

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 Ritchlin³, Laura C Coates⁴, Alexa P Kollmeier⁵, Bei Zhou⁶, Yusang Jiang⁶, Karen Benschley⁶, Koehn Im⁷, Rattandeep Batra⁸, Soumya D Chakravarty^{9,10}, Proton Rahman¹¹, Désirée van der Heijde¹²

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

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 outcomes³

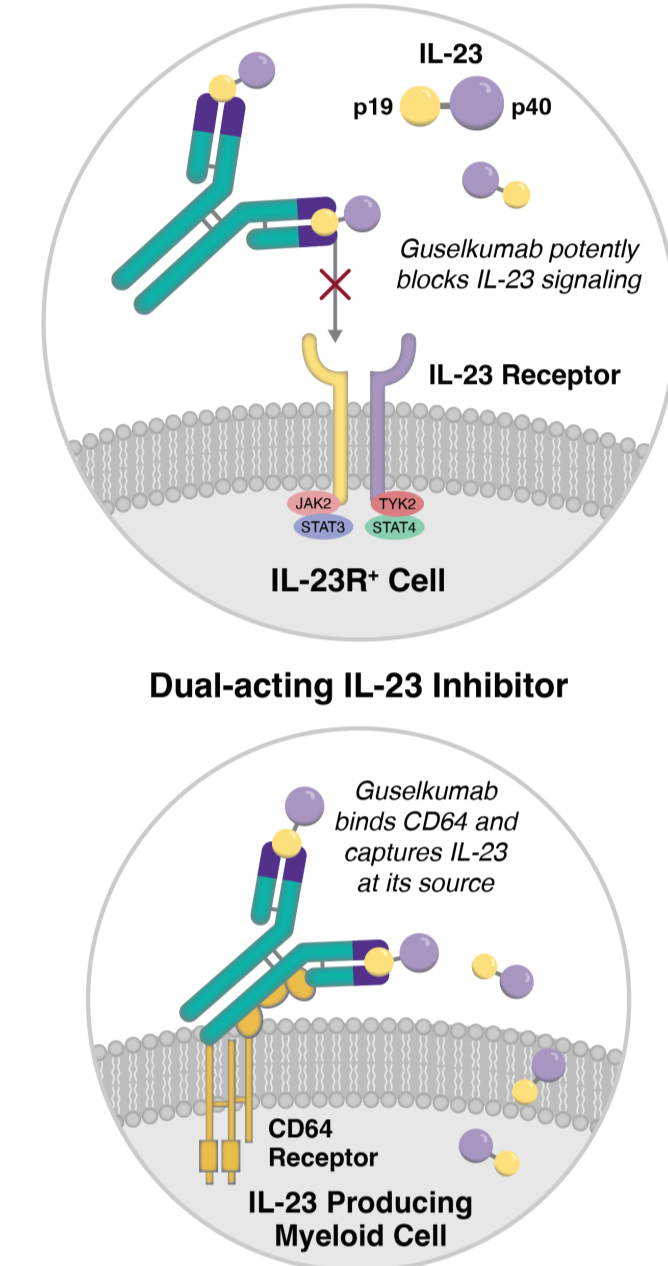
Guselkumab (GUS) is a fully human, dual-acting, monoclonal antibody that selectively inhibits the interleukin (IL)-23 subunit⁴

- Indicated to treat moderate-to-severe plaque psoriasis (PsO), active PsA, and moderately-to-severely active Crohn's disease and ulcerative colitis⁵

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 significance⁶

Objectives

Report findings through W24 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



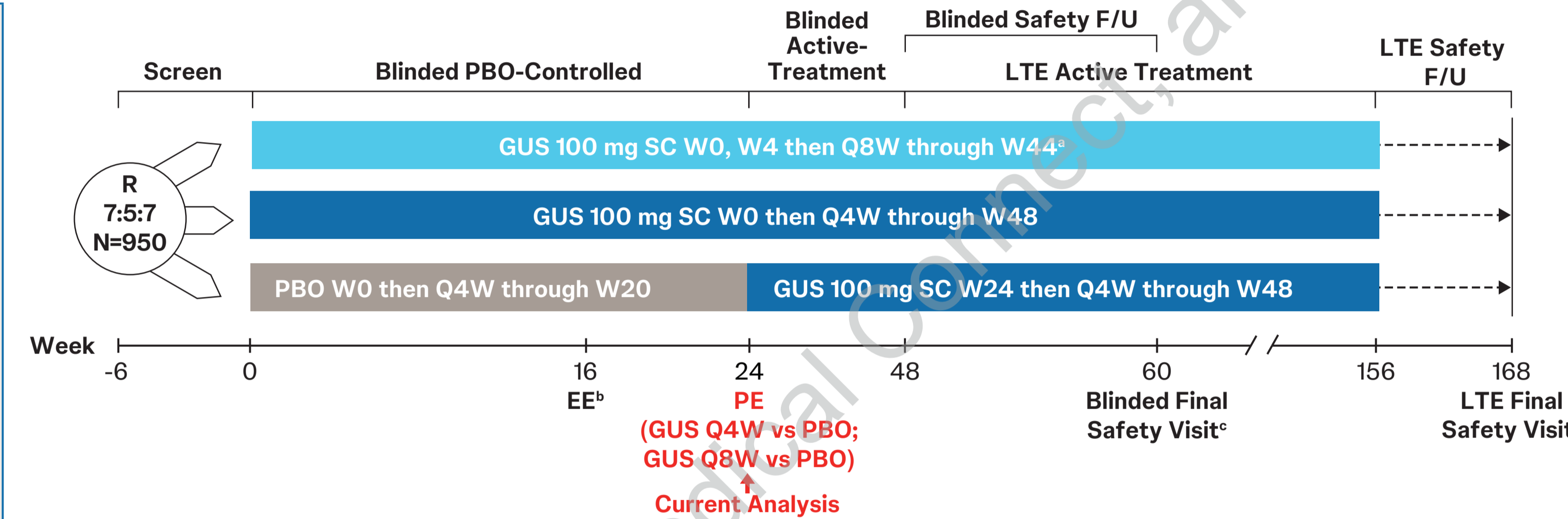
APEX Study Design

Inclusion Criteria

- Biologic-naïve
- 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



- 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)

¹PBO SC W0 then Q4W through W48 administered to maintain blinding. ²EE if <20% improvement from BL in both TJC and SJC at W16. ³EE pts may initiate/increase dose permitted medication up to the maximum dose, at the investigator's discretion. ⁴Final safety visit for those who do not enter LTE. ⁵Final safety visit for those who entered LTE. ⁶ACR=American College of Rheumatology; BL=baseline; CASPAR=CASPAR criteria for Psoriatic Arthritis; CRP=C-reactive protein; csDMARD=conventional synthetic disease modifying antirheumatic drug; EE=early escape; F/U=follow-up; LTE=long-term extension; NSAID=nonsteroidal anti-inflammatory drug; PE=primary endpoint; R=randomization; SC=subcutaneous; SJC=swollen joint count; TJC=tender joint count; vdH-S=van der Heijde-Score.

Results

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

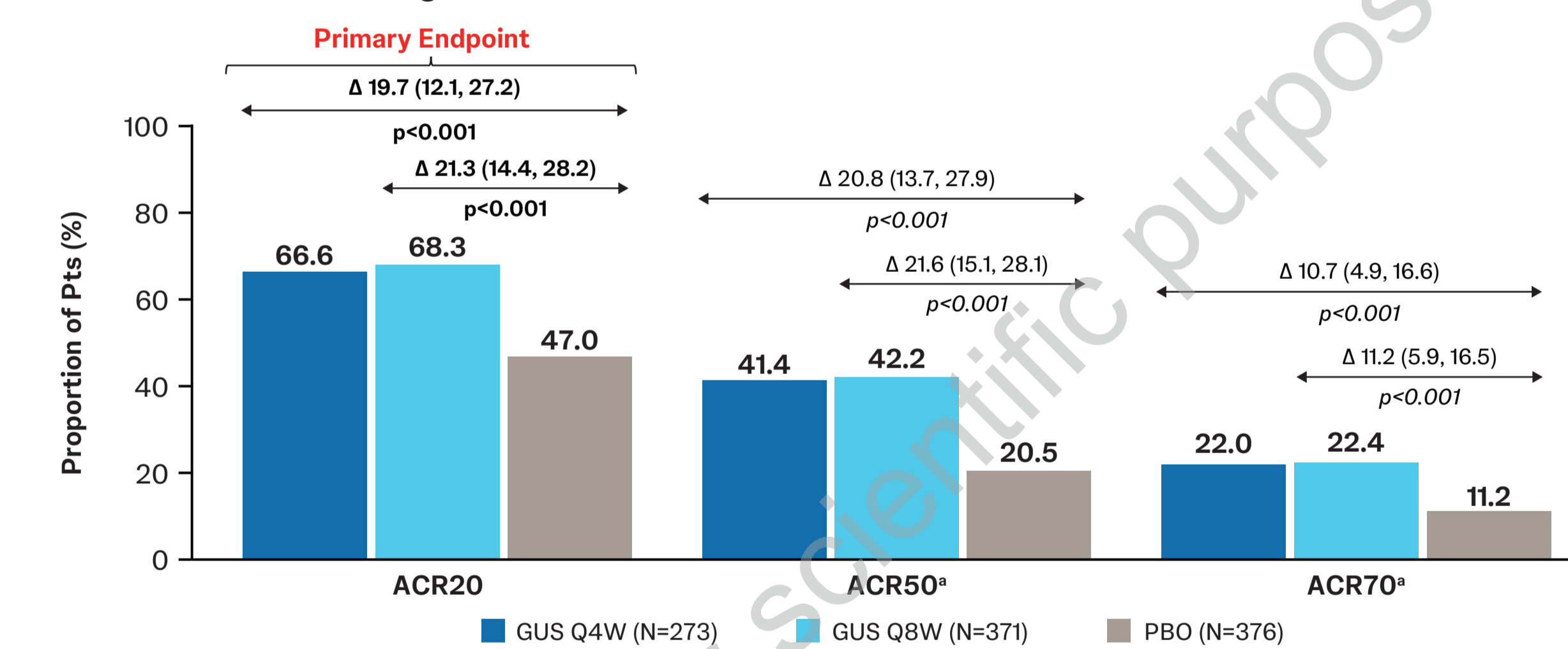
- Background PsA medication use and treatment completion through W24 (96-97%) were consistent across treatment groups

	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/m ²	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]	277 (47.6)	267 (43.4)	268 (42.2)	270 (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. ^aValues are median (IQR). BMI=Body Mass Index, BSA=body surface area, DSS=Dactylitis Severity Score, HAQ-DI=Health Assessment Questionnaire-Disability Index, IQR=interquartile range, JSN=joint space narrowing, LEI=Leeds Enthesitis Index, PASI=Psoriasis Area and Severity Index, SD=standard deviation.

GUS demonstrated significantly higher ACR20 response rates vs PBO at W24

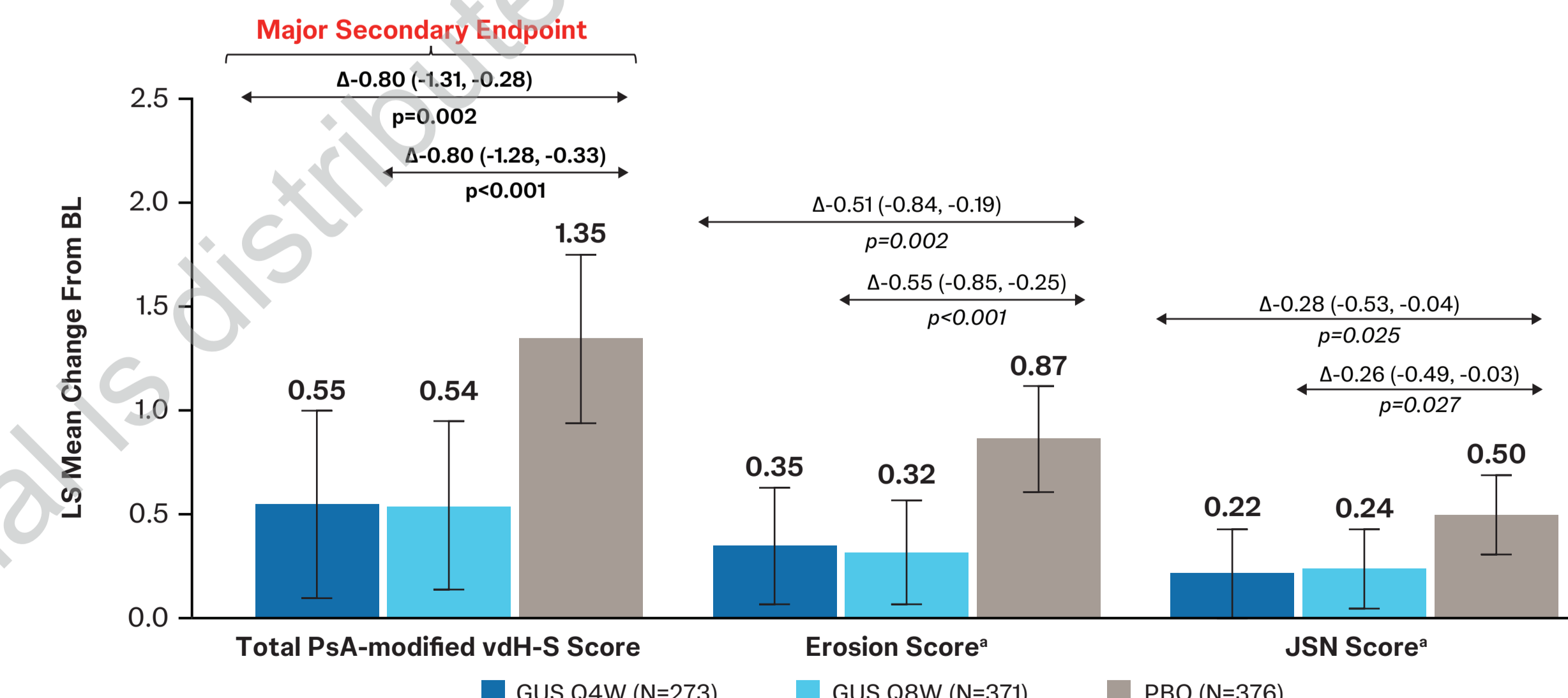
- GUS demonstrated higher rates of ACR50 and ACR70 vs PBO at W24



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. ^aItalicized p-values are nominal. ^bΔ=treatment difference (95% CI).

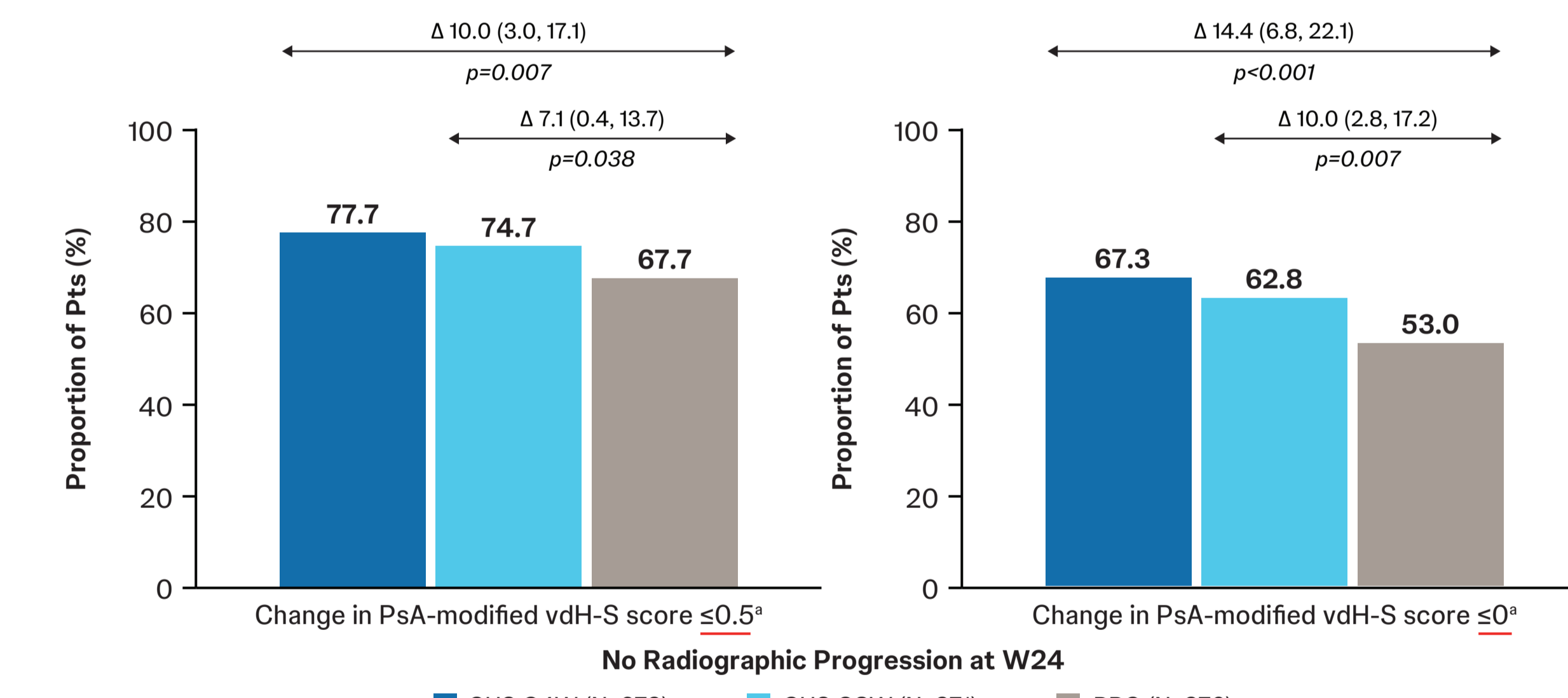
GUS exhibited significantly lower rates of radiographic progression vs PBO at W24

- GUS exhibited consistent treatment effects for both erosion and JSN scores



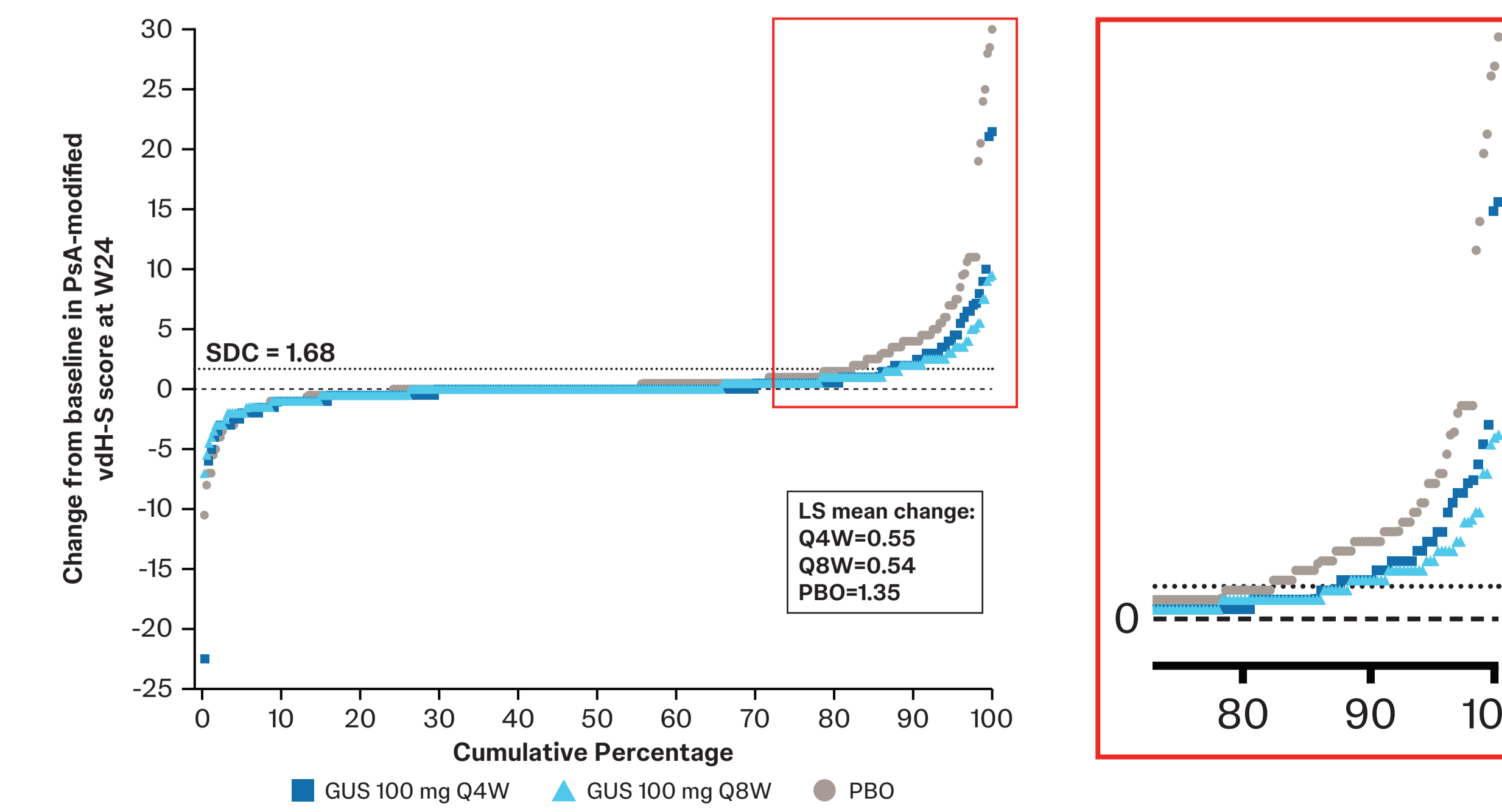
Major secondary endpoint (PsA-modified vdH-S score) p-values are multiplicity controlled using a fixed sequence testing procedure and can be used to determine statistical significance. Statistics are based on analysis of covariance across multiply imputed datasets. ^aItalicized p-values are nominal. ^bΔ=treatment difference (95% CI). ^cLS=least squares.

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



^aItalicized p-values are nominal. ^bΔ=treatment difference (95% CI).

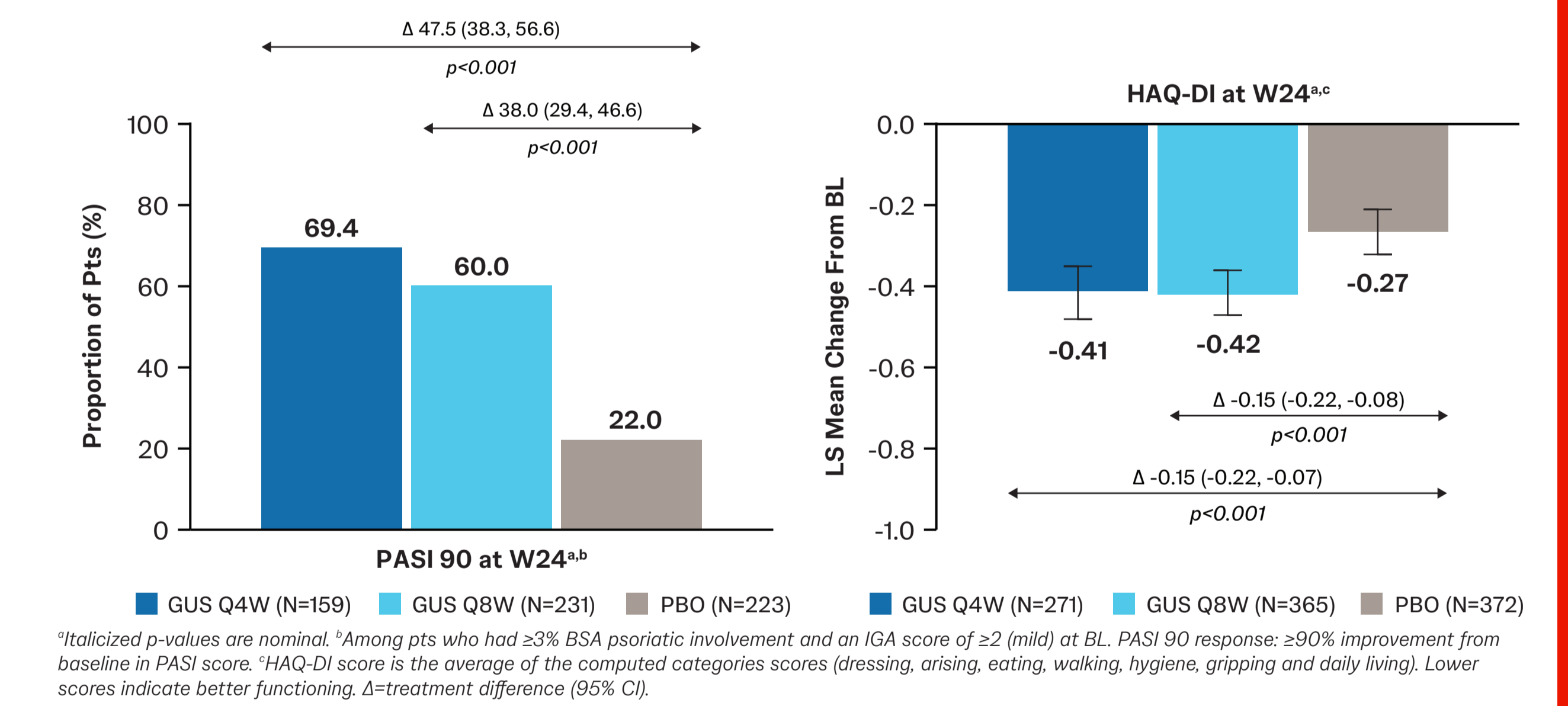
Pt-level data also showed clear separation between GUS and PBO



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

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



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. ^aClinically important hepatic disorders were prespecified as AE terms within the Medical Dictionary for Regulatory Activities 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, IBD=inflammatory bowel disease, MACE=major adverse cardiovascular event, SAE=serious AE.

- Study remains blinded through W48
- 2 pts with malignancy (prostate, renal); 1 MACE (myocardial infarction); 1 COVID-19 death in unvaccinated elderly pt
- No new-onset IBD