Achievement of Low Disease Activity/Remission in Guselkumab-Treated Patients with Moderately-Highly Active Psoriatic Arthritis Regardless of Baseline Characteristics: Pooled Post-Hoc Analysis of Two Phase 3/Randomized Studies

Philip J. Mease[1,2], Alice B. Gottlieb[3], Iain B. McInnes[4], Natalie J. Shiff[5,6], Emmanouil Rampakakis[7,8], Francois Nantel[9], Jenna Parrett[5], Frederic Lavie[10], Proton Rahman[11]

[1]Rheumatology Research, Providence Swedish Medical Center, Seattle, WA, USA; [2]University of Washington School of Medicine, Seattle, WA, USA; [3]Icahn School of Medicine at Mount Sinai, Department of Dermatology, New York, NY, USA; [4]University of Glasgow, College of Medical Veterinary and Life Sciences, Glasgow, UK; [5]Johnson & Johnson, Horsham, PA, USA; [6]University of Saskatchewan, Adjunct, Community Health and Epidemiology, Saskatoon, SK, Canada; [7]McGill University, Department of Pediatrics, Montreal, QC, Canada; [8]Scientific Affairs, JSS Medical Research Inc, Montreal, QC, Canada; [9]Nantel Medsci Consult, Montreal, QC, Canada; [10]Johnson & Johnson, Issy les Moulineaux, France; [11]Memorial University of Newfoundland, Faculty of Medicine, Division of Rheumatology, St. Johns, NL, Canada

Background

- Guselkumab (GUS), a fully human interleukin (IL)-23p19-subunit inhibitor monoclonal antibody, has demonstrated multidomain efficacy in patients (pts) with active psoriatic arthritis (PsA) in the Phase 3, double-blind, placebo (PBO)-controlled DISCOVER-1 and -2 studies[1,2]
- Clinical Disease Activity Index for PsA (cDAPSA):
  - Version of the DAPSA omitting C-reactive protein (CRP); focused on peripheral joint disease
  - Validated composite measure suitable for routine clinical practice
  - Established cut points for remission (REM) and low disease activity (LDA), moderate DA (ModDA), and high DA (HDA)
- Pt-specific factors may influence PsA treatment efficacy:[3]
  - Sex, body mass index (BMI), PsA duration, CRP, baseline (BL) DA/domain involvement

Objectives

- **Achievement of cDAPSA LDA/REM was assessed in a pooled (DISCOVER-1 and -2) post-hoc analysis of pts with ModDA/HDA at BL in pt subgroups defined by BL demographic and disease characteristics**

Methods

DISCOVER-1 and DISCOVER-2 Trial Designs

DISCOVER-1 (W0-W60)[4]	DISCOVER-2 (W0-W112)[4]
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 JAKi

CRP=C-reactive protein; JAKi=Janus kinase inhibitor; 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.

Post-Hoc Analyses

- Analysis population: Pooled DISCOVER-1 and DISCOVER-2 pts with cDAPSA ModDA (>13 to ≤27) or HDA (>27) at BL
- Outcome of interest: cDAPSA LDA/REM (≤13) response rates through Week (W)24: nonresponder imputation (NRI) for missing data
- Statistical methodology: Odds ratios (OR) and 95% confidence intervals (CI) comparing each GUS group vs PBO: logistic regression stratified by BL characteristics

Stratification Factors

Measure	Definition
Sex	Male/Female
BMI	<25; ≥25 to <30; ≥30 kg/m^2
PsA duration	<1; ≥1 to <3; ≥3 years
SJC/TJC	<10; ≥10 to ≤15; >15
cDAPSA	ModDA/HDA
CRP	<1; ≥1 to <2; ≥2 mg/dL
PASI	<12; ≥12 to <20; ≥20
BSA % with PsO	<3; ≥3 to <10; ≥10 to <20; ≥20
csDMARD use	None; Any; MTX
Prior TNFi use	Yes/No

BMI=Body mass index; BSA=Body surface area; cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis; csDMARD=Conventional synthetic disease-modifying antirheumatic drug; CRP= C-reactive protein; HDA=High disease activity; ModDA=Moderate disease activity; MTX=Methotrexate; PASI=Psoriasis Area and Severity Index; PsA= Psoriatic arthritis; PsO=Psoriasis; SJC=Swollen joint count; TJC=Tender joint count; TNFi=Tumor necrosis factor inhibitor.

Key Takeaways

- **In this cohort of PsA pts with highly active joint disease, significantly greater proportions of GUS-randomized pts vs PBO achieved cDAPSA LDA/REM at W24**
- **Both GUS dosing regimens showed consistent treatment effect in achieving low levels of joint disease activity across BL pt and disease characteristics including:**
  - **Sex, BMI, PsA duration**
  - **Joint disease activity**
  - **Skin disease activity**
  - **Concomitant csDMARD use**
  - **Prior TNFi exposure**
- **The findings from this post-hoc analysis support the use of GUS across diverse populations of pts with active PsA, including those with highly active joint disease**

Results

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

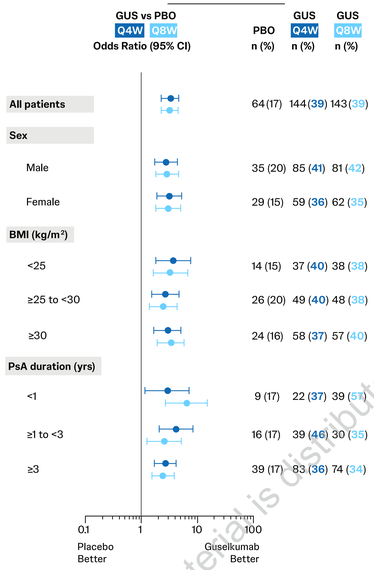
- BL demographic and disease characteristics were well-balanced across the treatment groups

BL Characteristics of DISCOVER-1 and -2 Pts with cDAPSA ModDA/HDA	GUS Q4W (N=372)	GUS Q8W (N=371)	PBO (N=370)
Demographics & Disease Duration			
Age, y	46.5 (11.5)	46.2 (11.9)	47.2 (11.5)
Male, n (%)	207 (55.6)	194 (52.3)	176 (47.6)
BMI, kg/m^2	29.4 (5.8)	29.1 (6.3)	29.2 (6.2)
PsA duration, y	5.9 (6.1)	5.6 (5.7)	6.3 (6.4)
Joint Disease			
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[a]	44.7 (20.3)	44.4 (20.2)	45.2 (19.8)
ModDA, n (%)	65 (17.5)	60 (16.2)	41 (11.1)
HDA, n (%)	307 (82.5)	311 (83.8)	329 (88.9)
CRP, mg/dL	1.6 (2.0)	1.9 (2.4)	1.9 (2.4)
Skin Disease			
PASI score [0-72][b]	10.4 (11.2)	9.3 (11.1)	8.8 (9.5)
% BSA with PsO [0-100][c]	17.1 (19.8)	15.7 (20.0)	15.4 (18.9)
Concomitant/Prior Medications, n (%)			
csDMARDs	251 (67.5)	250 (67.4)	253 (68.4)
MTX	217 (58.3)	207 (55.8)	226 (61.1)
Prior TNFi	38 (10.2)	41 (11.1)	39 (10.5)

Data presented as mean (standard deviation) unless otherwise noted. [a]cDAPSA disease activity=REM ≤4; LDA >4 to ≤13; ModDA >13 to ≤27; HDA >27. [b]PBO N=369. [c]BSA=Body surface area; cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis; CRP=C-reactive protein; csDMARDs=Conventional synthetic disease-modifying antirheumatic drugs; GUS=Guselkumab; HDA=High disease activity; ModDA=Moderate disease activity; MTX=Methotrexate; PASI=Psoriatic Area and Severity Index; PBO=Placebo; PsA=Psoriatic arthritis; PsO=Psoriasis; Pts=Patients; Q4W=Every 4 weeks; Q8W=Every 8 weeks; SJC=Swollen joint count; TJC=Tender joint count; TNFi=Tumor necrosis factor inhibitor; yr=Year.

Greater proportions of GUS-randomized pts vs PBO achieved cDAPSA LDA/REM at W24, regardless of BL pt demographics and PsA duration

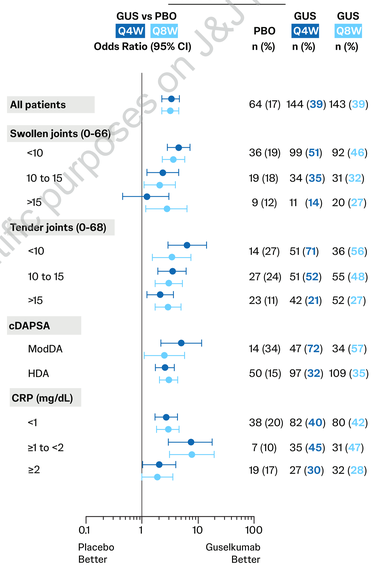
- OR of GUS vs PBO at W24: Sex=2.8-3.2; BMI=2.5-3.7; PsA duration=2.5-6.4



BMI=Body mass index; cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis; CI=Confidence interval; GUS=Guselkumab; LDA=Low disease activity; PBO=Placebo; PsA=Psoriatic arthritis; Q4W=Every 4 weeks; Q8W=Every 8 weeks; REM=Remission; yr=Years.

GUS-randomized pts generally had greater response rates vs PBO for achieving cDAPSA LDA/REM at W24 regardless of joint disease activity and systemic inflammation at BL

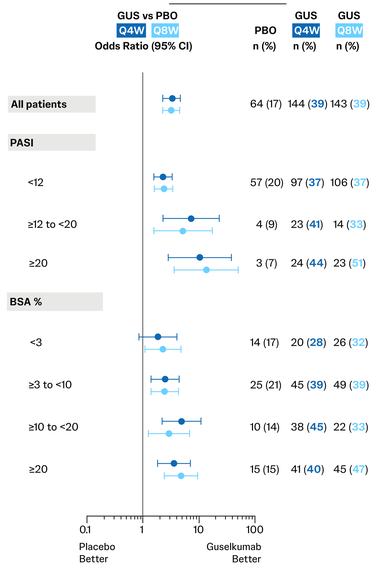
- OR of GUS vs PBO at W24: SJC=1.2-4.5; TJC=2.1-6.4; cDAPSA=2.5-5.0; CRP=1.9-7.7



cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis; CI=Confidence interval; CRP=C-reactive protein; GUS=Guselkumab; HDA=High disease activity; LDA=Low disease activity; ModDA=Moderate disease activity; PBO=Placebo; Q4W=Every 4 weeks; Q8W=Every 8 weeks; REM=Remission.

cDAPSA LDA/REM was achieved by higher proportions of pts receiving GUS vs PBO in subgroups of adequate sample size defined by BL psoriatic skin disease severity

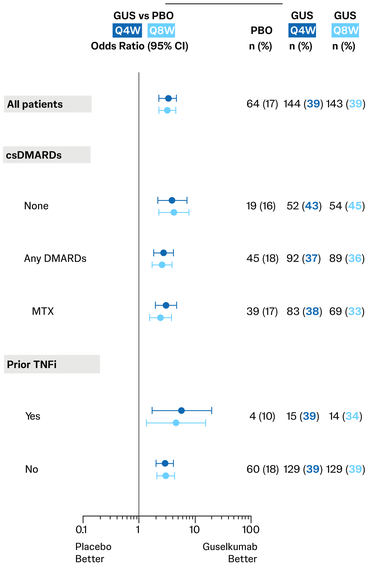
- OR of GUS vs PBO at W24: PASI=2.3-13.6; BSA %=1.9-5.0



BSA=Body surface area; cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis; CI=Confidence interval; GUS=Guselkumab; LDA=Low disease activity; PASI=Psoriasis Area and Severity Index; PBO=Placebo; Q4W=Every 4 weeks; Q8W=Every 8 weeks; REM=Remission.

Greater proportions of GUS-randomized pts vs PBO achieved cDAPSA LDA/REM regardless of concomitant csDMARD use or prior TNFi exposure

- OR of GUS vs PBO at W24: csDMARDs, None=3.9-4.2; Any/MTX=2.4-3.0; Prior TNFi (Yes/No)=2.8-5.7



cDAPSA=Clinical Disease Activity Index for Psoriatic Arthritis; CI=Confidence interval; csDMARDs=Conventional synthetic disease-modifying antirheumatic drug; DMARD=Disease-modifying antirheumatic drug; GUS=Guselkumab; LDA=Low disease activity; MTX=Methotrexate; PBO=Placebo; Q4W=Every 4 weeks; Q8W=Every 8 weeks; REM=Remission; TNFi=Tumor necrosis factor inhibitor.

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