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POS1024

GUSELKUMAB PROVIDES SUSTAINED DOMAIN-SPECIFIC AND COMPREHENSIVE EFFICACY AS ASSESSED USING COMPOSITE ENDPOINTS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Guselkumab (GUS) is a human monoclonal antibody specific to the p19-subunit of interleukin-23. GUS significantly improved signs and symptoms of PsA through Week24 (Wk24), and improvements were maintained through Wk52 in the Phase 3 DISCOVER-1¹ and DISCOVER-2² studies.

Objectives: Assess GUS efficacy through Wk52 in both studies utilizing composite indices.

Methods: Adult patients (pts) enrolled had active PsA despite standard therapies. Pts in DISCOVER-1 had ≥ 3 swollen and ≥ 3 tender joints and C-reactive protein (CRP) ≥ 0.3 mg/dL; in DISCOVER-2, pts had ≥ 5 swollen and ≥ 5 tender joints and CRP ≥ 0.6 mg/dL. 31% of DISCOVER-1 pts received 1-2 prior tumor necrosis factor inhibitors; DISCOVER-2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100mg every 4 weeks (Q4W); GUS 100mg at Wk0, Wk4, then every 8 weeks (Q8W); or placebo (PBO); PBO pts crossed over to GUS 100mg Q4W at Wk24. Composite endpoints pooled across the two studies were: Disease Activity Index for Psoriatic Arthritis (DAPSA), Psoriatic Arthritis Disease Activity Score (PASDAS), Minimal Disease Activity (MDA), and Very Low Disease Activity (VLDA). GUS vs PBO comparisons through Wk24 employed a Cochran-Mantel-Haenszel test with baseline stratification factors or Fisher's exact test; no treatment group comparisons were performed beyond Wk24. P-values were not adjusted for multiplicity. From Wk24 -Wk52, pts with missing data were considered nonresponders (>90% of pts completed study treatment through Wk52).

Results: In randomized and treated pts from DISCOVER-1 (N=381) and DISCOVER-2 (N=739), pooled baseline characteristics were generally well-balanced across treatment groups and reflected active disease. Differences in response rates between GUS Q4W or Q8W and PBO were seen as early as Wk8 and increased over time through Wk24. In pts continuing GUS Q4W or Q8W, respectively, post-Wk24 response rates associated with these composite indices continued to increase through Wk52, at which time they were 54.2% and 52.5% for DAPSA LDA, 45.3% and 41.9% for PASDAS LDA, 35.9% and 30.7% for MDA, 18.2% and 17.6% for DAPSA remission, and 13.1% and 14.4% for VLDA, with no discernable difference between the GUS Q4W and Q8W dosing regimens (Table 1 and Figure 1). After PBO pts crossed over to GUS Q4W at Wk24, response rates increased through Wk52.

Conclusion: GUS 100mg Q4W and Q8W provided robust and sustained benefits to pts with active PsA across multiple domains, indicating that GUS

may provide an alternative treatment option for the diverse manifestations of PsA.

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Table 1. Pooled response rates for DISCOVER-1 and DISCOVER-2 randomized and treated patients.

	DISCOVER-1&2		
	GUS Q4W	GUS Q8W	PBO → GUS Q4W ¹
Randomized and treated patients, n	373	375	372
PASDAS² LDA			
Wk 24	27.9%**	30.1%**	8.9%
Wk 52	45.3%	41.9%	36.8%
MDA³			
Wk 24	22.8%**	24.3%**	7.8%
Wk 52	35.9%	30.7%	28.2%
DAPSA⁴ Remission			
Wk 24	10.2%**	8.3%**	2.2%
Wk 52	18.2%	17.6%	11.0%
VLDA³			
Wk 24	6.4%**	4.3%*	1.3%
Wk 52	13.1%	14.4%	8.3%

Data reported as proportions of patients, %. Unadjusted p values at Wk24 vs PBO: *p<0.05; **p<0.001.

¹ Pts randomized to PBO crossed over to GUS Q4W at Wk24.

² PASDAS is derived from Pt global assessment of arthritis and psoriasis (0-100), Physician global assessment (0-100), swollen joint count (0-66), tender joint count (0-68), CRP (mg/L), Leeds enthesitis index score, tender dactylitis count, and the 36-item Short-Form Health Survey Physical Component Summary score. PASDAS LDA ≤ 3.2 .

³ MDA is 5/7 criteria met; VLDA is 7/7 criteria met: tender joint count ≤ 1 , swollen joint count ≤ 1 , Psoriasis Activity and Severity Index ≤ 1 , Pt assessment of pain ≤ 15 (0-100), Pt global assessment of disease activity ≤ 20 (0-100), Health Assessment Questionnaire-Disability Index score ≤ 0.5 , Tender entheses points ≤ 1 .

⁴ DAPSA Remission: score ≤ 4 (definition in Figure 1 legend).

Figure. Proportions of Pooled DISCOVER-1 and DISCOVER-2 Patients Achieving DAPSA LDA^a Through Week 52.

Missing data imputed as nonresponse.

*, **, † p < 0.05, 0.01, 0.001, respectively, vs placebo. Unadjusted (nominal) p values are not controlled for multiplicity and are descriptive/supportive only; no statistical significance should be implied.

^a The DAPSA score is derived from tender joint count (0–68), swollen joint count (0–66), CRP (mg/dL), patient assessment of pain (0–10 cm VAS), and patient global assessment of disease activity (arthritis, 0–10 cm VAS). DAPSA LDA: ≤ 4 . DAPSA Remission: ≤ 4 .

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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.
^ap<0.05, ^bp<0.005 for SF-36 MCS ≤ 38 vs > 38 strata.
^cStatistical comparisons between tofacitinib and PBO at M3 were via t-test.
^dStatistical 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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