of enthesitis, and resolution of dactylitis were maintained or further improved from wk 24¹ through wk 56; these proportions were generally greater for pts originally randomized to UPA vs ADA (Table 1). At wk 56, mean change from BL in mTSS was similar with UPA15, UPA30, and ADA. Improvements in pts who switched from PBO to UPA were generally similar to those originally randomized to UPA at wk 56. Through wk 56, the rates of TEAEs and serious AEs, including serious infections, were similar in the UPA15 and ADA arms and higher with UPA30 (Figure 1). The rate of herpes zoster was higher with UPA vs ADA in a dose-dependent manner. Malignancies were reported at similar rates among all treatment groups. Adjudicated venous thromboembolic events and major adverse cardiovascular events were reported in all groups with comparable rates. Two deaths were reported with UPA15, 2 with UPA30, and 1 with ADA; 1 death was reported with PBO during the 24-wk PBO-controlled period.

Conclusion: Efficacy responses were maintained or further improved with UPA15 and UPA30 over 56 wks and were numerically higher vs ADA. The inhibition of radiographic progression was maintained at wk 56 and was similar with UPA and ADA. At wk 56, improvements in efficacy were observed in pts who switched from PBO to UPA. No new safety findings were observed with longer exposure to UPA.

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Figure. Exposure-adjusted Event and Incidence Rates of Treatment-emergent AEs Through Week 56

ADA, adalimumab; AE, adverse event; CI, confidence interval; CPK, creatine phosphokinase; EAIR, exposure-adjusted incidence rate; ECV, every other visit; GI, gastrointestinal; MACE, major adverse cardiovascular events; defined as non-fatal myocardial infarction, nonfatal stroke, and cardiovascular death; NMSC, non-melanoma skin cancer; PY, patient-years; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolism defined as deep vein thrombosis (DVT) and pulmonary embolism (PE).

* Opportunistic infections excluding tuberculosis and herpes zoster; UPA15, one event each of candida urethritis, cryptococcal meningitis, and one lung infection; UPA30, one event each of cryptococcal meningitis, cryptococcal meningitis, and one lung infection; ADA, one event each of candida urethritis, cryptococcal meningitis, and one lung infection.

[†] Herpes zoster: most events were mild or moderate in severity, limited to <10 dermatomes, and did not lead to study drug discontinuation.

[‡] UPA15, 4 cases of carcinoma, 2 squamous cell carcinoma of skin, and 1 event each of endometrial adenocarcinoma, lung adenocarcinoma, lung cancer metastatic, malignant melanoma, and adenocarcinoma; UPA30, 2 cases of carcinoma, 2 squamous cell carcinoma of skin, and 1 event each of adenocarcinoma of colon, B-cell lymphoma, breast cancer, clear cell renal cell carcinoma, invasive breast carcinoma, lung adenocarcinoma, and plasma cell myeloma; ADA, 2 cases of carcinoma, and 1 event each of colon cancer metastatic, ovarian cancer, pancreatic carcinoma metastatic, and adenocarcinoma.

[§] VTE were reported in 1 patient; UPA15, 1; UPA30, 1; ADA, 1; in the PBO-controlled period in 1 patient who was discontinuing and experienced an unrelated event.

^{||} Deaths: UPA15, 1 due to metastatic lung cancer and 1 due to liver respiratory tract infection; UPA30, 1 due to coronavirus infection and 1 due to interstitial lung disease; ADA, 1 death was reported in the placebo group during the 24-week placebo-controlled period in a patient who was discontinuing and experienced an unrelated event.

Figure 1

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AB0524 EFFICACY OF GUSELKUMAB ACROSS BASDAI COMPONENTS IN TREATING AXIAL-RELATED SYMPTOMS OF PSORIATIC ARTHRITIS: RESULTS FROM TWO PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED STUDIES

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Background: The monoclonal antibody guselkumab (GUS; anti-IL-23p19-subunit) is approved to treat psoriatic arthritis (PsA). Post hoc analyses of DISCOVER-1&2 suggested that GUS may be effective in improving symptoms of axial manifestation of PsA.

Objectives: Evaluate the efficacy of GUS across components of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) in improving symptoms of axial manifestations of active PsA patients (pts) using data from Phase 3, randomized, placebo (PBO)-controlled studies.

Methods: DISCOVER-1&2 enrolled pts with active PsA; pts were randomized to subcutaneous injections of guselkumab 100 mg every 4 weeks (Q4W) or at Wk0, 4, and Q8W, or PBO. These post hoc analyses included pts who were identified by the investigator as having axial symptoms and sacroiliitis (prior X-ray or MRI or screening X-ray). BASDAI scores were assessed at Wks 0, 8, 16, 24, and 52. Mean BASDAI component scores through Wk52 are reported by treatment group. Pooled data from the two studies are reported. Mean BASDAI component scores are reported using observed data; total BASDAI scores with missing components were set to missing. The proportion of pts achieving ≥50% improvement in BASDAI (BASDAI 50) was also determined; pts with missing data or who met the treatment failure criteria (discontinued study agent or used prohibited medications) were considered nonresponders at all subsequent timepoints.

Results: These analyses included 312 pts from DISCOVER-1&2 (103 GUS Q4W, 91 GUS Q8W, 118 PBO); mean total BASDAI scores at Wk0 were 6.4, 6.5, and 6.6, respectively. Demographics and mean baseline BASDAI component scores (ie, fatigue, spinal pain, joint pain, enthesitis, qualitative morning stiffness, and quantitative morning stiffness) were similar across treatment groups (Table 1). In comparison with the total study population, this subgroup of pts had a higher mean C-reactive protein level at baseline and a higher proportion of pts with enthesitis and included a slightly higher proportion of males. Mean scores for all six BASDAI components, including spinal pain, decreased through

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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