Efficacy of Guselkumab, a Monoclonal Antibody That Specifically Binds to the p19-Subunit of IL-23, on Endpoints Related to Axial Involvement in Patients With Active Psoriatic Arthritis With Imaging-Confirmed Sacroiliitis: Week-24 Results From Two Phase-3, Randomized, Double-blind, Placebo-controlled Studies

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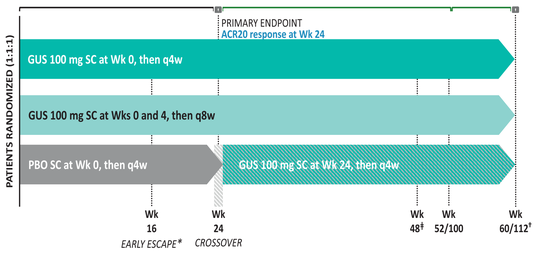
BACKGROUND

- Guselkumab (GUS), a human monoclonal antibody that specifically binds to the p19-subunit of interleukin (IL)-23, is approved for adults with moderate-to-severe psoriasis (100 mg every 8 weeks [q8w])
- In two phase-3 studies (DISCOVER-1 and DISCOVER-2)[1,2], GUS improved signs and symptoms of active psoriatic arthritis (PsA) and inhibited radiographic progression (DISCOVER-2) versus placebo at Week 24
- This post-hoc analysis from the pooled DISCOVER-1 and -2 studies evaluated the efficacy of GUS in PsA patients with imaging-confirmed axial inflammation consistent with sacroiliitis

METHODS

- In both DISCOVER-1 and DISCOVER-2 studies, patients with active PsA despite standard therapies were randomized 1:1:1 to GUS 100 mg q4w; GUS 100 mg at Week 0, Week 4, and then q8w; or placebo (Figure 1)

Figure 1. Study Design



*Early escape patients were eligible to initiate/increase background medications if <5% improvement from baseline in both tender/swollen joint counts at Week 16; ‡Last dose in DISCOVER-1 was at Week 48; Last dose in DISCOVER-2 was at Week 100; †Follow-up to Week 60 in DISCOVER-1 and from Week 100-112 in DISCOVER-2.
ACR, American College of Rheumatology; GUS, guselkumab; PBO, placebo; SC, subcutaneous; q4w, every 4 weeks; q8w, every 8 weeks; Wk, week

  - DISCOVER-1 (n=381 randomized and treated):
    - ≥3 swollen and ≥3 tender joints and C-reactive protein (CRP) ≥0.3 mg/dL
    - With or without tumor necrosis factor-α inhibitor (TNFi) experience
    - Approximately 30% patients in DISCOVER-1 had prior exposure to up to 2 TNFi
  - DISCOVER-2 (n=739 randomized and treated):
    - ≥5 swollen and ≥5 tender joints and CRP ≥0.6 mg/dL
    - Naïve to biologic agents and Janus kinase inhibitors
- Investigators confirmed sacroiliitis either by documented prior imaging or pelvic radiograph at screening
- Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)- and Ankylosing Spondylitis Disease Activity Score (ASDAS)-related axial efficacy endpoints were measured over 24 weeks
  - Patients with missing data at a visit were classified as non-responders at that visit
  - Patients meeting treatment failure criteria prior to a visit were classified as non-responders and had no change from baseline

RESULTS

- A total of 312 patients had axial involvement consistent with sacroiliitis at baseline and either a history of imaging confirmation (DISCOVER-1 and -2) or pelvic radiograph at screening (DISCOVER-2)
- Baseline characteristics were consistent among the groups (Table 1)

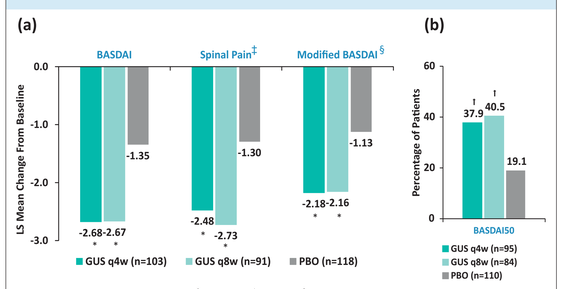
Table 1. Baseline Demographic and Disease Characteristics

	GUS q4w	GUS q8w	PBO	Total
Analysis set*, N	103	91	118	312
PsA disease duration (yrs)	5.5 (5.53)	4.8 (5.04)	6.7 (6.39)	5.7 (5.78)
Male, n (%)	68 (66.0)	54 (59.3)	69 (58.5)	191 (61.2)
BMI (kg/m²)	28.0 (6.13)	27.6 (6.50)	28.5 (6.21)	28.1 (6.26)
CRP (mg/dL)	2.3 (2.89)	2.7 (3.37)	2.4 (2.88)	2.5 (3.03)
Axial disease-related activity (0-10)				
BASDAI	6.5 (1.70)	6.5 (1.80)	6.6 (1.54)	6.5 (1.67)
Modified BASDAI (without Q3)	6.4 (1.79)	6.5 (1.85)	6.5 (1.62)	6.5 (1.74)
BASDAI Q2 (Spinal Pain)	6.6 (2.14)	6.5 (2.28)	6.7 (1.99)	6.6 (2.10)
ASDAS-CRP	3.9 (0.84)	3.9 (1.05)	4.0 (0.79)	3.9 (0.89)
HLA-B27 status available, N	63	56	71	190
HLA-B27 Positive, n (%)	22 (34.9)	17 (30.3)	18 (25.3)	57 (30.0)
HLA-B27 Negative, n (%)	41 (65.1)	39 (69.6)	53 (74.6)	133 (70.0)

Data presented are mean (SD) unless otherwise specified. *Patients with spondylitis and peripheral arthritis at baseline and either a history of imaging confirmation (DISCOVER-1 and -2) or pelvic radiograph at screening (DISCOVER-2).
ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; CRP, C-reactive protein; HLA, human leukocyte antigen; PBO, placebo; PsA, psoriatic arthritis; q4w, every 4 weeks; q8w, every 8 weeks

- Least squares mean changes from baseline to Week 24 in BASDAI, spinal pain and modified BASDAI were significantly greater in both GUS-treated groups versus placebo (p<0.001) (Figure 2a)
- BASDAI50 response rate at Week 24 was significantly greater in both GUS-treated groups versus placebo (p<0.01) (Figure 2b)

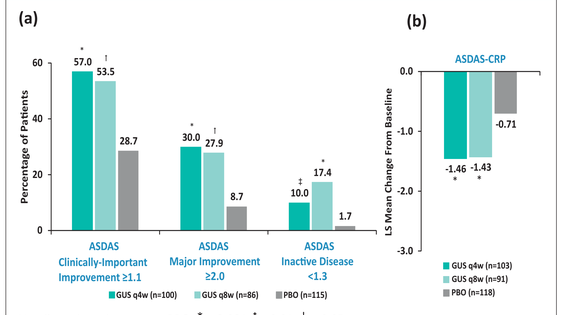
Figure 2. BASDAI Responses at Week 24 in GUS-treated PsA Patients with Axial Involvement Versus Placebo



Unadjusted p-value versus PBO: *p<0.001; †p<0.01. ‡Question 2 of the BASDAI (How would you describe the overall level of inflammatory neck, back or hip pain you have had?); §Excludes Question 3 of the BASDAI (How would you describe the overall level of pain/swelling in joints other than neck, back, hips you have had?).
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; GUS, guselkumab; LS, least squares; PBO, placebo; PsA, psoriatic arthritis; q4w, every 4 weeks; q8w, every 8 weeks

- Greater proportions of GUS-treated patients achieved ASDAS responses of clinically-important improvement, major improvement, and inactive disease at Week 24 versus placebo (Figure 3)

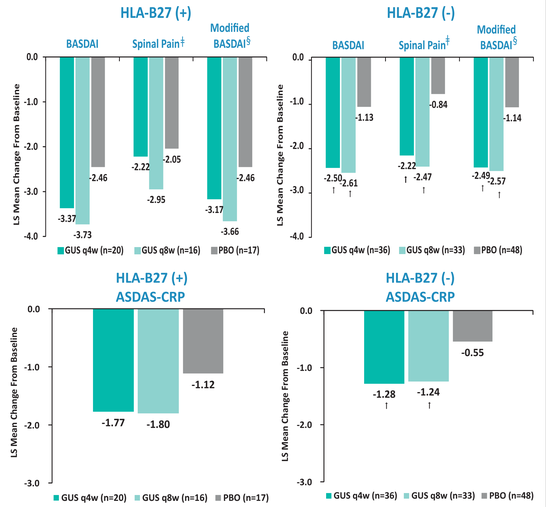
Figure 3. ASDAS Responses at Week 24 in GUS-treated PsA Patients with Axial Involvement Versus Placebo



Unadjusted p-values versus PBO: *p<0.001; †p<0.01; ‡p<0.05.
ASDAS, Ankylosing Spondylitis Disease Activity Score; CRP, C-reactive protein; GUS, guselkumab; LS, least squares; PBO, placebo; PsA, psoriatic arthritis; q4w, every 4 weeks; q8w, every 8 weeks

- Greater improvements in BASDAI- and ASDAS-related endpoints were observed in GUS-treated groups versus placebo irrespective of HLA-B27 status at Week 24 (Figure 4)

Figure 4. BASDAI and ASDAS-CRP Responses at Week 24 by HLA-B27 Status in GUS-treated PsA Patients Versus Placebo



Unadjusted p-value versus PBO. †p<0.01. ‡Question 2 of the BASDAI (How would you describe the overall level of inflammatory neck, back or hip pain you have had?); §Excludes Question 3 of the BASDAI (How would you describe the overall level of pain/swelling in joints other than neck, back, hips you have had?).
ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CRP, C-reactive protein; GUS, guselkumab; HLA, human leukocyte antigen; LS, least squares; PBO, placebo; PsA, psoriatic arthritis; q4w, every 4 weeks; q8w, every 8 weeks

CONCLUSIONS

- GUS 100 mg q4w and q8w improved axial symptoms over 24 weeks in active PsA patients with reported radiographic sacroiliitis
  - As measured by BASDAI- and ASDAS-related endpoints
- Improvements in axial symptoms were observed irrespective of HLA-B27 status

REFERENCES

1. Deodhar A, et al. *Lancet*. 2020;395:1115-1125; 2. Mease P, et al. *Lancet*. 2020;395:1126-1136

DISCLOSURES

P. Helliwell - Grants/research support paid to charity (AbbVie, Janssen, Novartis) or honoraria/consultation fees paid to charity (AbbVie, Amgen, Pfizer, UCB) or himself (Celgene, Galapagos); D. Gladman - Grants/research support: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, and UCB; Consultant of: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, and UCB; D. Poddubnyy - Grants/research support: AbbVie, MSD, Novartis, and Pfizer; Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, and UCB; Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer, Roche, and UCB; P. Mease - Grants/research support: AbbVie, Amgen, Bristol-Myers Squibb, Janssen, Eli Lilly, Novartis, Pfizer, Sun Pharma, and UCB; Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Galapagos, Gilead, Novartis, Pfizer, Sun Pharma, and UCB; Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Novartis, Pfizer, and UCB; X. Baraliakos - Grants/research support: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen; Consultant of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen; Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB and Werfen; A. Deodhar - Grants/research support: AbbVie, Eli Lilly, GSK, Novartis, Pfizer, and UCB; Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB; Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB; D. Van der Heijde - Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB; Director of Imaging Rheumatology BV; A. Kollmeier, E. Hsia, X. Xu, S. Sheng, P. Agarwal, and B. Zhou - employees of Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson) and own Johnson & Johnson stock or stock options; S. Chakravarty - employee of Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson) and owns Johnson & Johnson stock or stock options; M. Shawi and C. Karyekar - employees of Janssen Global Services, LLC (a subsidiary of Johnson & Johnson) and own Johnson & Johnson stock or stock options.

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