SUPPLEMENTARY MATERIAL

Response to Tofacitinib in Patients with Psoriatic Arthritis and Probable Anxiety/Depressive Disorder: A Post Hoc Analysis of Phase 3 Trials

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Supplementary Methods

OPAL Balance: study design

Patients who had participated in OPAL Broaden or OPAL Beyond could enter the open-label long-term extension (LTE) study, OPAL Balance, ≤ 3 months after completing the qualifying studies or discontinuing for reasons other than study drug-related adverse events. Patients received tofacitinib 5 mg twice daily (BID), regardless of treatment in the qualifying studies, with adjustments to 10 mg BID permitted after month 1 for inadequate symptom control, and reductions to 5 mg BID thereafter for safety reasons. Patients could continue to receive selected conventional synthetic disease-modifying antirheumatic drugs concomitantly.

Schedule of assessments

The Short Form-36 Health Survey (SF-36) [1] was assessed at baseline and at months 3, 6, 9, and 12 for OPAL Broaden, at months 3 and 6 for OPAL Beyond, and at months 6, 12, 18, 24, and 36 for OPAL Balance. The SF-36 Mental Component Summary (MCS) was derived using selected questions from the SF-36 [1]. Probable anxiety and/or depressive disorder (pADD) status was determined post hoc using the SF-36 MCS score (presence: SF-36 MCS ≤ 38, absence: SF-36 MCS > 38) [2].

Efficacy outcomes and other patient-reported outcomes were assessed at months 3 and 6 (OPAL Broaden and Beyond), months 9 and 12 (OPAL Broaden), and months 6–36 (OPAL Balance), stratified by baseline pADD status.

Safety was assessed up to month 3 (OPAL Broaden and Beyond, placebo-controlled phase) and to month 12 (data collected beyond month 6 is from OPAL Broaden only).

Statistical analysis

Binary and continuous change from baseline outcomes were assessed using longitudinal logistic regression models (PROC GLIMMIX in SAS software [SAS/Stat 14.1. SAS Institute Inc., Cary, NC]) and mixed effect linear models (PROC MIXED in SAS software), respectively. The independent variables included as main effects in the model were baseline pADD, treatment group, and visit. These variables were entered with three-way and all two-way interactions. Variables also added as main effects included age (years), sex, geographic region, baseline pain visual analog scale, smoking status (never-smoker, smoker, or ex-smoker), any history of alcohol use (yes or no), indicated employed on day 1 (completed a Work Limitations Questionnaire; yes or no), duration of psoriatic arthritis, and baseline Psoriatic Arthritis Disease Activity Score. The same was applied for the LTE study with the addition of parent study (ie, OPAL Broaden and OPAL Beyond) as a fixed effect, and only one treatment group instead.

The linear-regression models also included the baseline value of the dependent variable. Patients within each study were included as a random effect. For the analysis of data from OPAL Balance, the parent studies were also included as an effect.

Pseudo likelihood methods for binary models and restricted maximum likelihood methods for continuous models were used; a structured covariance matrix known as 'autoregressive of order one' was used in both models. If this model failed to converge, the following steps were taken: 1) a 'compound symmetric' covariance was used; 2) an unstructured model was fitted, and if these failed then the quadrature method (binary) or the method of MIVQUE0 (continuous) was fitted. Reporting of modeling results emphasized visit, treatment and smoking status in figures or tabular displays, including estimated differences using odds ratios and their 95% confidence intervals (CIs). Degrees of freedom were estimated using a method attributed to Satterthwaite; if degrees of freedom were not estimable using this method, the method attributed to Kenward-Roger was used (all are SAS software options).

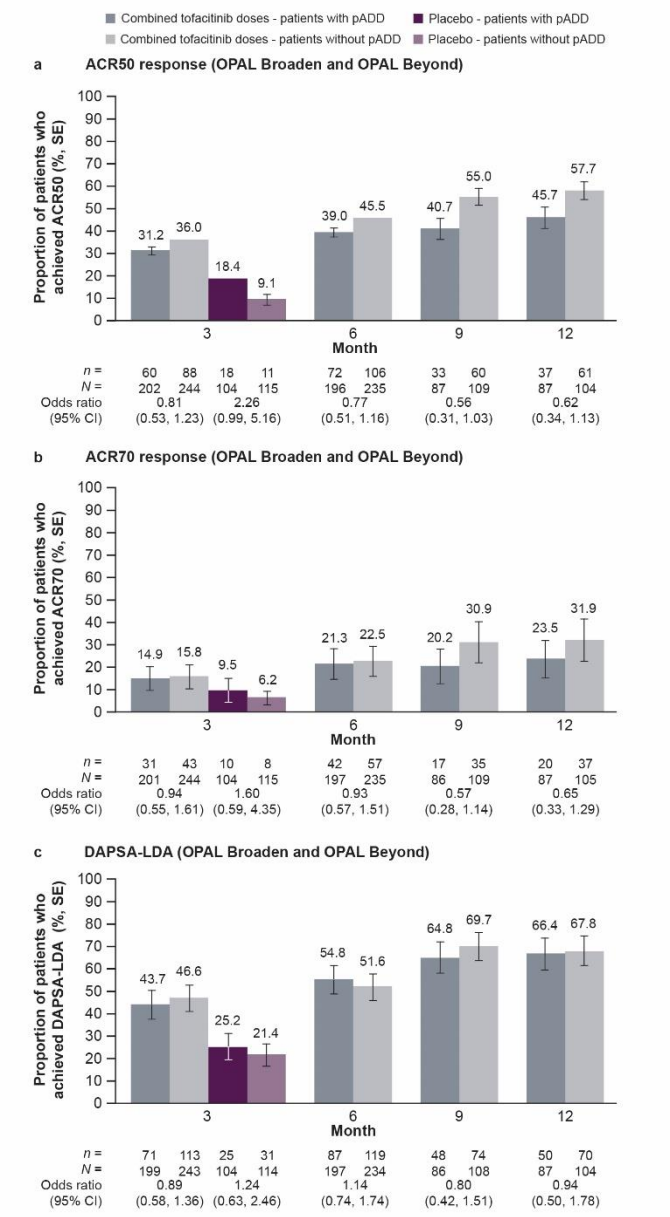
Within each treatment group/treatment sequence at each visit, comparisons between patients with and without baseline pADD were performed for that visit, by forming contrasts for the differences in estimates (rates or means), resulting in approximate t-tests and associated *p* values ($p < 0.05$ are reported); these were inverted to calculate 95% CIs. In the case of the logistic regressions, the differences were then exponentiated (ie, an inverse to the link was applied), resulting in odds ratios and their CIs. There was no adjustment for multiple comparisons, and *p* values should therefore be considered descriptive.

References

1. Ware JE, Jr., Kosinski M, Bjorner JB, Turner-Bowker DM, Gandek B, Maruish ME. User's manual for the SF-36v2® health survey (2nd ed.). Lincoln (RI): QualityMetric; 2007.

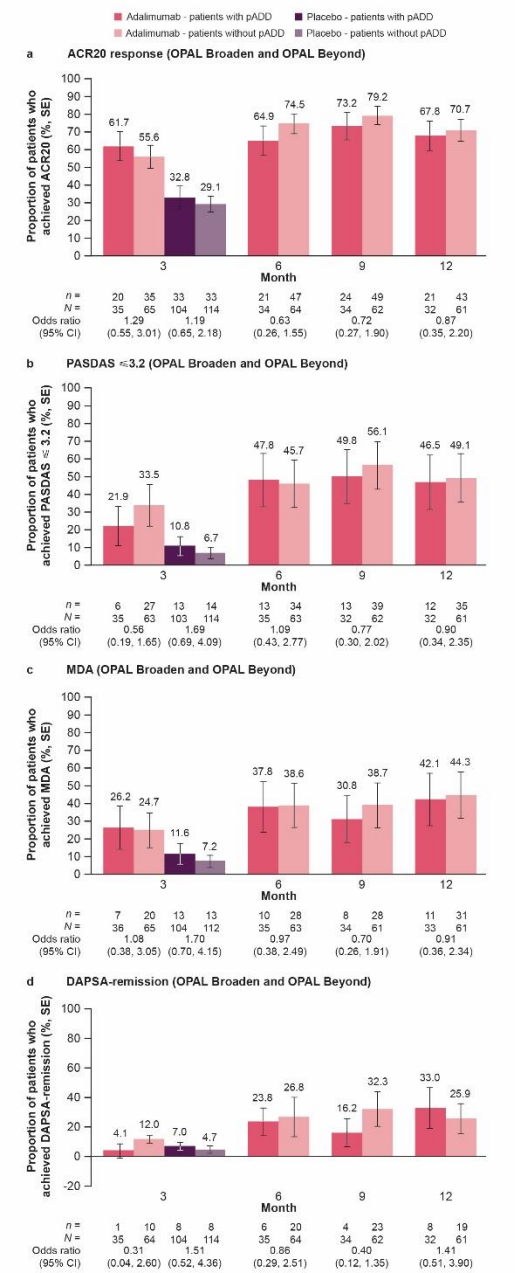
2. Matcham F, Norton S, Steer S, Hotopf M. Usefulness of the SF-36 Health Survey in screening for depressive and anxiety disorders in rheumatoid arthritis. BMC Musculoskelet Disord. 2016; 17:224.

Fig. S1 Proportions of patients achieving **a**, ACR50 response[a]; **b**, ACR70 response[b]; and **c**, DAPSA-LDA[c] with tofacitinib (combined doses; 5 or 10 mg BID) and placebo, stratified by patients with[d] and without[e] baseline pADD (OPAL Broaden and OPAL Beyond)



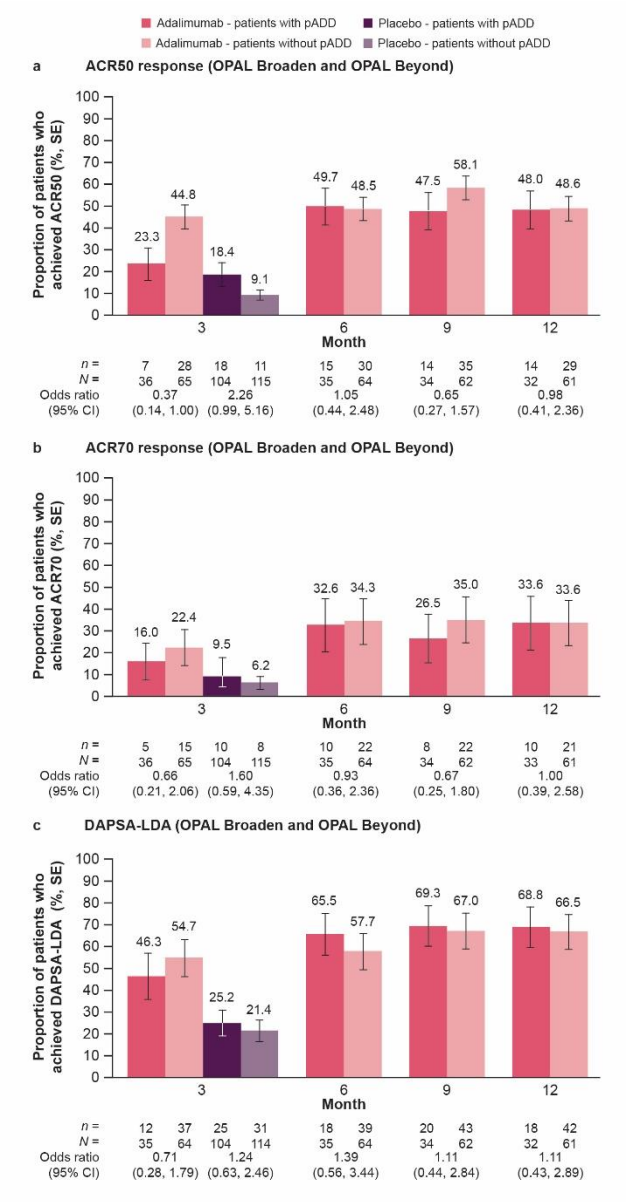
Error bars represent standard error (SE). SEs from the repeated measures mixed-effects model for proportions may not have been estimable for any given treatment group. The SEs for differences between treatment groups (odds ratios) are estimable, as well as their 95% CIs. Data for months 3 and 6 are pooled for OPAL Broaden and Beyond; data for months 9 and 12 are for OPAL Broaden only. Patients who initially received placebo and switched to tofacitinib at month 3 had their post-month 3 values excluded from the analysis. *n* and *N* represent observed counts. Odds ratios represent differences (expressed as ratios) between patients with and without baseline pADD. Response rates and odds ratios are estimated from the model. *$p < 0.05$, patients with[d] versus without[e] baseline pADD. [a] ≥ 50% improvement in ACR criteria. [b] ≥ 70% improvement in ACR criteria. [c]DAPSA score ≤ 14. [d]SF-36 MCS score ≤ 38. [e]SF-36 MCS score > 38. *ACR* American College of Rheumatology, *BID* twice daily, *CI* confidence interval, *DAPSA* Disease Activity Index for Psoriatic Arthritis, *LDA* low disease activity, *MCS* Mental Component Summary, *n* number of patients meeting response criteria, *N* number of patients evaluable at each time point stratified by patients with[d] versus without[e] baseline pADD, *pADD* probable anxiety and/or depressive disorder, *SF-36* Short Form-36 Health Survey

Fig. S2 Proportions of patients achieving **a**, ACR20 response[a]; **b**, PASDAS ≤ 3.2; **c**, MDA[b]; and **d**, DAPSA-remission[c] with adalimumab and placebo, stratified by patients with[d] and without[e] baseline pADD (OPAL Broaden and OPAL Beyond)



Error bars represent standard error (SE). Placebo data at month 3 are pooled for OPAL Broaden and Beyond; adalimumab data are from OPAL Broaden only. Patients who initially received placebo and switched to tofacitinib at month 3 had their post-month 3 values excluded from the analysis. *n* and *N* represent observed counts. Odds ratios represent differences (expressed as ratios) between patients with and without baseline pADD. Response rates and odds ratios are estimated from the model. *$p < 0.05$, patients with[d] versus without[e] baseline pADD. [a]≥ 20% improvement in ACR criteria. [b]MDA defined as achieving 5 of the 7 following criteria: TJC ≤ 1; SJC ≤ 1; PASI ≤ 1 or BSA ≤ 3%; pain VAS ≤ 15; PtGA VAS ≤ 20 mm; HAQ-DI ≤ 0.5; LEI ≤ 1. [c]DAPSA score ≤ 4. [d]SF-36 MCS score ≤ 38. [e]SF-36 MCS score > 38. *ACR* American College of Rheumatology, *BSA* body surface area, *CI* confidence interval, *DAPSA* Disease Activity Index for Psoriatic Arthritis, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *LEI* Leeds Enthesitis Index, *MCS* Mental Component Summary, *MDA* minimal disease activity, *n* number of patients meeting response criteria, *N* number of patients evaluable at each time point stratified by patients with[d] versus without[e] baseline pADD, *pADD* probable anxiety and/or depressive disorder, *PASDAS* Psoriatic Arthritis Disease Activity Score, *PASI* Psoriasis Area Severity Index, *PtGA* Patient Global Assessment of Disease Activity, *SF-36* Short Form-36 Health Survey, *SJC* swollen joint count, *TJC* tender joint count, *VAS* visual analog scale

Fig. S3 Proportions of patients achieving **a**, ACR50 response[a]; **b**, ACR70 response[b]; and **c**, DAPSA-LDA[c] with adalimumab and placebo, stratified by patients with[d] and without[e] baseline pADD (OPAL Broaden and OPAL Beyond)



Error bars represent standard error (SE). Placebo data at month 3 are pooled for OPAL Broaden and Beyond; adalimumab data are from OPAL Broaden only. Patients who initially received placebo and switched to tofacitinib at month 3 had their post-month 3 values excluded from the analysis. *n* and *N* represent observed counts. Odds ratios represent differences (expressed as ratios) between patients with and without baseline pADD. Response rates and odds ratios are estimated from the model. **p* < 0.05, patients with[d] versus without[e] baseline pADD. [a] ≥ 50% improvement in ACR criteria. [b] ≥ 70% improvement in ACR criteria. [c]DAPSA score ≤ 14. [d]SF-36 MCS score ≤ 38. [e]SF-36 MCS score > 38. *ACR* American College of Rheumatology, *CI* confidence interval, *DAPSA* Disease Activity Index for Psoriatic Arthritis, *LDA* low disease activity, *MCS* Mental Component Summary, *n* number of patients meeting response criteria, *N* number of patients evaluable at each time point stratified by patients with[d] versus without[e] baseline pADD, *pADD* probable anxiety and/or depressive disorder, *SF-36* Short Form-36 Health Survey

Fig. S4 Proportions of patients achieving **a**, ACR20 response[a]; **b**, PASDAS ≤ 3.2; **c**, MDA[b]; and **d**, DAPSA-remission[c] with tofacitinib, stratified by patients with[d] and without[e] baseline pADD (OPAL Balance)

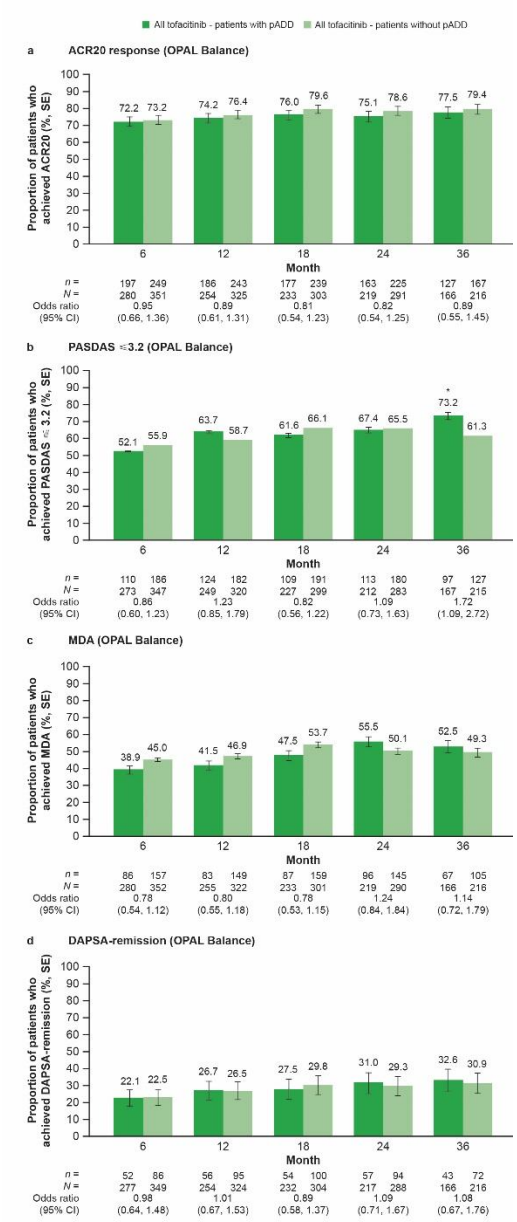


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Fig. S5 Proportions of patients achieving **a**, ACR50 response[a]; **b**, ACR70 response[b]; and **c**, DAPSA-LDA[c] with tofacitinib, stratified by patients with[d] and without[e] baseline pADD (OPAL Balance)

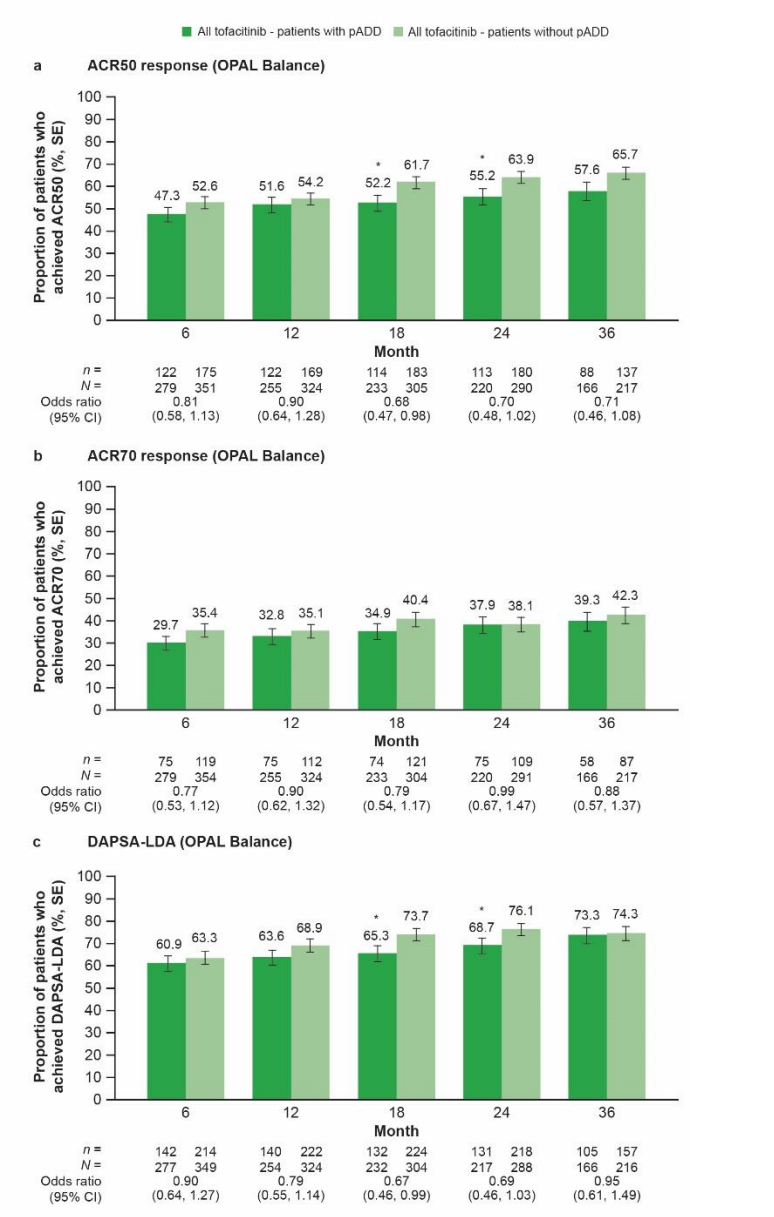

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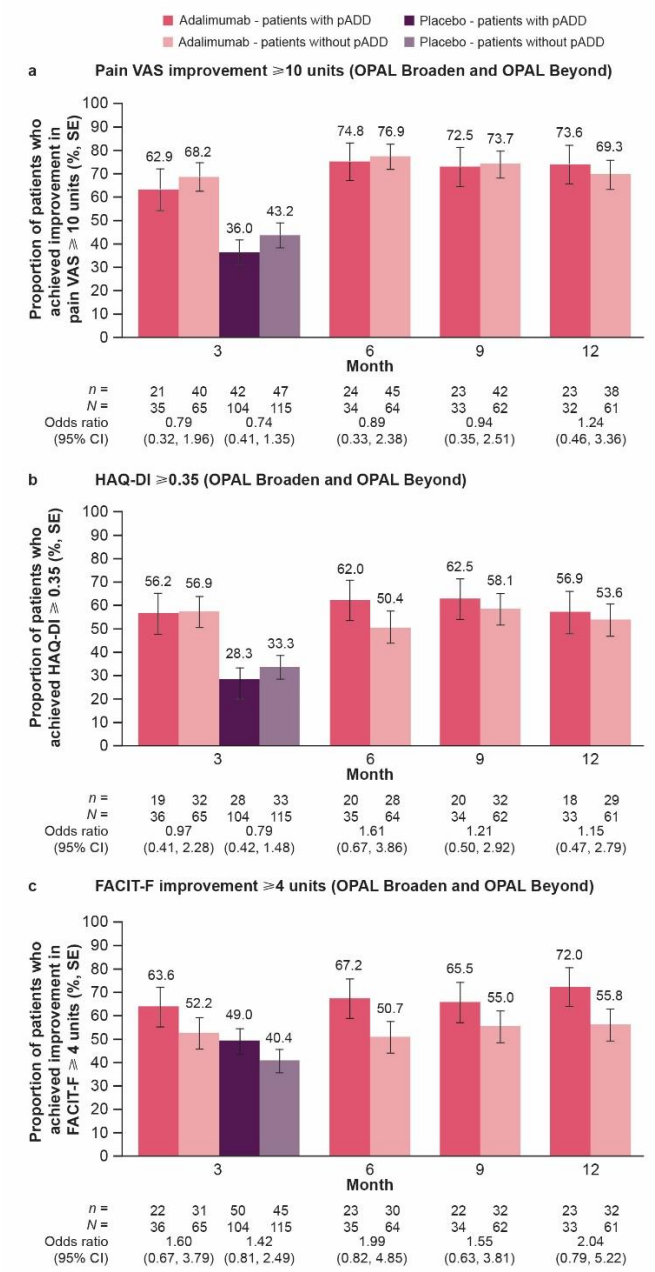
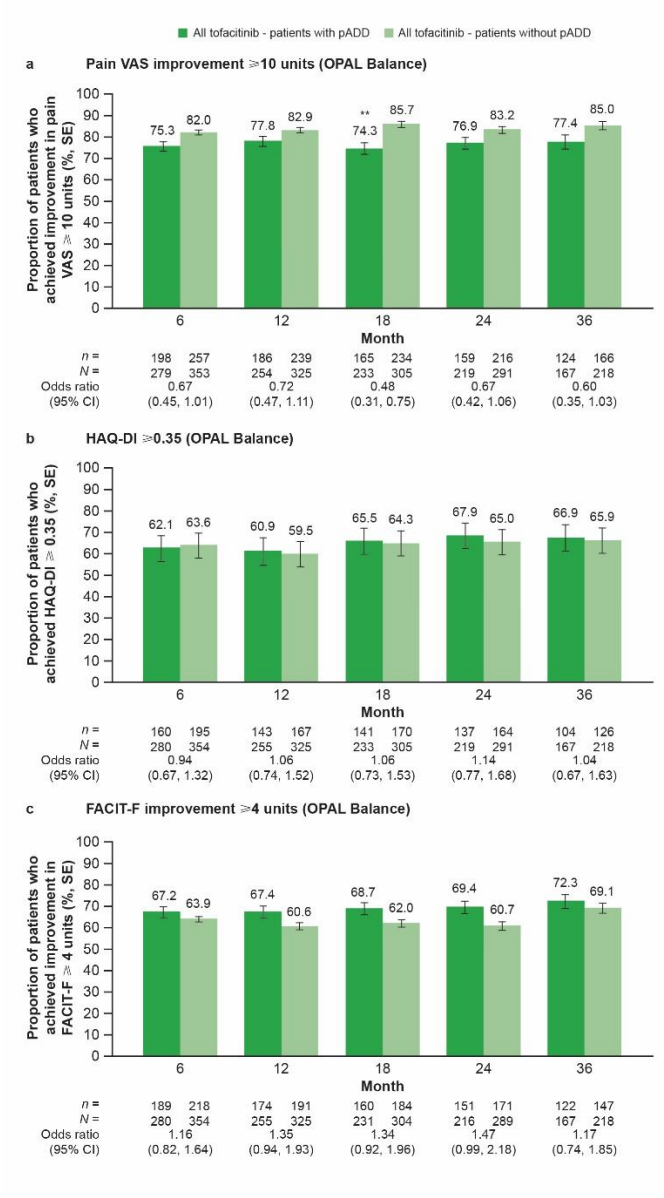
Fig. S6 Proportions of patients achieving MCID for **a**, pain VAS ≥10 units; **b**, HAQ-DI ≥0.35; and **c**, FACIT-F ≥4 with adalimumab, stratified by patients with[a] and without[b] baseline pADD (OPAL Broaden and OPAL Beyond)



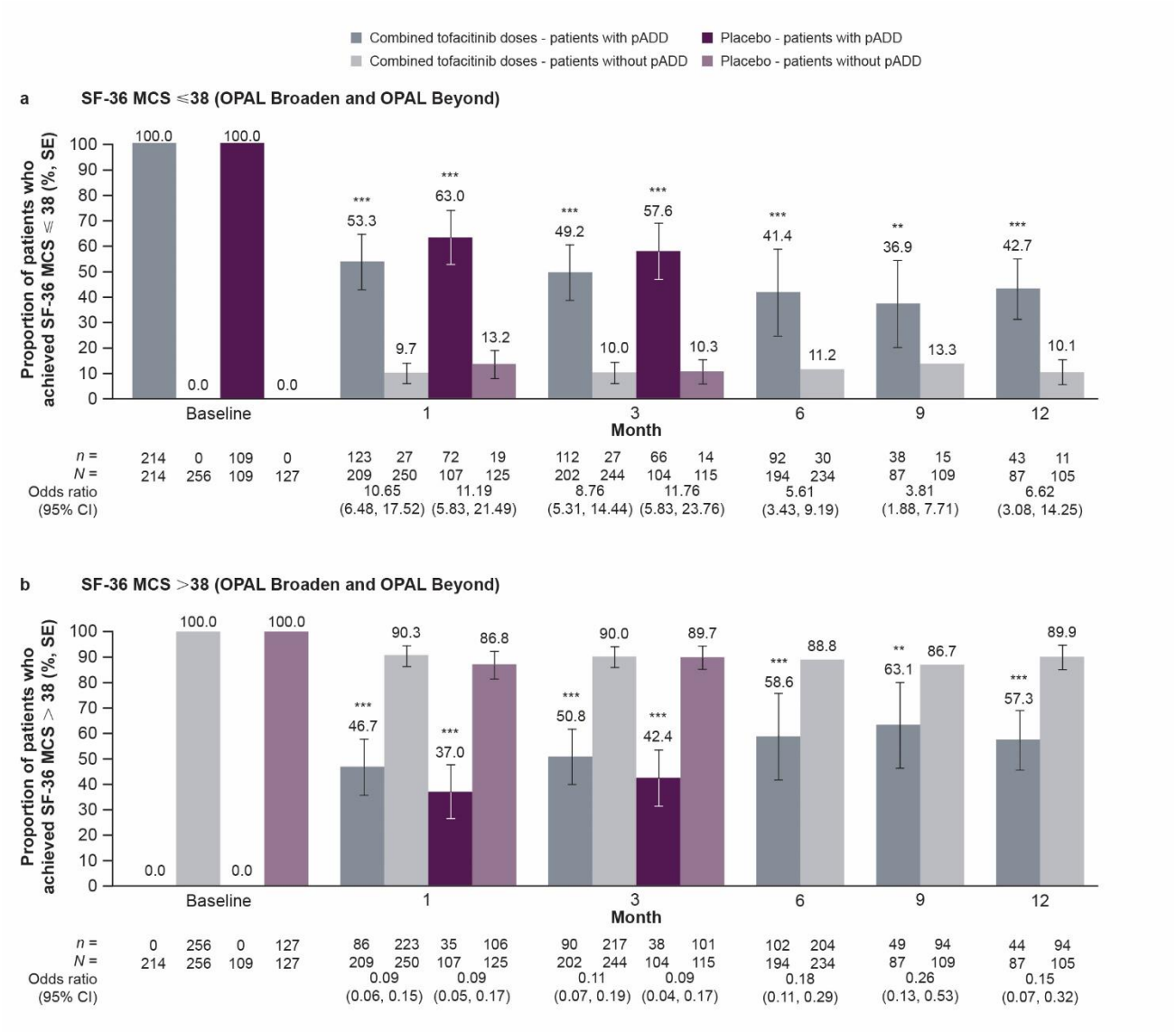
Error bars represent standard error (SE). Placebo data at month 3 are pooled for OPAL Broaden and Beyond; adalimumab data are from OPAL Broaden only. Patients who initially received placebo and switched to tofacitinib at month 3 had their post-month 3 values excluded from the analysis. *n* and *N* represent observed counts. Odds ratios represent differences (expressed as ratios) between patients with and without baseline pADD. Rates of MCID and odds ratios are estimated from the model. [a]SF-36 MCS score ≤ 38. [b]SF-36 MCS score > 38. *CI* confidence interval, *FACIT-F* Functional Assessment of Chronic Illness Therapy-Fatigue, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *MCID* minimal clinically important difference, *MCS* Mental Component Summary, *n* number of patients meeting response criteria, *N* number of patients evaluable at each time point stratified by patients with[a] versus without[b] baseline pADD, *pADD* probable anxiety and/or depressive disorder, *SF-36* Short Form-36 Health Survey, *VAS* visual analog scale

Fig. S7 Proportions of patients achieving MCID for **a**, pain VAS ≥10 units; **b**, HAQ-DI ≥0.35; and **c**, FACIT-F ≥4 with tofacitinib, stratified by patients with[a] and without[b] baseline pADD (OPAL Balance)



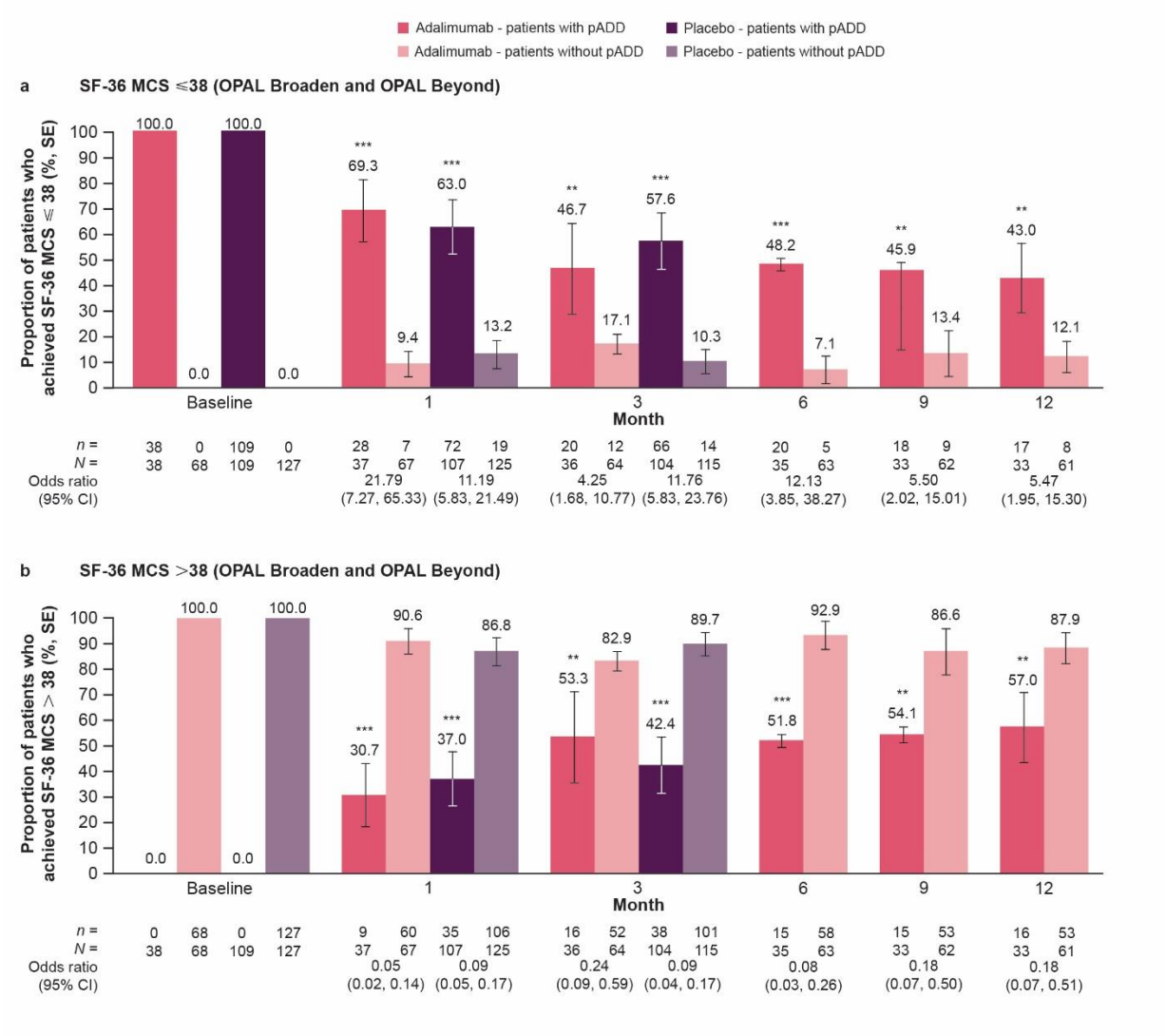
Error bars represent standard error (SE). *n* and *N* represent observed counts. Odds ratios represent differences (expressed as ratios) between patients with and without baseline pADD. Rates of MCID and odds ratios are estimated from the model. $^{**}p < 0.01$, patients with[a] versus without[b] baseline pADD. [a]SF-36 MCS score ≤ 38. [b]SF-36 MCS score > 3. *CI* confidence interval, *FACIT-F* Functional Assessment of Chronic Illness Therapy-Fatigue, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *MCID* minimal clinically important difference, *MCS* Mental Component Summary, *n* number of patients meeting response criteria, *N* number of patients evaluable at each time point stratified by patients with[a] versus without[b] baseline pADD, *pADD* probable anxiety and/or depressive disorder, *SF-36* Short Form-36 Health Survey, *VAS* visual analog scale

Fig. S8 Proportions of patients receiving tofacitinib (combined doses; 5 or 10 mg BID) and placebo with **a**, presence[a]; and **b**, absence[b] of pADD, stratified by patients with[a] and without[b] baseline pADD (OPAL Broaden and OPAL Beyond)



Error bars represent standard error (SE). SEs from the repeated measures mixed-effects model for proportions may not have been estimable for any given treatment group. The SEs for differences between treatment groups (odds ratios) are estimable, as well as their 95% CIs. Data for baseline, and months 1, 3, and 6 are pooled for OPAL Broaden and Beyond; data for months 9 and 12 are for OPAL Broaden only. Patients who initially received placebo and switched to tofacitinib at month 3 had their post-month 3 values excluded from the analysis. *n* and *N* represent observed counts. Odds ratios represent differences (expressed as ratios) between patients with and without baseline pADD. Proportions of patients and odds ratios are estimated from the model. $^{**}p < 0.01$; $^{***}p < 0.0001$, patients with[a] versus without[b] baseline pADD. [a]SF-36 MCS score ≤ 38. [b]SF-36 MCS score > 38. *BID* twice daily, *CI* confidence interval, *MCS* Mental Component Summary, *n* number of patients with characteristic, *N* number of patients evaluable at each time point stratified by patients with[a] versus without[b] baseline pADD, *pADD* probable anxiety and/or depressive disorder, *SF-36* Short Form-36 Health Survey

Fig. S9 Proportions of patients receiving adalimumab with **a**, presence[a]; and **b**, absence[b] of pADD, stratified by patients with[a] and without[b] baseline pADD (OPAL Broaden and OPAL Beyond)



Error bars represent standard error (SE). Placebo data at baseline, and months 1 and 3 are pooled for OPAL Broaden and Beyond; adalimumab data are from OPAL Broaden only. Patients who initially received placebo and switched to tofacitinib at month 3 had their post-month 3 values excluded from the analysis. *n* and *N* represent observed counts. Odds ratios represent differences (expressed as ratios) between patients with and without baseline pADD. Proportions of patients and odds ratios are estimated from the model. $^{**}p < 0.01$; $^{***}p < 0.0001$, patients with[a] versus without[b] baseline pADD. [a]SF-36 MCS score ≤ 38. [b]SF-36 MCS score > 38. *CI* confidence interval, *MCS* Mental Component Summary, *n* number of patients with characteristic, *N* number of patients evaluable at each time point stratified by patients with[a] versus without[b] baseline pADD, *pADD* probable anxiety and/or depressive disorder, *SF-36* Short Form-36 Health Survey

Fig. S10 Proportions of patients receiving tofacitinib with **a**, presence[a]; and **b**, absence[b] of pADD, stratified by patients with[a] and without[b] baseline pADD (OPAL Balance)

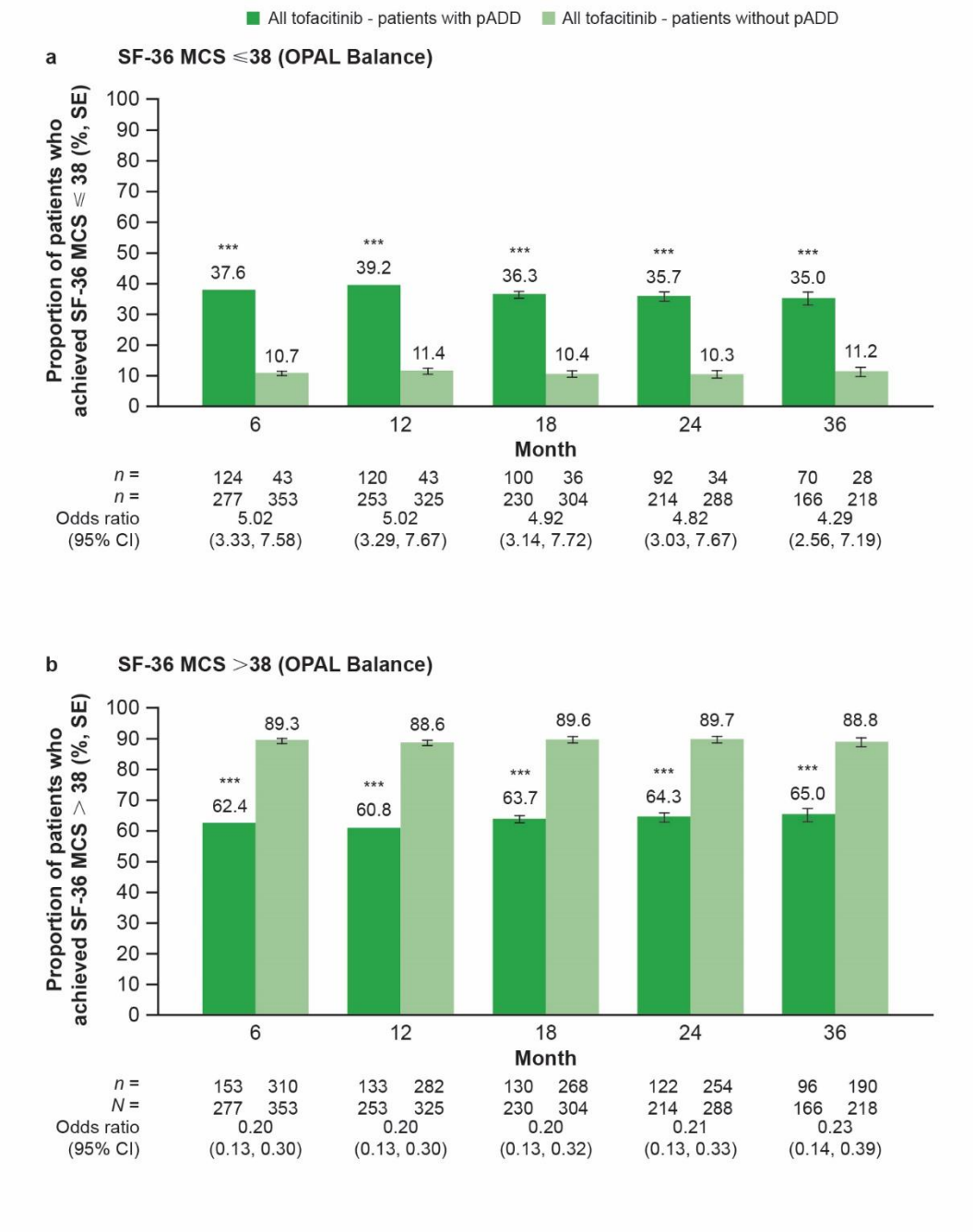


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Table S1 Baseline demographics and disease characteristics, stratified by patients with[a] and without[b] baseline pADD (OPAL Broaden and OPAL Beyond pooled)

	Combined tofacitinib doses (5 or 10 mg BID)		**Placebo**	
	With pADD[a] (*N* = 214)	**Without pADD[b] (*N* = 256)**	**With pADD[a] (*N* = 109)**	**Without pADD[b] (*N* = 127)**
Age (years), mean (SD)	49.1 (12.4)	49.6 (11.7)	47.4 (11.8)	49.3 (13.0)
Age >65 years, *n* (%)	18 (8.4)	16 (6.3)	7 (6.4)	14 (11.0)
Female, *n* (%)	131 (61.2)	125 (48.8)	69 (63.3)	67 (52.8)
BMI (kg/m^2), mean (SD)	30.1 (6.4)	30.0 (6.3)	29.6 (5.9)	28.8 (5.4)
BMI >30 kg/m^2, *n* (%)	96 (44.9)	110 (43.0)	53 (48.6)	50 (39.4)
SF-36 MCS, mean (SD)	29.7 (6.2)	48.9 (7.8)	29.7 (6.0)	49.1 (7.3)
SF-36 PCS, mean (SD)	33.7 (7.6)	34.4 (9.1)	34.9 (7.8)	35.6 (9.4)
PASI, mean (SD)	9.8 (7.6)[c]	9.4 (8.1)[d]	10.2 (8.8)[e]	10.4 (10.9)[f]
Use of ≥1 anti-anxiety or anti-depression medication on day 1, *n* (%)	36 (16.8)	44 (17.2)	23 (21.1)	22 (17.3)
PsA duration, years (SD)	7.6 (7.1)	8.3 (7.4)	7.4 (7.0)	8.6 (7.9)
Prior bDMARD treatments, *n* (%)	126 (58.9)	140 (54.7)	60 (55.0)	75 (59.1)
PASDAS, mean (SD)	6.4 (1.0)[g]	5.9 (1.2)[h]	6.1 (1.2)[i]	5.9 (1.2)[j]
DAPSA, mean (SD)	49.6 (23.2)	44.6 (23.5)	45.3 (23.8)	41.4 (21.7)

HAQ-DI, mean (SD)	1.4 (0.6)	1.1 (0.6)	1.3 (0.7)	1.1 (0.7)
CRP (mg/L), mean (SD)	13.6 (24.5)	11.0 (18.0)	9.5 (16.3)	12.9 (23.0)
FACIT-F total score, mean (SD)[k]	20.9 (9.2)	32.0 (9.8)	21.7 (8.5)	33.3 (9.4)
Pain VAS, mean (SD)	60.9 (22.3)	53.0 (22.7)	57.2 (26.6)	51.5 (22.2)

[a]SF-36 MCS score ≤ 38

[b]SF-36 MCS score > 38

[c]*N* = 153

[d]*N* = 159

[e]*N* = 79

[f]*N* = 89

[g]*N* = 209

[h]*N* = 250

[i]*N* = 105

[j]*N* = 126

[k]Lower scores represents greater fatigue

bDMARD biologic disease-modifying antirheumatic drug, *BID* twice daily, *BMI* body mass index, *CRP* C-reactive protein, *DAPSA* Disease Activity Index for Psoriatic Arthritis, *FACIT-F* Functional Assessment of Chronic Illness Therapy-Fatigue, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *MCS* Mental Component Summary, *n* number of

patients with characteristic, *N* number of patients evaluable at each time point stratified by patients with[a] versus without[b] baseline pADD, *pADD* probable anxiety and/or depressive disorder, *PASDAS* Psoriatic Arthritis Disease Activity Score, *PASI* Psoriasis Area Severity Index, *PCS* Physical Component Summary, *PsA* psoriatic arthritis, *SD* standard deviation, *SF-36* Short Form-36 Health Survey, *VAS* visual analog scale

Table S2 LS mean change from baseline in efficacy outcomes and PROs at months 3, 6, 9, and 12 with tofacitinib (combined doses; 5 or 10 mg BID), adalimumab, and placebo, stratified by patients with[a] and without[b] baseline pADD (OPAL Broaden and OPAL Beyond)

	Mean (SE)		**LS mean (SE) change from baseline**							
	Baseline		**Month 3**		**Month 6**		**Month 9**		**Month 12**	
	With pADD[a]	**Without pADD[b]**	**With pADD[a]**	**Without pADD[b]**	**With pADD[a]**	**Without pADD[b]**	**With pADD[a]**	**Without pADD[b]**	**With pADD[a]**	**Without pADD[b]**
PASDAS										
Combined tofacitinib doses	6.41 (0.07) [*N* = 209]	5.94 (0.08) [*N* = 250]	-1.97 (0.10) [*N* = 193]	-2.14 (0.09) [*N* = 235]	-2.37 (0.10) [*N* = 188]	-2.44 (0.09) [*N* = 224]	-2.59 (0.13) [*N* = 86]	-2.64 (0.12) [*N* = 104]	-2.72 (0.14) [*N* = 86]	-2.79 (0.13) [*N* = 100]
Adalimumab	6.44 (0.14) [*N* = 38]	5.63 (0.16) [*N* = 68]	-2.03 (0.23) [*N* = 35]	-2.12 (0.17) [*N* = 63]	-2.55 (0.23) [*N* = 35]	-2.49 (0.17) [*N* = 63]	-2.67 (0.23) [*N* = 32]	-2.72 (0.17) [*N* = 62]	-2.72 (0.24) [*N* = 32]	-2.62 (0.17) [*N* = 61]
Placebo	6.15 (0.11) [*N* = 105]	5.87 (0.11) [*N* = 126]	-1.06 (0.14) [*N* = 100]	-0.87 (0.13) [*N* = 113]	NA	NA	NA	NA	NA	NA

DAPSA										
Combined tofacitinib doses	49.57 (1.59) [*N* = 214]	44.64 (1.47) [*N* = 256]	-21.11 (1.22) [*N* = 199]	-21.30 (1.12) [*N* = 243]	-24.66 (1.23) [*N* = 197]	-23.99 (1.14) [*N* = 234]	-28.23 (1.51) [*N* = 86]	-27.16 (1.38) [*N* = 108]	-29.68 (1.65) [*N* = 87]	-28.25 (1.52) [*N* = 104]
Adalimumab	44.10 (2.79) [*N* = 37]	35.48 (2.21) [*N* = 68]	-19.75 (2.78) [*N* = 34]	-18.68 (2.08) [*N* = 64]	-25.58 (2.81) [*N* = 34]	-22.49 (2.10) [*N* = 64]	-27.26 (2.85) [*N* = 33]	-23.53 (2.12) [*N* = 62]	-26.36 (2.90) [*N* = 31]	-23.77 (2.14) [*N* = 61]
Placebo	45.26 (2.28) [*N* = 109]	41.36 (1.93) [*N* = 127]	-10.40 (1.66) [*N* = 104]	-10.30 (1.55) [*N* = 114]	NA	NA	NA	NA	NA	NA
HAQ-DI										
Combined tofacitinib doses	1.41 (0.04) [*N* = 214]	1.08 (0.04) [*N* = 256]	-0.37 (0.03) [*N* = 202]	-0.40 (0.03) [*N* = 245]	-0.42 (0.03) [*N* = 196]	-0.44 (0.03) [*N* = 235]	-0.48 (0.04) [*N* = 87]	-0.49 (0.04) [*N* = 108]	-0.53 (0.05) [*N* = 87]	-0.51 (0.04) [*N* = 105]
Adalimumab	1.43 (0.09) [*N* = 38]	0.91 (0.07) [*N* = 68]	-0.33 (0.08) [*N* = 36]	-0.41 (0.06) [*N* = 65]	-0.39 (0.08) [*N* = 35]	-0.45 (0.06) [*N* = 64]	-0.38 (0.08) [*N* = 34]	-0.46 (0.06) [*N* = 62]	-0.44 (0.08) [*N* = 33]	-0.46 (0.06) [*N* = 61]
Placebo	1.35 (0.07) [*N* = 109]	1.05 (0.06) [*N* = 127]	-0.17 (0.05) [*N* = 104]	-0.16 (0.04) [*N* = 115]	NA	NA	NA	NA	NA	NA

Pain VAS										
Combined tofacitinib doses	60.93 (1.53) [*N* = 214]	53.00 (1.42) [*N* = 256]	-18.59 (1.61)* [*N* = 202]	-23.67 (1.48) [*N* = 244]	-19.19 (1.63)** [*N* = 197]	-25.53 (1.50) [*N* = 235]	-23.80 (2.10) [*N* = 86]	-28.19 (1.90) [*N* = 109]	-24.95 (2.27) [*N* = 87]	-29.04 (2.09) [*N* = 105]
Adalimumab	57.32 (3.35) [*N* = 37]	47.06 (2.63) [*N* = 68]	-17.88 (3.68) [*N* = 35]	-21.87 (2.75) [*N* = 65]	-22.32 (3.74) [*N* = 34]	-24.22 (2.78) [*N* = 64]	-22.57 (3.79) [*N* = 33]	-23.59 (2.81) [*N* = 62]	-21.09 (3.84) [*N* = 32]	-23.79 (2.84) [*N* = 61]
Placebo	57.23 (2.55) [*N* = 109]	51.47 (1.97) [*N* = 127]	-6.85 (2.20) [*N* = 104]	-7.73 (2.06) [*N* = 115]	NA	NA	NA	NA	NA	NA
FACIT-F										
Combined tofacitinib doses	20.95 (0.63) [*N* = 214]	32.02 (0.61) [*N* = 256]	4.99 (0.65)* [*N* = 202]	7.09 (0.60) [*N* = 243]	6.14 (0.66)* [*N* = 197]	7.84 (0.61) [*N* = 235]	6.47 (0.83) [*N* = 87]	7.45 (0.75) [*N* = 109]	6.43 (0.90)* *N* = 87]	8.86 (0.82) [*N* = 105]
Adalimumab	21.34 (1.26) [*N* = 38]	34.88 (1.20) [*N* = 68]	5.25 (1.44) [*N* = 36]	5.97 (1.09) [*N* = 65]	6.13 (1.46) [*N* = 35]	6.70 (1.09) [*N* = 64]	5.40 (1.48) [*N* = 34]	7.11 (1.11) [*N* = 62]	7.00 (1.50) [*N* = 33]	7.08 (1.12) [*N* = 61]
Placebo	21.70 (0.82) [*N* = 109]	33.32 (0.84) [*N* = 127]	1.98 (0.87) [*N* = 104]	3.79 (0.82) [*N* = 115]	NA	NA	NA	NA	NA	NA

CRP										
Combined tofacitinib doses	13.58 (1.68) [*N* = 214]	11.03 (1.13) [*N* = 256]	-5.60 (0.88) [*N* = 199]	-6.28 (0.80) [*N* = 244]	-6.99 (0.89) [*N* = 197]	-7.51 (0.82) [*N* = 234]	-6.59 (1.23) [*N* = 87]	-7.50 (1.12) [*N* = 108]	-5.95 (1.30) [*N* = 87]	-7.52 (1.20) [*N* = 105]
Adalimumab	14.80 (4.15) [*N* = 38]	14.01 (2.96) [*N* = 68]	-7.67 (2.05) [*N* = 35]	-8.87 (1.52) [*N* = 64]	-9.35 (2.06) [*N* = 35]	-6.97 (1.52) [*N* = 64]	-7.63 (2.09) [*N* = 34]	-7.71 (1.54) [*N* = 62]	-7.76 (2.14) [*N* = 32]	-8.68 (1.56) [*N* = 61]
Placebo	9.49 (1.56) [*N* = 109]	12.94 (2.04) [*N* = 127]	-1.63 (1.21) [*N* = 104]	0.73 (1.13) [*N* = 114]	NA	NA	NA	NA	NA	NA
TJC										
Combined tofacitinib doses	23.12 (1.00) [*N* = 214]	20.92 (0.89) [*N* = 256]	-9.71 (0.72) [*N* = 202]	-9.37 (0.66) [*N* = 245]	-11.89 (0.73) [*N* = 197]	-10.76 (0.68) [*N* = 235]	-13.67 (0.90) [*N* = 87]	-12.37 (0.82) [*N* = 109]	-14.61 (0.99) [*N* = 87]	-12.92 (0.91) [*N* = 104]
Adalimumab	19.82 (2.04) [*N* = 38]	15.63 (1.23) [*N* = 68]	-7.91 (1.65) [*N* = 36]	-7.09 (1.23) [*N* = 65]	-11.16 (1.67) [*N* = 35]	-9.99 (1.24) [*N* = 64]	-12.45 (1.69) [*N* = 34]	-10.59 (1.26) [*N* = 62]	-11.97 (1.71) [*N* = 33]	-11.21 (1.27) [*N* = 61]
Placebo	21.64 (1.50) [*N* = 109]	18.91 (1.20) [*N* = 127]	-5.62 (0.99) [*N* = 104]	-5.19 (0.92) [*N* = 115]	NA	NA	NA	NA	NA	NA

SJC										
Combined tofacitinib doses	12.80 (0.63) [*N* = 214]	12.18 (0.67) [*N* = 256]	-7.11 (0.43) [*N* = 202]	-6.69 (0.40) [*N* = 245]	-7.96 (0.44) [*N* = 197]	-7.45 (0.40) [*N* = 235]	-9.11 (0.57) [*N* = 87]	-8.65 (0.52) [*N* = 109]	-9.60 (0.62) [*N* = 87]	-9.20 (0.57) [*N* = 104]
Adalimumab	10.89 (0.97) [*N* = 38]	9.24 (1.06) [*N* = 68]	-7.10 (0.99) [*N* = 36]	-6.25 (0.74) [*N* = 65]	-8.68 (1.01) [*N* = 35]	-7.02 (0.75) [*N* = 64]	-9.24 (1.02) [*N* = 34]	-7.56 (0.76) [*N* = 62]	-8.95 (1.03) [*N* = 33]	-6.94 (0.76) [*N* = 61]
Placebo	11.00 (0.84) [*N* = 109]	10.91 (0.80) [*N* = 127]	-3.38 (0.59) [*N* = 104]	-3.61 (0.55) [*N* = 115]	NA	NA	NA	NA	NA	NA
PtGA										
Combined tofacitinib doses	61.99 (1.48) [*N* = 214]	51.34 (1.39) [*N* = 256]	-18.42 (1.60)* [*N* = 202]	-22.71 (1.47) [*N* = 245]	-21.45 (1.62)* [*N* = 197]	-26.11 (1.49) [*N* = 235]	-24.02 (2.10) [*N* = 87]	-27.63 (1.91) [*N* = 109]	-23.94 (2.28) [*N* = 87]	-27.32 (2.09) [*N* = 105]
Adalimumab	60.37 (3.13) [*N* = 38]	45.07 (2.81) [*N* = 68]	-18.26 (3.66) [*N* = 36]	-21.13 (2.73) [*N* = 65]	-22.52 (3.72) [*N* = 35]	-22.27 (2.76) [*N* = 64]	-22.52 (3.76) [*N* = 34]	-22.10 (2.79) [*N* = 62]	-20.84 (3.82) [*N* = 33]	-23.85 (2.82) [*N* = 61]
Placebo	59.47 (2.32) [*N* = 109]	51.04 (1.93) [*N* = 127]	-6.19 (2.19) [*N* = 104]	-9.11 (2.04) [*N* = 115]	NA	NA	NA	NA	NA	NA

Baseline values presented are from simple statistics and not from the longitudinal model. Placebo data at baseline and month 3 are pooled for OPAL Broaden and Beyond; tofacitinib data for baseline, month 3, and month 6 are pooled for OPAL Broaden and Beyond, data for months 9 and 12 are for OPAL Broaden only; adalimumab data are from OPAL Broaden only. Patients who initially received placebo and switched to tofacitinib at month 3 had their post-month 3 values excluded from the analysis

*$p < 0.05$, **$p < 0.01$, patients with[a] versus without[b] baseline pADD

[a]SF-36 MCS score ≤ 38

[b]SF-36 MCS score > 38

BID twice daily, *CRP* C-reactive protein, *DAPSA* Disease Activity Index for Psoriatic Arthritis, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *FACIT-F* Functional Assessment of Chronic Illness Therapy-Fatigue, *LS* least squares, *MCS* Mental Component Summary, *N* number of patients evaluable at each time point stratified by patients with[a] versus without[b] baseline pADD, *NA* not applicable, *pADD* probable anxiety and/or depressive disorder, *PASDAS* Psoriatic Arthritis Disease Activity Score, *PRO* patient-reported outcome, *PtGA* Patient Global Assessment of Disease Activity, *SE* standard error, *SF-36* Short Form-36 Health Survey, *SJC* swollen joint count, *TJC* tender joint count, *VAS* visual analog scale

Table S3 LS mean change from baseline in efficacy outcomes and PROs at months 6, 12, 18, 24, and 36 with tofacitinib, stratified by patients with[a] and without[b] baseline pADD (OPAL Balance)

	Mean (SE)		**LS mean (SE) change from baseline**									
	Baseline		**Month 6**		**Month 12**		**Month 18**		**Month 24**		**Month 36**	
	With pADD[a]	**Without pADD[b]**	**With pADD[a]**	**Without pADD[b]**	**With pADD[a]**	**Without pADD[b]**	**With pADD[a]**	**Without pADD[b]**	**With pADD[a]**	**Without pADD[b]**	**With pADD[a]**	**Without pADD[b]**
PASDAS	6.36 (0.06) [*N* = 296]	5.81 (0.07) [*N* = 372]	-2.68 (0.09) [*N* = 268]	-2.79 (0.08) [*N* = 341]	-2.80 (0.09) [*N* = 243]	-2.87 (0.08) [*N* = 314]	-2.92 (0.09) [*N* = 222]	-2.98 (0.08) [*N* = 293]	-2.98 (0.10) [*N* = 207]	-3.00 (0.09) [*N* = 277]	-3.05 (0.10) [*N* = 164]	-2.98 (0.09) [*N* = 212]
DAPSA	48.37 1.36 [*N* = 303]	42.14 (1.17) [*N* = 378]	-27.87 (0.94) [*N* = 276]	-27.91 (0.85) [*N* = 349]	-29.16 (0.97) [*N* = 253]	-28.87 (0.87) [*N* = 324]	-29.36 (1.01) [*N* = 232]	-30.56 (0.90) [*N* = 304]	-31.12 (1.04) [*N* = 217]	-30.44 (0.92) [*N* = 288]	-32.60 (1.13) [*N* = 166]	-31.90 (1.00) [*N* = 216]
HAQ-DI	1.41 (0.04) [*N* = 304]	1.03 (0.03) [*N* = 378]	-0.47 (0.03) [*N* = 280]	-0.55 (0.03) [*N* = 354]	-0.46 (0.03) [*N* = 255]	-0.54 (0.03) [*N* = 325]	-0.51 (0.04) [*N* = 233]	-0.56 (0.03) [*N* = 305]	-0.53 (0.04) [*N* = 219]	-0.55 (0.03) [*N* = 291]	-0.56 (0.04) [*N* = 167]	-0.57 (0.04) [*N* = 218]
Pain VAS	59.87 (1.36) [*N* = 303]	51.12 (1.17) [*N* = 378]	-23.44 (1.41)** [*N* = 279]	-28.27 (1.26) [*N* = 353]	-24.64 (1.46) [*N* = 254]	-27.72 (1.30) [*N* = 325]	-24.88 (1.51)* [*N* = 233]	-29.31 (1.34) [*N* = 305]	-25.10 (1.55)* [*N* = 219]	-29.24 (1.38) [*N* = 291]	-27.54 (1.71) [*N* = 167]	-29.67 (1.51) [*N* = 218]

FACIT-F	21.60 (0.51) [*N* = 304]	33.07 (0.50) [*N* = 378]	6.94 (0.64) [*N* = 280]	8.54 (0.58) [*N* = 354]	6.69 (0.65)* [*N* = 255]	8.50 (0.59) [*N* = 325]	7.52 (0.67) [*N* = 231]	8.30 (0.61) [*N* = 304]	7.46 (0.69) [*N* = 216]	8.52 (0.62) [*N* = 289]	8.43 (0.75) [*N* = 167]	8.57 (0.66) [*N* = 218]
CRP	12.42 (1.25) [*N* = 304]	11.46 (1.00) [*N* = 378]	-7.89 (0.51) [*N* = 277]	-7.85 (0.46) [*N* = 350]	-7.79 (0.53) [*N* = 254]	-7.75 (0.47) [*N* = 325]	-7.34 (0.56) [*N* = 232]	-7.00 (0.49) [*N* = 304]	-8.24 (0.57) [*N* = 218]	-7.56 (0.50) [*N* = 288]	-7.77 (0.65) [*N* = 167]	-7.28 (0.57) [*N* = 217]
TJC	22.54 (0.86) [*N* = 304]	19.46 (0.71) [*N* = 378]	-13.74 (0.56) [*N* = 280]	-13.13 (0.51) [*N* = 354]	-14.22 (0.58) [*N* = 255]	-14.04 (0.52) [*N* = 324]	-14.28 (0.60) [*N* = 233]	-14.83 (0.54) [*N* = 305]	-15.30 (0.62) [*N* = 220]	-14.77 (0.55) [*N* = 291]	-16.42 (0.68) [*N* = 166]	-15.67 (0.60) [*N* = 217]
SJC	12.44 (0.53) [*N* = 304]	11.47 (0.51) [*N* = 378]	-8.66 (0.30) [*N* = 280]	-8.36 (0.27) [*N* = 354]	-9.29 (0.31)* [*N* = 255]	-8.48 (0.28) [*N* = 324]	-9.54 (0.32) [*N* = 233]	-9.24 (0.28) [*N* = 305]	-10.03 (0.33) [*N* = 220]	-9.32 (0.29) [*N* = 291]	-10.02 (0.37) [*N* = 166]	-9.79 (0.32) [*N* = 217]
PtGA	61.26 (1.28) [*N* = 304]	49.42 (1.17) [*N* = 378]	-23.31 (1.41)** [*N* = 280]	-28.31 (1.26) [*N* = 353]	-24.67 (1.46) [*N* = 255]	-28.27 (1.30) [*N* = 325]	-24.57 (1.51)* [*N* = 233]	-29.02 (1.35) [*N* = 305]	-25.76 (1.56) [*N* = 219]	-28.21 (1.38) [*N* = 299]	-26.79 (1.72) [*N* = 166]	-29.52 (1.52) [*N* = 218]

*$p < 0.05$, **$p < 0.01$, patients with[a] versus without[b] baseline pADD

[a]SF-36 MCS score ≤ 38

[b]SF-36 MCS score > 38

Baseline values presented are from simple statistics and not from the longitudinal model

CRP C-reactive protein, *DAPSA* Disease Activity Index for Psoriatic Arthritis, *HAQ-DI* Health Assessment Questionnaire-Disability Index,

FACIT-F Functional Assessment of Chronic Illness Therapy-Fatigue, *LS* least squares, *MCS* Mental Component Summary, *N* number of patients evaluable at each time point stratified by patients with[a] versus without[b] baseline pADD, *pADD* probable anxiety and/or depressive disorder, *PASDAS* Psoriatic Arthritis Disease Activity Score, *PRO* patient-reported outcome, *PtGA* Patient Global Assessment of Disease Activity, *SE* standard error, *SF-36* Short Form-36 Health Survey, *SJC* swollen joint count, *TJC* tender joint count, *VAS* visual analog scale