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TOFACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS: ANALYSIS OF DERMATOLOGIC ENDPOINTS FROM 2 PHASE 3 STUDIES

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Background: Psoriatic arthritis (PsA) is a chronic, systemic inflammatory disease; the onset of dermatologic symptoms often precedes rheumatic manifestations.[1] Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. It has been shown that tofacitinib can improve dermatologic symptoms in patients (pts) with PsA.[2,3]

Objectives: To investigate the efficacy of tofacitinib in improving additional dermatologic endpoints in adult pts with active PsA.

Methods: This analysis included data from 2 placebo (PBO)-controlled, double–blind, Phase 3 studies in pts with active PsA and an inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD) who were tumour necrosis factor inhibitor (TNFi)-naïve (OPAL Broaden [12 months; NCT01877668]; N=422)[2] or had an IR to ≥1 TNFi (OPAL Beyond [6 months; NCT01882439]; N=394).[3] Pts must have had active plaque psoriasis at screening only and were required to receive a stable dose of 1 csDMARD. Pts were randomised to tofacitinib 5 mg twice daily (BID), 10 mg BID, adalimumab 40 mg subcutaneous injection once every 2 weeks (OPAL Broaden only) or PBO (advanced to tofacitinib 5 or 10 mg BID at Month [M]3). Percentage (%) change from baseline (BL) (Δ) in Psoriasis Area and Severity Index (PASI) total score, % of pts achieving ≥75% PASI improvement from BL (PASI75) stratified by BL PASI severity (>0 to ≤10, or >10), and ΔPatient's Global Joint and Skin Assessment-Visual Analogue Scale Psoriasis question (PGJS–VAS Psoriasis) were measured at M1, 3, 6, and at M9 and 12 (OPAL Broaden only).% ΔPASI total score and PASI75 were measured only in pts with BL affected body surface area (BSA) ≥3% and PASI >0. Safety endpoints were also analysed.

Results: BL demographics were similar between treatment groups and studies. BL median PASI scores (pts with BL BSA ≥3% and PASI >0) ranged from 5.6 to 7.8 (OPAL Broaden) and 7.1 to 8.8 (OPAL Beyond). BL mean PGJS–VAS Psoriasis ranged from 51.0 to 54.8 (OPAL Broaden) and 53.5 to 58.9 (OPAL Beyond). At M1 and 3,% ΔPASI total score, PASI75 response rates in pts with mild or moderate/severe dermatologic symptoms at BL, and ΔPGJS–VAS Psoriasis were improved vs PBO in tofacitinib-treated pts; these improvements were maintained to M12 in OPAL Broaden and M6 in OPAL Beyond (Table). Similar effects were observed in adalimumab-treated pts vs PBO in OPAL Broaden across these endpoints. Serious adverse events (AEs) and discontinuations due to AEs were similar across treatment groups up to M6 in OPAL Beyond and M12 in OPAL Broaden.

Conclusion: In pts with PsA (TNFi-naïve or TNFi-IR), tofacitinib improved dermatologic endpoints, and responses were maintained to the end of each study. Tofacitinib may provide a treatment option for pts with active PsA, including the dermatologic symptoms of PsA.

REFERENCES:

[1] Gladman DD, et al. Ann Rheum Dis 2005;64:ii14-7.
[2] Mease P, et al. N Engl J Med 2017;377:1537-50.
[3] Gladman D, et al. N Engl J Med 2017;377:1525-36.

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Table. Dermatologic endpoints in OPAL Broaden and OPAL Beyond

Month	OPAL Broaden (up to M12; N=422) Tofacitinib 5 mg BID N=107	Tofacitinib 10 mg BID N=104	Adalimumab 40 mg SC Q2W N=106	PBO N=105	OPAL Beyond (up to M6; N=394) Tofacitinib 5 mg BID N=113	Tofacitinib 10 mg BID N=132	PBO N=131
LS mean (SE) percentage change from baseline in PASI total score[a,b]							
	n=82	n=70	n=77	n=82	n=79	n=79	n=84
1	-50.1 (5.0)***	-65.1 (5.3)***	-34.1 (5.1)**	-16.5 (5.1)	-25.9 (7.7)*	-33.6 (7.7)**	-8.0 (7.4)
3	-58.4 (5.7)***	-67.1 (6.0)***	-55.1 (5.9)***	-27.6 (6.0)	-36.5 (7.9)	-47.4 (7.7)**	-17.6 (7.7)
6	-61.7 (5.8)	-79.9 (5.8)	-71.3 (5.6)	-	-40.7 (7.2)	-53.1 (7.2)	-
9	-72.8 (5.2)	-85.5 (5.6)	-75.0 (5.4)	-	-	-	-
12	-80.2 (5.5)	-86.5 (5.9)	-75.0 (5.7)	-	-	-	-
Number of responders achieving PASI75/pts evaluable at visit (%) with baseline PASI >0 to ≤10[b,c,d]							
1	15/60 (25.0)	15/44 (34.1)	8/47 (17.0)	4/54 (7.4)	10/52 (19.2)	12/45 (26.7)	5/56 (8.9)
3	25/57 (50.9)	22/44 (50.0)	14/46 (30.4)	9/54 (16.7)	11/45 (24.4)	23/46 (50.0)	12/46 (25.0)
6	29/57 (50.9)	25/42 (59.5)	27/45 (51.3)	-	17/41 (35.4)	24/42 (57.1)	-
9	28/57 (49.1)	26/41 (60.3)	22/43 (51.2)	-	-	-	-
12	37/54 (68.5)	28/41 (68.3)	21/42 (50.0)	-	-	-	-
Number of responders achieving PASI75/pts evaluable at visit (%) with baseline PASI >10[b,c,d]							
1	6/21 (35.1)	6/25 (16.0)	3/28 (10.7)	0/26 (0.0)	2/27 (7.4)	3/33 (9.1)	0/28 (0.0)
3	6/21 (28.6)	9/25 (36.0)	16/28 (57.1)	3/25 (12.0)	6/27 (22.2)	12/30 (40.0)	0/25 (0.0)
6	9/20 (45.0)	17/25 (68.0)	19/28 (67.9)	-	10/27 (37.0)	13/29 (44.8)	-
9	8/20 (40.0)	20/25 (80.0)	23/28 (82.1)	-	-	-	-
12	9/19 (47.4)	19/24 (79.2)	22/28 (78.6)	-	-	-	-
LS mean (SE) change from baseline in PGJS-VAS Psoriasis question[a,e]							
	n=106	n=104	n=106	n=104	n=128	n=130	n=130
1	-18.6 (2.3)***	-22.1 (2.3)***	-15.0 (2.3)**	-6.7 (2.3)	-21.4 (2.0)***	-23.3 (2.0)***	-7.4 (2.0)
3	-28.3 (2.4)***	-29.7 (2.4)***	-23.4 (2.5)***	-10.6 (2.6)	-22.4 (2.3)***	-27.6 (2.3)***	-7.7 (2.3)
6	-27.0 (2.4)	-30.0 (2.4)	-26.1 (2.4)	-	-21.7 (2.3)	-27.8 (2.3)	-
9	-27.4 (2.4)	-32.3 (2.4)	-27.0 (2.5)	-	-	-	-
12	-27.8 (2.5)	-30.4 (2.5)	-27.0 (2.5)	-	-	-	-

[a]Measured in patients with baseline BSA ≥3% and PASI >0. [b]This analysis was pre-specified; the total number of patients by treatment group included in the longitudinal model is shown as n. [c]Post hoc analysis. [d]PASI >0 to ≤10 was considered "mild"; "PASI >10 was considered "moderate/severe". [e]Patients answered the question "At all the ways your psoriasis affects you, how would you rate the way it–which you felt over the past week?", and their response was recorded on a VAS of 0–100 mm (0 = excellent; 100 = poor). N = number of patients in the full analysis set.

*Nominal p≤0.05; **p<0.01; ***p<0.001 vs PBO. No imputation was applied for missing values.

For percentage change from baseline in PASI total score and change from baseline in PGJS-VAS, the data were analysed using a repeated-measures model with fixed effects for treatment group, visit, interaction of the treatment group by visit, geographic location and baseline value. The model used a common unstructured variance–covariance matrix, without imputation for missing data. Two models were used. In the analyses of results through the first 3 months, the two PBO-to-tofacitinib sequences were combined into a single PBO group (pooled PBO group); the results through M3 were from this model. In the analyses of results after M3 (including all post-baseline data through M6 for OPAL Beyond and M12 for OPAL Broaden), the PBO-to-tofacitinib sequences were kept separate; the results after M3 were from this model.

#BID, twice daily; BSA, body surface area; Q2W, once every 2 weeks; LS, least squares; M, month; PASI, Psoriasis Area and Severity Index; PASI75, ≥75% PASI improvement from baseline; PBO, placebo; PGJS-VAS Psoriasis, Patient's Global Joint and Skin Assessment-Visual Analogue Scale Psoriasis question; pts, patients; SC, subcutaneous; SE, standard error; VAS, visual analogue scale