Guselkumab Re-Treatment After Withdrawal: Rapid Regain of Disease Control in Super-Responders With Moderate-to-Severe Plaque Psoriasis - Final Week 220 Phase 3b GUIDE Findings

Khusru Asadullah,[1,2] Andreas Pinter,[3] Kilian Eyerich,[4] Peter Weisenseel,[5] Carle Paul,[6] Friedemann Taut,[7] Simmy Jacobsen,[8] Jörg Schmitz,[8] Judita Makuc,[9] Nikolas Spindler,[8] Knut Schäkel[9]

[1]Dept. of Dermatology, Venereology and Allergology, Charité – Universitätsmedizin, Berlin, Germany; [2]Dermatology Potsdam MVZ, Potsdam, Germany; [3]University Hospital Frankfurt am Main, Frankfurt, Germany; [4]Dept. of Dermatology and Venereology, Medical Center, University of Freiburg, Germany; [5]Dermatologikum Hamburg, Hamburg, Germany; [6]Toulouse University, Toulouse, France; [7]Taut Science and Service GmbH, Konstanz, Germany; [8]Johnson & Johnson, Neuss, Germany; [9]Dept. of Dermatology, and Interdisciplinary Center for Inflammatory Diseases, Heidelberg University Hospital, Heidelberg, Germany

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Background

The Phase 3b GUIDE trial investigated early intervention with guselkumab (GUS) for disease modification in adults with moderate-to-severe plaque psoriasis (PSO)[1,2]

- GUIDE Part 1 (Week [W]0-W28): Early GUS intervention (≤2 years from symptom onset) and bionaïve-status increased the likelihood of achieving super response (SRe; PSO Area and Severity Index [PASI]=0 at W20 and W28)[2]

Dose interval extensions and biologic treatment interruptions in PSO may be necessary due to medical events or patient preference

- GUIDE Part 2 (W28-W68): GUS dosed every 16W (q16w) demonstrated non-inferiority to q8w in maintaining disease control (PASI <3) at W68 among SRes[3]
- GUIDE Part 3 (W68-W220): 273 SRes with disease control at W68 were withdrawn from GUS. Upon loss of response (PASI>5; Figure 1), treatment was re-initiated with 3 doses (R0/R8/R16), allowing for evaluation of disease control after withdrawal, re-treatment efficacy, and potential disease-modifying effects

Objectives

To assess PASI and DLQI outcomes within 24W of GUS re-treatment among SRes who lost response (PASI >5) after W68 GUS withdrawal

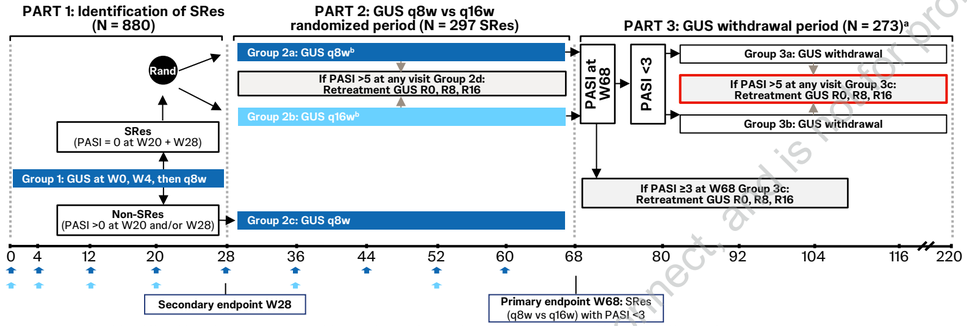
Methods

Key inclusion criteria [NCT03818035]

- Adults with moderate-to-severe PSO
- ~40% with PSO for ≤2 years

Analysis

- NRI was applied to handle missing categorical data; continuous data are presented as observed unless otherwise specified
- All p-values are nominal



PASI evaluates the extent and severity of psoriasis and provides a score from 0 (no PSO) to 72 (severe). [a]Patients entering Part 3 from the q8w and q16w arms of Part 2 received their last guselkumab dose at W60 and W52, respectively. [b]Blinded treatment.
DLQI=Dermatology Life Quality Index, ***NRI***=non-responder imputation, ***R***=re-treatment, ***Rand***=randomization.

Key Takeaways

- **Among SRes who remained treatment-free for a median of 302 days following GUS withdrawal[5] and were re-treated with GUS after loss of response in Part 3 of the GUIDE study:**
  - ✓ **77% regained disease control within 8W (R8) after one GUS dose; 60% achieved complete skin clearance at R24**
  - ✓ **73% achieved DLQI 0/1 (no impact of PSO on quality of life) at R24; having DLQI 0/1 at the time of withdrawal at W68 increased the likelihood of regaining DLQI 0/1**
  - ✓ **No new safety signals were identified**
- **GUS re-treatment effectively restored disease control, skin clearance, and quality of life after withdrawal in the majority of SRes**
  - ✓ **Complete skin clearance before withdrawal increased the likelihood of achieving complete skin clearance with re-treatment, supporting disease modification through long-term control**
  - ✓ **Patients with longer maintenance of disease control after withdrawal were more likely to achieve clear skin with re-treatment, possibly suggesting deeper remission**

Results

Baseline characteristics were generally comparable between SRes with completely clear skin and PASI > 0 at time of withdrawal (W68)

- Of 273 SRes who maintained disease control (PASI <3) at W68 who were withdrawn from GUS, 227 were re-treated after loss of response (PASI >5)
  - A higher proportion of SRes with PASI >0 at W68 had BMI >30 compared with those with PASI=0 (28.3% vs 22.8%)
  - SRes with PASI >0 at W68 were more likely to have had LDD at baseline (60.9% vs 52.2%), while those with PASI=0 at W68 (47.8% vs 39.1%) were more likely to have had SDD

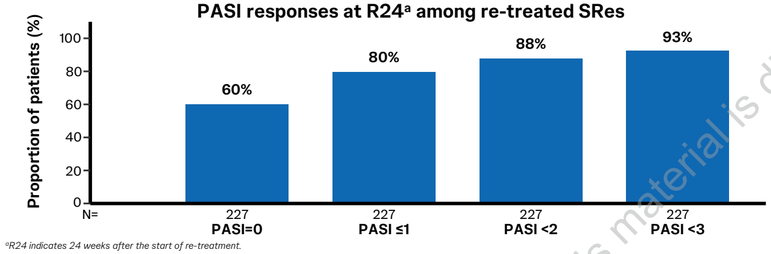
Baseline characteristics of SRes re-treated with GUS after loss of response	SRes with PASI=0 at W68 (N = 180)	SRes with PASI >0 at W68 (N = 46)	All SRes (N = 226)[a]
Demographics			
Mean age, years (SD)	40.1 (13.3)	37.1 (13.5)	39.5 (13.3)
Male, n (%)	123 (68.3)	33 (71.7)	156 (69.0)
Mean weight, kg (SD)	83.3 (18.8)	85.7 (19.6)	83.8 (18.9)
BMI >30 kg/m², n (%)	41 (22.8)	13 (28.3)	54 (23.9)
Disease Characteristics			
Mean PSO duration, years (SD)	11.1 (13.2)	11.6 (11.6)	11.2 (12.8)
LDD (>2 years), n (%)	94 (52.2)	28 (60.9)	122 (54.0)
SDD (≤2 years), n (%)	86 (47.8)	18 (39.1)	104 (46.0)
Mean BSA with PSO, % (SD)	24.6 (14.7)	25.0 (16.0)	24.7 (14.9)
Mean PASI, (0-72) (SD)	18.4 (7.0)	20.3 (9.2)	18.8 (7.5)
Prior PSO Medication			
Biologic-naïve, n (%)	166 (92.2)	41 (89.1)	207 (91.6)
1 or more biologics, n (%)	14 (7.8)	5 (10.9)	19 (8.4)

[a]226 of the 227 SRes had available PASI data at W68. ***BMI***=body mass index, ***BSA***=body surface area, ***LDD***=long disease duration, ***SD***=standard deviation, ***SDD***=short disease duration,

60% of SRes who lost response after GUS withdrawal achieved completely clear skin (PASI=0) at W24 after initiating re-treatment

- The majority (88%) of re-treated SRes achieved PASI <2 (new PSO treat-to-target goal in Germany[4]) at R24

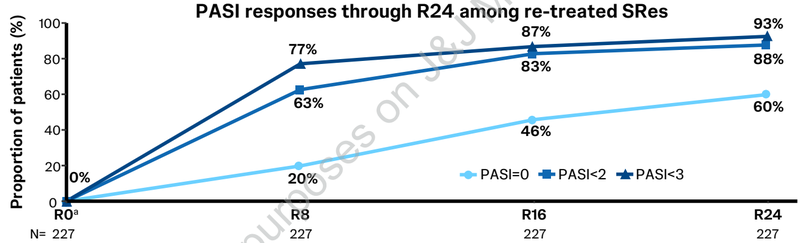
PASI responses at R24[a] among re-treated SRes



[a]R24 indicates 24 weeks after the start of re-treatment.

77% of SRes who lost response after GUS withdrawal regained disease control (PASI <3) after 1 dose of GUS, increasing to 93% after 3 doses

PASI responses through R24 among re-treated SRes



[a]R0 indicates the start of re-treatment.

SRes with PASI=0 at W68 had a higher rate of complete skin clearance at R24 than those with PASI >0, despite having generally comparable baseline characteristics

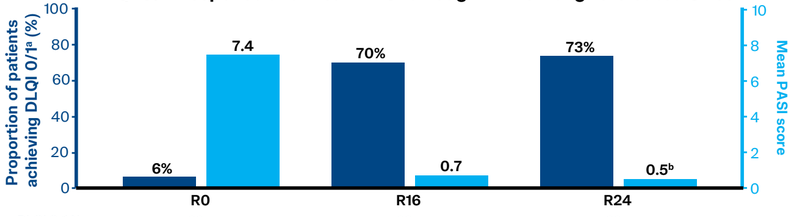
- SRes initiating re-treatment after W92 had higher rates of complete skin clearance and PASI <1 (data not shown) at R24 than those initiating re-treatment at or before W92
- No differences were observed across subgroups for the less stringent PASI<3 response at R24 (data not shown)

PASI=0 achievement at R24 among subgroups of re-treated SRes		n/N (%)	Nominal p-value
Sex			
	Male	96/157 (61.1)	0.5717
	Female	40/70 (57.1)	
Weight			
	≤90 kg	99/163 (60.7)	0.6872
	>90 kg	37/64 (57.8)	
BMI			
	<26.5 kg/m²	68/113 (60.2)	0.9353
	≥26.5 kg/m²	68/114 (59.6)	
PSO duration			
	SDD (≤2 years)	65/104 (62.5)	0.4631
	LDD (>2 years)	71/123 (57.7)	
GUS regimen in GUIDE Part 2			
	q8w	65/112 (58.0)	0.5690
	q16w	71/115 (61.7)	
PASI at W68			
	PASI=0	121/180 (67.2)	<0.0001
	PASI>0	15/46 (32.6)	
Re-treatment time point			
	≤W92	58/112 (51.8)	0.0125
	>W92	78/115 (67.8)	

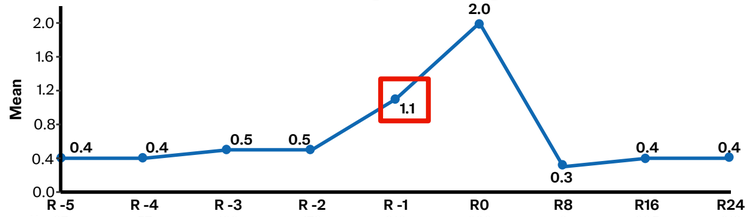
Quality of life and PASI scores improved rapidly among SRes re-treated with GUS after loss of response following withdrawal

- The proportion of SRes with DLQI 0/1 (no impact of PSO on quality of life) increased rapidly from 6% at R0 to 73% at R24 with GUS re-treatment (top panel)
  - SRes with DLQI 0/1 at W68 were more likely to achieve DLQI 0/1 at R24 (79%) compared with those with DLQI >1 at W68 (37%), despite similar proportions with DLQI 0/1 at initiation of re-treatment (R0) in both subgroups (data not shown)
- Mean PASI scores decreased rapidly from 7.4 at R0 to 0.5 at R24 with GUS re-treatment (top panel)
- Itching, pain, and stinging (DLQI Item 1 scores) worsened at R -1 suggesting an impending relapse, but normalized at R8 after 1 dose of GUS retreatment (bottom panel)

DLQI 0/1[a] response and mean PASI through R24 among re-treated SRes



DLQI item 1[c] scores through R24 among re-treated SRes[d]



[a]Indicating no effect of skin disease on patient's quality of life. [b]Last observation carried forward was applied for missing data. [c]DLQI item 1 (Over the last week, how itchy, sore, painful or stinging has your skin been?) range: 0 (Not at all), 1 (A little), 2 (A lot), 3 (Very much). [d]The regular study visits prior to R0 were termed R-5 (re-treatment minus 5 visits) to R-1 and occurred at the 12-weekly visits between W68 and W220. All re-treated patients are shown cumulatively. Data <W68 were excluded for R -X assessments.

PRESENTED AT: AAD Annual Meeting; March 27-31, 2026; Denver, Colorado, USA. **REFERENCES: 1.** Eyerich K. *BMJ Open.* 2021;11:e049822. **2.** Schäkel K. *J Eur Acad Dermatol Venereol.* 2023;37:2016–27. **3.** Eyerich K. *JAMA Dermatol.* 2024;160:953–63. **4.** Nast, A. 2025. https://register.awmf.org/assets/guidelines/013-001e_S3_Therapie-Psoriasis-vulgaris_2025-08.pdf. **5.** Schäkel K. EADV. 2025;Abstract:1909. Medical writing support was provided by JSS Medical Research, Inc, under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298-1304). This study was sponsored by Johnson & Johnson. **DISCLOSURES: KA:** Advisory board/speaker/clinical trials/grants: AbbVie, Akribes, Almirall-Hermal, Antabio, Bayer, DEKA Biosciences, Enerviti Pharma, Galderma, Incyte, Johnson & Johnson, LEO Pharma, L'Oréal, Novartis, Pierre Fabre, Sanofi Genzyme, and UCB. **AP:** Advisor/speaker/grants/clinical trials: AbbVie, Almirall-Hermal, Amgen, Biogen Idec, BioNTech, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Galderma, GSK, Hexal, Johnson & Johnson, Klinge Pharma, LEO Pharma, MC2, Medac, Merch Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi Genzyme, Schering-Plough, Tigercat Pharma, UCB, and Zuellig Pharma. **KE:** Speaker/advisory board: AbbVie, Almirall-Hermal, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Hexal, Johnson & Johnson, LEO Pharma, Novartis, Pfizer, Sanofi Genzyme, Sityrx, and UCB. Co-founder/shareholder: Dermagnostix, and Dermagnostix R&D. **PW:** Advisory board/speaker/clinical trials/grants: AbbVie, Almirall-Hermal, Biogen Idec, Bristol Myers Squibb, Celgene, Eli Lilly, Johnson & Johnson, LEO Pharma, Medac, Novartis, Pfizer, and UCB. **CP:** Advisory board/speaker/clinical trials/grants: AbbVie, Almirall-Hermal, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Johnson & Johnson, LEO Pharma, Merck, Mylan, Novartis, Pfizer, Pierre Fabre, Sanofi Genzyme, and UCB. **FT:** Owns Taut Science and Service GmbH, a consultancy specializing in clinical development and medical affairs. Consulting fees: Johnson & Johnson. **SJ, JS, JM, NS:** Employees of Johnson & Johnson; may own stock/stock options in Johnson & Johnson. **KS:** Advisory board/consultant/speaker/clinical trials/honoraria/grants: AbbVie, Apogee, Alumis, Amgen, Almirall-Hermal, Biogen Idec, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Celldex Therapeutics, Chugai, Galderma, Incyte, Johnson & Johnson, LEO Pharma, Eli Lilly, MSD, Morphosys, Nektar Therapeutics, Novartis, Regeneron, Sanofi Genzyme, Smerud, and UCB.