

Guselkumab Response and Inhibition of Structural Damage Progression in Active Psoriatic Arthritis Across APEX Participant Subgroups

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 Koehn Im,⁷ Rattandeep Batra,⁸ Karissa Lozenski,⁹ Soumya D Chakravarty,^{9,10} Proton Rahman,¹¹ 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.



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Background

Guselkumab (GUS), a fully-human monoclonal antibody able to bind to the CD64-receptor and simultaneously inhibit the interleukin (IL)-23p19 subunit, is indicated for moderate-to-severe plaque psoriasis, active psoriatic arthritis (PsA), and moderately-to-severely active Crohn's disease/ulcerative colitis

 The ongoing phase 3b, randomized, double-blind, placebo (PBO)-controlled **APEX study (NCT04882098)** is further evaluating GUS effects on clinical and radiographic progression outcomes in **participants (pts) with active and erosive PsA**

 APEX met primary (American College of Rheumatology $\geq 20\%$ improvement [ACR20]) and major secondary (PsA-modified van der Heijde-Sharp [vdH-S] score change from baseline) endpoints, such that **GUS Q4W and Q8W demonstrated significantly higher rates of clinical improvement and significant inhibition of structural damage progression** vs PBO at Week(W)24

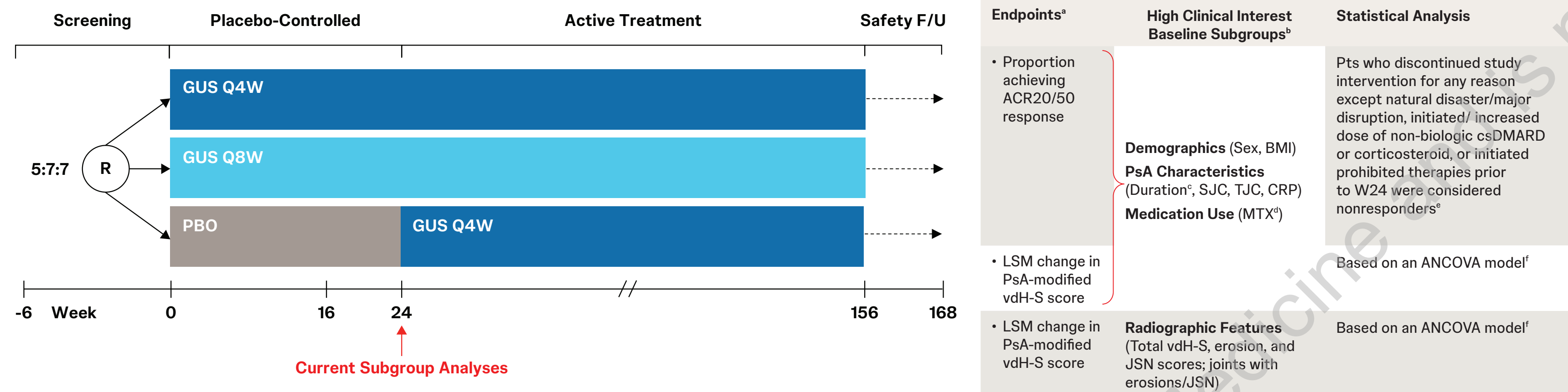
Objective

 Evaluate consistency in GUS clinical response and radiographic progression inhibition across subgroups of pts of high clinical interest

APEX Study Design and Analysis Methods

Inclusion Criteria

- ✓ Biologic-naïve adults
≥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
radiographs of
hands/feet**
- ✓ Active plaque
psoriasis



^aOver 200 MRI datasets, 29 subgroups were predefined to evaluate treatment consistency over baseline characteristics (*n=7*), disease characteristics (*n=12*), medication use (*n=5*), and radiographic features (*n=5*): those of high clinical interest are reported here. Predefined PSA duration subgroup categories were <121 to <323 years, however, <323 presented due to small sample size in <1 year category. Predefined as csDMARD used at baseline, however, MTX component presented separately based on MTX representing the majority of csDMARD used at baseline. Data impacted by or missing due to, natural disaster/major disruption were imputed using NRI; other missing data were imputed using NNRI. Exploratory model variables: baseline vHS-V score, treatment group, and randomization stratification level; data impacted by natural disaster/major disruption and missing data imputed using NNRI. ACR-American College of Rheumatology; ANCOVA-analysis of covariance; BMI-body mass index; CVD-cardiovascular disease; CSF-erythrocyte sedimentation rate; CRP-C-reactive protein; csDMARD-conventional synthetic disease-modifying antirheumatic drug; F/U-follow-up; HLA-Human Leukocyte Antigen; IGA-Infliximab; IL-6-interleukin 6; IL-8-interleukin 8; IL-10-interleukin 10; IL-17-interleukin 17; IL-23-interleukin 23; IL-27-interleukin 27; IL-36-interleukin 36; IL-37-interleukin 37; IL-38-interleukin 38; IL-39-interleukin 39; IL-40-interleukin 40; IL-41-interleukin 41; IL-42-interleukin 42; IL-43-interleukin 43; IL-44-interleukin 44; IL-45-interleukin 45; IL-46-interleukin 46; IL-47-interleukin 47; IL-48-interleukin 48; IL-49-interleukin 49; IL-50-interleukin 50; IL-51-interleukin 51; IL-52-interleukin 52; IL-53-interleukin 53; IL-54-interleukin 54; IL-55-interleukin 55; IL-56-interleukin 56; IL-57-interleukin 57; IL-58-interleukin 58; IL-59-interleukin 59; IL-60-interleukin 60; IL-61-interleukin 61; 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Results

Similar proportions of pts comprised baseline characteristic subgroups across treatment arms

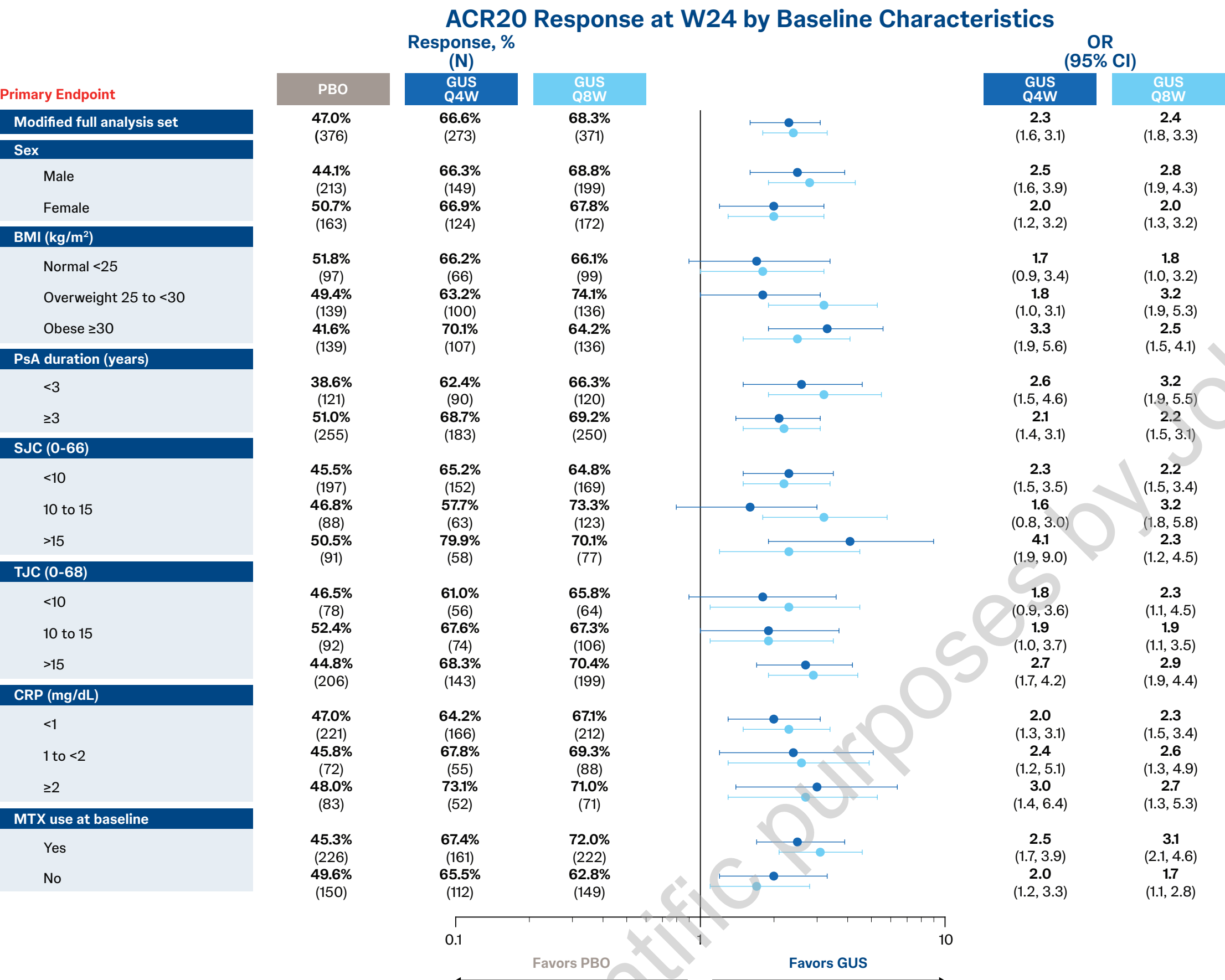
- Pts with active and erosive PsA: median disease duration=5 years
SJC=9, TJC=16, and CRP=0.8 mg/dL

Modified full analysis set*	PBO (N=376)	GUS Q4W (N=273)	GUS Q8W (N=371)	Total (N=1020)
Sex				
Male	57%	55%	54%	55%
Female	43%	45%	46%	45%
BMI, kg/m ²				
Normal <25	26%	24%	27%	26%
Overweight ≥25 to <30	37%	37%	37%	37%
Obese ≥30	37%	39%	37%	37%
PsA disease duration, yrs				
<3	32%	33%	32%	32%
≥3	68%	67%	68%	67%
SJC (0–66)				
<10	52%	56%	46%	51%
10 to 15	23%	23%	33%	27%
>15	24%	21%	21%	22%
TJC (0–68)				
<10	21%	21%	17%	19%
10 to 15	24%	27%	29%	27%
>15	55%	52%	54%	54%
CRP, mg/dL				
<1	59%	61%	57%	59%
1 to <2	19%	20%	24%	21%
≥2	22%	19%	19%	20%
MTX use at baseline				
Yes	60%	59%	60%	60%
No	40%	41%	40%	40%

All randomized pts except those from Ukraine sites rendered unable to support key study operations due to major disruptions (N=1020). **BMI**=body mass index, **CRP**=C-reactive protein, **GUS**=guselkumab, **MTX**=methotrexate, **PBO**=placebo, **psA**=psoriatic arthritis, **pts**=participants, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **SJC**=swollen joint count, **TJC**=tender joint count.

GUS treatment effect on joint disease activity was consistent across subgroups

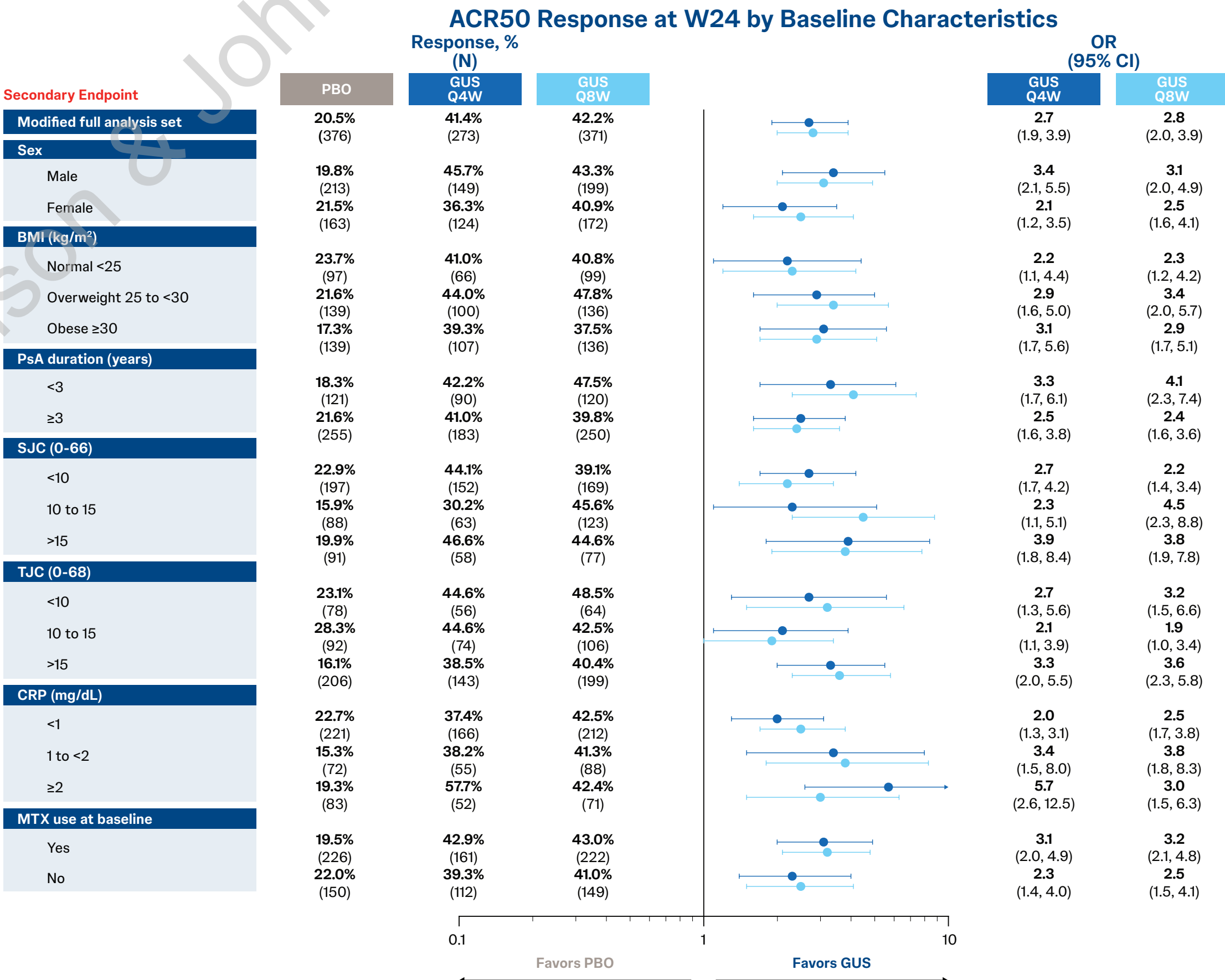
- Aligned with primary endpoint results, GUS-treated pts had approximately 2-4 times higher odds of achieving ACR20 response than PBO-treated pts



CR=American College of Rheumatology, BMI=body mass index, CI=confidence interval, CRP=C-reactive protein, GUS=guselkumab, MTX=methotrexate, R=odds ratio, PBO=placebo, PsA=psoriatic arthritis, Q4W=every 4 weeks, Q8W=every 8 weeks, SJC=swollen joint count, TJC=tender joint count, W=week.

GUS effect on the more stringent ACR50 response was also consistent across subgroups

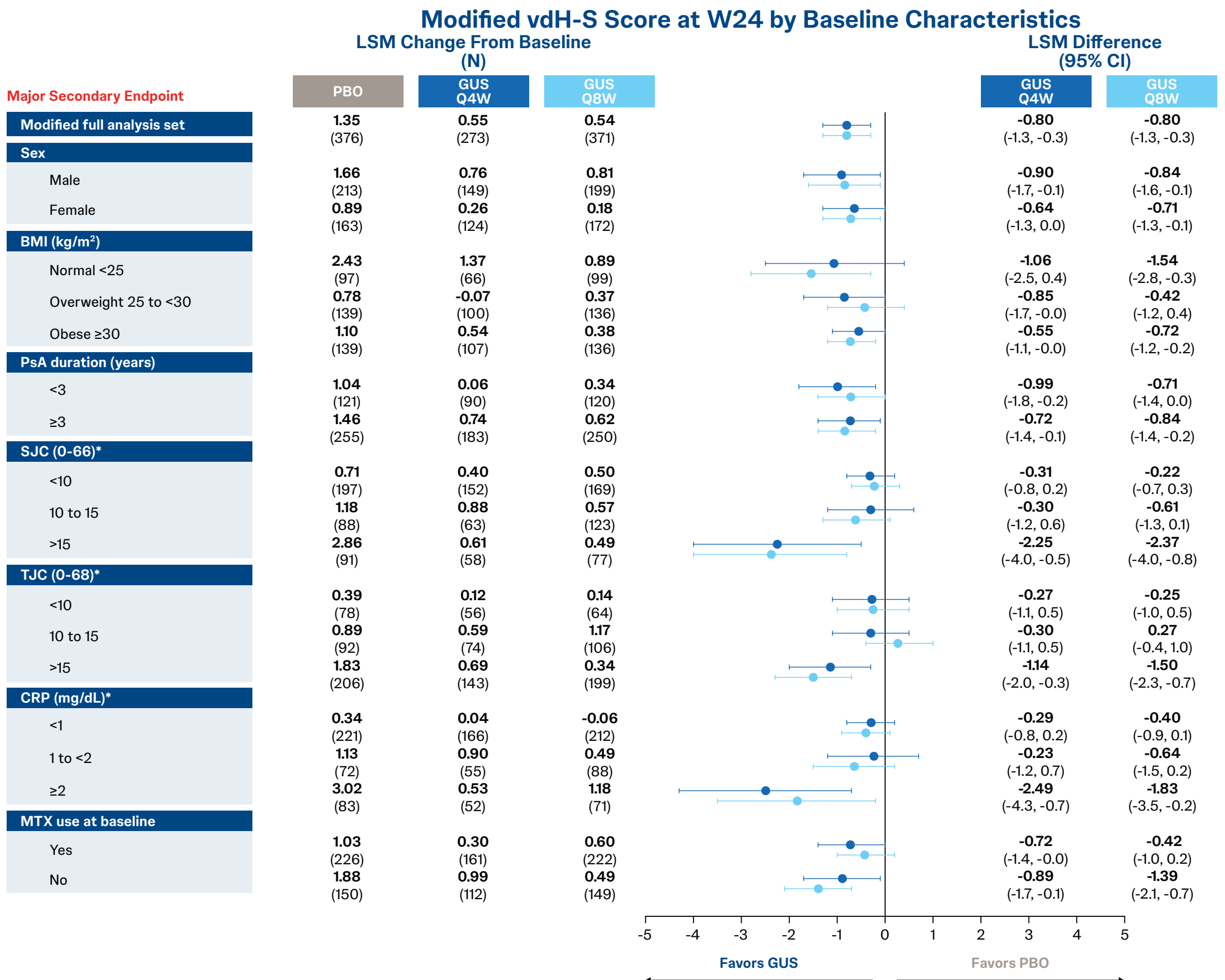
- Aligned with overall ACR50 results, GUS-treated pts had approximately 2-6 times higher odds of achieving ACR50 response than PBO-treated pts



OR=American College of Rheumatology, BMI=body mass index, CI=confidence interval, CRP=C-reactive protein, GUS=guselkumab, MTX=methotrexate, OR=odds ratio, PBO=placebo, PsA=psoriatic arthritis, Q4W=every 4 weeks, Q8W=every 8 weeks, SJC=swollen joint count, TJC=tender joint count, W=week.

Significant inhibition of structural damage progression with GUS was generally consistent across baseline pt subgroups

- Concordant with known risk factors, PBO-treated pts with SJC >15 & CRP ≥2 mg/dL exhibited notably higher degrees of radiographic progression, leading to even more robust GUS effects in these groups



Interaction p-value <0.05 for SJC GUS Q4W and Q8W; JC GUS Q8W; CRP GUS Q4W. **BMi**=body mass index, **CI**=confidence interval, **CRP**=C-reactive protein, **GUS**=guselkumab, **LSM**=least squares mean, **MTX**=methotrexate, **PBO**=placebo, **PsA**=psoriatic arthritis, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **SJC**=swollen joint count, **TJC**=tender joint count, **vdH-S**=van der Heijde-Swery score, **W**=week.

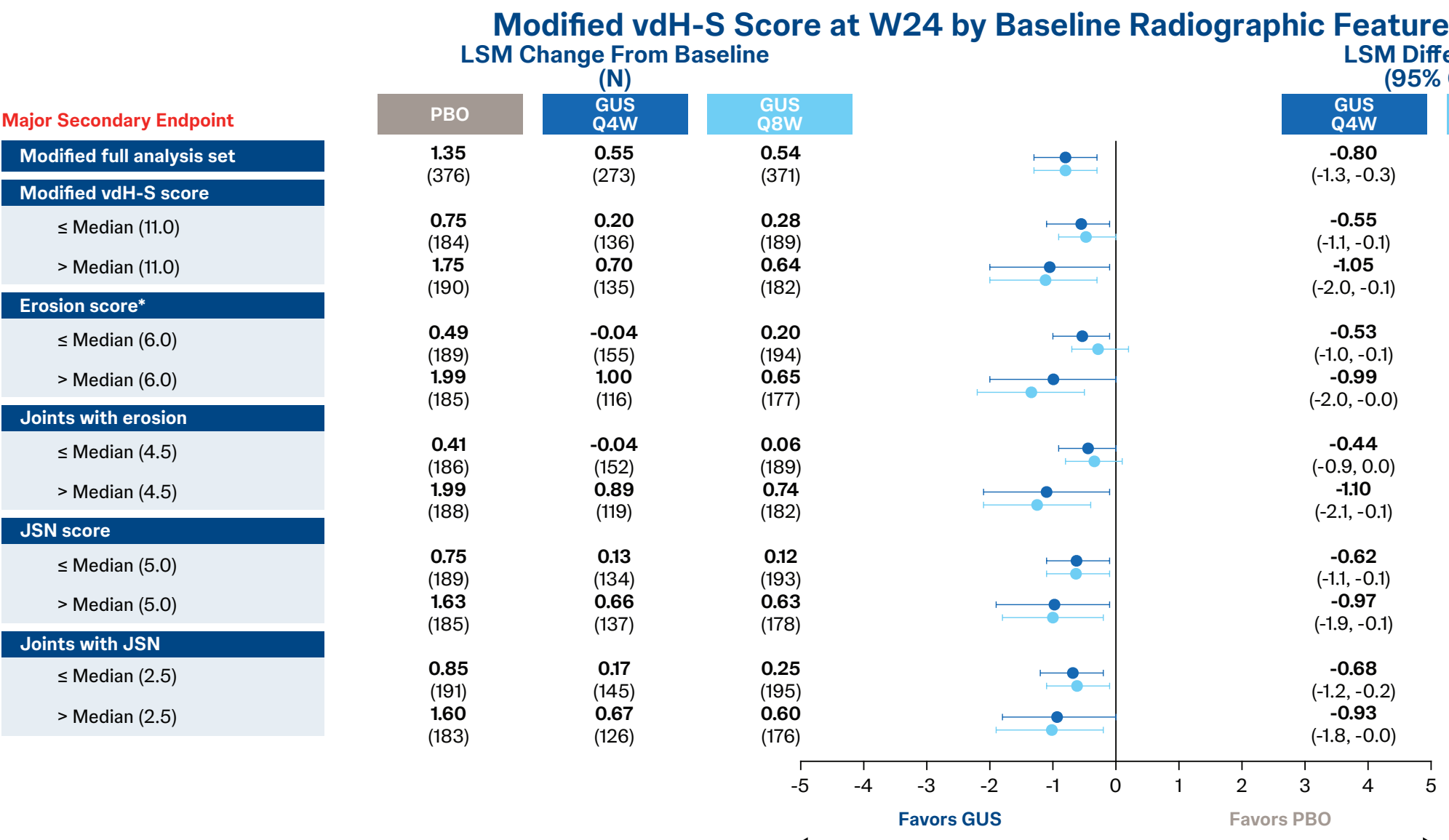
Baseline radiographic joint damage was of moderate degree and similar across treatment groups

		PBO (N=374)	GUS Q4W (N=271)	GUS Q8W (N=371)	Total (N=1016)
Baseline Radiographic Features					
	Total vdH-S score [0-528]	11.5 [5.0–27.5]	11.0 [4.5–26.5]	11.0 [4.5–25.0]	11.0 [5.0–26.5]
	Erosion score [0-320]	6.0 [2.5–13.0]	5.5 [2.5–13.0]	6.0 [2.5–14.0]	6.0 [2.5–13.5]
	JSN score [0-208]	5.0 [1.5–14.0]	5.5 [1.5–14.9]	5.0 [1.0–14.5]	5.0 [1.5–14.5]

values are median [interquartile range]. **GUS**=guselkumab, **JSN**=joint space narrowing, **PBO**=placebo, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **vdH-S**=van der Heijde-Sharp score, **W**=week.

Inhibition of structural damage progression with GUS was largely consistent regardless of baseline radiographic features

- PBO-treated pts with a vdH-S erosion score >6 and >4.5 erosive joints at baseline had the most radiographic progression at W24



interaction p -value <0.05 for erosion score GUS Q8W. **CI**=confidence interval, **GUS**=guselkumab, **JSN**=joint space narrowing, **LSM**=least squares mean, **PBO**=placebo, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks, **vdH-S**=van der Heijde-Sharp score, **W**=week.