Inhibition of Structural Damage Progression With Guselkumab, a Selective IL-23i, in Participants With Active PsA: Results Through Week 24 of the Phase 3b/Randomized/Double-Blind/Placebo-Controlled APEX Study

Philip J. Mease,[1,2] Christopher T. Ritchlin,[3] Laura C. Coates,[4] Alexa P. Kollmeier,[5] Bei Zhou,[6] Yusang Jiang,[6] Karen Bensley,[6] Koeun Im,[7] Rattandeep Batra,[8] Soumya D. Chakravarty,[9,10] Proton Rahman,[11] Désirée van der Heijde[12]

[1]Rheumatology Research, Providence Swedish Medical Center, Seattle, WA, USA; [2]University of Washington School of Medicine, Seattle, WA, USA; [3]Department of Medicine, Allergy/Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, USA; [4]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Botnar Research Centre, Oxford, UK; [5]Johnson & Johnson, San Diego, CA, USA; [6]Johnson & Johnson, Spring House, PA, USA; [7]Johnson & Johnson, Cambridge, MA, USA; [8]Johnson & Johnson, Toronto, ON, Canada; [9]Johnson & Johnson, Horsham, PA, USA; [10]Drexel University College of Medicine, Philadelphia, PA, USA; [11]Craig L Dobbin Genetics Research Centre, Faculty of Medicine, Division of Rheumatology, Memorial University of Newfoundland, St. Johns, NL, Canada; [12]Leiden University Medical Center, Leiden, The Netherlands

Key Takeaways

✓ At W24 of the ongoing Phase 3b APEX study of GUS, a dual-acting selective IL-23i for PsA, the Q4W & Q8W regimens demonstrated:

- ✓ Significantly higher ACR20 response rates vs PBO
- ✓ Significantly lower rates of radiographic progression (Δ GUS vs PBO = -0.80)
- ✓ Consistent effects on erosion & JSN scores
- ✓ Higher proportion of pts with no progression of structural damage vs PBO
- ✓ Higher rates of ACR50, ACR70, PASI 90 & greater improvement in physical function vs PBO; similar AE profile for GUS and PBO; no new GUS safety signal

✓ GUS is the only selective IL-23i to demonstrate significant inhibition of structural damage progression

Background

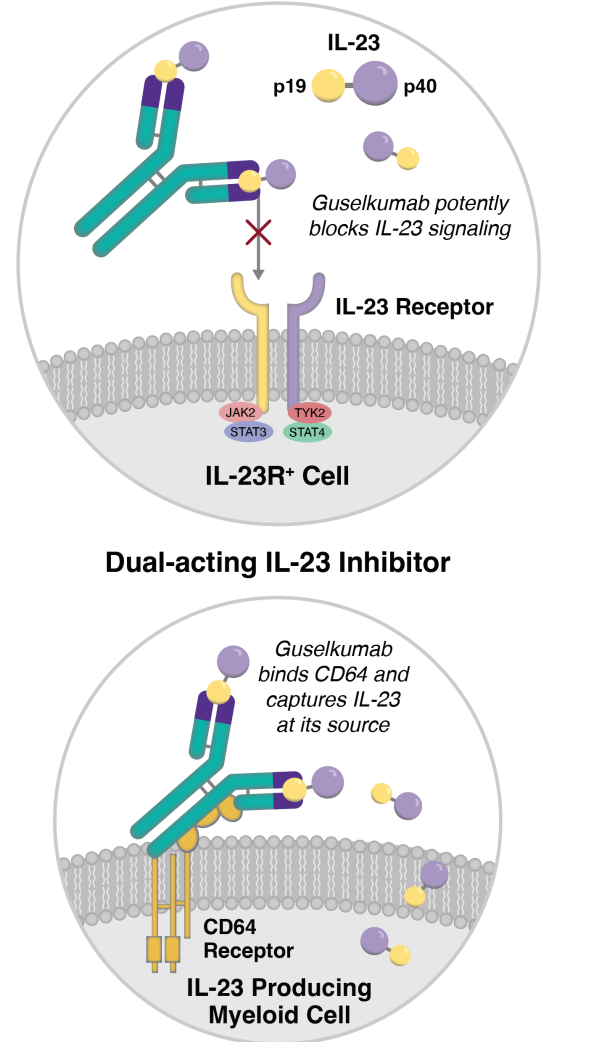
Psoriatic arthritis (PsA), a chronic, heterogeneous, inflammatory disease affecting joints and skin, can substantially impact health-related quality of life[1,2]

- Structural damage resulting from chronic inflammation leads to poorer outcomes[3]

Guselkumab (GUS) is a fully human, dual-acting, monoclonal antibody that selectively inhibits the interleukin (IL)-23p19 subunit[4]

- Indicated to treat moderate-to-severe plaque psoriasis (PsO), active PsA, and moderately-to-severely active Crohn's disease and ulcerative colitis[5]

In DISCOVER-2, biologic-naïve participants (pts) with active PsA receiving GUS every 4 weeks (Q4W) exhibited significantly less radiographic progression vs placebo (PBO); the lower rate of radiographic progression seen with GUS every 8 weeks (Q8W) vs PBO did not reach statistical significance[6]



Objectives

Report findings through Week (W)24 of the ongoing Phase 3b, randomized, double-blind, placebo-controlled APEX study (NCT04882098), intended to further evaluate GUS effects on clinical and radiographic progression outcomes in pts with active PsA

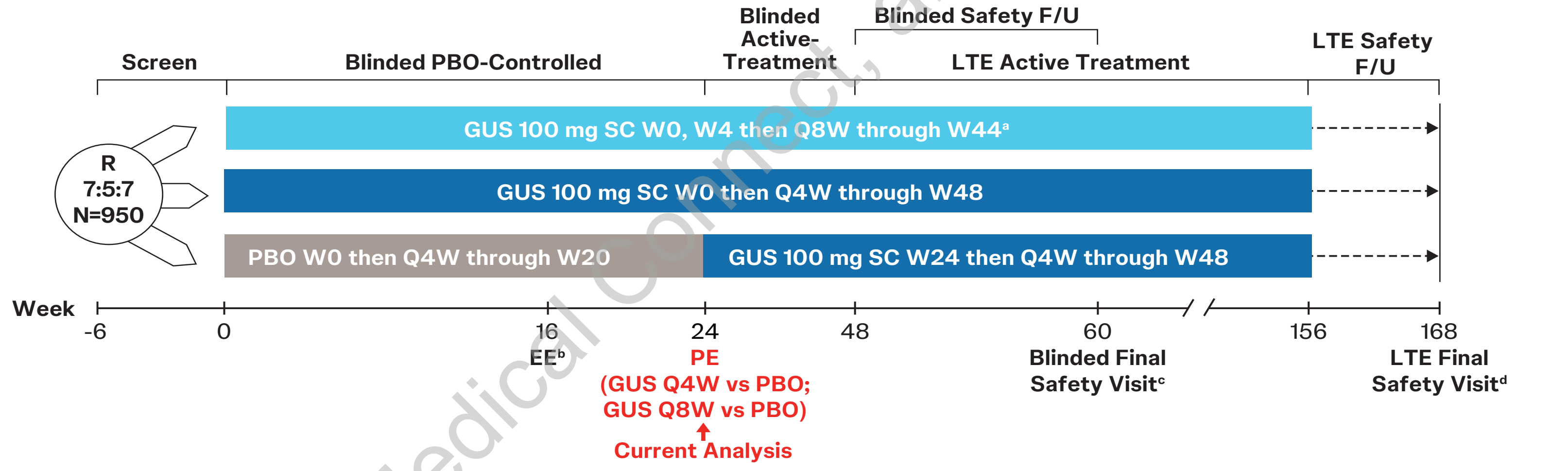
APEX Study Design

Inclusion Criteria

- ✓ Biologic-naive
- ✓ Age ≥18 years
- ✓ Active PsA ≥6 months (despite prior csDMARD, apremilast, NSAID); CASPAR criteria met
- ✓ ≥3 SJC; ≥3 TJC; CRP ≥0.3 mg/dL
- ✓ **≥2 erosive joints on hand/foot radiographs**
- ✓ Active plaque PsO (≥1 PsO plaque ≥2 cm and/or nail PsO)

Multiplicity-Controlled Endpoints

- **Primary:** ACR20 response at W24
- **Major Secondary:** Mean change in total PsA-modified vdH-S score at W24


Screen
Blinded PBO-Controlled
Blinded Active-Treatment
Blinded Safety F/U
LTE Active Treatment
LTE Safety F/U
R 7:5:7 N=950
GUS 100 mg SC W0, W4 then Q8W through W44[a]
GUS 100 mg SC W0 then Q4W through W48
PBO W0 then Q4W through W20
GUS 100 mg SC W24 then Q4W through W48
Week -6 0 16 24 48 60 156 168
16: EE[b]
24: PE (GUS Q4W vs PBO; GUS Q8W vs PBO) ↑ Current Analysis
60: Blinded Final Safety Visit[c]
168: LTE Final Safety Visit[d]

- **Modified full analysis set (mFAS):** All randomized pts excluding those from Ukraine sites rendered unable to support key study operations due to major disruptions; employed as the main efficacy analysis set (N=1020)
- **Safety analysis set:** All pts who received ≥1 administration of any study intervention (N=1054)

[a]PBO SC W8 then Q8W through W48 administered to maintain blinding. [b]EE if <20% improvement from BL in both TJC and SJC at W16. EE pts may initiate/increase dose permitted medication up to the maximum dose, at the investigator's discretion. [c]Final safety visit for those who do not enter LTE. [d]Final safety visit for those who entered LTE. **ACR**=American College of Rheumatology, **BL**=baseline, **CASPAR**=ClASsification criteria for Psoriatic ARthritis, **CRP**=C-reactive protein, **csDMARD**=conventional synthetic disease modifying antirheumatic drug, **EE**=early escape, **F/U**=follow-up, **GUS**=guselkumab, **LTE**=long-term extension, **NSAID**=nonsteroidal anti-inflammatory drug, **PBO**=placebo, **PE**=primary endpoint, **PsA**=psoriatic arthritis, **PsO**=psoriasis, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **R**=randomization, **SC**=subcutaneous, **SJC**=swollen joint count, **TJC**=tender joint count, **vdH-S**=van der Heijde-Sharp, **W**=week.

Results

Characteristics of APEX pts with active and erosive PsA were comparable across groups

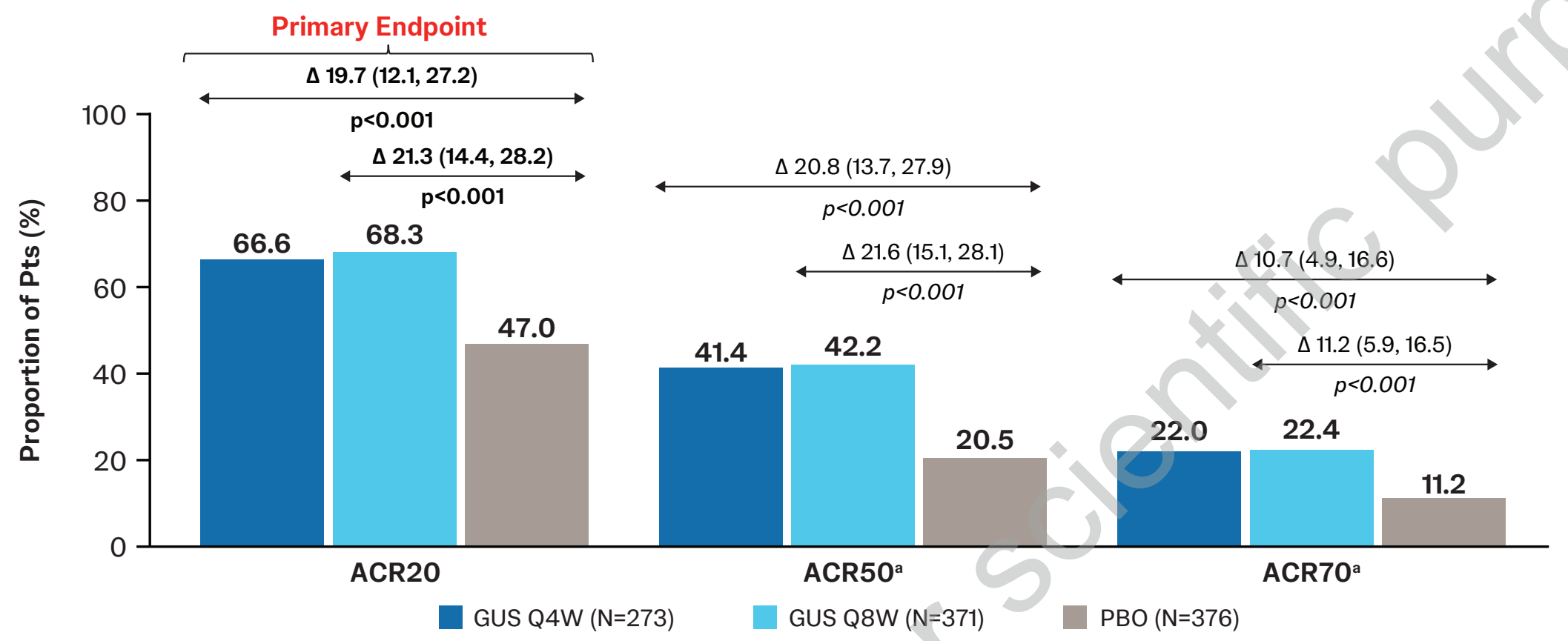
- Background PsA medication use and treatment completion through W24 (96–97%) were consistent across treatment groups

	GUS Q4W (N=273)	GUS Q8W (N=371)	PBO (N=376)	Total (N=1020)
Baseline Demographics				
Age, years	52.2 (13.2)	53.2 (12.9)	53.5 (13.0)	53.0 (13.0)
Male	55%	54%	57%	55%
Weight, kg	85.6 (20.1)	83.2 (17.4)	83.1 (18.2)	83.8 (18.5)
BMI, kg/m²	29.4 (6.0)	29.0 (5.6)	28.9 (5.7)	29.1 (5.7)
PsA Characteristics				
PsA disease duration, years	7.5 (7.1)	7.2 (7.6)	7.2 (6.9)	7.3 (7.2)
SJC [0–66][a]	9.0 (6.0; 14.0)	10.0 (6.0; 14.0)	9.0 (6.0; 15.0)	9.0 (6.0; 14.0)
TJC [0–68][a]	16.0 (10.0; 27.0)	17.0 (11.0; 26.0)	16.6 (10.0; 25.5)	16.1 (10.0; 26.0)
HAQ-DI [0–3]	1.2 (0.7)	1.2 (0.6)	1.2 (0.7)	1.2 (0.7)
CRP, mg/dL[a]	0.7 (0.4; 1.5)	0.8 (0.4; 1.6)	0.8 (0.4; 1.8)	0.8 (0.4; 1.6)
Enthesitis / Dactylitis	58% / 44%	59% / 39%	59% / 45%	58% / 43%
Mean LEI [1–6] / DSS [1-60]	3.2 / 10.8	3.0 / 11.0	3.0 / 10.2	3.1 / 10.6
PsO Characteristics				
% BSA	15.0 (19.2)	16.5 (21.9)	16.3 (21.5)	16.0 (21.0)
PASI [0–72]	7.6 (8.3)	8.3 (10.1)	8.2 (9.5)	8.1 (9.4)
Radiographic Characteristics				
PsA-modified vdH-S score [0–528]	27.7 (47.6)	26.7 (43.4)	26.8 (42.2)	27.0 (44.1)
Erosion score [0–320]	13.7 (24.3)	13.4 (21.9)	13.4 (20.7)	13.5 (22.1)
JSN score [0–208]	14.0 (24.2)	13.3 (22.8)	13.4 (22.4)	13.5 (23.0)

Values are reported as mean (SD) for pts with nonmissing data unless otherwise noted. [a]Values are median (IQR). **BMI**=body mass index, **BSA**=body surface area, **CRP**=C-reactive protein, **DSS**=Dactylitis Severity Score, **GUS**=guselkumab, **HAQ-DI**=Health Assessment Questionnaire-Disability Index, **IQR**=interquartile range, **JSN**=joint space narrowing, **LEI**=Leeds Enthesitis Index, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **PsA**=psoriatic arthritis, **PsO**=psoriasis, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **SD**=standard deviation, **SJC**=swollen joint count, **TJC**=tender joint count, **vdH-S**=van der Heijde-Sharp.

GUS demonstrated significantly higher ACR20 response rates vs PBO at W24

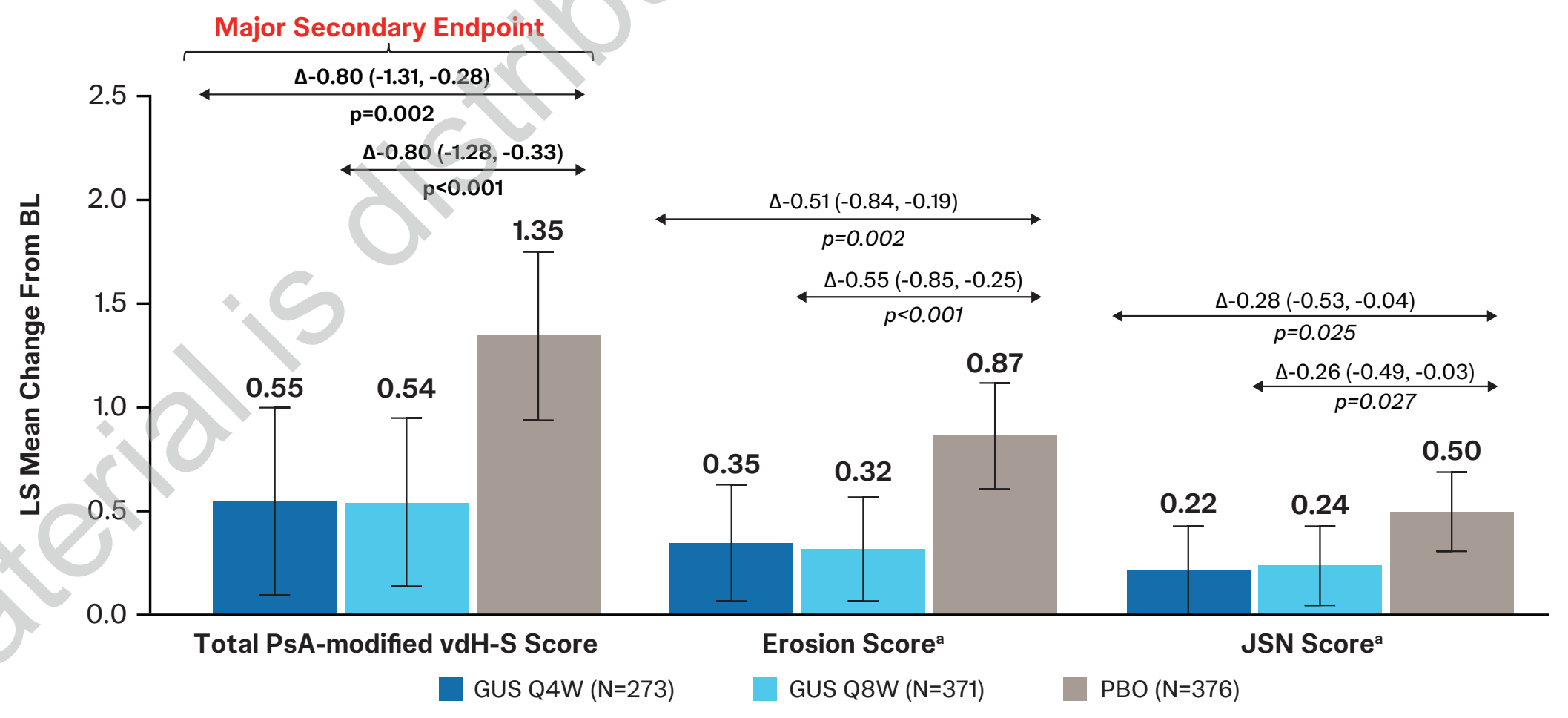
- GUS demonstrated higher rates of ACR50 and ACR70 vs PBO at W24



Primary endpoint p-values are multiplicity controlled using a fixed sequence testing procedure and can be used to determine statistical significance. Statistics are based on Cochran-Mantel-Haenszel across multiply imputed datasets. [a]Italicized p-values are nominal. Δ=treatment difference (95% CI). **ACR**=American College of Rheumatology, **CI**=confidence interval, **GUS**=guselkumab, **PBO**=placebo, **Pts**=participants, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks.

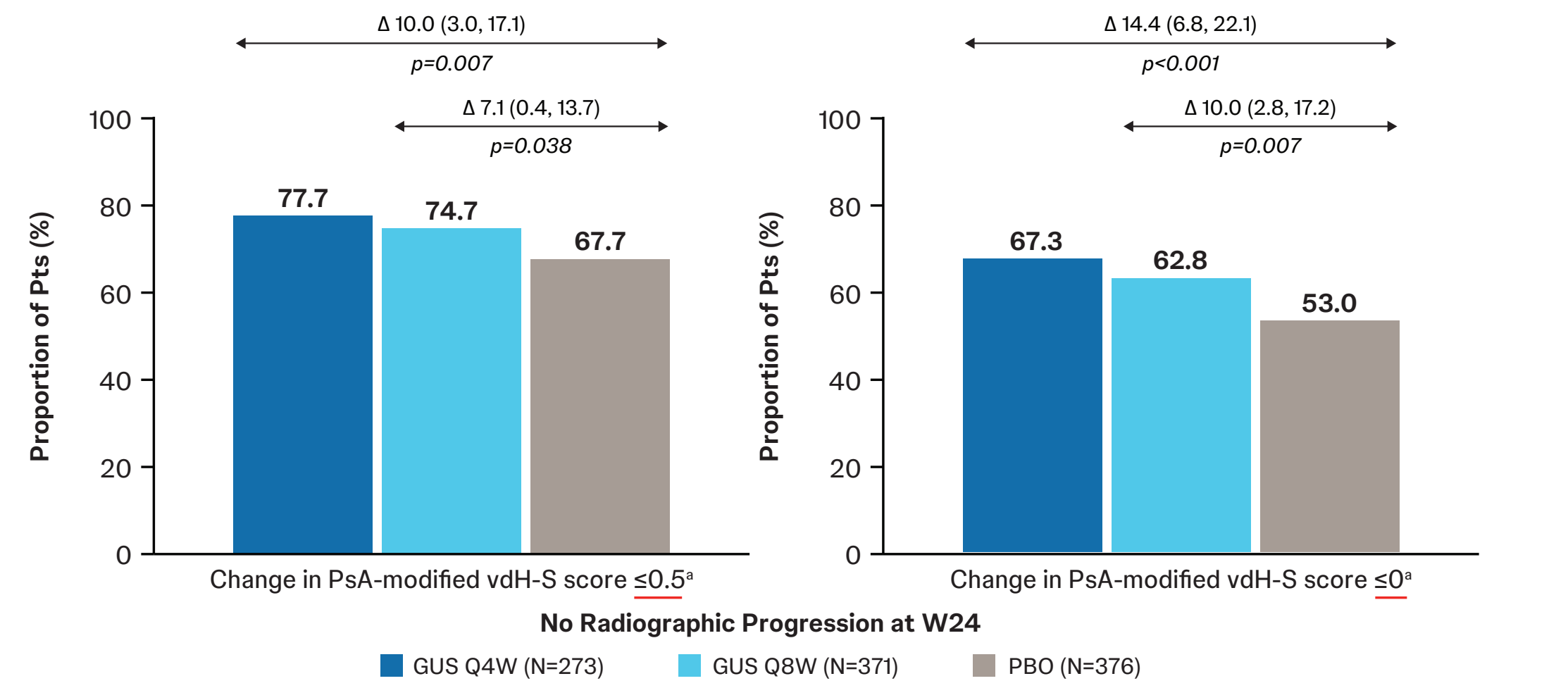
GUS exhibited significantly lower rates of radiographic progression vs PBO at W24

- GUS exhibited consistent treatment effects for both erosion and joint space narrowing (JSN) scores



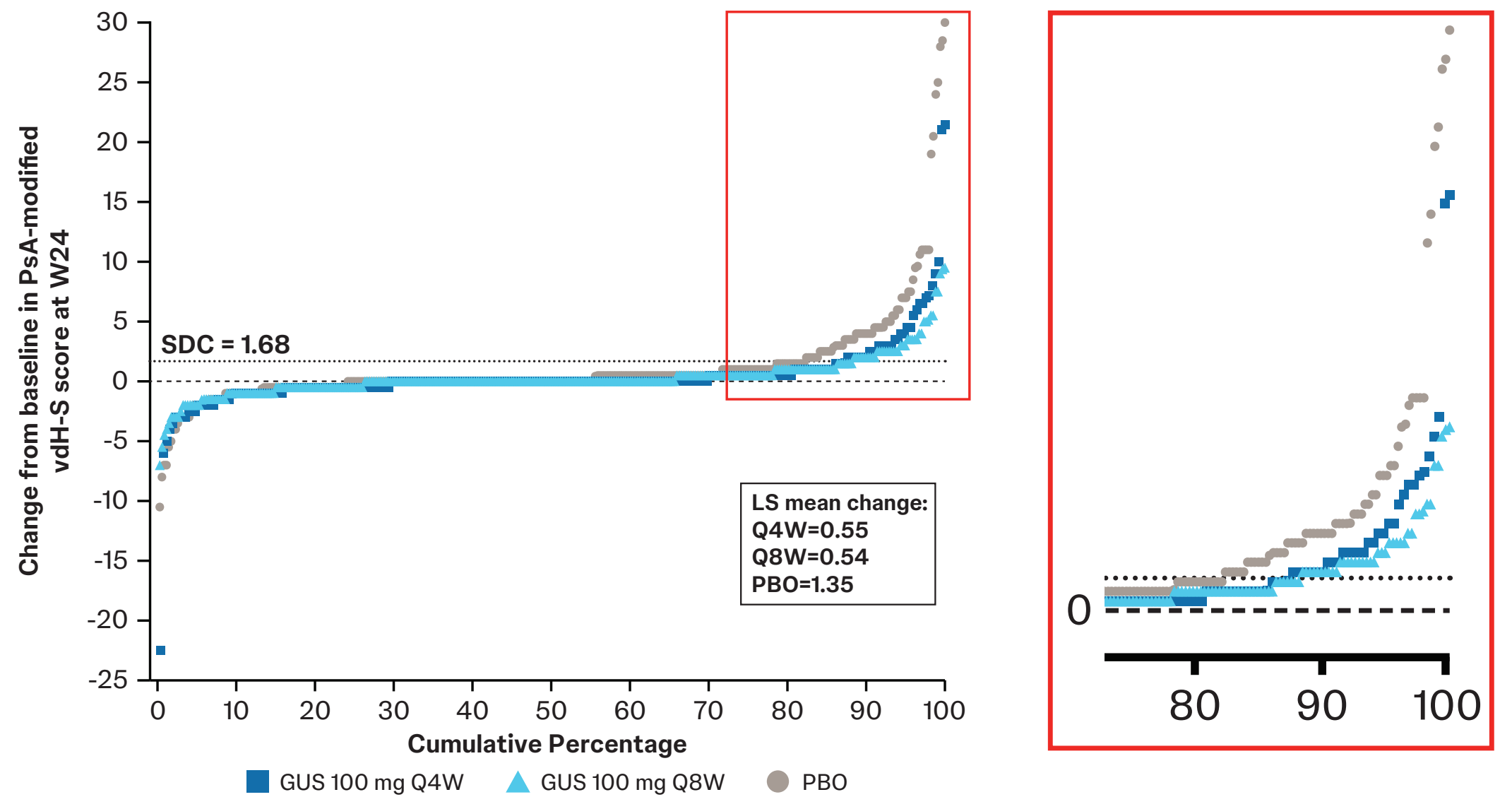
Major secondary endpoint (PsA-modified vdH-S score) p-values are multiplicity controlled using a fixed sequence testing procedure and can be used to determine statistical significance. Statistics are based on analysis of covariance across multiply imputed datasets. [a]Italicized p-values are nominal. Δ=treatment difference (95% CI). **BL**=baseline, **CI**=confidence interval, **GUS**=guselkumab, **JSN**=joint space narrowing, **LS**=least squares, **PBO**=placebo, **PsA**=psoriatic arthritis, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **vdH-S**=van der Heijde-Sharp.

Higher proportions of GUS vs PBO-treated pts showed no radiographic progression



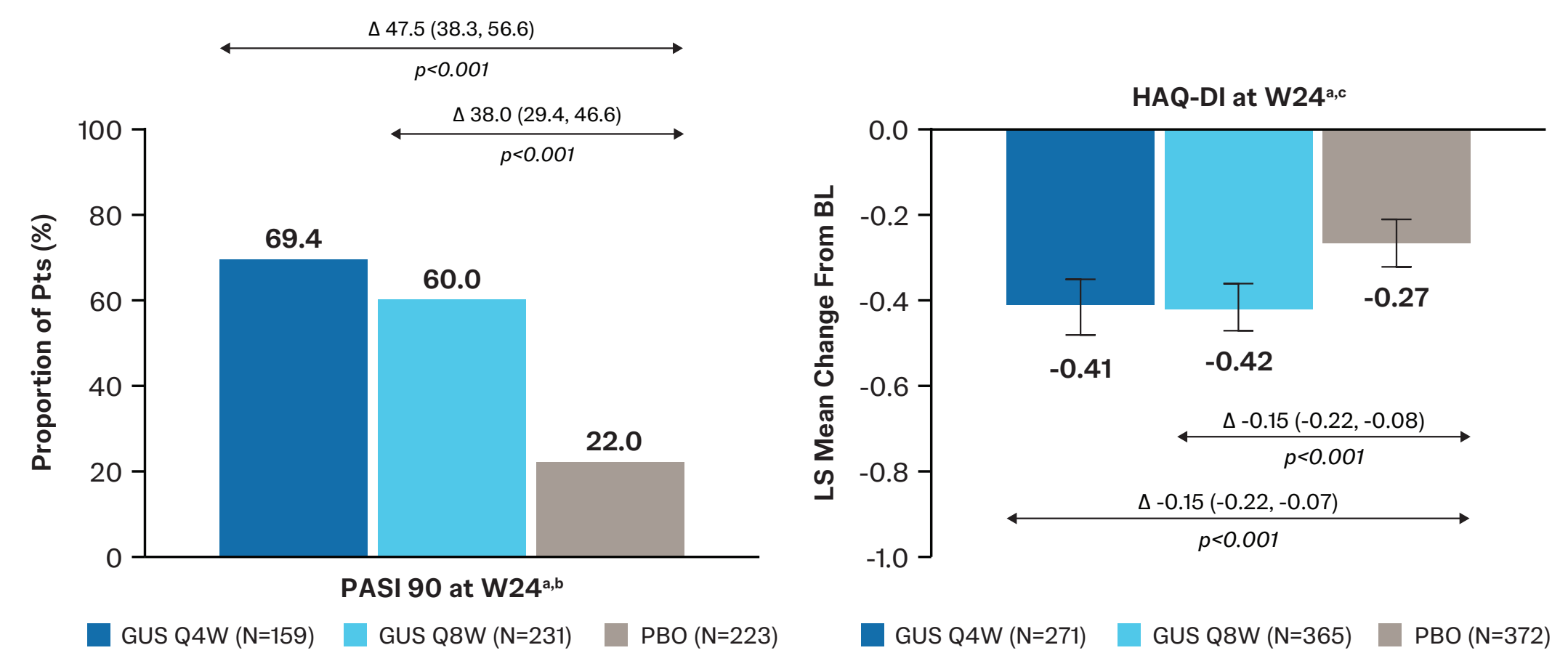
[a]Italicized p-values are nominal. Δ=treatment difference (95% CI). **CI**=confidence interval, **GUS**=guselkumab, **PBO**=placebo, **PsA**=psoriatic arthritis, **Pts**=patients, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **vdH-S**=van der Heijde-Sharp, **W**=week.

Pt-level data also showed clear separation between GUS and PBO



GUS=guselkumab, **LS**=least squares, **PBO**=placebo, **PsA**=psoriatic arthritis, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **SDC**=smallest detectable change, **vdH-S**=van der Heijde-Sharp, **W**=week.

Higher skin clearance rates and greater improvement in physical function with GUS vs PBO



[a]Italicized p-values are nominal. [b]Among pts who had ≥3% BSA psoriatic involvement and an IGA score of ≥2 (mild) at BL. PASI 90 response: ≥90% improvement from baseline in PASI score. [c]HAQ-DI score is the average of the computed categories scores (dressing, arising, eating, walking, hygiene, gripping and daily living). Lower scores indicate better functioning. Δ=treatment difference (95% CI). **BL**=baseline, **BSA**=body surface area, **CI**=confidence interval, **GUS**=guselkumab, **HAQ-DI**=Health Assessment Questionnaire-Disability Index, **IGA**=Investigator's Global Assessment, **LS**=least squares, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **Pts**=participants, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **W**=week.

GUS AE profile through W24 was similar to PBO

Safety Through W24	GUS Q4W (N=280)	GUS Q8W (N=388)	PBO (N=386)
Mean weeks of follow-up	24.0	23.9	23.8
Pts with ≥1:			
AE	107 (38.2%)	165 (42.5%)	144 (37.3%)
SAE	5 (1.8%)	12 (3.1%)	10 (2.6%)
AE leading to study agent d/c	2 (0.7%)	6 (1.5%)	1 (0.3%)
Infection	52 (18.6%)	91 (23.5%)	81 (21.0%)
Serious infection	2 (0.7%)	5 (1.3%)	1 (0.3%)
Active tuberculosis	0	0	0
Opportunistic infection	0	0	0
Venous thromboembolism event	1 (0.4%)	1 (0.3%)	1 (0.3%)
Anaphylactic or serum sickness reaction	0	0	0
Clinically important hepatic disorder[a]	0	0	0

Safety analysis set. AEs are coded using MedDRA Version 27.0. Data are n (%) unless otherwise noted. [a]Clinically important hepatic disorders were prespecified as AE terms within the MedDRA category of Drug-Related Hepatic Disorders that met the criteria for an SAE or led to study agent d/c. **AE**=adverse event, **d/c**=discontinuation, **GUS**=guselkumab, **MedDRA**=Medical Dictionary for Regulatory Activities, **PBO**=placebo, **Pts**=participants, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **SAE**=serious adverse event, **W**=week.

- **Study remains blinded through W48**
- **2 pts with malignancy (prostate, renal); 1 major adverse cardiac event (myocardial infarction); 1 COVID-19 death in unvaccinated elderly pt**
- **No new-onset inflammatory bowel disease**

PRESENTED AT: Congress of Clinical Rheumatology–West (CCR-W) 2025; Huntington Beach, CA, USA; September 18–21, 2025. **REFERENCES: 1.** Gladman DD, et al. *Q J Med.* 1987;62:127–41. **2.** Ritchlin CT. *J Rheumatol.* 2008;35:1434–7. **3.** van der Heijde D, et al. *Arthritis Res Ther.* 2020;22:18. **4.** Sachen KL, et al. *Front Immunol.* 2025;16:1532852. **5.** Janssen Biotech, Inc. *US FDA website.* Revised March 2025. **6.** Mease PJ, et al. *Lancet.* 2020;395:1126–36. **ACKNOWLEDGMENTS:** Medical writing support was provided by Mona Patel, PharmD, under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298–1304). This study was sponsored by Johnson & Johnson. **DISCLOSURES: PJM:** Grants: AbbVie, Acelyrin, Amgen, Bristol Myers Squibb, Eli Lilly, Johnson & Johnson, Novartis, and UCB; Consulting fees: AbbVie, Acelyrin, Amgen, Bristol Myers Squibb, Eli Lilly, Immagene, Johnson & Johnson, Novartis, Pfizer, UCB, and Ventyx; and Speaker fees: AbbVie, Amgen, Eli Lilly, Johnson & Johnson, Novartis, Pfizer, and UCB. **CTR:** Received grant/research support from AbbVie, Amgen, and UCB and consulting fees from AbbVie, Amgen, Eli Lilly, Gilead, Johnson & Johnson, Novartis, Pfizer, and UCB. **LCC:** Has received grants/research support from AbbVie, Amgen, Celgene, Eli Lilly, Johnson & Johnson, Novartis, Pfizer, and UCB; worked as a paid consultant for AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Galapagos, Johnson & Johnson, Moonlake, Novartis, Pfizer, and UCB; and has been paid as a speaker for AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Johnson & Johnson, Medac, Novartis, Pfizer, and UCB. **APK, BZ, YJ, KB, KI, RB,** and **SDC:** are employees of Johnson & Johnson; employees may own stock/stock options in Johnson & Johnson. **PR:** received consulting fees from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Johnson & Johnson, Merck, Novartis, Pfizer, and UCB; meeting attendance/travel support from Johnson & Johnson; and research grants from Johnson & Johnson, and Novartis. **DvdH:** received consulting fees from AbbVie, Alfasigma, ArgenX, Bristol Myers Squibb, Eli Lilly, Grey-Wolf Therapeutics, Janssen, Novartis, Pfizer, Takeda, and UCB; serves as the Associate Editor of Annals of Rheumatic Diseases, on the editorial board member Journal of Rheumatology, and as the director of Imaging Rheumatology BV. **Previously presented at:** European Alliance of Associations for Rheumatology (EULAR) 2025; Barcelona, Spain; June 11–14, 2025.