Pharmacokinetics of Guselkumab in Super Responders and Long-Term Psoriasis Disease Control: Insights From the Phase 3b GUIDE Trial

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Kilian Eyerich,[1] Khusru Asadullah,[2,3] Andreas Pinter,[4] Peter Weisenseel,[5] Carle Paul,[6] Fabian Kreimendahl,[7] Katharine Henry,[8] Julian Wilke,[7] Nenja Krüger,[7] Nikolas Spindler,[7] Steve Fakharzadeh,[9] Knut Schäkel[10]

[1]Department of Dermatology and Venereology, Medical Center, University of Freiburg, Freiburg, Germany; [2]Department 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, Neuss, Germany; [8]Johnson & Johnson, Cambridge, MA, USA; [9]Johnson & Johnson, Horsham, PA, USA; [10]Department of Dermatology, and Interdisciplinary Center for Inflammatory Diseases, Heidelberg University Hospital, Heidelberg, Germany

Background

- GUIDE is a Phase 3b, randomized, double-blind trial investigating the potential of disease modification with guselkumab in patients with moderate-to-severe plaque psoriasis[1,2]
- Our previous biomarker findings demonstrated a sustained effect of guselkumab on inflammatory processes underlying psoriasis, which allowed for disease control with an extended (every 16 weeks [q16w]) dosing interval in super responder (SRe) patients (defined as those with Psoriasis Area and Severity Index [PASI]=0[a] at Week (W)20 and W28 with guselkumab treatment),[3] and may account for the long-term maintenance of response observed following withdrawal of treatment for >1 year[4]

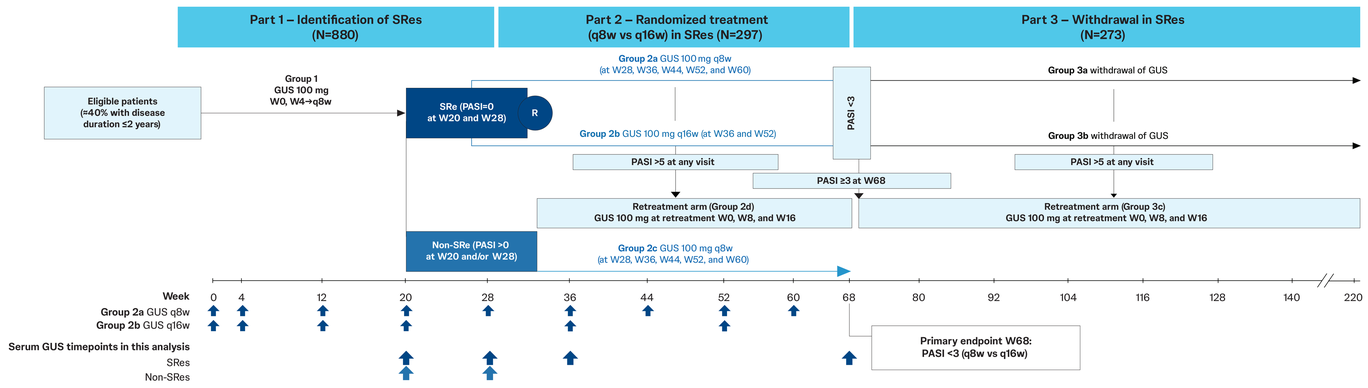
Objective

- **In this analysis, we analyze the relationship of serum guselkumab concentration with dosing interval (every 8 weeks [q8w] and q16w) and clinical outcomes in GUIDE to further assess the potential of disease modification with guselkumab treatment**

Methods

- In Part 1 of GUIDE (W0–W28), 880 patients were enrolled to receive guselkumab 100 mg at W0, W4, W12, and W20 (**Figure 1**)
- In Part 2 (W28–W68), SRes were randomized to receive either guselkumab 100 mg q8w (five injections) or q16w (two injections)
- In Part 3 (W68–W220), SRes with PASI <3 at W68 were withdrawn from guselkumab (N=273)[b]. Patients who worsened to PASI >5 after W68 received guselkumab q8w dosing at retreatment W0, W8, and W16[c]
- In this analysis, we report guselkumab serum concentration, measured using an immunoassay, in blood samples collected before dosing at W20, W28, W36, and W68. All *P* values are nominal

Figure 1. GUIDE study design



[a]*PASI evaluates the extent and severity of psoriasis and provides a score from 0 (no psoriasis) to 72 (severe).* [b]*Patients entering Part 3 from the q8w and q16w arms of Part 2 received their last guselkumab dose at W60 and W52, respectively.* [c]*Unlike in Part 1, the retreatment phase in Part 3 does not include an induction scheme, i.e., the retreatment dosing interval was q8w.* ***GUS****=guselkumab,* ***PASI****=Psoriasis Area and Severity Index,* ***q8w****=every 8 weeks,* ***q16w****=every 16 weeks,* ***R****=randomization,* ***SRe****=super responder,* ***W****=week.*

Key Takeaways

- Previous GUIDE data showed non-inferiority of guselkumab q16w vs q8w dosing in SRes for maintenance of disease control at W68.[3] In this GUIDE analysis of serum guselkumab concentration, we further investigated the relationship between dosing interval, clinical outcomes, and the potential for disease modification with guselkumab
- **SRes** had slightly **higher serum guselkumab concentrations** early in the treatment course (**W20 and W28**) vs non-SRes. Regression analysis found that BMI, but not other patient characteristics known to influence SRe status[2] (i.e., disease duration and prior biologic use), affected serum guselkumab concentration
- Subsequently, SRes who received guselkumab **q16w had five-fold lower serum guselkumab concentrations than q8w-dosed SRes** at W68
  - ✓ With both dosing regimens, high rates of complete skin clearance were achieved, with **~3 out of 4 SRes** achieving **PASI=0** at W68. The rate of complete skin clearance was higher in q8w- vs q16w-dosed SRes
  - ✓ Nevertheless, **PASI <3 response rates** at W68 and subsequent **treatment-free duration** were similar between dosing groups. These findings suggest that following achievement of super response, the subsequent dosing interval may be less critical for maintenance of disease control, indicating a reduced need for treatment
- In summary, super response was associated with **higher serum guselkumab** concentration early during treatment, after which an extended dosing interval effectively **controlled disease activity,** despite a **five-fold lower serum guselkumab concentration.** While higher serum guselkumab concentration corresponded to greater efficacy early in the treatment course, serum guselkumab concentration did not affect maintenance of disease control after W28, suggesting potential disease-modifying effects of guselkumab in SRes. Together with previous findings showing sustained normalization of serum and skin biomarkers,[3,5] these data further support the hypothesis that disease modification, as recently defined in a Delphi consensus,[6] may be possible with guselkumab in SRes

Results

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

Patient disposition

- Serum guselkumab data were available for 821/880 (93.3%) patients at W20, of whom 298 (36.3%) were SRes and 523 (63.7%) were non-SRes (**Table 1**)
- Baseline characteristics were similar between all enrolled patients[2] and subgroups with available serum guselkumab data
- SRe and non-SRe baseline characteristics are consistent with those previously published for all enrolled (SRe and non-SRe) patients[2]; SRes had a shorter mean duration of psoriasis and were less likely to have received prior biologic therapy than non-SRes

Table 1. Patient characteristics at baseline

Characteristic	All enrolled patients[2] N=880	Patients with guselkumab serum data at W20		
		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)

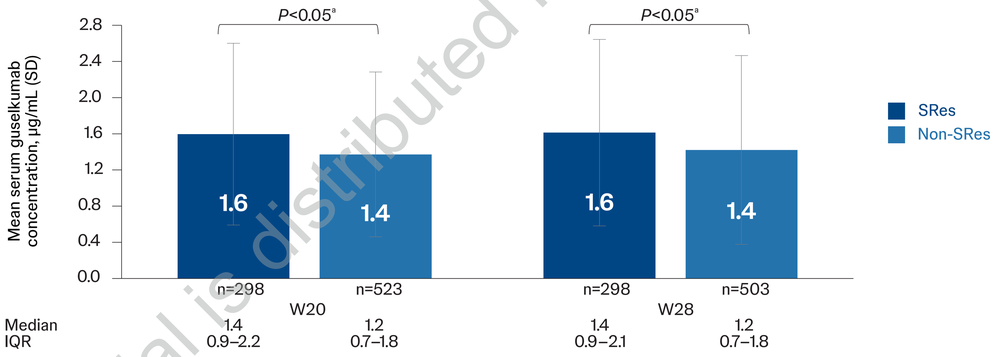
BMI*=Body Mass Index,* ***DLQI****=Dermatology Life Quality Index,* ***PASI****=Psoriasis Area and Severity Index,* ***SD****=standard deviation,* ***SRe****=super responder,* ***W****=week.*

SRes had significantly higher serum guselkumab concentrations than non-SRes early during treatment

Serum guselkumab concentration at W20 and W28

- Higher mean serum guselkumab concentration was observed in SRes vs non-SRes (1.6 vs 1.4 µg/mL) at both W20 and W28 (**Figure 2**)

Figure 2. Mean serum guselkumab concentration at W20 and W28 by SRe status



[a]*Using the Wilcoxon rank sum test with continuity correction.* ***IQR****=interquartile range,* ***SD****=standard deviation,* ***SRe****=super responder,* ***W****=week.*

Impact of patient characteristics on guselkumab pharmacokinetics

- Factors previously investigated for their impact on achieving SRe status[2] were evaluated in a regression model to determine their effect on serum guselkumab concentration (**Table 2**)
- Body Mass Index (BMI) was the most impactful factor affecting serum guselkumab concentration, accounting for 14.9% of the variation in concentration at W20

Table 2. Regression analysis of patient characteristics against serum guselkumab concentration at W20 (n=821)

Characteristic	Proportion of variation in guselkumab concentration accounted for at W20, 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

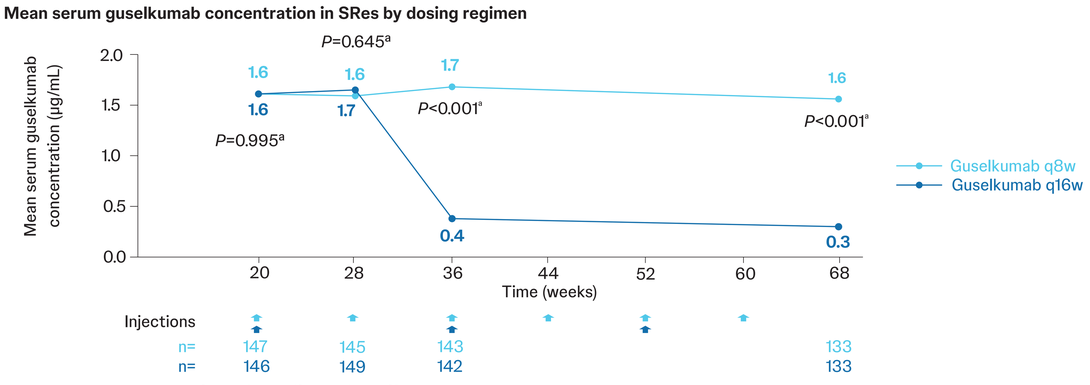
BMI*=Body Mass Index,* ***PASI****=Psoriasis Area and Severity Index,* R^2*=coefficient of determination,* ***W****=week.*

Despite five-fold lower serum guselkumab concentration, SRes dosed q16w achieved PASI <3 at a similar rate to q8w SRes at W68

Serum guselkumab concentration and clinical response

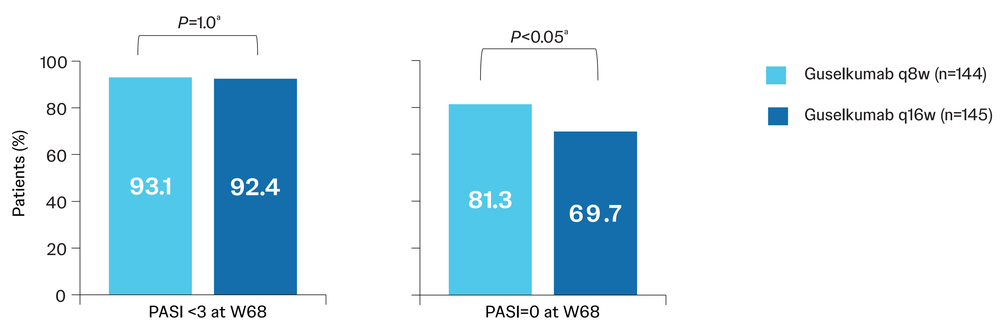
- Although SRes dosed q16w had a five-fold lower mean serum guselkumab concentration at W68 than SRes dosed q8w (0.3 vs 1.6 µg/mL; **Figure 3**), a similar proportion:
  - Achieved PASI <3 at W68 (92.4% vs 93.1%; **Figure 4**)
  - Remained treatment free through W164 **(Figure 5)**
- High PASI=0 response 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%; **Figure 4**)
- Among q16w-dosed SRes, those who achieved PASI=0 at W68 had a slightly higher serum guselkumab concentration vs those with PASI >0 (W68: 0.3 vs 0.2 µg/mL; *P*<0.05 [using the Wilcoxon rank sum test with continuity correction]; data not shown)

Figure 3. Mean serum guselkumab concentration in SRes by dosing regimen



[a]*Using the Wilcoxon rank sum test with continuity correction.* ***q8w****=every 8 weeks,* ***q16w****=every 16 weeks,* ***SRe****=super responder.*

Figure 4. Proportion of patients achieving PASI <3 or PASI=0 at W68



[a]*Using the Fisher's exact test.* ***PASI****=Psoriasis Area and Severity Index,* ***q8w****=every 8 weeks,* ***q16w****=every 16 weeks,* ***W****=week.*

Figure 5. Treatment-free duration after guselkumab withdrawal

q8w*=every 8 weeks,* ***q16w****=every 16 weeks,* ***W****=week.*

PRESENTED AT: 6th Inflammatory Skin Disease Summit (ISDS); New York, NY, USA; November 12–15, 2025. **REFERENCES: 1.** Eyerich K et al. ***BMJ Open.*** 2021;11:e049822; **2.** Schäkel K et al. ***J Eur Acad Dermatol Venereol.*** 2023;37:2016–27; **3.** Eyerich K et al. ***JAMA Dermatol.*** 2024;160:953–63; **4.** Schäkel K et al. Presented at AAD Congress 2024; San Diego, CA, USA; March 8–12, 2024. P502:36; **5.** Angsana J et al. Presented at ISID 2023; Tokyo, Japan; May 10–13, 2023. P587; **6.** Eyerich K et al. ***J Eur Acad Dermatol Venereol.*** 2024;38:e424–7. **ACKNOWLEDGMENTS:** This study was supported by Johnson & Johnson. Medical writing support was provided by Jenny Pateman, PhD, at AMICULUM Business Services Ltd, funded by Johnson & Johnson (Germany). Layout design and formatting for this encore presentation was provided by Sandeep Chavan of SIRO Medical Writing Pvt. Ltd., India (funded by Johnson & Johnson). **DISCLOSURES:** The authors disclose that they were an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: **KE:** AbbVie, Almirall, BMS, Boehringer Ingelheim, Eli Lilly, Janssen-Cilag GmbH, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; **KA:** AbbVie, Akribes, Almirall, Antabio, Bayer, DEKA Biosciences, Emeriti Pharma, Galderma, Incyte, Janssen-Cilag GmbH, LEO Pharma, LOréal, Novartis, Pierre Fabre, Sanofi Genzyme, and UCB Pharma; **AP:** AbbVie, Almirall, Amgen, Biogen Idec, BioNTech, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Galderma, GSK, Hexal, Janssen-Cilag GmbH, Klinge Pharma, LEO Pharma, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi Genzyme, Schering-Plough, Tigercat Pharma, and UCB Pharma; **PW:** AbbVie, Almirall, Biogen, BMS, Celgene, Eli Lilly, Janssen-Cilag GmbH, LEO Pharma, Medac, Novartis, Pfizer, and UCB Pharma; **CP:** AbbVie, Almirall, Amgen, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen-Cilag GmbH, LEO Pharma, Merck, Mylan, Novartis, Pfizer, Pierre Fabre, Sanofi, and UCB Pharma; **FK, JW, NK, NS** and **SF** are employees of Johnson & Johnson Innovative Medicine; **KH** is an employee of Johnson & Johnson Innovative Medicine, R&D; **KS:** AbbVie, Almirall, Antabio, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, Janssen-Cilag GmbH, LEO Pharma, Novartis, Pfizer, and UCB Pharma.
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