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

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Key Takeaways

- **GUS-treated biologic-naïve pts with active and erosive PsA demonstrated significantly greater clinical improvement and significant inhibition of structural damage progression vs PBO at W24**
- **GUS effects were generally consistent across diverse subgroups of pts defined by baseline demographics, disease characteristics, medication use, and radiographic features of interest**
  - Benefit in ACR20/50 clinical improvement was similar regardless of sex, BMI, PsA duration, joint involvement, CRP, and MTX use at baseline
  - Inhibition of radiographic progression observed across clinical and radiographic feature subgroups

Background

Guselkumab (GUS), a fully-human monoclonal antibody able to bind to the CD64-receptor and simultaneously inhibit the 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 ≥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

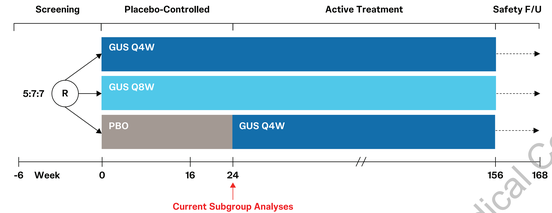
Objective

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



Endpoints[a]	High Clinical Interest Baseline Subgroups[b]	Statistical Analysis
• Proportion achieving ACR20/50 response	**Demographics** (Sex, BMI) **PsA Characteristics** (Duration[c], SJC, TJC, CRP) **Medication Use** (MTX[d])	Pts who discontinued study intervention for any reason except natural disaster/major disruption, initiated/increased dose of csDMARD or corticosteroid, or initiated prohibited therapies prior to W24 were considered nonresponders[e]
• LSM change in PsA-modified vdH-S score		Based on an ANCOVA model[f]
• LSM change in PsA-modified vdH-S score	**Radiographic Features** (Total vdH-S, erosion, and JSN scores; joints with erosions/JSN)	Based on an ANCOVA model[f]

[a]Over 200 MI datasets. [b]29 subgroups were predefined to evaluate treatment consistency over baseline demographics (n=7), disease characteristics (n=12), medication use (n=5), and radiographic features (n=5); those of high clinical interest are reported here. [c]Predefined PsA duration subgroups categories were <1/≥1 to <3/≥3 years, however, <3/≥3 presented due to small sample size in <1 year category. [d]Predefined as csDMARD use at baseline, however, MTX component presented separately based on MTX regressing the majority of csDMARD use at baseline. [e]Data impacted by, or missing due to, natural disaster/major disruption were imputed using NRI; for missing MI, other missing data were imputed using NRI. [f]Explanatory model variables: baseline vdH-S score, treatment group, and randomization stratification level; data impacted by natural disaster/major disruption and missing data imputed using MI. **ANCOVA**=analysis of covariance, **BMI**=body mass index, **CASPAR**=CASsification criteria for Psoriatic Arthritis, **CRP**=C-reactive protein, **csDMARD**=conventional synthetic disease-modifying antirheumatic drug, **F/U**=follow-up, **JSN**=joint space narrowing, **LSM**=least squares mean, **MI**=multiple imputation, **MTX**=methotrexate, **NRI**=nonresponder imputation, **NSAID**=nonsteroidal anti-inflammatory drug, **R**=randomization, **SJC**=swollen joint count, **TJC**=tender joint count.

Results

Similar proportions of pts comprised baseline characteristic subgroups across treatment arms

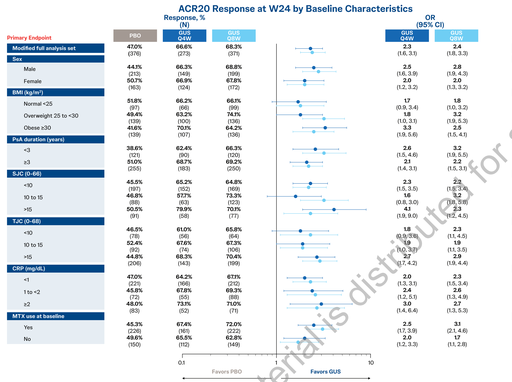
- Pts with active and erosive PsA: median disease duration=5 years, SJC=9, TJC=16, and CRP=0.8 mg/dL

Modified full analysis set[a]	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%	68%
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%

[a]*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,* ***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

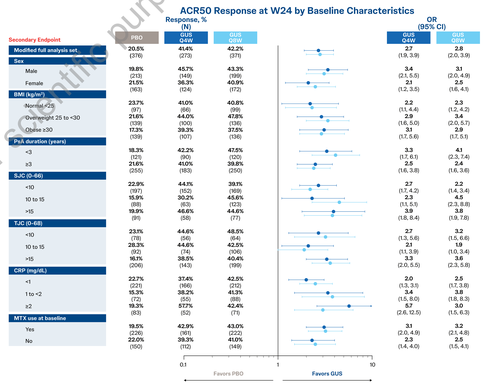
- Aligned with primary endpoint results, GUS-treated pts had approximately 2- to 4-times higher odds of achieving ACR20 response than PBO-treated pts



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.*

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

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



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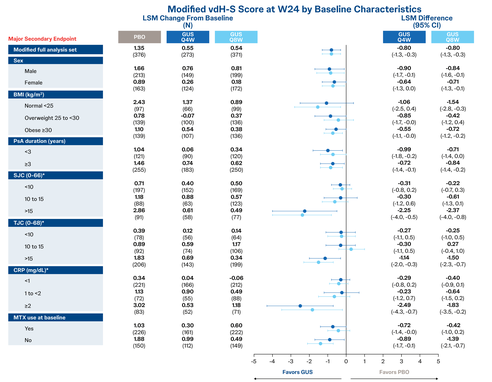
Significant inhibition of structural damage progression with GUS was generally consistent across baseline pt subgroups

- 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; TJC 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-Sharp,* ***W***=*week.*

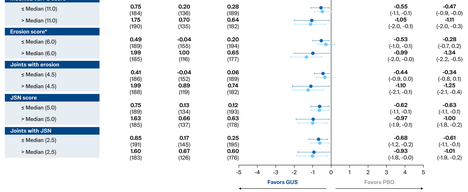
Baseline radiographic joint damage was of moderate degree and similar across treatment groups

	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.*

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; ***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,* ***W***=*week.*

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