FRI0509 SAFETY AND EFFICACY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, UP TO 24 MONTHS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: INTERIM DATA FROM OPAL BALANCE, AN OPEN-LABEL, LONG-TERM EXTENSION STUDY

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Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for psoriatic arthritis (PsA). Interim data (database not locked) from ≤24 months' participation (3 years' total treatment duration) for patients (pts) with active PsA in an ongoing, open-label, long-term extension study (LTE; NCT01976364 OPAL Balance) is reported.

Objectives: To evaluate the safety, tolerability and efficacy of tofacitinib in pts with active PsA.

Methods: Eligible pts from 2 pivotal Phase 3 tofacitinib PsA studies (NCT01877668 OPAL Broaden, NCT01882439 OPAL Beyond) could enter a 3-year LTE ≤3 months after completing the qualifying study or discontinuing for non study-drug-related reasons. Pts were to receive tofacitinib 5 mg twice daily (BID) for 1 month, after which an increase to 10 mg BID or reduction back to 5 mg BID was permitted at any time for efficacy or safety reasons. Concomitant treatment with a single conventional synthetic disease-modifying antirheumatic drug (csDMARD) was allowed but not required. Primary endpoints were incidence and severity of adverse events (AEs) and change from baseline in laboratory values. Efficacy was a secondary endpoint.

Results: 680/685 enrolled pts were treated. 608 (89.4%) remained at data cut-off. Mean (range) duration of tofacitinib exposure in this LTE was 206 (3–741) days. 661 (97.2%) pts took a csDMARD on Day 1, and 73 (11.0%) later discontinued csDMARD. To Month 24, 860 AEs were reported in 367 (54.0%) pts, 41 (6.0%) pts had serious AEs and 24 (3.5%) pts discontinued due to AEs. Special interest AEs included 6 serious infections (0.9%), 10 herpes zoster events (1.5%) including 1 serious event, 2 major adverse cardiovascular events (0.3%) and 2 malignancies (0.3%). There were 3 deaths (not attributed to treatment, as assessed by the investigator) due to metastatic pancreatic carcinoma, acute cardiac failure and pulmonary embolism. No GI perforation, inflammatory bowel disease or uveitis cases were reported. One AE of latent TB was reported. One pt met discontinuation criteria for laboratory values due to increased serum creatinine >50% and >0.5 mg/dL over the average of screening and baseline creatinine. Small mean decreases in absolute lymphocyte and neutrophil counts, and small mean increases in serum lipid markers, were observed; 18 (2.6%) pts started new lipid-lowering medication during the LTE (80 [11.8%] pts were on lipid-lowering drug at baseline). Efficacy was maintained in the LTE (Table 1).

Table 1. Summary of efficacy through to Month 15[a]

	Tofacitinib (all patients) (N=680)				
	Month 3	Month 6	Month 9	Month 12	Month 15
ACR20, n/N1 (%)	421/606 (69.5)	326/470 (69.4)	219/307 (71.3)	109/154 (70.8)	48/66 (72.7)
ACR50, n/N1 (%)	264/607 (43.5)	217/469 (46.3)	160/308 (52.0)	77/153 (50.3)	31/66 (47.0)
ACR70, n/N1 (%)	154/608 (25.3)	140/471 (29.7)	92/308 (29.9)	48/153 (31.4)	19/67 (28.4)
ΔHAQ-DI, mean (SD) [N1]	-0.5 (0.6) [606]	-0.5 (0.6) [472]	-0.5 (0.6) [308]	-0.5 (0.6) [154]	-0.5 (0.6) [67]
PASI75 response rate, n/N1 (%)[b]	219/387 (56.6)	180/304 (59.2)	113/202 (55.9)	55/100 (55.0)	31/45 (68.9)
ΔLEI, mean (SD)[c] [N1]	-1.6 (1.8) [399]	-1.5 (1.8) [312]	-1.6 (1.8) [204]	-1.4 (2.0) [102]	-1.8 (2.1) [48]
ΔDSS, mean (SD)[c] [N1]	-6.9 (7.8) [330]	-6.8 (8.3) [254]	-6.9 (7.2) [164]	-6.9 (6.6) [83]	-7.3 (7.4) [39]
ΔPain, mean (SD)[d] [N1]	-25.3 (26.8) [604]	-26.3 (28.0) [471]	-28.7 (28.9) [308]	-28.7 (29.2) [154]	-31.4 (29.1) [67]

Baseline values represent those at the start of the qualifying study

Only evaluable pts at a visit of interest were included in the analysis and missing values were not imputed

[a]Efficacy data is reported to Month 15 as sample sizes were too small beyond this time point; [b]Among patients with baseline BSA ≥3% and PASI >0; [c]Among patients with baseline score >0; [d]Patient's assessment of arthritis pain measured using VAS (mm)

Δ, change from baseline; ACR, American College of Rheumatology; ACR20/50/70, ACR20%/50%/70% response rate; BSA body surface area; DSS, Dactylitis Severity Score; HAQ-DI, Health Assessment Questionnaire Disability Index; LEI, Leeds Enthesitis Index; N, number of patients in full analysis set; N1, number of evaluable patients at a visit; n, number of responders; PASI75, Psoriasis Area Severity Index 75% improvement; PsA, psoriatic arthritis; SD, standard deviation; VAS, visual analogue scale

Conclusions: Over 24 months in the LTE, the safety profile of tofacitinib in pts with active PsA was generally similar to that of the pivotal Phase 3 studies. No new safety signals were identified. Efficacy was maintained over time.

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FRI0510 CORRELATION OF THE ROUTINE ASSESSMENT OF PATIENT INDEX DATA (RAPID-3) WITH OTHER PSORIATIC ARTHRITIS COMPOSITE DISEASE ACTIVITY MEASURES IN PATIENTS RECEIVING ADALIMUMAB

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Background: There is increased interest across rheumatologic disease to utilize patient (pt)-reported outcomes (PROs) in disease assessment. Several measures entirely derived from PROs, such as the 3-component routine assessment of pt index data (RAPID-3), have been shown to be closely correlated with physician rheumatoid arthritis assessments using traditional composite scores.[1]

Objectives: To assess the correlation between the RAPID-3 and other psoriatic arthritis (PsA) composite indices [eg, disease activity index for PsA (DAPSA), minimal disease activity (MDA)] in pts with PsA receiving adalimumab (ADA) or placebo (PBO).

Methods: This post hoc analysis used data from the ADEPT trial, which included pts with active PsA despite prior DMARD therapy who were randomized to receive ADA or PBO for 24 weeks (wks). Mean RAPID-3 was summarized by visit for each treatment group. Correlations between RAPID-3 and DAPSA over time were assessed through Pearson and Spearman coefficient. Pts were categorized at wk 24 according to DAPSA [Remission: ≤4; low disease activity (LowDA): >4 – ≤14; moderate disease activity (ModDA): >14 – ≤28; high disease activity (HighDA): >28) and MDA [achievement of 5 of 7 or the more stringent 7 of 7 criteria (very low disease activity [VLDA]): yes, no], and assessed for the numbers of pts in each respective RAPID-3 disease activity state (Remission: ≤3; LowDA: >3 – ≤6; ModDA: >6 – ≤12; HighDA: >12). The Kappa statistic was used to describe the agreement between the numbers of pts in respective disease activity categories by RAPID-3, DAPSA, and MDA. Data were as observed.

Results: Amongst the 151 and 162 pts randomized to receive ADA and PBO, respectively, both groups exhibited HighDA when assessed by RAPID-3 [13.1 for both groups; 55% (ADA) and 54% (PBO) in HighDA]. At wk 24, mean RAPID-3 remained in HighDA for the PBO group (12.6), whereas it decreased to a state of LowDA (6.8) in those receiving ADA. Following 24 wks of treatment, 39% and 24% in the ADA group were in remission by RAPID-3 and DAPSA, respectively. Fewer pts in the PBO group were in remission by either definition at wk 24 (8% and 3%, respectively). At baseline, there was moderate correlation between RAPID-3 and DAPSA in both treatment groups (ADA: 0.512; PBO: 0.510). At wk 24, the correlations in both treatment groups increased, with the correlation observed in the ADA group outpacing the PBO group (ADA: 0.721; PBO: 0.590). Similarly, disease activity categorizations by RAPID-3 correlated with DAPSA and MDA categorizations (Table).

Conclusions: In a PBO-controlled trial of ADA in pts with PsA, there was good correlation between disease activity captured by pt's self-assessment, via the RAPID-3, and physician assessment, underscoring the potential utility of pt-derived measures in assessing disease activity.

References:

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