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POS1025

TOFACITINIB TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS AND PROBABLE DEPRESSION AND/OR ANXIETY: A POST HOC ANALYSIS OF TWO PHASE 3 CLINICAL TRIALS

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Background: Depression and anxiety are highly prevalent in patients (pts) with psoriatic arthritis (PsA),¹ with inflammation a key pathogenic feature of depression in these pts.² Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. It acts by modulating immune and inflammatory responses. The link between major depressive disorder/generalised anxiety disorder (MDD/GAD), inflammation and tofacitinib effectiveness has not been fully explored.

Objectives: Analyse the prevalence of probable MDD/GAD in pts with PsA initiating tofacitinib treatment and the impact of baseline (BL) probable MDD/GAD status on tofacitinib efficacy in these pts.

Methods: This was a post hoc analysis of data from pts who received tofacitinib 5 or 10 mg twice daily (BID), or placebo (PBO), pooled from two Phase 3 trials (12-month OPAL Broaden [NCT01877668];³ 6-month OPAL Beyond [NCT01882439]).⁴ Pts with BL probable MDD and/or GAD were identified by a Short Form-36 Health Survey (SF-36) Mental Component Summary score (MCS) ≤ 38 . Pt demographics/BL characteristics and outcomes were stratified by the presence (SF-36 MCS ≤ 38) or absence (SF-36 MCS > 38) of BL probable MDD/GAD. At Months (M)3/6/9/12, changes from BL in SF-36 MCS were evaluated, and efficacy assessed by the proportions of pts who achieved: Psoriatic Arthritis Disease Activity Score (PASDAS) ≤ 3.2 , Health Assessment Questionnaire-Disability Index (HAQ-DI) improvement ≥ 0.35 and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) improvement ≥ 4 . BL global pain was measured via visual analogue scale.

Results: Of the 706 pts included in this analysis, BL probable MDD/GAD was identified in 46.2%, 44.9% and 46.2% of pts in the tofacitinib 5 mg BID (108/234), tofacitinib 10 mg BID (106/236) and PBO (109/236) groups, respectively. BL disease activity was similar across the three treatment groups, independent of probable MDD/GAD status (mean PASDAS: 6.1–6.4 in pts with vs 5.8–6.1 in pts without probable MDD/GAD). In the tofacitinib 5 mg BID group, mean BL scores for HAQ-DI (1.4 vs 1.0), FACIT-F total score (20.5 vs 32.4) and global pain (61.3 vs 51.5) indicated worse disability, fatigue and pain, respectively, for pts with vs without BL probable MDD/GAD. Similar findings were seen in the tofacitinib 10 mg BID and PBO groups. At M3, improvements from BL in SF-36 MCS in pts with probable MDD/GAD were numerically, but not significantly, greater with tofacitinib 5 and 10 mg BID vs PBO, and these changes were largely sustained to M12 (Figure 1a). At M3, numerically greater proportions of pts achieved improvements in PASDAS, HAQ-DI and FACIT-F with tofacitinib 5 or 10 mg BID vs PBO, regardless of BL probable MDD/GAD status (Figure 1b–d). Through M3–12, the proportions of pts who achieved PASDAS ≤ 3.2 with tofacitinib 5 or 10 mg BID were generally significantly greater in pts without vs with probable MDD/GAD (Figure 1b). At all timepoints, rates of improvement in HAQ-DI with tofacitinib 5 mg BID were numerically greater in pts with vs without probable MDD/GAD, whereas the opposite was true for tofacitinib 10 mg BID (Figure 1c). FACIT-F improvement rates with tofacitinib 10 mg BID were consistently numerically greater in pts with vs without probable MDD/GAD, while findings were mixed for tofacitinib 5 mg BID (Figure 1d).

Figure. Efficacy measures at M3/6/9/12, (pooled data from OPAL Broaden and Beyond): a) change from BL in SF-36 MCS in pts with BL probable MDD/GAD (SF-36 MCS ≤ 38); b) proportion of pts achieving b) PASDAS ≤ 3.2 ; c) HAQ-DI ≥ 0.35 ; d) FACIT-F ≥ 4 , stratified by presence (SF-36 MCS ≤ 38) or absence (SF-36 MCS > 38) of BL probable MDD/GAD

Missing data were not imputed.
* $p < 0.05$, ** $p < 0.005$ for SF-36 MCS ≤ 38 vs > 38 strata.
†Statistical comparisons between tofacitinib and PBO at M3 were via t-test.
‡Statistical comparisons between SF-36 MCS ≤ 38 vs > 38 strata were via chi-squared test.
N, number of evaluable patients; SE, standard error.

Conclusion: Around 46% of pts with PsA treated with tofacitinib had BL probable MDD/GAD (SF-36 MCS ≤ 38). Pts with BL probable MDD/GAD treated with tofacitinib had sustained changes in SF-36 MCS. Rates of clinical improvement with tofacitinib were generally greater in pts without vs with probable MDD/GAD, whereas findings for disability and fatigue improvements varied between tofacitinib doses. Further research is required to evaluate the relationship between PsA and depression, to improve treatment targets and the quality of life of pts with PsA.

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POS1026

GUSELKUMAB PROVIDES SUSTAINED IMPROVEMENTS IN WORK PRODUCTIVITY AND NON-WORK ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS THROUGH 1 YEAR OF A PHASE 3 TRIAL

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Background: DISCOVER-2 was a Phase 3 trial of the first-in-class anti-IL-23-specific mAb guselkumab (GUS) in patients (pts) with psoriatic arthritis (PsA). PsA impacts patients' productivity at work and in daily activity.¹

Objectives: To evaluate the effect of GUS on work productivity and daily activity in DISCOVER-2 through 1 year using the Work Productivity and Activity Impairment Questionnaire: PsA (WPAI- PsA).

Methods: Bio-naïve adults with active PsA despite nonbiologic DMARDs &/or NSAIDs received subcutaneous GUS 100 mg every 4 weeks (Q4W); GUS 100 mg W0, W4, then Q8W; or placebo (PBO). At W24, PBO pts crossed over to GUS 100 mg Q4W. WPAI-PsA assesses PsA-related work time missed (absenteeism), impairment while working (presenteeism), impaired overall work productivity (absenteeism + presenteeism), and daily activity during the previous week. A shift analysis evaluated proportions of pts employed vs unemployed (regardless of desire to work) over time. Among pts working at baseline, least-squares (LS) mean changes from baseline in WPAI-PsA domains were determined using a mixed-effects model for repeated measures analysis, whereby mean changes in WPAI-PsA domains were calculated for each multiple imputation (MI) dataset using an analysis of covariance (ANCOVA); the reported LSmean is the average of all MI datasets. Also, among pts employed at baseline, indirect savings from improved overall work productivity were estimated using 2020 EU mean yearly wage estimate (all occupations).²

Results: In pts working at baseline, significant improvement in work productivity and non-work activity vs PBO was observed at W24. Productivity gains seen with GUS at W24 continued to improve through 1 year (Table 1). Shift analysis showed relatively stable employment in pts employed at baseline (62% of shift analysis cohort) through 1 year of GUS (>91% continued to work when assessed at W16, W24, and W52 [data not shown]). For those unemployed at baseline (38% of cohort), the proportion of pts working increased by ~10% following 1 year of GUS (Figure 1). Potential yearly indirect savings from improved overall work productivity were: €7409 GUS Q4W and €7039 GUS Q8W vs €4075 PBO at W24 and were €8520 GUS Q4W, €9632 GUS Q8W, and €6668 PBO→GUS Q4W at W52.

Conclusion: Improvement in work productivity and non-work activity was greater with GUS vs PBO among pts with active PsA through W52. Improvements demonstrated may result in reduction in PsA costs associated with work productivity.

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Table 1. Model-based estimates of LSmean change^a (95% CI) from baseline in WPAI-PsA domains among pts working at baseline and with an observed change through W24 (N=474) and W52 (N=475)

Change from baseline	GUS 100mg Q4W		GUS 100mg Q8W		PBO (W0-24)	PBO → GUS 100 mg Q4W (W24-52)
Visit	W24	W52	W24	W52	W24	W52
Absenteeism, N						
LSmean	145	145	147	147	162	163
	-3.4	-4.1	-3.0	-4.0	-3.0 (-6.0, 0.0)	-3.0
	(-6.5, -0.3)	(-6.8, -1.5)	(-6.0, 0.1)	(-6.6, -1.3)	0.04	(-5.5, -0.4)
Diff vs. PBO	-0.4		-0.01 (-4.2, 4.2)			
	(-4.6, 3.8)					
Presenteeism, N						
LSmean	145	145	147	147	162	163
	-20.1	-22.4	-19.6	-25.7	-10.5	-18.5
	(-23.7, -16.6)	(-26.3, -18.6)	(-23.2, -16.1)	(-29.5, -21.8)	(-13.9, -7.0)	(-22.2, -14.7)
Diff vs PBO	-9.7*		-9.2*			
	(-14.4, -5.0)		(-13.9, -4.5)			
Work productivity, N						
LSmean	145	145	147	147	162	163
	-20.1	-22.6	-19.2	-25.9	-10.6	-17.6
	(-24.1, -16.1)	(-26.8, -18.3)	(-23.1, -15.2)	(-30.0, -21.7)	(-14.4, -6.8)	(-21.7, -13.6)
Diff vs PBO	-9.5*		-8.6*			
	(-14.8, -4.2)		(-13.9, -3.3)			
Non-work Activity, N						
LSmean	242	242	246	246	245	245
	-20.5	-25.7	-21.2	-25.4	-9.9	-22.3
	(-23.3, -17.7)	(-28.6, -22.7)	(-23.9, -18.4)	(-28.4, -22.5)	(-12.6, -7.1)	(-25.3, -19.4)
Diff vs PBO	-10.6*		-11.3*			
	(-14.4, -6.8)		(-15.1, -7.5)			

CI=Confidence interval

a. LSmean for each MI dataset is calculated based on an ANCOVA model for the change from baseline at W24/W52. The combined LSmean, which is the average of the LSmean, taken over all the MI datasets, is presented.

*p<0.05

Figure. Shift Analysis of Working Status: Not Employed at Baseline

GUS 100 mg Q4W (N = 92), GUS 100 mg Q8W (N = 97), PBO → GUS 100 mg Q4W (W24-52) (N = 74)
 * GUS 100 mg Q4W: W16, 3.3%; W24, 2.2%; GUS 100 mg Q8W: W16, 1.0%; W24, 2.1%; PBO → GUS 100 mg Q4W (W24-52): W16, 1.4%; W24, 1.4%.

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POS1027

EFFICACY AND SAFETY OF GUSELKUMAB, A MONOCLONAL ANTIBODY SPECIFIC TO THE p19-SUBUNIT OF INTERLEUKIN-23, THROUGH 2 YEARS: RESULTS FROM A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY CONDUCTED IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Guselkumab (GUS), a selective IL-23 inhibitor dosed every 4 or 8 weeks (Q4W or Q8W), demonstrated efficacy for joint and skin symptoms, inhibition of structural damage progression (Q4W), and safety vs. placebo (PBO) through Week 24 (W24) of the Ph3, double-blind, PBO-controlled trial in biologic-naïve pts with PsA (DISCOVER-2).¹ Favorable benefit-risk was also seen through 1 year.²

Objectives: To assess GUS efficacy and safety through 2 years.