Impact of Prior Tumor Necrosis Factor Inhibitor Treatment and Baseline Psoriatic Arthritis Disease Activity on Minimal Clinically Important Improvement Thresholds for Efficacy Outcomes: Post hoc Analysis of Three Phase 3 Studies of Guselkumab in Patients with Active Psoriatic Arthritis

Alexis Ogdie,[1] Philip Mease,[2,3] Francois Nantel,[4] Frederic Lavie,[5] Mohamed Sharaf,[6] Emmanouil Rampakakis,[7,8] Helena Marzo-Ortega,[9] Laure Gossec[10]

[1]Division of Rheumatology, University of Pennsylvania School of Medicine, Philadelphia, PA, USA; [2]Rheumatology Research, Providence Swedish Medical Center, Seattle, WA, USA; [3]University of Washington School of Medicine, Seattle, WA, USA; [4]Nantel Medsci Consult, Montreal, QC, Canada; [5]Johnson & Johnson, Issy les Moulineaux, France; [6]Johnson & Johnson, Dubai, UAE; [7]Department of Pediatrics, McGill University, Montreal, QC, Canada; [8]Scientific Affairs, JSS Medical Research, Inc, Montreal, QC, Canada; [9]NIHR Leeds Biomedical Research Centre, Chapel Allerton Hospital and Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK; [10]Sorbonne Université and AP-HP, Pitié-Salpêtrière Hospital, Paris, France

Key Takeaways

- **Acknowledging differences in methodologies, MCII thresholds estimated in RCT participants were generally more stringent than those previously reported**
- **In a pooled RCT population of patients with moderately-to-highly active PsA, estimated MCII thresholds were consistent across biologic-naïve and TNFi-experienced participants**
  - ✓ **Patients receiving GUS every 8 weeks (Q8W) were more likely to achieve early (W8) MCII across disease domains when compared with placebo (PBO), irrespective of prior TNFi use**
- **MCII cutoffs were greater for patients with higher baseline cDAPSA disease activity, indicating baseline joint disease activity may impact assessment of improvement**
  - ✓ **Despite greater cDAPSA thresholds, patients with HDA at baseline remained more likely to achieve early (W8) MCII with GUS Q8W than with PBO**

Background

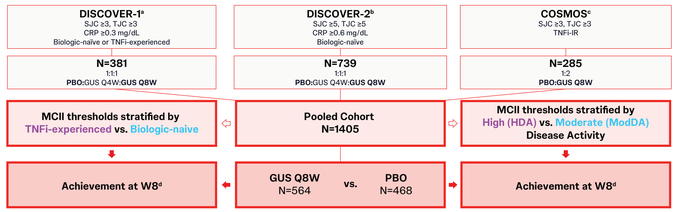
- Psoriatic arthritis (PsA) disease activity and impact on patients are measured with clinical and patient-reported outcomes (PROs)[1]
- Minimal clinically important improvement (MCII), the smallest improvement perceived by patients as clinically meaningful[2], has been defined for multiple PsA outcome measures, mainly using observational data[3,4]
- Guselkumab (GUS), a fully human monoclonal antibody targeting the interleukin (IL)-23p19 subunit, is approved for the treatment of adults with active PsA
  - GUS demonstrated early, significant, and sustained multi-domain efficacy across 3 Phase 3 randomized controlled trial (RCT) populations of PsA patients with variable treatment history[5-7]
  - MCII thresholds for PsA outcomes have not yet been evaluated across lines of treatment or varying levels of disease activity in PsA patients treated with GUS

Objectives

MCII thresholds for efficacy outcomes were determined in subsets of PsA patients, stratified by treatment history and baseline disease activity, utilizing pooled data from 3 Phase 3 RCTs

Methods

Patients with active PsA from 3 RCTs were pooled



[a]NCT03162796. [b]NCT03158285. [c]NCT03796858. [d]First time point assessed common to all 3 RCTs. **CRP**=C-reactive protein, **GUS**=Guselkumab, **HDA**=High disease activity, **IR**=Inadequate response, **MCII**=Minimal clinically important improvement, **ModDA**=Moderate disease activity, **PBO**=Placebo, **Q4W**=At W0, W4, and every 4 weeks, **Q8W**=At W0, W4, and every 8 weeks, **RCT**=Randomized controlled trial, **SJC**=Swollen joint count, **TJC**=Tender joint count, **TNFi**=Tumor necrosis factor inhibitor, **W**=Week

Assessments and analyses

MCII Thresholds From 3 RCTs
Efficacy Outcomes in TNFi-experienced and Biologic-naïve Cohorts | **cDAPSA and PASDAS in Patients With HDA vs. ModDA**

Efficacy outcomes:
Joint: cDAPSA, PtGA Arthritis
Skin: PtGA Psoriasis
PROs: Patient Pain, HAQ-DI, FACIT-Fatigue
Overall: PASDAS

Assessed using 3 distribution-based methods:
#1: baseline SD x √ 1 – Cronbach's alpha
#2: 0.5 x baseline SD
#3: (last visit score – first visit score)/(baseline SD) x (√1 – Cronbach's alpha)[a]

PsA disease activity thresholds:
cDAPSA (0-154):
HDA: >27; ModDA: >13 and ≤27

PASDAS (0-10):
HDA: >5.4; ModDA: >3.2 and ≤5.4

Assessed using a distribution-based method:
0.5 x SD of change in outcome from baseline to W24

Achievement of MCII thresholds with GUS vs. PBO
W8: 1st timepoint common to all outcomes across 3 RCTs
GUS Q8W: GUS regimen common to 3 RCTs
Logistic regression: among patients with baseline score >MCII
Non-responder imputation: applied for missing data

[a]Triangulated from estimated thresholds derived for each subsequent visit pair between baseline and W24. **cDAPSA**=Clinical Disease Activity Index for PsA, **FACIT**=Functional Assessment of Chronic Illness Therapy, **GUS**=Guselkumab, **HAQ-DI**=Health Assessment Questionnaire–Disability Index, **HDA**=High disease activity, **MCII**=Minimal clinically important improvement, **ModDA**=Moderate disease activity, **PASDAS**=PsA Disease Activity Score, **PBO**=Placebo, PsA=Psoriatic arthritis, **PtGA**=Patient Global Assessment, **RCT**=Randomized controlled trial, **SD**=Standard deviation, **TNFi**=Tumor necrosis factor inhibitor, **W**=Week

Results

Baseline characteristics were generally well-balanced across tumor necrosis factor inhibitor (TNFi)-experienced and biologic-naïve cohorts

	TNFi-experienced (N=403)	Biologic-naïve (N=1002)	All (N=1405)
Demographics			
Age, yrs	49.4 (11.7)	46.2 (11.7)	47.1 (11.8)
Male	50%	52%	51%
White/Asian	86%/14%	97%/3%	96%/4%
Weight, kg	86.0 (19.4)	84.8 (19.4)	85.2 (19.4)
Characteristics			
cDAPSA (0-154)	43.7 (19.8)	44.4 (19.9)	44.2 (19.8)
ModDA: >13 and ≤27	16%	15%	15%
HDA: >27	84%	84%	84%
PASDAS (0-10)	6.4 (1.0)	6.5 (1.1)	6.5 (1.1)
ModDA: >3.2 and ≤5.4	16%	16%	16%
HDA: >5.4	84%	84%	84%
PtGA-Arthritis (0-100 VAS)	65.0 (17.9)	63.6 (19.7)	64.0 (19.2)
PtGA-Psoriasis (0-100 VAS)	61.4 (24.1)	60.5 (24.3)	60.8 (24.2)
Patient Pain (0-100 VAS)*	63.7 (18.7)	60.8 (19.9)	61.6 (19.6)
HAQ-DI (0-3)**	1.3 (0.6)	1.2 (0.6)	1.3 (0.6)
FACIT-Fatigue (0-52)	29.0 (10.9)	30.1 (9.9)	29.8 (10.2)
Medication use at baseline			
csDMARDs	66%	67%	67%
Methotrexate	58%	58%	58%

Nominal *p<0.05; **p<0.01 for TNFi-experienced vs. biologic-naïve based on a 2-sample t-test for continuous variables. Data shown are mean (SD), unless otherwise indicated. **cDAPSA**=Clinical Disease Activity for PsA, **csDMARD**=Conventional synthetic disease-modifying antirheumatic drug, **FACIT**=Functional Assessment of Chronic Illness Therapy, **HAQ-DI**=Health assessment questionnaire-disability index, **HDA**=High disease activity, **ModDA**=Moderate disease activity, **PASDAS**=PsA Disease Activity Score, **PtGA**=Patient Global Assessment, **SD**=Standard deviation, **TNFi**=Tumor necrosis factor inhibitor, **VAS**=Visual analog scale, **yrs**=Years

Mean MCII thresholds were generally consistent across prior treatment cohorts

- Estimated MCIIs represented **16-39% mean improvement** from baseline
- **Some variation** was observed among methods
- MCII thresholds estimated in RCT participants were generally more stringent than those previously reported

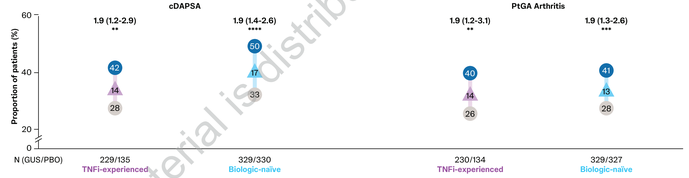
Outcome	Estimated MCII Range[a]		Mean (SD) MCII[b]		Reference MCII
	TNFi-exp.	Biologic-naïve	TNFi-exp.	Biologic-naïve	
cDAPSA (0-154)	11.0-19.8	11.0-19.8	14.7 (4.59)	14.7 (4.60)	3.25[3]-5.7[4]
PASDAS (0-10)	0.6-1.5	0.6-1.7	1.0 (0.48)	1.1 (0.57)	0.8[4,8-10]
PtGA Arthritis (0-100)	10.0-21.1	10.9-21.4	16.3 (5.76)	17.4 (5.63)	15[11]
PtGA Psoriasis (0-100)	13.3-32.2	13.5-32.2	23.2 (9.49)	23.3 (9.39)	15[11]
Patient Pain (0-100)	10.3-20.5	11.0-20.3	16.5 (5.43)	17.1 (5.24)	15[11]
HAQ-DI (0-3)	0.3-0.6	0.3-0.6	0.4 (0.15)	0.4 (0.14)	0.35[12]
FACIT-Fatigue (0-52)	6.0-10.9	5.5-9.9	8.9 (2.54)	8.3 (2.46)	4[13]

Among **403 TNFi-experienced and 1002 biologic-naïve** patients. [a]Range of estimated MCII from the following methods: Distribution method #1: baseline SD x √ 1–r; Distribution method #2: 0.5 x baseline SD; Distribution method #3: (last visit score – first visit score)/baseline SD) x (√ 1 – Cronbach's alpha). Estimates shown were triangulated from thresholds derived for each subsequent visit pair between baseline and W24. [b]Mean of estimated MCIIs from distribution methods #1, #2, and #3. [c]Threshold predicated on anchor-based (minimal important change=0.67)[7] and distribution (minimal clinically important difference=0.76)[8] methods, and indicative of a moderate response in majority of patients with psoriatic arthritis.[14] **cDAPSA**=Clinical Disease Activity for PsA, **FACIT**=Functional Assessment of Chronic Illness Therapy, **HAQ-DI**=Health assessment questionnaire-disability index, **MCII**=Minimal clinically important improvement, **PASDAS**=PsA Disease Activity Score, **PtGA**=Patient Global Assessment, **SD**=Standard deviation, **TNFi**=Tumor necrosis factor inhibitor

GUS-treated patients were more likely to achieve early (Week [W] 8) MCII in joint outcomes, irrespective of treatment history

- Clinical Disease Activity for Psoriatic Arthritis (cDAPSA) MCII thresholds estimated in RCT participants (14.7 in both cohorts) were more stringent than previously reported (3.25[3]/5.7[4])

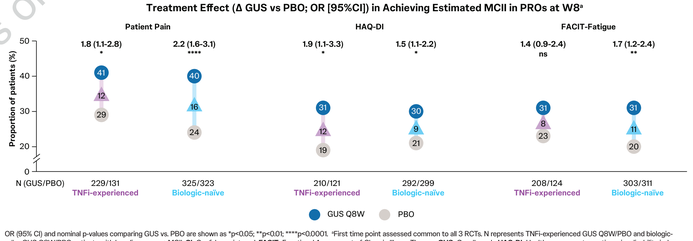
Treatment Effect (Δ GUS vs PBO; OR [95%CI]) in Achieving Estimated MCII in Joint Disease Activity at W8[a]



Odds ratio (OR; 95% confidence interval [CI]) and nominal p-values comparing GUS vs. PBO are shown as **p<0.01, ***p<0.001; ****p<0.0001. [a]First time point assessed common to all 3 RCTs. N represents TNFi-experienced GUS Q8W/PBO and biologic-naïve GUS Q8W/PBO patients with baseline scores >MCII. **cDAPSA**=Clinical Disease Activity for PsA, **CI**=Confidence interval, **GUS**=Guselkumab, **MCII**=Minimal clinically important improvement, **OR**=Odds ratio, **PBO**=Placebo, **PtGA**=Patient Global Assessment, **Q8W**=Every 8 weeks, **RCT**=Randomized controlled trial, **TNFi**=Tumor necrosis factor inhibitor, **W**=Week

GUS-treated patients were more likely to achieve early (W8) MCII in PROs, regardless of prior TNFi use

Treatment Effect (Δ GUS vs PBO; OR [95%CI]) in Achieving Estimated MCII in PROs at W8[a]



OR (95% CI) and nominal p-values comparing GUS vs. PBO are shown as *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001. [a]First time point assessed common to all 3 RCTs. N represents TNFi-experienced GUS Q8W/PBO and biologic-naïve GUS Q8W/PBO patients with baseline scores >MCII. **CI**=Confidence interval, **FACIT**=Functional Assessment of Chronic Illness Therapy, **GUS**=Guselkumab, **HAQ-DI**=Health assessment questionnaire-disability index, **MCII**=Minimal clinically important improvement, **ns**=Not significant, **PBO**=Placebo, **PRO**=Patient-reported outcome, **Q8W**=Every 8 weeks, **RCT**=Randomized controlled trials, **TNFi**=Tumor necrosis factor inhibitor, **W**=Week

GUS-treated patients were more likely to achieve early (W8) MCII in Patient Global Assessment (PtGA) Psoriasis and Psoriatic Arthritis Disease Activity Score (PASDAS), across prior treatment cohorts

Treatment Effect (Δ GUS vs PBO; OR [95%CI]) in Achieving Estimated MCII in Overall Disease Activity at W8[a]

OR (95% CI) and nominal p-values comparing GUS vs. PBO are shown as ***p<0.001; ****p<0.0001. [a]First time point assessed common to all 3 RCTs. N represents TNFi-experienced GUS Q8W/PBO and biologic-naïve GUS Q8W/PBO patients with baseline scores >MCII. **CI**=Confidence interval, **GUS**=Guselkumab, **MCII**=Minimal clinically important improvement, **OR**=Odds ratio, **PASDAS**=PsA Disease Activity Score; **PBO**=Placebo, **PtGA**=Patient Global Assessment, **Q8W**=Every 8 weeks, **RCT**=Randomized controlled trials, **TNFi**=Tumor necrosis factor inhibitor, **W**=Week

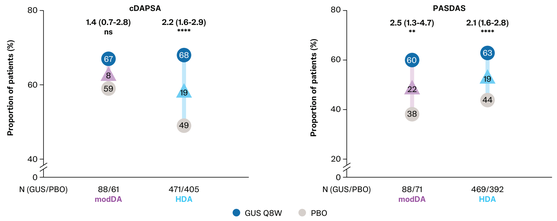
MCII thresholds for joint disease activity were greater in PsA RCT participants with high disease activity (HDA) vs. moderate disease activity (ModDA)

Outcome measure / disease activity at baseline	Estimated MCII	Reference MCII
cDAPSA	8.7	3.25[3]-5.7[4]
Patients with ModDA	4.1	
Patients with HDA	9.1	
PASDAS	0.8	0.8[4,8-10]
Patients with ModDA	0.7	
Patients with HDA	0.8	

Distribution method: 0.5 x SD of change in outcome from baseline to W24. [a]Threshold predicated on anchor-based (minimal important change=0.67)[7] and distribution (minimal clinically important difference=0.76)[8] methods, and indicative of a moderate response in majority of patients with psoriatic arthritis.[14] **cDAPSA**=Clinical Disease Activity for PsA, **HDA**=High disease activity, **MCII**=Minimal clinically important improvement, **ModDA**=Moderate disease activity, **PASDAS**=PsA Disease Activity Score, **SD**=Standard deviation

GUS-treated patients were more likely to achieve cDAPSA and PASDAS disease activity-specific MCIIs at W8

Treatment Effect (Δ GUS vs PBO; OR [95%CI]) in Achieving Estimated MCII in cDAPSA and PASDAS Stratified by Disease Activity at W8[a]



OR (95% CI) and nominal p-values comparing GUS vs. PBO are shown as **p<0.01; ****p<0.0001. [a]First time point assessed common to all 3 RCTs. **cDAPSA ModDA: >13 and ≤27; cDAPSA HDA: >27; PASDAS ModDA: >3.2 and ≤5.4; PASDAS HDA: >5.4.** N represents GUS Q8W/PBO with baseline scores >MCII. **cDAPSA**=Clinical Disease Activity for PsA, **CI**=Confidence interval, **GUS**=Guselkumab, **HDA**=High disease activity, **MCII**=Minimal clinically important improvement, **ModDA**=Moderate disease activity, **ns**=Not significant, **OR**=Odds ratio, **PASDAS**=PsA Disease Activity Score, **PBO**=Placebo, **Q8W**=Every 8 weeks, **RCT**=Randomized controlled trial, **W**=Week

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REFERENCES: 1. Ogdie, A. *Arthritis Care Res.* 2020;72:823. **2.** Kvien, T.K. *Ann Rheum Dis.* 2007;66:ii40. **3.** Karmacharya, P. *Arthritis Care Res.* 2022;75:2182. **4.** Ogdie, A. *Ann Rheum Dis.* 2020;79:1173. **5.** Deodhar, A. *Lancet.* 2020;395:1115-25. **6.** Mease, P.J. *Lancet.* 2020;395:1126-36. **7.** Coates, L.C. *Ann Rheum Dis.* 2022;81:359-69. **8.** Mulder, M.L.M. *Rheumatology.* 2022;61:4119. **9.** Tillett, W. *Ann Rheum Dis.* 2021;80:135. **10.** Helliwell, P.S. *J Rheumatol.* 2014;41:1212. **11.** Institute for Quality and Efficiency in Health Care. *General Methods* V6.1. Jan 2022. **12.** Mease, P.J. *J Rheumatol.* 2011;38:2461. **13.** Cella, D. *J Rheumatol.* 2005;32:811.
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