AAD 2025: GUIDE DATA

Pharmacokinetics of guselkumab in super responders and long-term psoriasis disease control: Insights from the Phase 3b GUIDE trial

P61980

K. Eyerich,[1] K. Asadullah,[2,3] A. Pinter,[4] P. Weisenseel,[5] C. Paul,[6] F. Kreimendahl,[7] K. Henry,[8] J. Wilke,[7] N. Krüger,[7] N. Spindler,[7] K. Schäkel[9]

[1]Dept. of Dermatology and Venereology, Medical Center, University of Freiburg, Freiburg, Germany; [2]Dept. of Dermatology, Venereology and Allergology, Charité – Universitätsmedizin, Berlin, Germany; [3]Dermatology Potsdam MVZ, Potsdam, Germany; [4]University Hospital Frankfurt am Main, Frankfurt, Germany; [5]Dermatologikum Hamburg, Hamburg, Germany; [6]Toulouse University, Toulouse, France; [7]Johnson & Johnson Innovative Medicine, Neuss, Germany; [8]Johnson & Johnson Innovative Medicine, R&D, Cambridge, MA, USA; [9]Dept. of Dermatology, and Interdisciplinary Center for Inflammatory Diseases, Heidelberg University Hospital, Heidelberg, Germany

J&J Innovative Medicine

Immunology

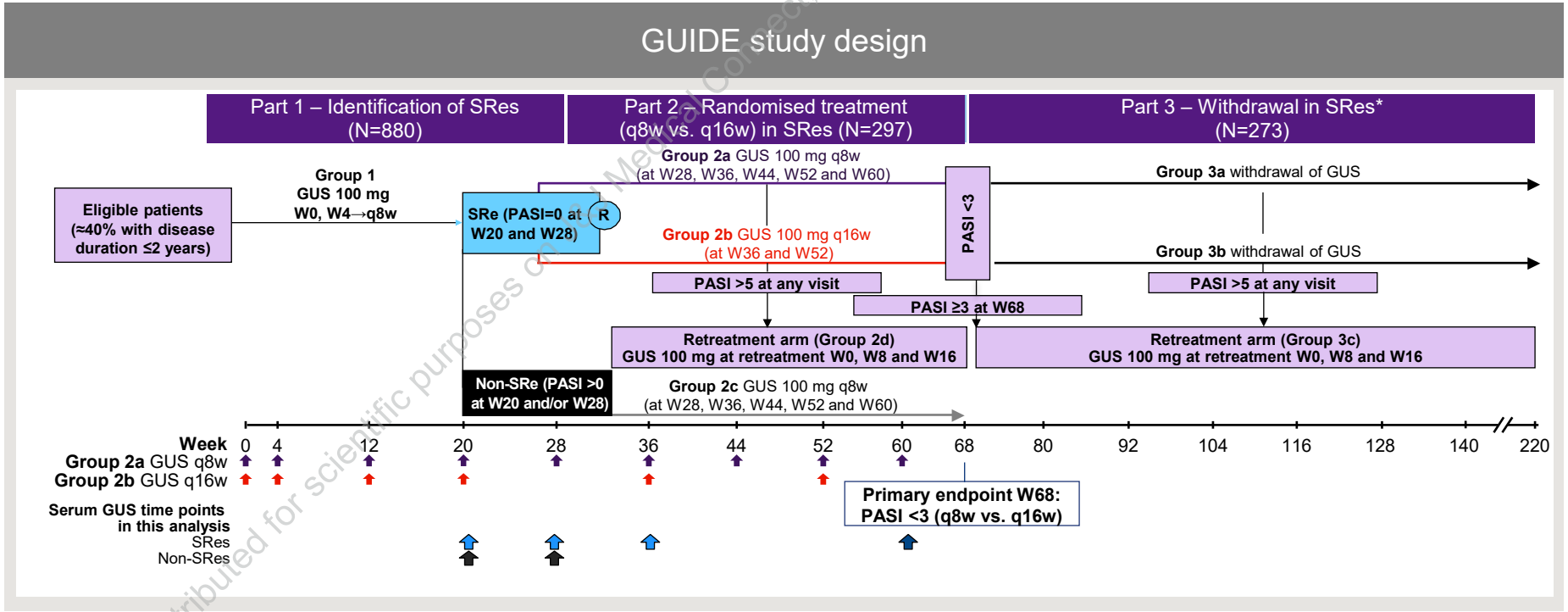
Pharmacokinetics of GUS in SRes and long-term PsO disease control: Insights from the Phase 3b GUIDE trial

Aim

- To analyse the relationship of serum GUS concentration with dosing interval (q8w and q16w) and clinical outcomes in GUIDE to further assess the potential of disease modification with GUS treatment

Methods

- GUS serum concentrations were measured using an immunoassay, in blood samples collected before dosing at Weeks 20, 28, 36 and 68
- All p-values are nominal



*Patients entering Part 3 from the q8w and q16w arms of Part 2 received their last guselkumab dose at W60 and W52, respectively. Unlike Part 1, the retreatment phase in Part 3 did not include an induction scheme - the retreatment dosing interval was q8w.
GUS, guselkumab; IL-23, interleukin-23; MOA, mode of action; PASI, Psoriasis Area and Severity Index; MOA, mode of action; PsO, psoriasis; q8w, every 8 weeks; q16w, every 16 weeks; R, randomisation; RCT, randomised controlled trial; SRe, super responder; W, Week.

Eyerich K, et al. Presented at AAD, Orlando, FL, US, 7–11 March 2025. P61980.

Patient characteristics at baseline (including those with available serum data)

Patient characteristics at baseline

Characteristic	All enrolled patients (N=880)	Patients with GUS serum data at Week 20		
		Overall (n=821)	SRe (n=298)	Non-SRe (n=523)
Mean age, years (SD)	42.5 (14.7)	42.2 (14.5)	39.4 (14.1)	43.7 (14.4)
Sex, n (%)				
Male / female	620 (70.5) / 260 (29.5)	584 (71.1) / 237 (28.9)	203 (68.1) / 95 (31.9)	381 (72.8) / 142 (27.2)
Mean BMI, kg/m² (SD)	28.3 (6.0)	28.3 (6.1)	27.0 (5.2)	29.0 (6.4)
Mean weight, kg (SD)	88.0 (21.1)	88.0 (21.2)	83.5 (18.6)	90.6 (22.1)
Mean duration of psoriasis, years (SD)	12.5 (13.8)	12.5 (13.8)	9.9 (12.4)	14.0 (14.4)
Mean PASI (SD)	19.1 (7.9)	19.1 (7.9)	18.8 (7.6)	19.2 (8.1)
Mean DLQI (SD)	19.0 (5.3)	19.1 (5.1)	18.9 (5.0)	19.2 (5.2)
Prior biologic therapy, n (%)	123 (14.0)	117 (14.3)	21 (7.0)	96 (18.4)

Key result

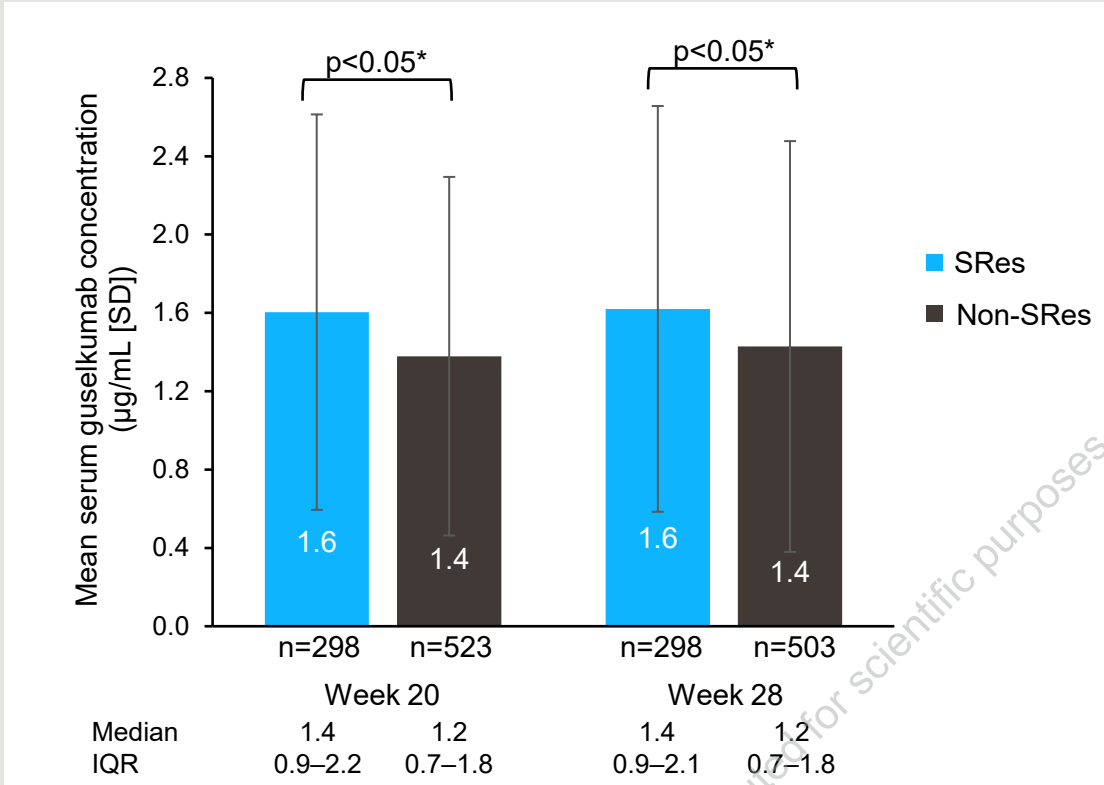
- Baseline characteristics were similar between all enrolled patients and subgroups with available serum GUS data
- SRe and non-SRe baseline characteristics are consistent with those previously published for all enrolled (SRe and non-SRe) patients; SRes had a shorter mean duration of PsO and were less likely to have received prior biologic therapy than non-SRes

BMI, body mass index; DLQI, Dermatology Life Quality Index; GUS, guselkumab; IL-23, interleukin-23; MOA, mode of action; PASI, Psoriasis Area and Severity Index; PsO, psoriasis; RCT, randomised controlled trial; SD, standard deviation; SRe, super responder; W, week.

Eyerich K, et al. Presented at AAD, Orlando, FL, US, 7–11 March 2025. P61980.

Super responders had significantly higher serum GUS concentrations than non-super responders early during treatment

Mean serum GUS concentration at Week 20 and Week 28 by SRe status



Regression analysis of patient characteristics against serum GUS concentration at Week 20†

Characteristic	Proportion of variation in GUS concentration accounted for at Week 20, R^2 (%)
Baseline BMI	14.9
Baseline PASI	0.8
Prior biologic therapy	0.7
Baseline age	0.4
Sex	0.3
Duration of psoriasis	0.1

Key result

- Factors previously investigated for their impact on achieving SRe status were evaluated in a regression model to determine their effect on serum GUS concentration
- BMI was the most impactful factor affecting serum GUS concentration, accounting for 14.9% of the variation in concentration at W20

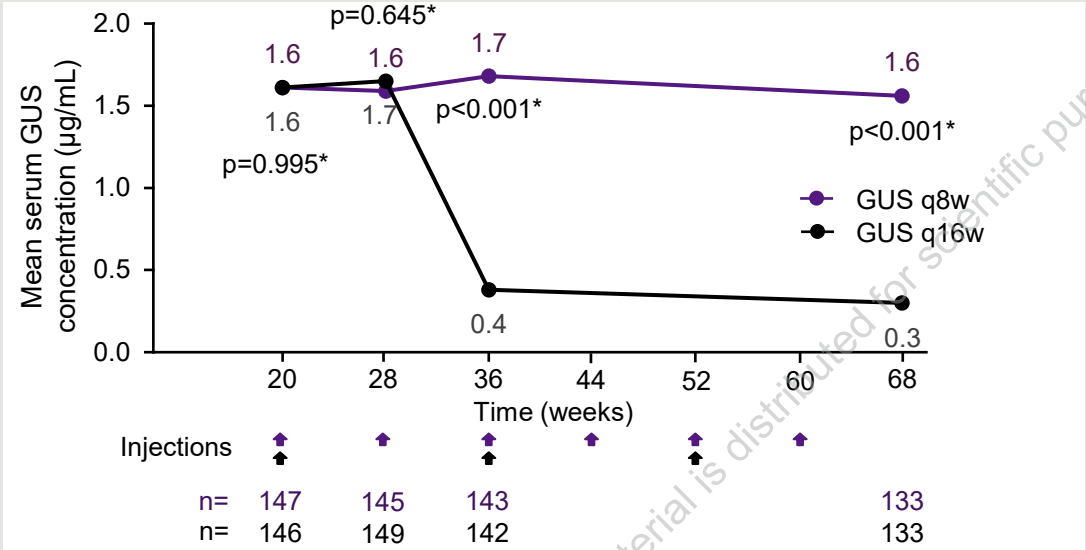
*Using the Wilcoxon rank sum test with continuity correction; †n=821.
BMI, body mass index; GUS, guselkumab; IL-23, interleukin-23; IQR, interquartile range; MOA, mode of action; PASI, Psoriasis Area and Severity Index; PsO, psoriasis; R^2,coefficient of determination; RCT, randomised controlled trial; SD, standard deviation; SRe, super responder; W, week.
Eyerich K, et al. Presented at AAD, Orlando, FL, US, 7–11 March 2025. P61980.

Despite five-fold lower serum GUS concentration, super responders dosed q16w achieved PASI <3 at a similar rate to q8w super responders at Week 68

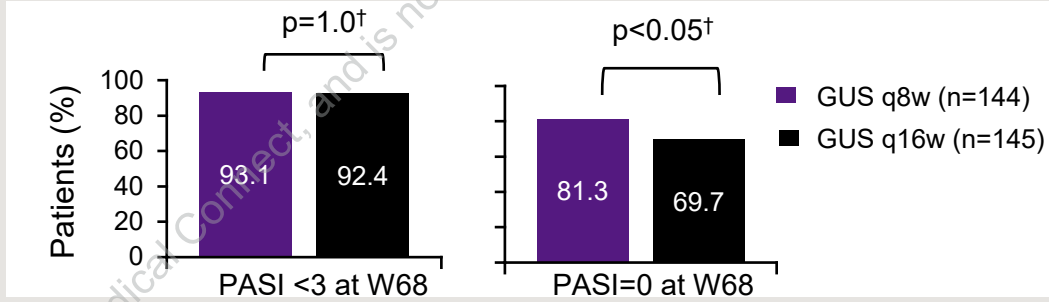
Key result

- Although SRes dosed q16w had a five-fold lower mean serum GUS concentration at Week 68 than SRes dosed q8w (0.3 vs. 1.6 µg/mL), a similar proportion:
  - Achieved PASI <3 at Week 68 (92.4% vs. 93.1%)
  - Remained treatment-free through Week 104
- High PASI =0 response rates were observed for both q8w- and q16w-dosed SRes at W68; however, q8w-dosed SRes had higher response rates (81.3% vs 69.7%)

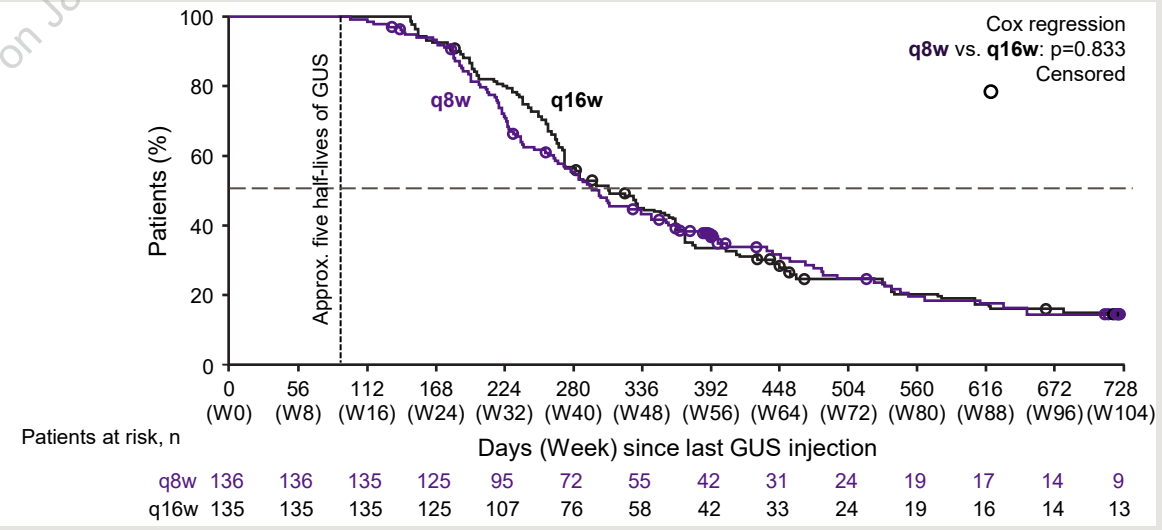
Mean serum GUS concentration in SRes by dosing regimen



Proportion of patients achieving PASI <3 or PASI=0 at Week 68



Treatment-free duration after GUS withdrawal



*Using the Wilcoxon rank sum test with continuity correction; †Using the Fisher's exact test.
GUS, guselkumab; IL-23, interleukin-23; MOA, mode of action; PASI, Psoriasis Area and Severity Index; PsO, psoriasis; q8w, every 8 weeks; q16w, every 16 weeks; RCT, randomised controlled trial; SD, standard deviation; SRE, super responder; W, week.
Eyerich K, et al. Presented at AAD, Orlando, FL, US, 7–11 March 2025. P61980.

Conclusions

- SRes had slightly higher serum GUS concentrations early in the treatment course (Week 20 and Week 28) vs. non-SRes. Regression analysis found that BMI affected serum GUS concentration

- SRes who received GUS q16w had five-fold lower serum GUS concentrations than q8w-dosed SRes at Week 68
  - With both dosing regimens, high rates of complete skin clearance were achieved, with approximately three out of four SRes achieving PASI=0 at Week 68. The rate of complete skin clearance was higher in q8w-dosed vs. q16w-dosed SRes
  - PASI <3 response rates at Week 68 and subsequent treatment-free durations were similar between dosing groups

- Super response was associated with higher serum GUS concentration early during treatment, after which an extended dosing interval effectively controlled disease activity, despite a five-fold lower serum GUS concentration. While higher serum GUS concentration corresponded to greater efficacy early in the treatment course, serum GUS concentration did not affect maintenance of disease control after Week 28, suggesting potential disease-modifying effects of GUS in SRes

BMI, body mass index; GUS, guselkumab; IL-23, interleukin-23; MOA, mode of action; PASI, Psoriasis Area and Severity Index; PsO, psoriasis; q8w, every 8 weeks; q16w, every 16 weeks; RCT, randomised controlled trial; SRe, super responder.

Eyerich K, et al. Presented at AAD, Orlando, FL, US, 7–11 March 2025. P61980.

GUIDE Phase 3b trial results: Early intervention with guselkumab results in higher rates of fingernail psoriasis clearance and maintenance of nail response following treatment withdrawal

P62281

K. Schäkel,[1] K. Eyerich,[2] A. Pinter,[3] P. Weisenseel,[4] C. Paul,[5] J. Wilke,[6] N. Trenkler,[6] Y. Chen,[7] N. Spindler,[6] N. Krüger,[6] K. Asadullah[8,9]

[1]Dept. of Dermatology, and Interdisciplinary Center for Inflammatory Diseases, Heidelberg University Hospital, Heidelberg, Germany; [2]Dept. of Dermatology and Venereology, Medical Center, University of Freiburg, Germany; [3]University Hospital Frankfurt am Main, Frankfurt, Germany; [4]Dermatologikum Hamburg, Hamburg, Germany; [5]Toulouse University, Toulouse, France; [6]Johnson & Johnson Innovative Medicine, Neuss, Germany; [7]Johnson & Johnson Innovative Medicine R&D, LLC, San Diego, CA, USA; [8]Dept. of Dermatology, Venereology and Allergology, Charité – Universitätsmedizin, Berlin, Germany; [9]Dermatology Potsdam MVZ, Potsdam, Germany

J&J Innovative Medicine

Immunology

GUIDE Phase 3b trial results: Early intervention with GUS results in higher rates of fingernail psoriasis clearance and maintenance of nail response following treatment withdrawal

Background

- Nail PsO, a distinct manifestation of PsO that is difficult to treat, can have a substantial impact on a patient's appearance and QoL. It is considered a predictor of disease progression and PsA development. PsO management guidelines consider nail PsO as an upgrade criterion for defining PsO severity

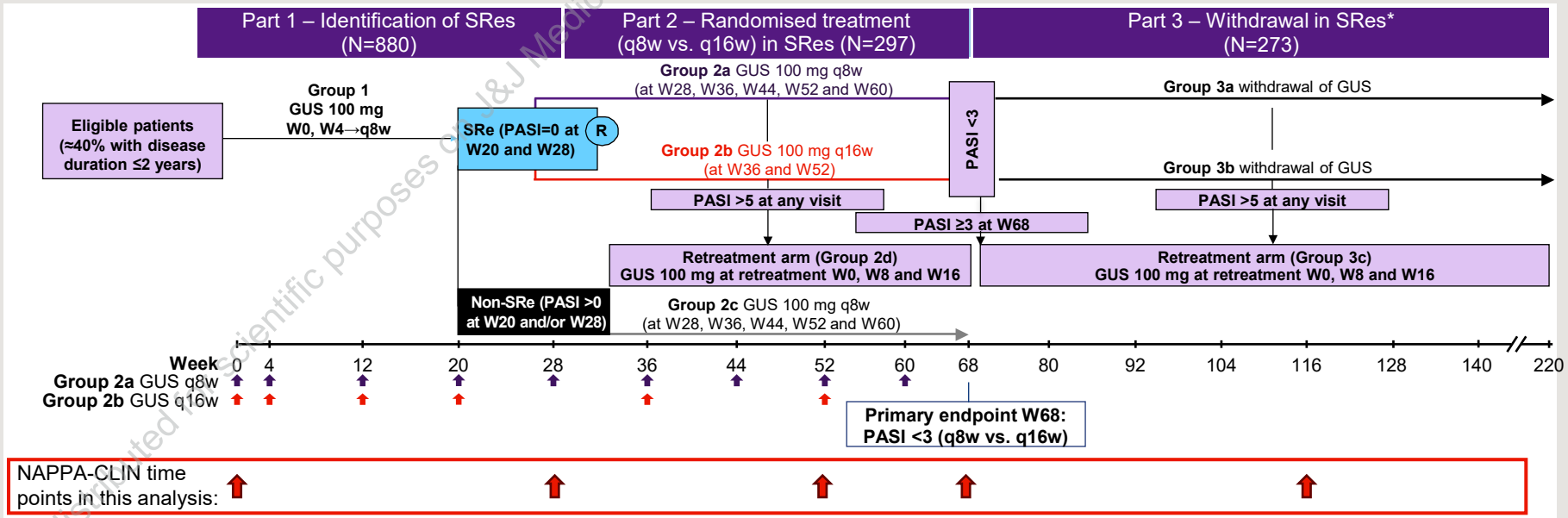
Aim

- To evaluate the impact of SRe status and disease duration (SDD: ≤2 years; LDD: >2 years) on fingernail PsO among patients treated with GUS (up to Week 68) and on maintenance of fingernail response following treatment withdrawal for >1 year (Week 116)

Methods

- Observed NAPPA-CLIN† outcomes were reported in the ITT population (hands only)
- NAPPA-CLIN assesses the least and the worst involved nail of both hands, providing a score from 0 (no nail PsO) to 16 (severe)
- All p-values are nominal

GUIDE study design



*Patients who worsened to PASI >5 after Week 68 received guselkumab q8w dosing at retreatment Weeks 0, 8 and 16; †A shortened version of the Nail Psoriasis Severity Index that evaluates only four digits.

GUS, guselkumab; IL-23, interleukin-23; ITT, intent-to-treat; LDD, long disease duration; MOA, mode of action; NAPPA-CLIN, Nail Assessment In Psoriasis And Psoriatic Arthritis–Clinical; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PsO, psoriasis; q8w, every 8 weeks; q16w, every 16 weeks; QoL, quality of life; R, randomisation; RCT, randomised controlled trial; SDD, short disease duration; SRe, super responder; W, Week.

Schäkel K, et al. Presented at AAD, Orlando, FL, US, 7–11 March 2025. P62281.

Fingernail psoriasis affected approximately half of all patients in the GUIDE study at baseline and was more prevalent in patients with long vs. short disease duration

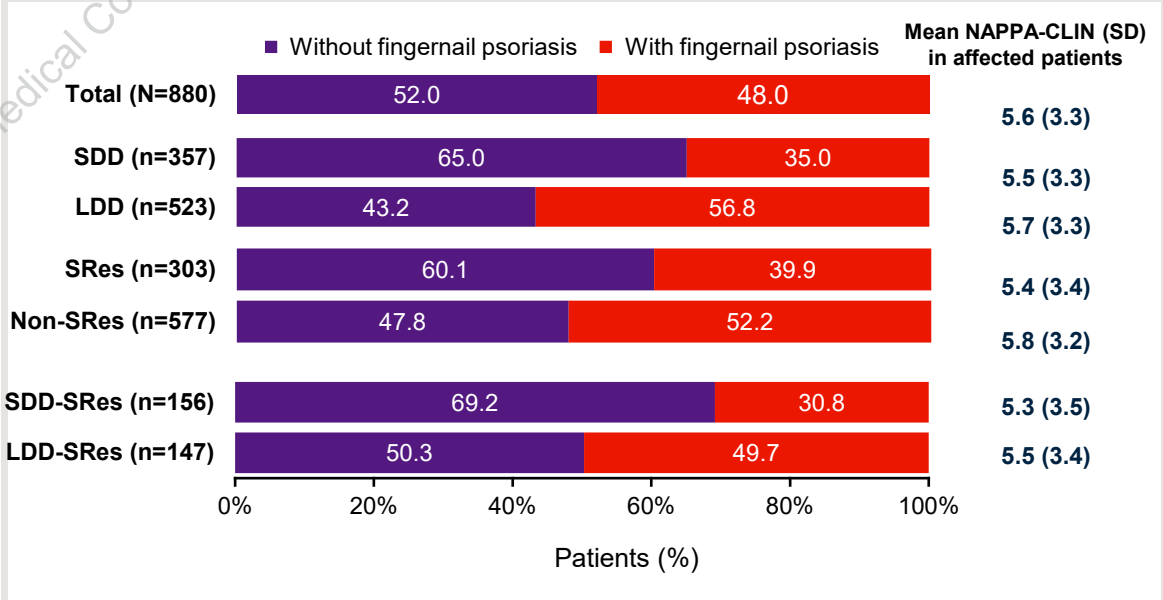
Key result

- While a lower proportion of patients with SDD than with LDD had fingernail psoriasis (35.0% [125/357] vs 56.8% [297/523]), the mean NAPPA-CLIN score was similar among those affected (5.5 vs 5.7, respectively)

Patient characteristics at baseline

Characteristic	Patients		
	Without fingernail psoriasis (n=458)	With fingernail psoriasis (n=422)	Total (N=880)
Mean age, years (SD)	41.1 (15.5)	44.0 (13.7)	42.5 (14.7)
Sex, n (%)			
Male / female	277 (60.5) / 181 (39.5)	343 (81.3) / 79 (18.7)	620 (70.5) / 260 (29.5)
Mean BMI, kg/m² (SD)	27.8 (6.1)*	28.9 (6.0)	28.3 (6.0)†
Duration of psoriasis Mean, years (SD) ≤2 years (SDD), n (%) >2 years (LDD), n (%)	 10.1 (12.9) 232 (50.7) 226 (49.3)	 15.1 (14.2) 125 (29.6) 297 (70.4)	 12.5 (13.8) 357 (40.6) 523 (59.4)
Mean PASI (SD)	18.3 (7.6)	20.0 (8.2)	19.1 (7.9)
Mean DLQI (SD)	18.7 (5.4)	19.3 (5.1)	19.0 (5.3)
Prior biologic therapy, n (%)	58 (12.7)	65 (15.4)	123 (14.0)

Fingernail involvement at baseline by patient group



*n=457; †n=879.

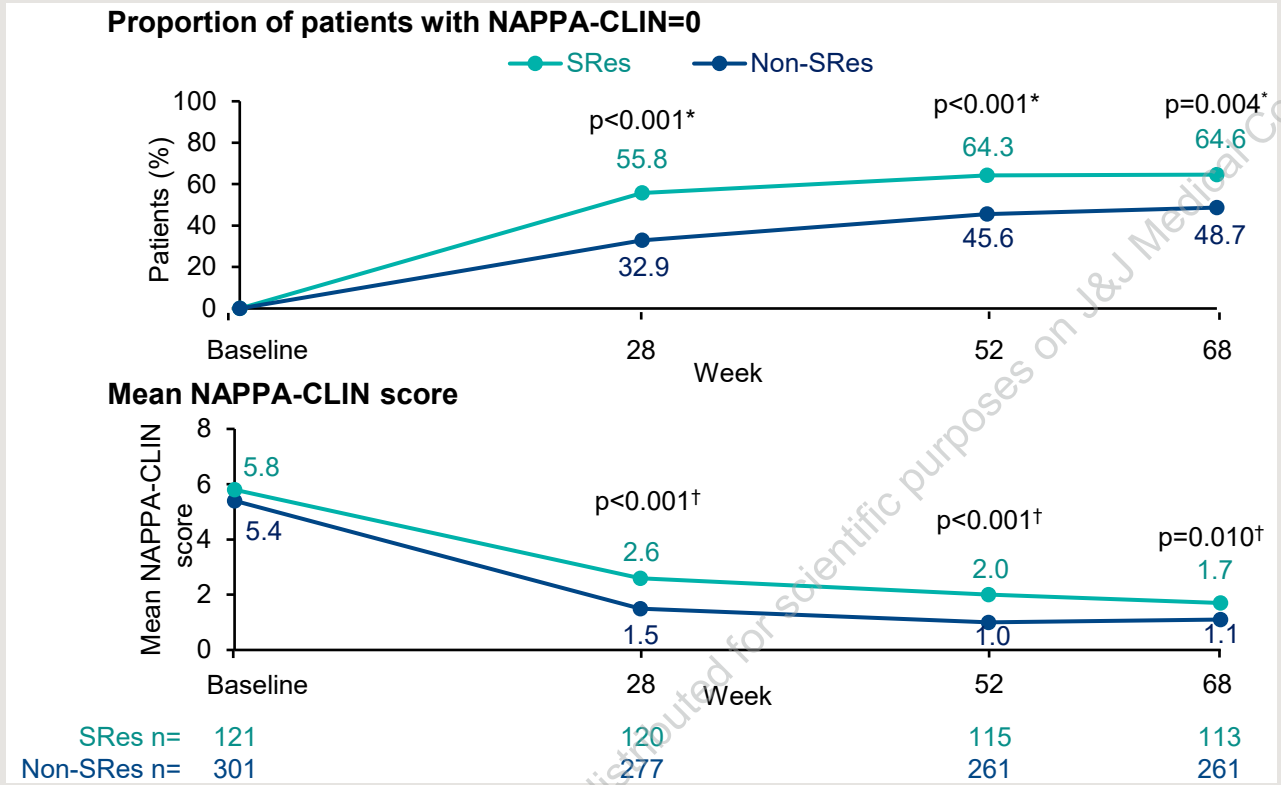
BMI, body mass index; DLQI, Dermatology Life Quality Index; GUS, guselkumab; IL-23, interleukin-23; LDD, long disease duration; MOA, mode of action; NAPPA-CLIN, Nail Assessment In Psoriasis And Psoriatic Arthritis–Clinical; PASI, Psoriasis Area and Severity Index; PsO, psoriasis; RCT, randomised controlled trial; SD, standard deviation; SDD, short disease duration; SRe, super responder.

Schäkel K, et al. Presented at AAD, Orlando, FL, US, 7–11 March 2025. P62281.

Super responders had a higher rate of complete clearance of fingernail psoriasis, vs. non-super responders, through 68 weeks of GUS treatment

Key result: SRes achieved a higher rate of complete fingernail clearance and a lower mean NAPPA-CLIN score than non-SRs at Week 68

Fingernail psoriasis through Week 68 by SRe status among patients with fingernail psoriasis at baseline

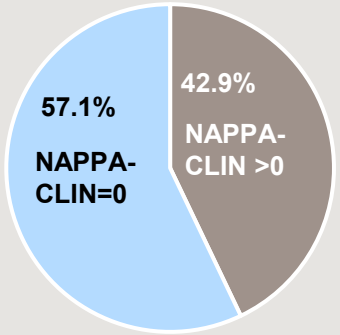


Mean NAPPA-CLIN scores among patients with fingernail psoriasis at baseline

Week	GUS q8w-treated patients‡	
	Total	Score vs. baseline
0	5.7 (n=337)	–
28	2.5 (n=335)	p<0.001
52	1.8 (n=318)	p<0.001
68	1.7 (n=316)	p<0.001

Fingernail response >1 year after withdrawal (n=21)

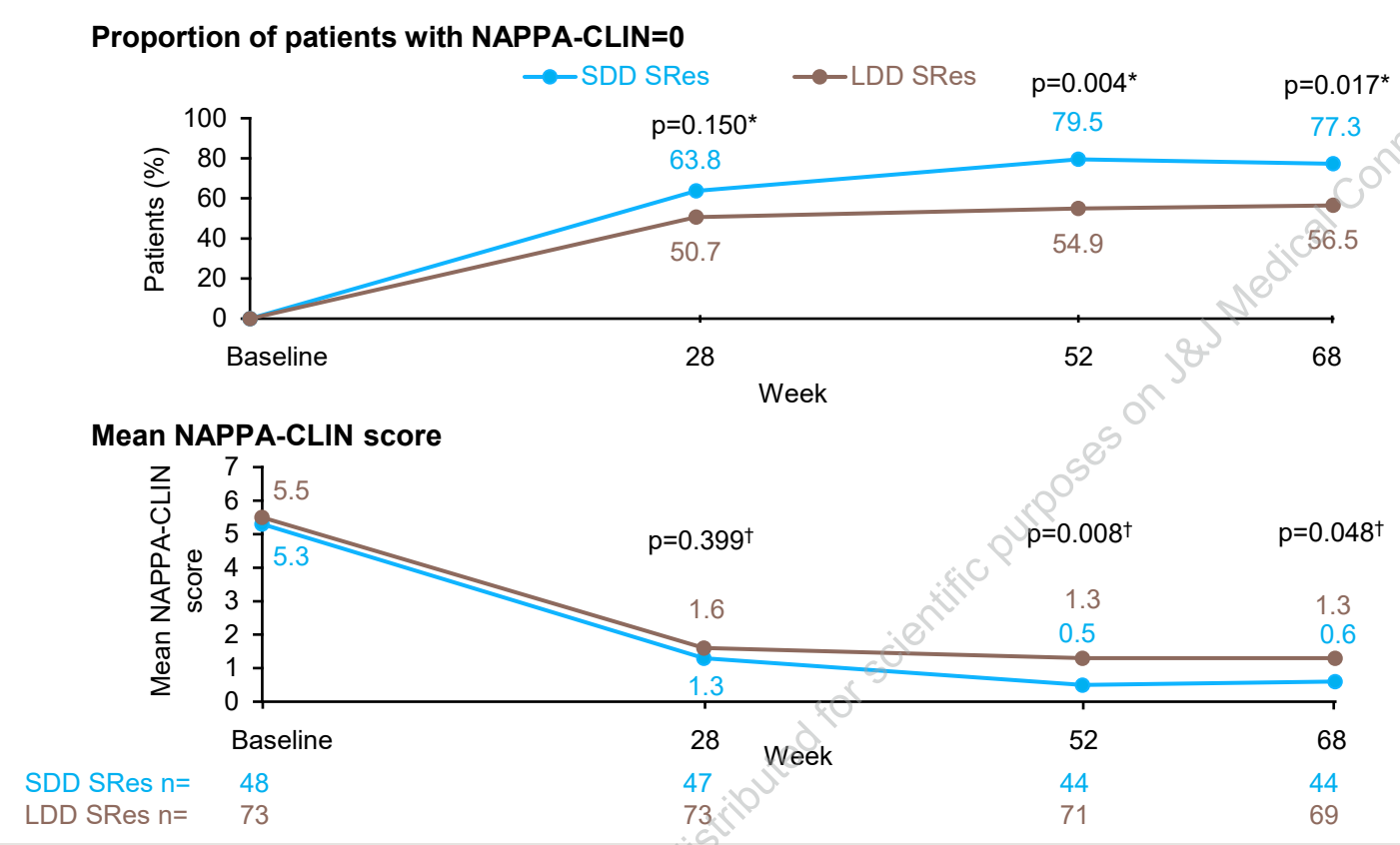
Among 74 SRes who remained treatment-free for >1 year after GUS withdrawal, 21 had fingernail psoriasis at baseline



*Two-sided two-group normal approximation Wald Z-test (SRes vs. non-SRs); †Two-sided non-adjusted two-group t-test (SRes vs. non-SRes); ‡Paired t-test without adjustments for covariates (each visit week vs. baseline).
GUS, guselkumab; IL-23, interleukin-23; MOA, mode of action; NAPPA-CLIN, Nail Assessment In Psoriasis And Psoriatic Arthritis–Clinical; PsO, psoriasis; q8w, every 8 weeks; RCT, randomised controlled trial; SRe, super responder.
Schäkel K, et al. Presented at AAD, Orlando, FL, US, 7–11 March 2025. P62281.

Short disease duration is associated with a higher rate of complete fingernail clearance in super responders

Fingernail psoriasis through Week 68 in SRes by disease duration among patients with fingernail psoriasis at baseline

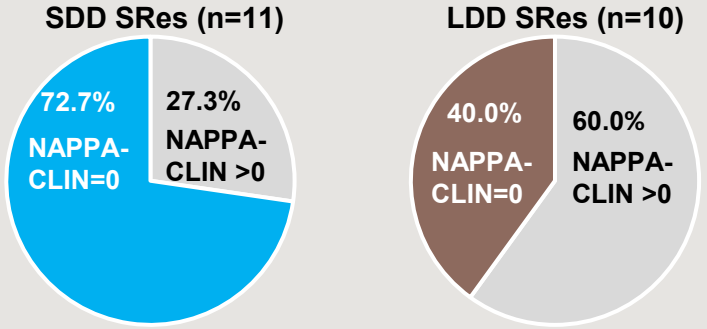


Mean NAPPA-CLIN scores among patients with fingernail psoriasis at baseline

Week	GUS q8w-treated SRes			
	SDD	LDD	SDD vs. LDD†	Total
0	5.4 (n=26)	5.3 (n=33)	–	5.4 (n=59)
28	1.6 (n=25)	2.0 (n=33)	p=0.587	1.8 (n=58)
52	0.5 (n=23)	1.5 (n=33)	p=0.034	1.1 (n=56)
68	0.6 (n=23)	1.7 (n=31)	p=0.043	1.2 (n=54)

Fingernail response at Week 116 by disease duration

>1 year after withdrawal (Week 116), SDD SRes had a higher rate of complete fingernail clearance (72.7% vs 40.0%) and a lower mean NAPPA-CLIN score (0.7 vs 3.6) compared with LDD SRes



*Two-sided two-group normal approximation Wald Z-test (SDD SRes vs. LDD SRes); †Two-sided non-adjusted two-group t-test (SRe vs. non-SRe groups).
GUS, guselkumab; IL-23, interleukin-23; LDD, long disease duration; MOA, mode of action; NAPPA-CLIN, Nail Assessment In Psoriasis And Psoriatic Arthritis–Clinical; PsO, psoriasis; q8w, every 8 weeks; RCT, randomised controlled trial; SDD, short disease duration; SRe, super responder.
Schäkel K, et al. Presented at AAD, Orlando, FL, US, 7–11 March 2025. P62281.

Conclusions

- The proportion of patients with nail PsO, but not the severity of nail involvement, was lower among those with short vs. long disease duration. Of note, patients with fingernail PsO were able to attain SRe status
- At Week 68, mean NAPPA-CLIN score was substantially reduced from baseline in all patient groups, with >50% of patients achieving complete fingernail clearance. SRes achieved better fingernail improvements (mean NAPPA-CLIN) with higher rates of complete fingernail clearance through Week 68 vs. non-SRes
- SDD was associated with a higher rate of complete fingernail clearance in SRes both during GUS treatment and after withdrawal vs. those with LDD
- Previous findings highlighted the impact of early intervention for disease modification in PsO with GUS. In line, a greater effect of treatment on fingernail PsO in SRes with SDD was observed, emphasising the benefits of early intervention with GUS in patients with nail involvement. Nail PsO is a recognised indicator of disease progression and a predictor of PsA development. Achievement of complete fingernail clearance may reflect mitigating risk for PsA
- Currently, there are hints for protective effects of IL-23 inhibition on progression to PsA, which are being further investigated for GUS in the PAMPA study. Consistent with previous GUIDE data showing earlier immunological normalisation and better skin efficacy in patients with SDD, our data on nail psoriasis reiterate the importance of timely GUS treatment to increase chances of modifying the course of disease

GUS, guselkumab; IL-23, interleukin-23; LDD, long disease duration; MOA, mode of action; NAPPA-CLIN, Nail Assessment In Psoriasis And Psoriatic Arthritis–Clinical; PsA, psoriatic arthritis; PsO, psoriasis; RCT, randomised control trial; SDD, short disease duration; SRe, super responder.

Schäkel K, et al. Presented at AAD, Orlando, FL, US, 7–11 March 2025. P62281.