Effects of Guselkumab on Articular Components of American College of Rheumatology (ACR) Score and Skin Responses in Patients With Active Psoriatic Arthritis (PsA): Results From the Phase-3 DISCOVER-2 Study

A.B. Gottlieb,[1] P.J. Mease,[2] J.F. Merola,[3] A.P. Kollmeier,[4] E.C. Hsia,[4,5] X.L. Xu,[4] P. Agarwal,[4] D. van der Heijde,[6] I.B. McInnes,[7] W.-H. Boehncke[8]

[1]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Swedish Medical Center and University of Washington, Seattle, WA, USA; [3]Department of Medicine, Division of Rheumatology, Allergy and Immunology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA; [4]Janssen Research & Development, LLC, Spring House, PA, USA; [5]University of Pennsylvania, Philadelphia, PA, USA; [6]Leiden University Medical Center, Leiden, The Netherlands; [7]Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, UK; [8]Service de Dermatologie, Hôpital Universitaire de Genève, Geneva, Switzerland

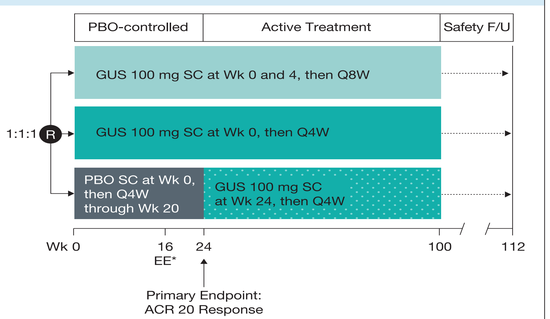
OBJECTIVE

- To evaluate efficacy results from the phase-3 DISCOVER-2 study of guselkumab (GUS) in biologic-naïve patients with active psoriatic arthritis (PsA) based on American College of Rheumatology (ACR) response criteria and skin clearance

METHODS

- This study included adults with active PsA for ≥6 months and active plaque psoriasis, nail changes, or history of plaque psoriasis
  - Active PsA was defined as swollen joint count (SJC) ≥5, tender joint count (TJC) ≥5, and C-reactive protein (CRP) level ≥0.6 mg/dL
- Patients were randomized 1:1:1 to subcutaneous 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)
- The primary endpoint was ACR 20 response at Week 24
- Efficacy assessments performed based on ACR component responses included mean changes from baseline to Week 24 in the following:
  - SJC (0-66)
  - TJC (0-68)
  - Patient assessment of pain (0-10 cm visual analog scale [VAS])
  - Patient global assessment of disease activity (PtGA; 0-10 cm VAS)
  - Physician global assessment of disease activity (PGA; 0-10 cm VAS)
  - Health Assessment Questionnaire-Disability Index (HAQ-DI) scores (0-3)
  - CRP (mg/dL)
- Skin clearance was determined based on achievement of Psoriasis Area and Severity Index (PASI) 100 or Investigator's Global Assessment (IGA) 0 (cleared) in patients with ≥3% body surface area (BSA) affected and IGA score ≥2 at baseline
- Safety was evaluated based on rates of adverse events through Week 24

Figure 1. Study Design



*EE occurred if patients had <5% improvement from baseline in both SJC and TJC at Week 16. These patients could initiate or increase the dose of allowed background medications while continuing study treatment.

ACR=American College of Rheumatology; EE=Early escape; F/U=Follow-up; GUS=Guselkumab; PBO=Placebo; Q4W=Every 4 weeks; Q8W=Every 8 weeks; R=Randomization; SC=Subcutaneous; SJC=Swollen joint count; TJC=Tender joint count; Wk=Week.

RESULTS

- A total of 739 patients were included in the full analysis set. Baseline demographic and disease characteristics for these patients are shown in Table 1.
- Primary endpoint results showed that ACR 20 response at Week 24 was 32.9% for placebo, 64.1% for GUS 100 mg Q8W, and 63.7% for GUS 100 mg Q4W (p<0.001 for GUS vs placebo)

Table 1. Baseline Demographic and Disease Characteristics

	Placebo	GUS 100 mg Q8W	GUS 100 mg Q4W
Full analysis set, n	246	248	245
Age (y), mean (SD)	46.3 (11.68)	44.9 (11.89)	45.9 (11.47)
Male, n (%)	117 (47.6)	129 (52.0)	142 (58.0)
Weight (kg), mean (SD)	84.0 (19.67)	83.0 (19.31)	85.8 (19.53)
BMI (kg/m^2), mean (SD)	29 (6.35)	28.7 (6.25)	29.1 (5.91)
SJC (0-66), median (range)	10 (5-55)	9.5 (5-46)	11 (5-56)
TJC (0-68), median (range)	18 (5-68)	16 (5-64)	19 (5-66)
Patient assessment of pain (0-10 VAS), mean (SD)	6.28 (1.773)	6.31 (1.958)	6.15 (1.987)
PtGA (0-10 VAS), mean (SD)	6.51 (1.790)	6.53 (1.932)	6.39 (1.943)
PGA (0-10 VAS), mean (SD)	6.65 (1.490)	6.56 (1.606)	6.62 (1.538)
HAQ-DI (0-3), mean (SD)*	1.29 (0.558)	1.28 (0.627)	1.25 (0.567)
CRP (mg/dL), median (range)	1.16 (0.01-19.30)	1.31 (0.03-18.80)	1.16 (0.01-19.00)
BSA (%), mean (SD)†	17.1 (19.99)	17.0 (20.98)	18.2 (20.39)
PASI score (0-72), mean (SD)*	9.3 (9.79)	9.7 (11.72)	10.8 (11.68)
IGA score (0-4), n (%)*			
Mild (2)	94 (38.4)	87 (35.1)	84 (34.3)
Moderate (3)	101 (41.2)	85 (34.3)	90 (36.7)
Severe (4)	14 (5.7)	23 (9.3)	27 (11.0)

*Placebo, n=245. †Placebo, n=245; GUS 100 mg Q8W, n=246.

BMI=Body mass index; BSA=Body surface area; CRP=C-reactive protein; GUS=Guselkumab; HAQ-DI=Health Assessment Questionnaire-Disability Index; IGA=Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; PGA=Physician global assessment; PtGA=Patient global assessment; Q4W=Every 4 weeks; Q8W=Every 8 weeks; SD=Standard deviation; SJC=Swollen joint count; TJC=Tender joint count; VAS=Visual analog scale.

- Median percent change from baseline to Week 24 in each of the 7 articular components of the ACR score is shown in Figure 2
- Mean (SD) changes from baseline to Week 24 in each component are shown in Table 2

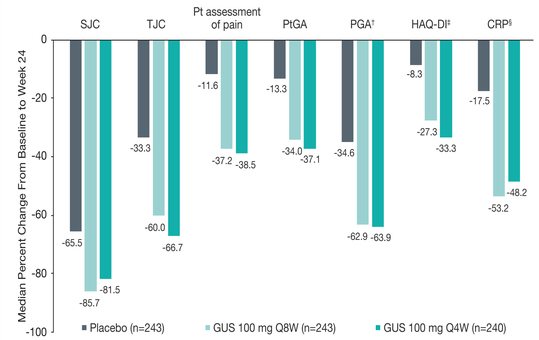
Table 2. Mean (SD) Changes From Baseline to Week 24 in ACR Component Scores (Observed Data)

	Placebo (n=243)	GUS 100 mg Q8W (n=243)	GUS 100 mg Q4W (n=240)
SJC	-6.4 (7.20)	-8.1 (6.07)	-8.8 (5.46)
TJC	-7.3 (11.15)	-10.4 (9.48)	-11.8 (9.88)
Patient assessment of pain	-1.08 (2.42)	-2.53 (2.47)	-2.39 (2.35)
PtGA	-1.24 (2.58)	-2.51 (2.47)	-2.42 (2.40)
PGA*	-2.46 (2.26)	-3.82 (2.31)	-3.90 (2.23)
HAQ-DI†	-0.16 (0.53)	-0.40 (0.54)	-0.43 (0.50)
CRP, mg/dL‡	-0.54 (2.55)	-1.08 (2.20)	-1.04 (2.11)

*GUS 100 mg Q8W, n=242; GUS 100 mg Q4W, n=238. †Placebo, n=242. ‡Placebo, n=240; GUS 100 mg Q4W, n=239.

ACR=American College of Rheumatology; CRP=C-reactive protein; GUS=Guselkumab; HAQ-DI=Health Assessment Questionnaire-Disability Index; PGA=Physician global assessment; PtGA=Patient global assessment; Q4W=Every 4 weeks; Q8W=Every 8 weeks; SD=Standard deviation; SJC=Swollen joint count; TJC=Tender joint count.

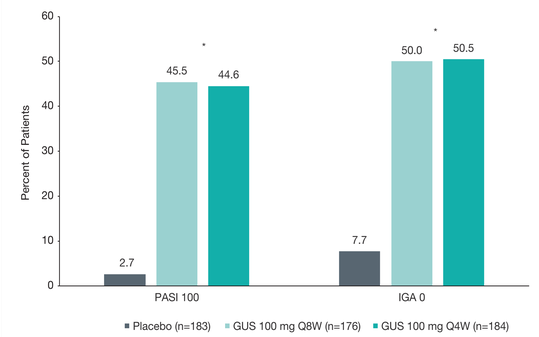
Figure 2. Median Percent Change From Baseline to Week 24 in the Articular Components of ACR Score* (Observed Data)



*Lower score in each component indicates less severe PsA.
†GUS 100 mg Q8W, n=242; GUS 100 mg Q4W, n=238.
‡Placebo, n=239; GUS 100 mg Q8W, n=233; GUS 100 mg Q4W, n=237.
§Placebo, n=240; GUS 100 mg Q4W, n=239.
ACR=American College of Rheumatology; CRP=C-reactive protein; GUS=Guselkumab; HAQ-DI=Health Assessment Questionnaire-Disability Index; PGA=Physician global assessment; PsA=Psoriatic arthritis; Pt=Patient; PtGA=Patient global assessment; Q4W=Every 4 weeks; Q8W=Every 8 weeks; SJC=Swollen joint count; TJC=Tender joint count.

- Skin clearance results based on achievement of PASI 100 and IGA 0 at Week 24 are shown in Figure 3
- Key safety results are summarized in Table 3

Figure 3. PASI 100 and IGA 0 Response Rates for Patients With ≥3% BSA Affected and IGA Score ≥2 at Baseline†



*Nominal p<0.001 for GUS vs placebo; p-values were calculated using the Cochran-Mantel-Haenszel test stratified by baseline use of nonbiologic disease-modifying antirheumatic drug and CRP prior to randomization (<2.0 vs ≥2.0 mg/dL).
†All patients, including those with imputed data. Patients with missing data were assumed to be non-responders.
BSA=Body surface area; CRP=C-reactive protein; GUS=Guselkumab; IGA=Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; Q4W=Every 4 weeks; Q8W=Every 8 weeks.

Table 3. Key Safety Results Through Week 24

	Placebo	GUS 100 mg Q8W	GUS 100 mg Q4W
Safety analysis set, n	246	248	245
Average duration of follow-up, weeks	24.0	23.9	23.8
Average number of study agent administrations	5.9	5.9	5.9
Patients with ≥1 of the following events:			
AE, n (%)	100 (40.7)	114 (46.0)	113 (46.1)
SAE, n (%)	7 (2.8)	3 (1.2)	8 (3.3)
AE leading to discontinuation of study agent, n (%)	4 (1.6)	2 (0.8)	6 (2.4)
Infections, n (%)	45 (18.3)	40 (16.1)	49 (20.0)
Serious infections, n (%)	1 (0.4)	1 (0.4)	3 (1.2)
Injection-site reactions, n (%)	1 (0.4)	3 (1.2)	3 (1.2)
Suicidal ideation, n (%)	1 (0.4)	0	1 (0.4)
Malignancy, n (%)	1 (0.4)	1 (0.4)	0

AE=Adverse event; GUS=Guselkumab; Q4W=Every 4 weeks; Q8W=Every 8 weeks; SAE=Serious adverse event.

- Investigators are blinded to the individual treatment groups until final database lock; therefore, to maintain blinding at study sites, treatment group information is not provided for the following safety outcomes:
  - No deaths
  - 1 major adverse cardiovascular event of ischemic stroke
  - No opportunistic infections or active tuberculosis
  - No suicidal behavior or non-suicidal self-injurious behavior
  - No anaphylactic or serum sickness reactions
  - 1 case of suspected inflammatory bowel disease

CONCLUSIONS

- Across all ACR components of articular disease activity, treatment with GUS 100 mg Q4W or Q8W provided greater improvements compared with placebo in patients with active PsA
- Roughly half of patients with mild to severe psoriasis at baseline achieved complete skin clearance at Week 24 with GUS therapy
- Both GUS dose regimens were safe and well tolerated through Week 24 and consistent with the safety profile established for GUS in the treatment of psoriasis, as described in the label

Author disclosures:

A.B. Gottlieb, P.J. Mease, J.F. Merola, D. van der Heijde, I.B. McInnes, and W.-H. Boehncke are advisors, investigators, and/or speakers for Janssen. A.P. Kollmeier, E.C. Hsia, X.L. Xu, and P. Agarwal are employees of Janssen Research & Development, LLC.

This poster was supported by Janssen Research & Development, LLC
Previously presented at American Academy of Dermatology 2020

Presented at Rheumatology Nurses Society, August 5-8, 2020