Wk24 in GUS-treated pts, with separation from PBO observed as early as Wk8; improvements were maintained at Wk52. At Wk24, BASDAI 50 response rates were higher in the Q4W and Q8W groups vs PBO (38% and 40% vs 19%).¹ At Wk52, mean BASDAI component scores for PBO pts who crossed over to GUS Q4W at Wk24 were similar to those for pts who were randomized to GUS.² A similar trend was observed for BASDAI50 response.

Conclusion: Among PsA pts with axial symptoms and sacroiliitis (via investigator-confirmed imaging) in the DISCOVER-1&2 trials, GUS treatment resulted in lower mean scores for all six BASDAI components compared with PBO as early as Wk 8 and through Wk24, with mean scores maintained at Wk52.

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Table 1. Baseline demographic and disease characteristics for patients who were identified by physicians as having symptoms consistent with spondylitis and had sacroiliitis confirmed via prior radiograph/MRI or screening radiograph

	GUS Q4W	GUS Q8W	Placebo
Patients, n	103	91	118
Male, n (%)	68 (66)	54 (59)	69 (59)
Age, years	44.9 ± 11.8	45.0 ± 10.7	45.3 ± 11.0
BASDAI			
Patients, n	95	84	110
Score	6.4 ± 1.7	6.5 ± 1.8	6.6 ± 1.5
BASDAI Components			
Fatigue	6.4 ± 2.0	6.7 ± 1.9	6.5 ± 1.9
Spinal pain	6.6 ± 2.1	6.5 ± 2.3	6.7 ± 2.0
Joint pain	6.3 ± 1.9	6.5 ± 2.2	6.8 ± 1.7
Enthesitis	6.3 ± 2.1	6.4 ± 2.2	6.3 ± 2.2
Qualitative morning stiffness	6.8 ± 2.1	6.7 ± 2.5	7.0 ± 2.0
Quantitative morning stiffness	6.2 ± 2.9	5.7 ± 2.9	6.1 ± 2.8

Data are mean ± standard deviation unless otherwise noted. BASDAI, Bath ankylosing spondylitis disease activity index

Figure. Mean scores of BASDAI components at week 24, DISCOVER-1 and DISCOVER-2

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AB0525

GUSELKUMAB TREATMENT SHOWS RAPID ONSET OF EFFECT ON COMPONENTS OF AMERICAN COLLEGE OF RHEUMATOLOGY RESPONSE CRITERIA: RESULTS OF 2 RANDOMIZED PHASE 3 TRIALS

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Background: Guselkumab (GUS), an anti-interleukin-23p19-subunit monoclonal antibody, demonstrated efficacy vs placebo (PBO) in achieving American College of Rheumatology 20% improvement (ACR20) response in patients (pts) with active psoriatic arthritis (PsA) in two phase 3 trials, DISCOVER-1 & 2.^{1,2}

Objectives: To assess the differential treatment effects of GUS across individual components of ACR response in PsA pts participating in the DISCOVER-1 & 2 trials.

Methods: In DISCOVER-1 & 2, 1120 pts were randomized & treated with GUS 100 mg every 4 weeks (Q4W; N=373); GUS 100 mg at Week (W)0 and W4, then Q8W (N=375); or matching PBO (N=372). Pts were evaluated by independent joint assessors at study visits. ACR20 response is defined as ≥20% improvement from baseline in both tender joint count (0-68 [TJC68]) and swollen joint count (0-66 [SJC66]) and ≥20% improvement from baseline in ≥3 of 5 assessments: Patient Assessment of Pain [Pt Pain], Patient Assessment of Global Disease Activity (arthritis) [PtGA], Physician Assessment of Global Disease Activity [PGA], Patient assessment of physical function as measured by Disability Index of the Health Assessment Questionnaire (HAQ-DI), and C-reactive protein (CRP). For each ACR component, achievement of ≥20% improvement from baseline was assessed over time through W24 for the combined (Q4W+Q8W) GUS groups, and median time to onset of treatment effect was determined with Kaplan-Meier curves by randomized group.

Results: Median time to response for all components except SJC66 occurred earlier with GUS than PBO. Time to onset of ACR20 treatment effect is shown in Figure 1. CRP data show 56% of GUS-treated pts had diminution of systemic inflammation by W4 (Table 1). Reduction in systemic inflammation was accompanied or rapidly followed by GUS-related improvement in both PtGA and PGA (median W4-8). Although SJC66/TJC68 data showed similar patterns, there was also a high PBO response (data not shown). Consistent with early reductions in systemic inflammation, 48-61% of GUS-treated pts had ≥20% improvement in TJC68/SJC66/PGA at W4 (Table 1), and 45-48% had ≥20% improvement in HAQ-DI, PtGA, and Pt Pain by W8. By W24, >80% of GUS-treated pts had ≥20% improvement in SJC66/TJC68/PGA, followed by 63-64% with this degree of improvement in PtGA, CRP, and Pt Pain, and 57% for HAQ-DI.

Conclusion: GUS demonstrated ACR20 improvements with separation from PBO in ACR components as early as W4, which is consistent with reduced inflammation by GUS and prior serological studies.³ At early study time points, both pts and physicians were able to discern improvements in signs and symptoms of arthritis that rapidly followed reductions in systemic inflammation (CRP). The predominant drivers of ACR20 response rates at W24 in GUS pts were SJC66/TJC68/PGA.

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Table 1.

	W4	W8	W12	W16	W20	W24
ACR20	20	39	50	56	60	61
HAQ-DI score	36	45	52	54	56	57
SJC66	61	74	84	86	87	88
TJC68	48	65	75	79	80	81
PGA	50	67	74	78	81	81
Pt Pain	35	48	58	59	62	64
Pt Pain	32	48	55	58	61	63
CRP	56	60	62	63	64	64

Figure. Median time to ACR20 response.

Data shown at W2 were derived solely from DISCOVER-2, as DISCOVER-1 did not include assessments at W2. The intersection of horizontal and vertical dashed lines denotes the time at which 50% of patients in a treatment group achieved ACR20 response.

Figure 1

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AB0526

SUSTAINED GUSELKUMAB RESPONSE IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS REGARDLESS OF BASELINE DEMOGRAPHIC AND DISEASE CHARACTERISTICS: POOLED RESULTS THROUGH WEEK 52 OF TWO PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED STUDIES

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Background: In the Phase 3 DISCOVER-1¹ & DISCOVER-2² trials, guselkumab (GUS), a human monoclonal antibody targeting the IL-23p19-subunit, was effective in psoriatic arthritis (PsA) across joint & skin endpoints. At Week 24 (W24), GUS benefit was consistent regardless of baseline (BL) demographic & disease characteristics.³

Objectives: We assessed whether GUS efficacy was sustained through W52 in pooled DISCOVER-1 & -2 patients (pts) across select BL subgroups.

Methods: Adults with active PsA despite standard therapies were enrolled in DISCOVER-1 (swollen [SJC] ≥3 & tender joint count [TJC] ≥3, C-reactive protein [CRP] ≥0.3 mg/dL) & DISCOVER-2 (SJC ≥5 & TJC ≥5, CRP ≥0.6 mg/dL). 31% of DISCOVER-1 pts had received 1-2 prior tumor necrosis factor inhibitors; DISCOVER-2 pts were biologic naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO). Pts randomized to PBO received GUS 100 mg Q4W starting at W24 & were excluded from these analyses assessing maintenance of effect from W24 to W52. GUS effects on joint (American College of Rheumatology [ACR]20/50/70) & skin (Investigator's Global Assessment [IGA=0/1 + ≥2-grade reduction from W0] in pts with ≥3% body surface area [BSA] with psoriasis & IGA ≥2 at W0) endpoints were evaluated by pt BL SJC, TJC, conventional synthetic disease-modifying antirheumatic drug (csDMARD) use, body mass index (BMI), PsA duration, & % BSA with psoriasis. Missing data were imputed as non-response through W52.

Results: BL pt characteristics in DISCOVER-1 (N=381) & DISCOVER-2 (N=739) were well balanced across randomized groups.^{1,2} Among 1120 pooled pts, mean SJC was 11, mean TJC was 21, & 68% used csDMARDs (primarily methotrexate [MTX]). At W24, 62% (232/373) & 60% (225/375), respectively, of GUS Q4W- & Q8W-treated pts achieved ACR20 vs 29% (109/372) of PBO, with GUS effect consistently observed across pt BL subgroups (Figure 1). ACR20 response rates were sustained or increased at W52 in the GUS Q4W (72%) & Q8W (70%) groups & across SJC (61-79%), TJC (68-76%), & csDMARD use (68-80%) subgroups (Table 1) & pt subgroups defined by BL BMI, PsA duration, & % BSA with psoriasis (data not shown). ACR50 & 70 response patterns were similar to ACR20 (Table 1). In pts with ≥3% BSA psoriasis & IGA ≥2 at BL, 71% (193/273) & 66% (171/258) of GUS Q4W- & Q8W-treated pts, respectively, vs 18% (47/261) of PBO, achieved IGA 0/1 at W24, with GUS effect consistently observed across pt BL subgroups (Figure 1). IGA 0/1 response rates were also sustained or increased at W52 in the GUS Q4W (80%) & Q8W (71%) groups & across % BSA with psoriasis (67-87%) & csDMARD use (68-87%) subgroups (Table 1) & pt subgroups defined by BL BMI and PsA duration (data not shown).

Conclusion: Treatment with GUS 100 mg Q4W & Q8W resulted in sustained improvement in signs & symptoms of active PsA through W52 regardless of pt BL characteristics.

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