SAT0317 TOFACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS AND METABOLIC SYNDROME: A POST-HOC ANALYSIS OF PHASE 3 STUDIES

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of psoriatic arthritis (PsA). PsA is often associated with comorbid metabolic syndrome (MetS), which is linked to increased inflammation and severity of underlying PsA, and higher cardiovascular risk.[1,2] Patients (pts) with PsA and comorbid MetS frequently demonstrate decreased therapeutic responses and lower probability of achieving minimal disease activity.[3,4]

Objectives: To compare key efficacy and safety endpoints in tofacitinib-treated pts with PsA and MetS in Phase (P) 3 studies.

Methods: Two double-blind P3 studies enrolled pts with active PsA who either had an inadequate response (IR) to ≥1 conventional synthetic (cs)DMARD and were TNFi-naïve (OPAL Broaden; n=422; 12 months; NCT01877668) or IR to ≥1 TNFi (OPAL Beyond; n=395; 6 months; NCT01882439). Pts were randomised to receive tofacitinib 5 mg BID, tofacitinib 10 mg BID, adalimumab 40 mg Q2W (OPAL Broaden only) or placebo (PBO); all pts continued on a single, stable csDMARD. In this analysis, data for tofacitinib- and PBO-treated pts were pooled from both studies; efficacy and safety endpoints at Month (M) 3 were descriptively reported according to the presence or absence of MetS at baseline (defined as ≥3 of the following: hypertension, elevated triglycerides, reduced HDL cholesterol, large waist size and elevated fasting glucose levels[5]). Efficacy endpoints included: ACR20 response; change from baseline in HAQ-DI; PASI75 response; and changes from baseline in Pt's Global Assessment of Arthritis and C-reactive protein (CRP). Safety endpoints included: treatment-emergent adverse events (AEs); fasting lipid levels (LDL, HDL and total cholesterol, and triglycerides).

Results: This analysis included 294 pts with MetS (tofacitinib 5 mg, n=99; 10 mg, n=101; PBO, n=94) and 416 pts without (tofacitinib 5 mg, n=139; 10 mg, n=135; PBO, n=142). At baseline, pts with MetS had a higher mean age (53.2 vs 46.2 years) and mean BMI (33.2 vs 27.3 kg/m^2), and a greater proportion of pts with MetS had a CRP level >2.87 mg/L (upper limit of normal) (67.7 vs 58.9%) and were taking lipid-lowering medications (Day 1: 26.5 vs 3.8%). Tofacitinib efficacy was generally similar in pts with and without MetS (Table). LDL, HDL and total cholesterol, and triglyceride levels generally increased from baseline to M3 (Table). Among pts with MetS, AEs occurred in 55.6% treated with tofacitinib 5 mg (serious AEs [SAEs], 2%) and in 42.6% treated with tofacitinib 10 mg (SAEs, 2%). Among those without MetS, AEs occurred in 42.4% treated with tofacitinib 5 mg (SAEs, 1.4%) and in 54.8% treated with tofacitinib 10 mg (SAEs, 1.5%).

Abstract SAT0317 – Table 1. Efficacy and safety endpoints at Month 3 in OPAL Broaden and OPAL Beyond

Efficacy	Tofacitinib 5 mg BID				Tofacitinib 10 mg BID				Placebo			
	With metabolic syndrome	N	Without metabolic syndrome	N	With metabolic syndrome	N	Without metabolic syndrome	N	With metabolic syndrome	N	Without metabolic syndrome	N
ACR20 response, % (SE)	54.6 (5.0)	99	46.8 (4.2)	139	47.5 (5.0)	101	57.0 (4.3)	135	20.6 (4.6)	94	28.9 (3.8)	142
ΔHAQ-DI, LSM (SE)	-0.43 (0.05)	97	-0.39 (0.04)	130	-0.42 (0.06)	96	-0.42 (0.04)	127	-0.20 (0.06)	88	-0.21 (0.04)	131
PASI75 response,† % (SE)	32.8 (5.9)	64	31.6 (4.7)	98	42.6 (6.3)	61	41.4 (5.2)	90	14.1 (4.4)	64	14.4 (3.5)	104
APGA (VAS, mm), LSM (SE)	-21.9 (2.5)	97	-22.3 (2.1)	130	-23.2 (2.7)	96	-26.1 (2.1)	127	-12.6 (2.7)	88	-9.6 (2.1)	131
ΔCRP (mg/L), LSM (SE)	-5.9 (1.4)	95	-5.6 (1.3)	130	-4.5 (1.5)	95	-8.8 (1.3)	126	-1.1 (1.5)	88	-0.9 (1.3)	130
Safety‡												
LDL cholesterol (mg/dL), mean (SD) Δ mean, % (SD)	131.9 (39.4) 10.6 (23.0)	84 83	121.6 (33.2) 8.2 (18.4)	128 125	135.6 (41.2) 11.9 (25.8)	93 87	130.6 (40.0) 16.0 (25.9)	120 114	124.1 (35.9) 4.5 (17.7)	81 79	113.6 (31.6) 4.2 (20.0)	126 126
HDL cholesterol (mg/dL), mean (SD) Δ mean, % (SD)	53.4 (16.1) 11.1 (19.7)	89 89	66.0 (18.6) 8.6 (20.6)	128 125	55.6 (17.5) 16.4 (18.9)	94 90	69.3 (22.6) 12.6 (18.8)	122 116	47.5 (12.8) 0.4 (15.2)	86 84	59.9 (18.1) -1.3 (16.3)	128 127
Total cholesterol (mg/dL), mean (SD) Δ mean, % (SD)	224.5 (47.4) 9.6 (14.6)	90 90	210.7 (40.3) 7.4 (13.9)	128 125	228.1 (49.7) 10.2 (18.8)	94 91	223.2 (46.5) 13.9 (18.3)	122 117	206.7 (43.5) 2.5 (13.0)	86 84	196.1 (39.1) 1.7 (13.8)	128 127
Triglycerides (mg/dL), mean (SD) Δ mean, % (SD)	198.0 (112.7) 9.2 (44.8)	90 90	116.0 (47.5) 9.4 (36.5)	128 125	188.7 (97.1) 7.6 (43.1)	94 90	120.9 (77.3) 24.1 (63.0)	122 116	167.4 (124.1) 7.4 (48.6)	86 84	113.5 (56.5) 11.4 (43.6)	128 127
Concomitant lipid-lowering medications												
Patients taking concomitant lipid-lowering medications at baseline, n (%)	25 (25.3)	99	4 (2.9)	139	32 (31.7)	101	7 (5.2)	135	21 (22.3)	94	5 (3.5)	142
Patients taking new concomitant lipid-lowering medications, n (%)	1 (1.0)	99	1 (0.7)	139	5 (5.0)	101	1 (0.7)	135	2 (2.1)	94	0 (0.0)	142

†For patients with baseline BSA ≥3% and baseline PASI >0; ‡This summary included data on lipids for patients in fasting state only
ACR20 was calculated as a ≥20% improvement from baseline in tender and swollen joint counts and ≥20% improvement from baseline in 3 of the 5 remaining ACR Core Set measures: patient and physician global assessments, pain, disability and an acute-phase reactant
Missing value for ACR20 and PASI75 was considered as non-response to treatment
LSM was calculated using a longitudinal model without imputation for missing values
Existing concomitant lipid-lowering medications are defined as drugs taken on Day 1
New concomitant lipid-lowering medications are defined as drugs taken on or after Day 2, which are not the same as those taken on Day 1
Δ, change from baseline to Month 3; ACR, American College of Rheumatology; BID, twice daily; BSA, body surface area; CRP, C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LSM, least squares mean; N, number of patients in analysis; n, number of patients meeting criteria; PASI75, Psoriasis Area and Severity Index decrease from baseline of ≥75%; PGA, Patient's Global Assessment of Arthritis; SD, standard deviation; SE, standard error; VAS, Visual Analogue Scale

Conclusions:

Across 2 P3 studies, tofacitinib showed generally similar efficacy and safety in pts with PsA with or without MetS.

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SAT0318 DO PATIENTS IN REMISSION IN PSORIATIC ARTHRITIS, HAVE LESS FATIGUE? AND DOES THIS DEPEND ON THE DEFINITION OF REMISSION? AN ANALYSIS OF 304 PATIENTS

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Background: Fatigue is a critical element of life impact for patients with Psoriatic Arthritis (PsA) and is not considered in remission definitions. In PsA, remission can be defined using composite scores (Minimal Disease Activity (MDA), Disease Activity in PSoriatic Arthritis (DAPSA)≤4), Patient Acceptable Symptom State (PASS), Patient Global Assessment (PGA)(for example ≤1/10), or as a single for remission item.

Objectives: To explore the relationship between fatigue and remission in PsA, when using different definitions of remission.

Methods: ReFlaP (NCT03119805) is a cross-sectional study in 14 countries of consecutive adult patients with definite PsA and more than 2 years of disease duration. Patient-perceived fatigue was assessed by a 11-point numerical rating scale. Remission status was defined from the physician's perspective as MDA, DAPSA≤4 and physician-perceived remission (single question yes/no), and from the patient's perspective as PASS, PGA ≤1 and patient-perceived remission (single question yes/no). We calculated fatigue group means and deltas by remission status and compared these by Student's t test. For known groups validity of each remission definition we used ROC curves and corresponding areas under the curve (AUC).

Results: Of 366 patients, 304 had both fatigue and remission data available: 148 (49.8%) were male, mean age was 53.9±12.3 years, mean disease duration was 10.8±7.7 years; 90.3% had predominant peripheral disease, 56.3% were taking methotrexate, 66.5% a biologic and 19.4% oral glucocorticoids. Disease activity was moderate: 41.1% had no current psoriasis skin lesions, mean Tender Joint Count (TJC) was 4.3±8.9, mean Swollen Joint Count (SJC) was 2.66±8.3, mean Physician's global assessment was 3.0±2.4, mean PGA was 4.19%±2.7. 80.6% patients had DAPSA levels<28 (ie, remission, low or moderate disease activity). Mean patient's assessment of fatigue was 4.26±3.0. The frequency of remission varied from 17.4% to 64.8% (the most stringent definition being DAPSA and the least PASS). Fatigue levels were much lower in remission than non-remission with group differences in fatigue ranging from 1.66±0.3) (Physician remission single question yes/no) to 3.81±0.3 (DAPSA remission) (all p<0.0001) (figure 1). Corresponding AUCs ranged from 0.66 (Physician's remission question) to 0.87 (DAPSA).