.1, 23.0)	35.8* (27.7, 44.6)	38.7* (30.7, 47.3)	13.7 (5.7, 26.3)	23.2 (13.9, 34.9)	28.1 (17.0, 41.5)
CDAI≤2.8[b]	0.7 (0.2, 1.8)	6.4* (5.0, 8.2)	9.0* (7.3, 11.0)	1.0 (0.0, 5.6)	6.7* (3.1, 12.4)	6.3* (2.9, 11.7)	0.0 (0.0, 7.0)	4.3 (0.9, 12.2)	5.3 (1.1, 14.6)
SDAI≤11[a]	14.2 (11.4, 17.3)	34.6* (31.6, 37.6)	41.1* (38.0, 44.2)	14.4 (8.1, 23.0)	35.3* (27.3, 44.1)	41.1* (32.9, 49.7)	11.8 (4.4, 23.9)	23.2 (13.9, 34.9)	31.6* (19.9, 45.2)

Parameter, % (95% CI)	bDMARD-naïve			1 previous TNFi			≥2 previous TNFi		
	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
	N=638	N=1043	N=1066	N=113	N=145	N=154	N=58	N=77	N=62
SDAI≤3.3[b]	0.7 (0.2, 1.8)	6.4* (4.9, 8.1)	9.3* (7.6, 11.3)	0.0 (0.0, 3.7)	7.5* (3.7, 13.4)	8.5* (4.5, 14.4)	0.0 (0.0, 7.0)	5.8* (1.6, 14.2)	7.0* (1.9, 17.0)
DAS28-4(ESR)<3.2[a]	4.5 (3.0, 6.5)	16.6* (14.3, 19.2)	22.9* (20.3, 25.8)	6.7 (2.7, 13.3)	13.1 (7.8, 20.1)	16.2* (10.4, 23.5)	0.0 (0.0, 6.8)	13.0* (6.1, 23.3)	15.3* (7.2, 27.0)
DAS28-4(ESR)<2.6[b]	2.3 (1.2, 3.8)	7.3* (5.7, 9.2)	11.5* (9.5, 13.7)	1.9 (0.2, 6.7)	6.9 (3.2, 12.7)	8.1* (4.1, 14.0)	0.0 (0.0, 6.8)	7.2* (2.4, 16.1)	5.1 (1.1, 14.1)
HAQ-DI≤0.5	18.2 (14.8, 22.1)	40.3* (37.0, 43.6)	46.1* (42.8, 49.5)	20.6 (13.4, 29.5)	30.9 (23.4, 39.3)	40.4* (32.4, 48.8)	19.6 (10.2, 32.4)	32.0 (21.7, 43.8)	36.7* (24.6, 50.1)
LS mean (95% CI) change from baseline in DAS28-4(ESR)	-0.8 (-0.9, -0.7)	-1.9* (-2.0, -1.8)	-2.1* (-2.2, -2.0)	-0.8 (-1.1, -0.4)	-1.7* (-2.1, -1.4)	-2.0* (-2.4, -1.7)	-0.6 (-1.1, -0.0)	-1.8* (-2.3, -1.3)	-2.1* (-2.6, -1.5)
LS mean (95% CI) change from baseline in HAQ-DI	-0.1 (-0.2, -0.1)	-0.5* (-0.5, -0.4)	-0.5* (-0.6, -0.5)	-0.1 (-0.2, 0.0)	-0.3* (-0.4, -0.2)	-0.5* (-0.6, -0.4)	-0.1 (-0.3, 0.1)	-0.4* (-0.5, -0.2)	-0.4* (-0.5, -0.2)

*p<0.05 vs placebo. No preservation of type I error or multiple-comparisons correction was applied to p values as statistical significance defined as p<0.05 was exploratory in nature; 95% CIs are confidence intervals based on exact binomial for single proportions, and normal approximation for continuous variables

[a]Low disease activity

[b]Disease remission

N, number of patients with available ACR data at Month 3; all data were FAS, NRI, except CDAI and SDAI (FAS, observed case) and change from baseline data (FAS, longitudinal model); percentages were based on the number of patients available for each parameter analysis

ACR, American College of Rheumatology criteria; bDMARD, biologic disease-modifying antirheumatic drug; BID, twice daily; CDAI, Clinical Disease Activity Index; CI, confidence interval; DAS, disease activity score; ESR, erythrocyte sedimentation rate; FAS, full analysis set; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS, least squares; NRI, non-responder imputation; P2/P3, Phase 2/Phase 3; SDAI, Simplified Disease Activity Index; TNFi, tumour necrosis factor inhibitor

Online Supplementary Table 2. Incidence rates (patients with event per 100 patient-years; 95% CI) for safety events of special interest in the P3 cohort plus/minus concomitant glucocorticoid treatment

Safety event, incidence rate (patients with event per 100 patient-years; 95% CI)	P3 cohort minus glucocorticoids			P3 cohort plus glucocorticoids		
	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID	Placebo	Tofacitinib 5 mg BID	Tofacitinib 10 mg BID
	N=246	N=442	N=462	N=435	N=774	N=752
Exposure, patient-years	71.8	400.8	423.5	130.9	732.0	724.8
All SAEs	7.0 (2.9, 16.8)	7.4 (5.1, 10.6)	8.9 (6.5, 12.3)	19.5 (13.2, 28.8)	15.5 (12.8, 18.7)	10.8 (8.7, 13.6)
Discontinuations due to AEs	11.2 (5.6, 22.3)	8.8 (6.3, 12.3)	9.0 (6.6, 12.4)	12.3 (7.5, 20.1)	10.9 (8.7, 13.5)	11.4 (9.2, 14.1)
All serious infections	0	1.2 (0.5, 3.0)	2.8 (1.6, 5.0)	2.3 (0.7, 7.1)	4.4 (3.1, 6.2)	3.7 (2.6, 5.4)
Herpes zoster (all – serious and non-serious)	2.8 (0.7, 11.3)	2.5 (1.4, 4.7)	3.9 (2.4, 6.4)	0.8 (0.1, 5.4)	5.2 (3.8, 7.2)	5.3 (3.8, 7.3)

Herpes zoster (serious)	0	0	0	0	0.5 (0.2, 1.5)	0.6 (0.2, 1.5)
Herpes zoster (non-serious)	2.8 (0.7, 11.3)	2.5 (1.4, 4.7)	3.9 (2.4, 6.4)	0.8 (0.1, 5.4)	4.7 (3.3, 6.6)	4.8 (3.5, 6.8)

Safety was assessed during Months 0–6 for the placebo group and Months 0–24 for the tofacitinib groups. Patients who advanced from placebo to tofacitinib are counted in the placebo group until advancement in the various studies – some patients advanced at Month 3, while others advanced at Month 6 unless they did not achieve a 20% improvement in swollen/tender joint counts at Month 3, in which case they advanced to active treatment (ORAL Sync, ORAL Scan and ORAL Standard)

bDMARD, biologic disease-modifying antirheumatic drug; BID, twice daily; CI, confidence interval; IR, inadequate responders; N, number of patients included in analysis; P3, Phase 3; SAE, serious adverse event