Guselkumab Effect on cDAPSA and Its Association with Long-Term Radiographic Progression in Moderately-Highly Active Psoriatic Arthritis

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Background

- Guselkumab (GUS), a fully human interleukin (IL)-23p19-subunit inhibitor, given 100 mg every 4 weeks (Q4W) or Q8W significantly improved joint and skin symptoms vs. placebo (PBO) in the Phase 3 DISCOVER-1 and -2 studies[1,2] in patients (pts) with active psoriatic arthritis (PsA)
  - GUS showed significantly (Q4W) and numerically (Q8W) lower rates of radiographic progression vs. PBO at W24, with durable suppression of radiographic progression through W100 across dosing regimens in DISCOVER-2[2,3]
- Clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA) was developed as a simplified tool to assess PsA disease activity, with established cut points for remission and low/moderate/high disease activity states

Objective

These post hoc analyses of the DISCOVER studies evaluated:

- **The transition between cDAPSA disease activity states through W52 in a mixed population of PsA pts (pooled DISCOVER-1 and -2) treated with GUS vs. PBO**
- **The association between earlier clinical improvement in joint disease activity with GUS and long-term radiographic progression through W100 in DISCOVER-2 biologic-naïve pts**

Methods

Phase 3 DISCOVER-1 and -2 studies[1-3]

DISCOVER-1 (W0-W60)	DISCOVER-2 (W0-W112)[a]
Randomized 1:1:1 (N=381)	Randomized 1:1:1 (N=739)
GUS 100 mg at W0, W4, then Q4W GUS 100 mg at W0, W4, then Q8W PBO Q4W through W20; GUS 100 mg at W24 and then Q4W	
History of or current PsO, ≥3 SJC and ≥3 TJC, CRP ≥0.3 mg/dL	History of or current PsO, ≥5 SJC and ≥5 TJC, CRP ≥0.6 mg/dL
~31% of pts previously received 1-2 TNFi	Naïve to biologic agents and Janus kinase inhibitors

[a]Efficacy was assessed through W100 (study visit window of ±7 days); safety was assessed through W112 (safety visit window of ±14 days). CRP=C-reactive protein; GUS=Guselkumab; PBO=Placebo; PsO=Psoriasis; Q4W=Every 4 weeks; Q8W=Every 8 weeks; SJC=Swollen joint count; TJC=Tender joint count; TNFi=Tumor necrosis factor inhibitor; W=Week.

- Among DISCOVER-1 and -2 pts with moderate (>13 to ≤27) or high (>27) levels of joint disease activity (ModDA/HDA; cDAPSA >13) at baseline (BL):
  - Rates of cDAPSA low disease activity or remission (LDA/REM; ≤13) through W24: GUS vs. PBO with logistic regression adjusting for prior TNFi use, BL use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), and BL cDAPSA
  - Rates of cDAPSA LDA/REM through W52: GUS-treated pts using nonresponder imputation (NRI) for missing data
  - Maintenance of cDAPSA LDA/REM at W52: Observed data among GUS-randomized pts achieving response at W24
- GUS-randomized biologic-naïve pts in DISCOVER-2, in whom radiographic progression was evaluated:
  - Predictive model (mixed linear) assessed associations between early (W8) shift from cDAPSA ModDA/HDA→LDA/REM and changes in total PsA-modified van der Heijde-Sharp [vdH-S] score through W100, after adjusting for known BL determinants of radiographic progression,[4-8] vdH-S score, age, sex, and CRP

Key Takeaways

- **Among DISCOVER-1 and -2 PsA pts with cDAPSA ModDA/HDA at BL:**
  - **GUS was associated with significantly greater rates of cDAPSA LDA/REM achievement vs. PBO as early as W8 (after 2 doses) and at W24**
  - **LDA/REM response rates were achieved by 53-54% of GUS-randomized pts at W52**
  - **The vast majority (84-88%) of pts who achieved cDAPSA LDA/REM at W24 maintained low/remitted levels of joint disease activity through W52**
- **Among DISCOVER-2 biologic-naïve GUS-randomized pts, early improvements in joint disease activity (cDAPSA ModDA/HDA→LDA/REM at W8) associated with significantly lower rates of radiographic progression through W100**
- **Findings suggest cDAPSA's utility in routine care to monitor both short- and long-term improvements in joint disease activity among GUS-treated PsA pts**

Results

Of the 1113 pts included in this analysis, 947 (85%) had HDA and 166 (15%) had ModDA

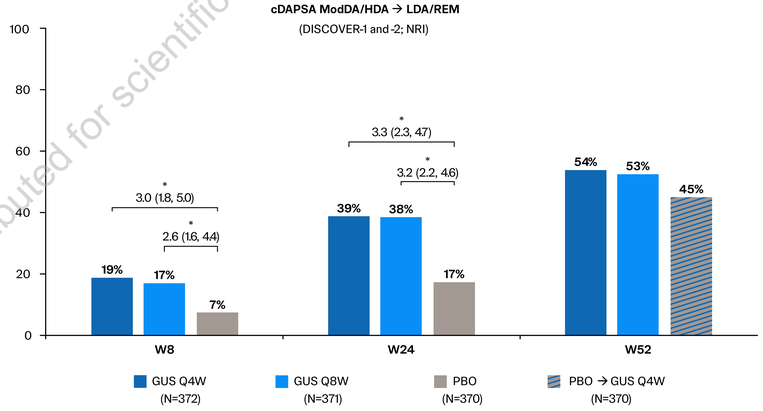
- BL PsA disease characteristics and demographics of pts with ModDA/HDA were well balanced across the treatment groups

BL Characteristics of Pts with cDAPSA ModDA/HDA	GUS Q4W (N=372)	GUS Q8W (N=371)	PBO (N=370)
DISCOVER-1 and -2 Demographics			
Age, yrs	46.5 (11.5)	46.2 (11.9)	47.2 (11.5)
Male, %	56%	52%	48%
White, %	98%	95%	96%[a]
BMI, kg/m^2	29.4 (5.8)	29.1 (6.3)	29.2 (6.2)
DISCOVER-1 and -2 PsA Characteristics			
PsA disease duration, yrs	5.9 (6.1)	5.6 (5.7)	6.3 (6.4)
SJC (0-66)	11.4 (7.5)	11.5 (7.7)	11.6 (7.0)
TJC (0-68)	20.9 (13.5)	20.1 (12.8)	21.1 (13.5)
cDAPSA (0-154)*	44.7 (20.3)	44.4 (20.2)	45.2 (19.8)
CRP, mg/dL	1.6 (2.0)	1.9 (2.4)	1.9 (2.4)
PASI (0-72)	10.4 (11.2)	9.3 (11.1)	8.8 (9.5)[b]
PtGA (0-100 VAS)	66.4 (19.6)	68.4 (19.6)[c]	66.7 (19.8)[b]
Pain (0-100 VAS)	60.7 (19.6)	62.5 (19.5)	61.4 (19.1)
DISCOVER-1 and -2 Medication Use at BL, %			
csDMARDs	68%	67%	68%
Methotrexate	58%	56%	61%
Oral Corticosteroids	17%	18%	19%
NSAIDs	64%	64%	66%
DISCOVER-2 Structural Damage	N=221	N=228	N=215
vdH-S	28.0 (43.6)	23.9 (40.4)	25.6 (42.4)

*Data are mean (SD) unless otherwise specified. *ModDA defined as score >13 to ≤27; HDA defined as score >27. [a]N=368; [b]N=369; [c]N=370. BL=Baseline; BMI=Body mass index; cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis; CRP=C-reactive protein; csDMARD=Conventional synthetic disease-modifying antirheumatic drug; GUS=Guselkumab; HDA=High disease activity; ModDA=Moderate Disease Activity; NSAID=Nonsteroidal anti-inflammatory drug; PASI=Psoriasis Area and Severity Index; PBO=Placebo; PsA=Psoriatic arthritis; 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; vdH-S: van der Heijde-Sharp.*

cDAPSA LDA/REM response rates were significantly higher with GUS vs. PBO as early as W8

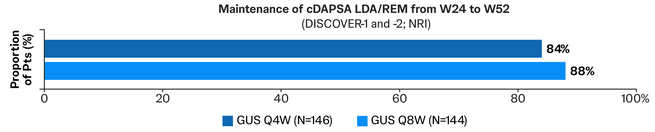
- cDAPSA LDA/REM response rates remained significantly higher with GUS vs. PBO at W24
- **53-54%** of GUS-randomized pts with cDAPSA ModDA/HDA at BL achieved LDA/REM at W52



[a]Nominal p≤0.0001 for GUS vs PBO. cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis; CI=Confidence interval; GUS=Guselkumab; HDA=High disease activity; LDA/REM=Low disease activity/remission; ModDA=Moderate disease activity; OR=Odds ratio; NRI=Nonresponder imputation; PBO=Placebo; Q4W=Every 4 weeks; Q8W=Every 8 weeks; W=Week.

84-88% of GUS-randomized pts achieving cDAPSA LDA/REM at W24 maintained low/remitted levels of joint disease activity at W52

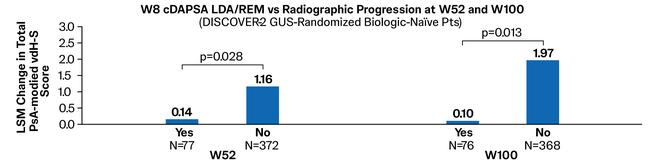
- **31-36%** of GUS-randomized pts not achieving cDAPSA LDA/REM at W24 did so at W52



cDAPSA=Clinical Activity Index for Psoriatic Arthritis; GUS=Guselkumab; LDA/REM=Low disease activity/remission; NRI=Nonresponder imputation; Pts=Patients; Q4W=Every 4 weeks; Q8W=Every 8 weeks; W=Week.

Achievement of cDAPSA LDA/REM as early as W8 with GUS was associated with significantly lower rates of radiographic progression at W52 and W100

- The effect of W8 cDAPSA LDA/REM achievement vs. non-achievement on future radiographic progression strengthened over time



cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis; GUS=Guselkumab; LDA/REM=Low disease activity/remission; LSM=Least squares mean; PsA=Psoriatic arthritis; Pts=Patients; vdH-S=Van der Heijde-Sharp; W=Week.

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