

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

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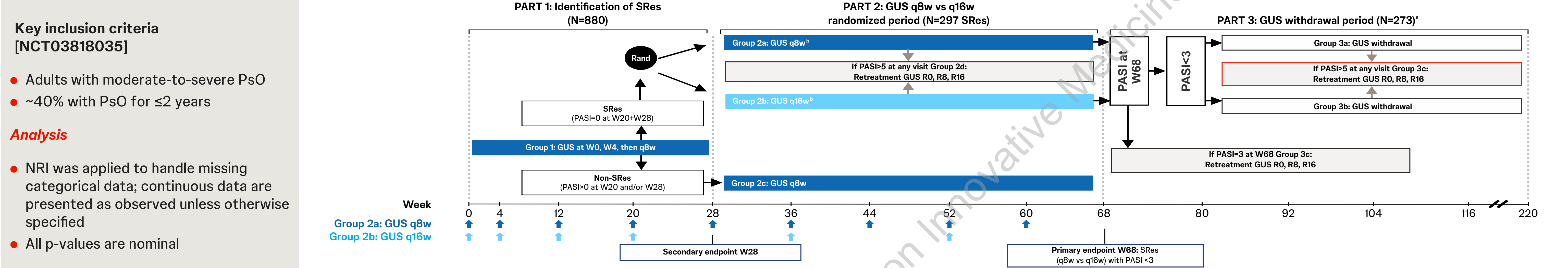
Background

- 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; Psoriasis 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 every 8W (q8w) in maintaining disease control (PASI <3) at W68 among SRes³
 - GUIDE Part 3 (W68–W220): 273 SRes with disease control at W68 were withdrawn from GUS.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 Dermatology Life Quality Index (DLQI) outcomes within 24W of GUS re-treatment among SRes who lost response (PASI >5) after W68 GUS withdrawal

Methods



PASI evaluates the extent and severity of psoriasis and provides a score from 0 (no PsO) to 72 (severe). *Patients entering Part 3 from the q8w and q16w arms of Part 2 received their last guselkumab dose at W60 and W52, respectively. *Blinded treatment. GUS=guselkumab, NRI=non-responder imputation, Non-SRes=non-super response, PASI=Psoriasis Area and Severity Index, PsO=psoriasis, q8w=every 8 weeks, q16w=every 16 weeks, R=re-treatment, Rand=randomization, SRes=super response, W=week.

Results

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

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

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

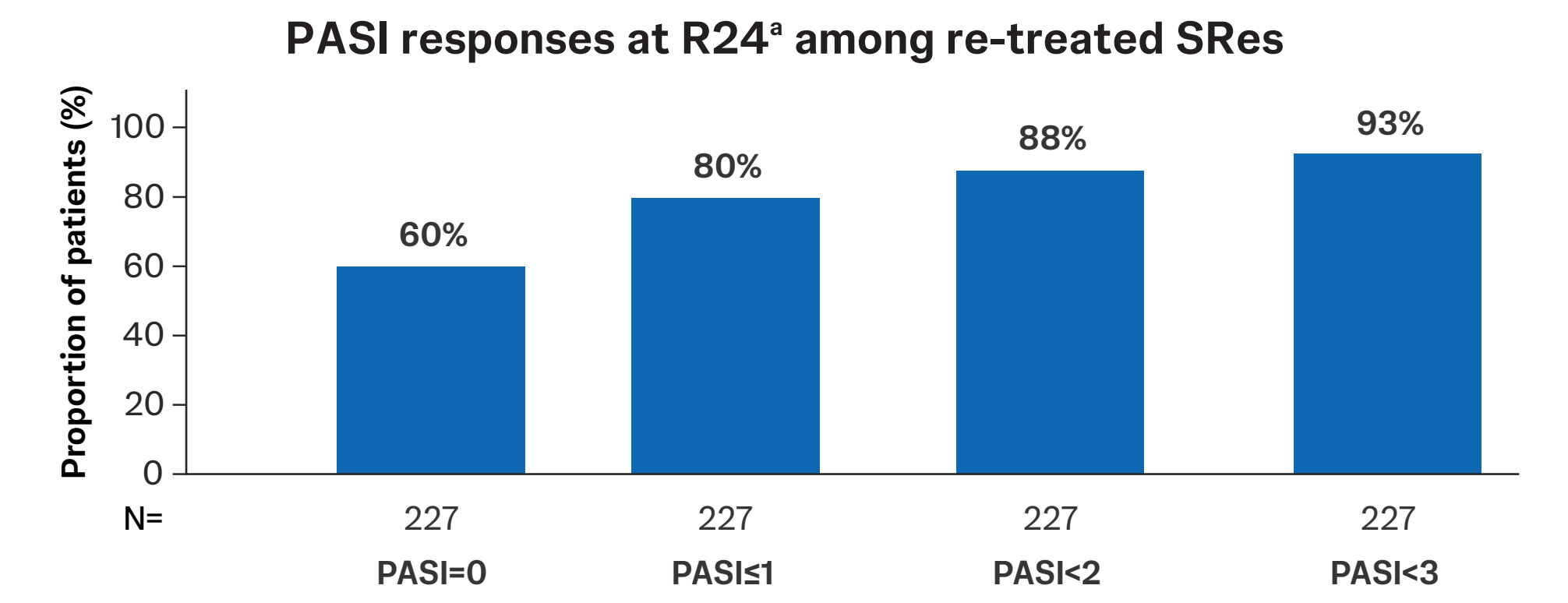
- Of 273 SRes who maintained disease control (PASI <3) at W68 who were withdrawn from GUS, 227 were re-treated after loss of response (PASI >5)
 - A higher proportion of SRes with PASI >0 at W68 had BMI >30 compared with those with PASI=0 (28.3% vs 22.8%)
 - SRes with PASI >0 at W68 were more likely 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/m ² , 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)

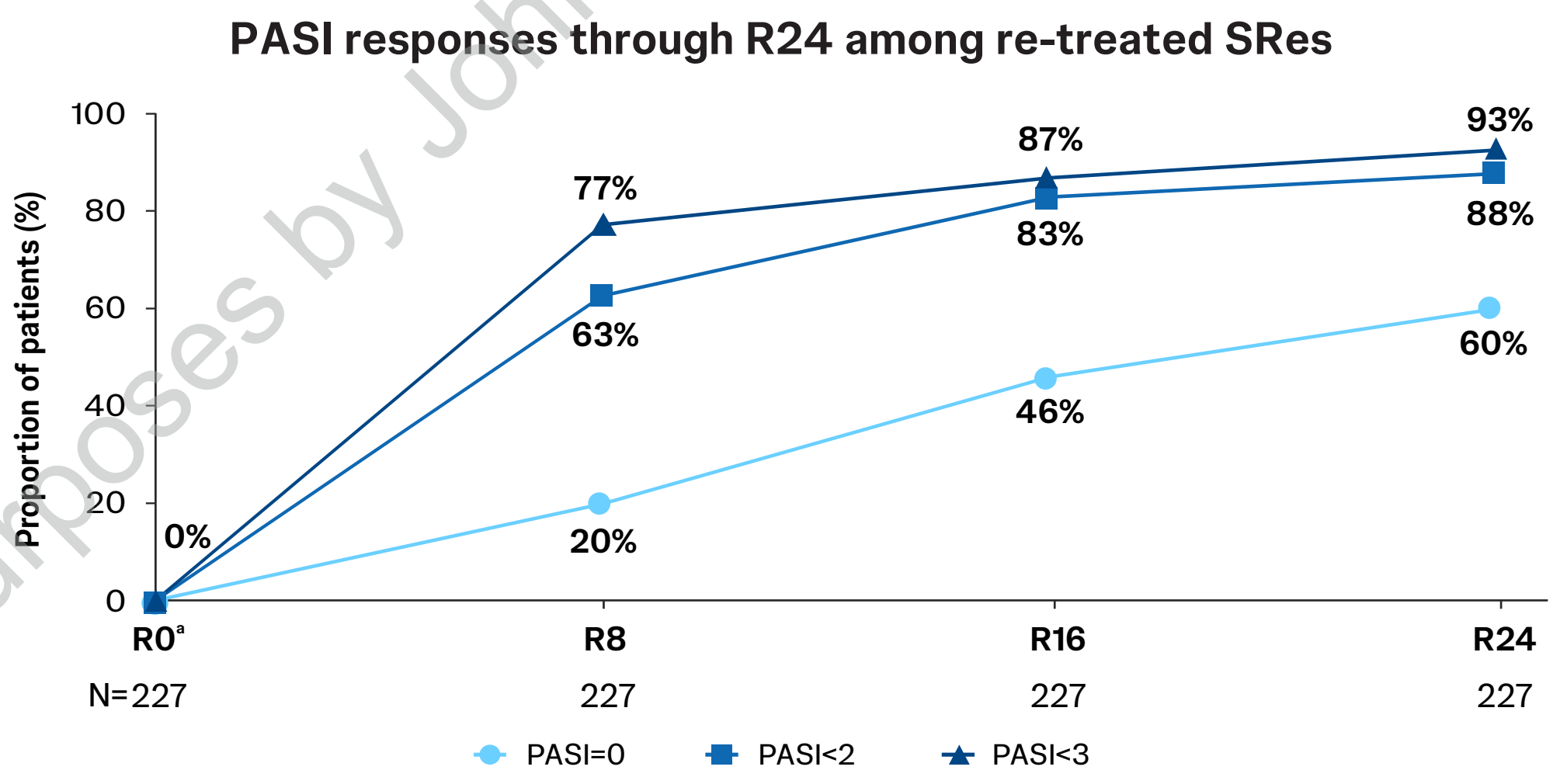
^a226 of the 227 SRes had available PASI data at W68. BMI=body mass index, BSA=body surface area, LDD=long disease duration, PASI=Psoriasis Area and Severity Index, PsO=psoriasis, SD=standard deviation, SDD=short disease duration, SRes=super response, W=week.

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 Germany⁴) at R24



^aR24 indicates 24 weeks after the start of re-treatment. GUS=guselkumab, PASI=Psoriasis Area and Severity Index, R=re-treatment, SRes=super response, W=week.



^aR0 indicates the start of re-treatment. GUS=guselkumab, PASI=Psoriasis Area and Severity Index, R=re-treatment, SRes=super response.

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/m ²		68/113 (60.2)	0.9353
≥26.5 kg/m ²		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)	

BMI=body mass index, GUS=guselkumab, LDD=long disease duration, PASI=Psoriasis Area and Severity Index, PsO=psoriasis, R=re-treatment, SDD=short disease duration, SRes=super response, W=week.

Key Takeaways

- Among SRes who remained treatment-free for a median of 302 days following GUS withdrawal⁵ 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