Effects of Guselkumab on Musculoskeletal Features in Patients With Active Psoriatic Arthritis by Baseline Skin Disease: Results From the Phase-3 DISCOVER-1 and DISCOVER-2 Studies

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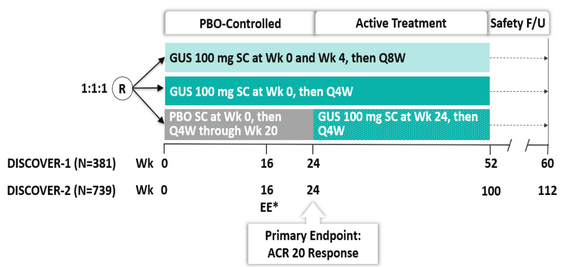
OBJECTIVE

- To evaluate the impact of treatment with Guselkumab (GUS) on musculoskeletal features of psoriatic arthritis (PsA) by baseline skin disease using pooled data from the phase-3 DISCOVER-1 and DISCOVER-2 studies

METHODS

- In both DISCOVER-1 and DISCOVER-2, patients were randomized 1:1:1 to subcutaneous (SC) GUS 100 mg every 4 weeks (Q4W), GUS 100 mg at Week 0 and Week 4, then every 8 weeks (Q8W), or placebo (Figure 1)
- Both studies included adults with active PsA for ≥6 months and active plaque psoriasis, nail changes, or history of plaque psoriasis
  - o In DISCOVER-1, active PsA was defined as swollen joint count (SJC) ≥3, tender joint count (TJC) ≥3, and C-reactive protein (CRP) ≥0.3 mg/dL
  - o In DISCOVER-2, active PsA was defined as SJC ≥5, TJC ≥5, and CRP ≥0.6 mg/dL

Figure 1. DISCOVER-1 and DISCOVER-2 Study Design



*EE=Early escape; patients were eligible to initiate/increase background medications if they had <5% improvement from baseline in both SJC and TJC at Week 16.
ACR=American College of Rheumatology; F/U=Follow-up; GUS=Guselkumab; PBO=Placebo; Q4W=Every 4 weeks; Q8W=Every 8 weeks; R=Randomization; SJC=Swollen joint count; TJC=Tender joint count; Wk=Week

- Some patients (31%) in DISCOVER-1 had prior exposure to up to 2 tumor necrosis factor-α inhibitors
- Patients in DISCOVER-2 were required to be biologic naïve
- The primary endpoint in both studies was American College of Rheumatology 20% improvement (ACR 20) response at Week 24
- Secondary endpoints included Psoriasis Area and Severity Index (PASI) 75, 90, and 100; Investigator's Global Assessment (IGA) response; ACR 50 response; and Health Assessment Questionnaire-Disability Index (HAQ-DI) scores at Week 24
- Pooled DISCOVER-1 and DISCOVER-2 results for ACR 20 and ACR 50 response rates and HAQ-DI changes from baseline were analyzed by baseline PASI score <12, ≥12 to <20, and ≥20 and by IGA score <2 and ≥2

RESULTS

- Baseline characteristics were similar across groups (Table 1)
  - o At baseline, 70.2% (261/372) of patients in the placebo group, 68.8% (258/375) in the GUS 100 mg Q8W group, and 73.2% (273/373) in the GUS 100 mg Q4W group had ≥3% BSA affected and an IGA score of ≥2

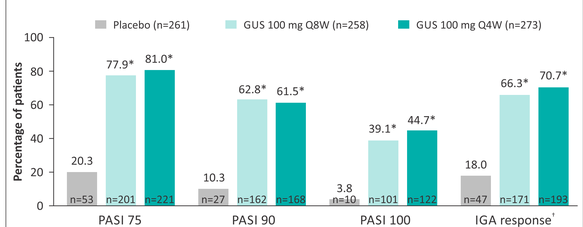
Table 1. Baseline Demographic and Disease Characteristics

	Placebo n=372	GUS 100 mg Q8W n=375	GUS 100 mg Q4W n=373	Total N=1120
Age (y), mean (SD)	47.2 (11.54)	46.2 (11.90)	46.5 (11.52)	46.6 (11.65)
Male, n (%)	178 (47.8)	197 (52.5)	208 (55.8)	583 (52.1)
Weight (kg), mean (SD)	84.4 (19.53)	84.1 (19.56)	86.1 (18.90)	84.9 (19.28)
BMI (kg/m^2), mean (SD)	29.2 (6.14)	29.1 (6.31)	29.4 (5.76)	29.2 (6.07)
SJC (0-66), median (range)	9 (3-55)	9 (3-58)	9 (2-56)	9 (2-58)
TJC (0-68), median (range)	17 (3-68)	16 (3-67)	17 (3-66)	16.5 (3-68)
HAQ-DI (0-3), mean (SD)*	1.28 (0.596)	1.26 (0.617)	1.20 (0.601)	1.24 (0.605)
CRP (mg/dL), median (range)	0.9 (0-19)	1.0 (0-19)	0.9 (0-19)	0.9 (0-19)

*Placebo, n=371; total, n=1119.
BMI=Body Mass Index; CRP=C-reactive protein; GUS=Guselkumab; HAQ-DI=Health Assessment Questionnaire-Disability Index; Q4W=Every 4 weeks; Q8W=Every 8 weeks, SD=Standard deviation; SJC=Swollen joint count; TJC=Tender joint count

- Pooled skin disease improvement results at Week 24 for all patients with ≥3% BSA affected and an IGA score ≥2 at baseline are shown in Figure 2

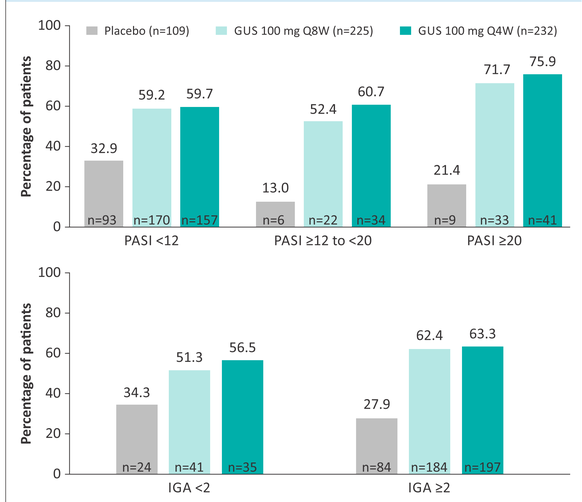
Figure 2. Skin Disease Improvement Results at Week 24 for Patients With ≥3% BSA Affected and IGA Score ≥2 at Baseline



*Nominal p<0.001 vs placebo; p-values calculated based on the Cochran-Mantel-Haenszel test.
†IGA response was defined as a score of 0 or 1 and ≥2 grade reduction from baseline.
BSA=Body surface area; GUS=Guselkumab; IGA=Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; Q4W=Every 4 weeks; Q8W=Every 8 weeks

- ACR 20 response rates at Week 24 were 29.3% (109/372) with placebo, 60.0% (225/375) with GUS 100 mg Q8W, and 62.2% (232/373) with GUS 100 mg Q4W
  - o ACR 20 response rates by baseline skin disease are shown in Figure 3

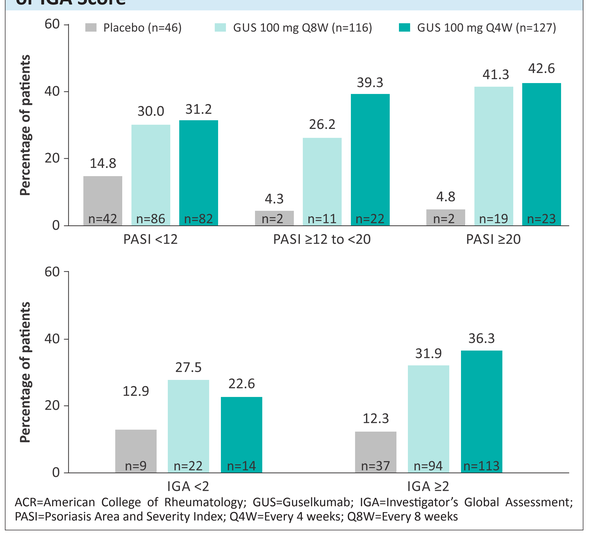
Figure 3. ACR 20 Response Rates at Week 24 by Baseline PASI or IGA Score



ACR=American College of Rheumatology; GUS=Guselkumab; IGA=Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; Q4W=Every 4 weeks; Q8W=Every 8 weeks

- ACR 50 response rates at Week 24 were 12.4% (46/372) with placebo, 30.9% (116/375) with GUS 100 mg Q8W, and 34.0% (127/373) with GUS 100 mg Q4W
  - o ACR 50 response rates by baseline skin disease are shown in Figure 4

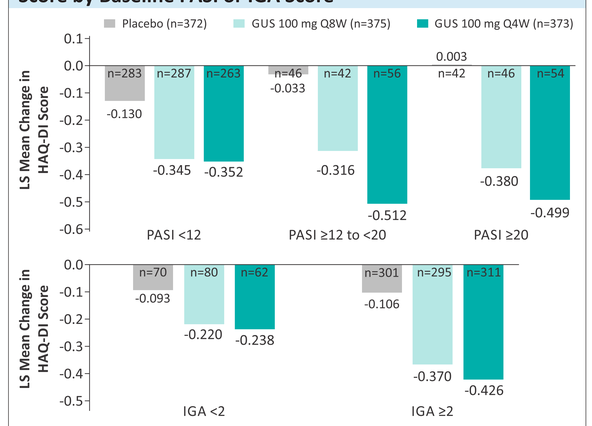
Figure 4. ACR 50 Response Rates at Week 24 by Baseline PASI or IGA Score



ACR=American College of Rheumatology; GUS=Guselkumab; IGA=Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; Q4W=Every 4 weeks; Q8W=Every 8 weeks

- Least squares (LS) mean changes in HAQ-DI from baseline to Week 24 by baseline skin disease are shown in Figure 5; statistical comparisons of GUS 100 mg Q8W and Q4W vs placebo are shown in Table 2

Figure 5. LS Mean Change From Baseline to Week 24 in HAQ-DI Score by Baseline PASI or IGA Score*



*Missing data were imputed by multiple imputations. LS mean changes were calculated using an analysis of covariance model. Lower HAQ-DI scores are indicative of better functioning.
GUS=Guselkumab; HAQ-DI=Health Assessment Questionnaire-Disability; IGA=Investigator's Global Assessment; LS=Least squares; PASI=Psoriasis Area and Severity Index; Q4W=Every 4 weeks; Q8W=Every 8 weeks

Table 2. LS Mean Difference Between GUS and Placebo in HAQ-DI Score Change From Baseline to Week 24 by Baseline PASI or IGA Score

	LS Mean Difference (95% CI) GUS 100 mg Q8W vs Placebo	Interaction *P*-value*	LS Mean Difference (95% CI) GUS 100 mg Q4W vs Placebo	Interaction *P*-value*
PASI <12	–0.215 (–0.29, –0.14)	0.313	–0.222 (–0.30, –0.14)	0.005
PASI ≥12 to <20	–0.283 (–0.46, –0.10)		–0.479 (–0.64, –0.31)	
PASI ≥20	–0.382 (–0.60, –0.17)		–0.501 (–0.71, –0.29)	
IGA <2	–0.128 (–0.29, 0.04)	0.228	–0.146 (–0.32, 0.03)	0.063
IGA ≥2	–0.263 (–0.34, –0.19)		–0.320 (–0.39, –0.25)	

*Based on the composite estimand and calculated using an analysis of covariance model.
CI=Confidence interval; GUS=Guselkumab; HAQ-DI=Health Assessment Questionnaire-Disability; IGA=Investigator's Global Assessment; LS=Least squares; PASI=Psoriasis Area and Severity Index; Q4W=Every 4 weeks; Q8W=Every 8 weeks

CONCLUSION

- Regardless of baseline skin disease severity, patients with active PsA achieved consistently greater improvements in musculoskeletal features of PsA with GUS than with placebo

Author disclosures
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