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Early Intervention With Guselkumab is Associated With Greater Efficacy and Higher Rates of Complete Skin Clearance Independent of Super Responder Status: The Phase 3b GUIDE Trial in Psoriasis

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Conflicts of Interest

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.

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Background

Psoriasis (PSO)

- Chronic, immune-driven, relapsing-remitting inflammatory skin disease[1]
- Primarily driven by dysregulation of the IL-23/IL-17 axis[2]
- Despite effective therapy options, patients with PSO often start adequate treatment later in their disease course[3]

Guselkumab (GUS)

- Fully human mAb that selectively inhibits IL-23 by targeting its p19 subunit
- Proven efficacy in patients with moderate-to-severe plaque PSO[4–7]
- Approved to treat moderate-to-severe PSO, active psoriatic arthritis and moderately-to-severely active ulcerative colitis and Crohn's disease[8]

GUIDE study

- Prospective Phase 3b RCT investigating early intervention with GUS in patients with moderate-to-severe PSO[8]
- Among the 880 enrolled patients, 40.6% had short disease duration (SDD; ≤24 months)

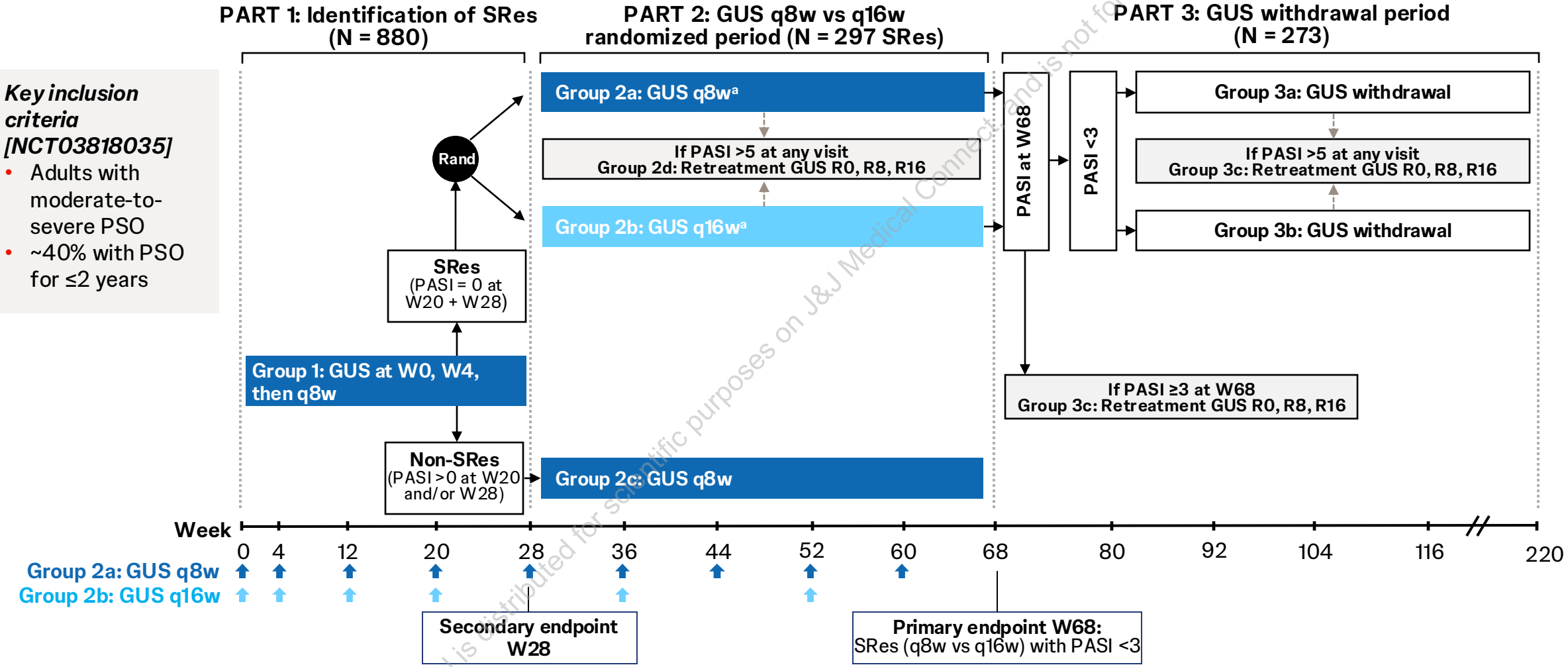
1. Siemińska I et al. *Clin Rev Allergy Immunol* 2024;66(2):164-191. **2.** Menter A et al. *Dermatol Ther (Heidelb)* 2021;11(2):385-400. **3.** Heidbrede T et al. *J Dtsch Dermatol Ges*. 2023 Jun;21(6):611-619. **4.** Blauvelt A et al. *J Am Acad Dermatol* 2017;76:405–17. **5.** Reich K et al. *J Am Acad Dermatol* 2017;76:418–31. **6.** Langley RG et al. *Br J Dermatol* 2018;178:114–23. **7.** Reich K et al. *Lancet* 2019;394:831–9. **8.** Tremfya Product Information: https://www.ema.europa.eu/en/documents/product-information/tremfya-epar-product-information_en.pdf. **mAb**=monoclonal antibody, **RCT**=randomized controlled trial.

Methods

GUIDE study design – Parts 1, 2 and 3

Key inclusion criteria [NCT03818035]

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



[a]Blinded treatment. **GUS**=guselkumab, **PASI**=Psoriasis Area and Severity Index, **PSO**=psoriasis, **q8w**=every 8 weeks, **q16w**=every 16 weeks, **R**=retreatment, **Rand**=randomization, **SRe**=super responder, **W**=week.

GUIDE study design – Parts 1 and 2

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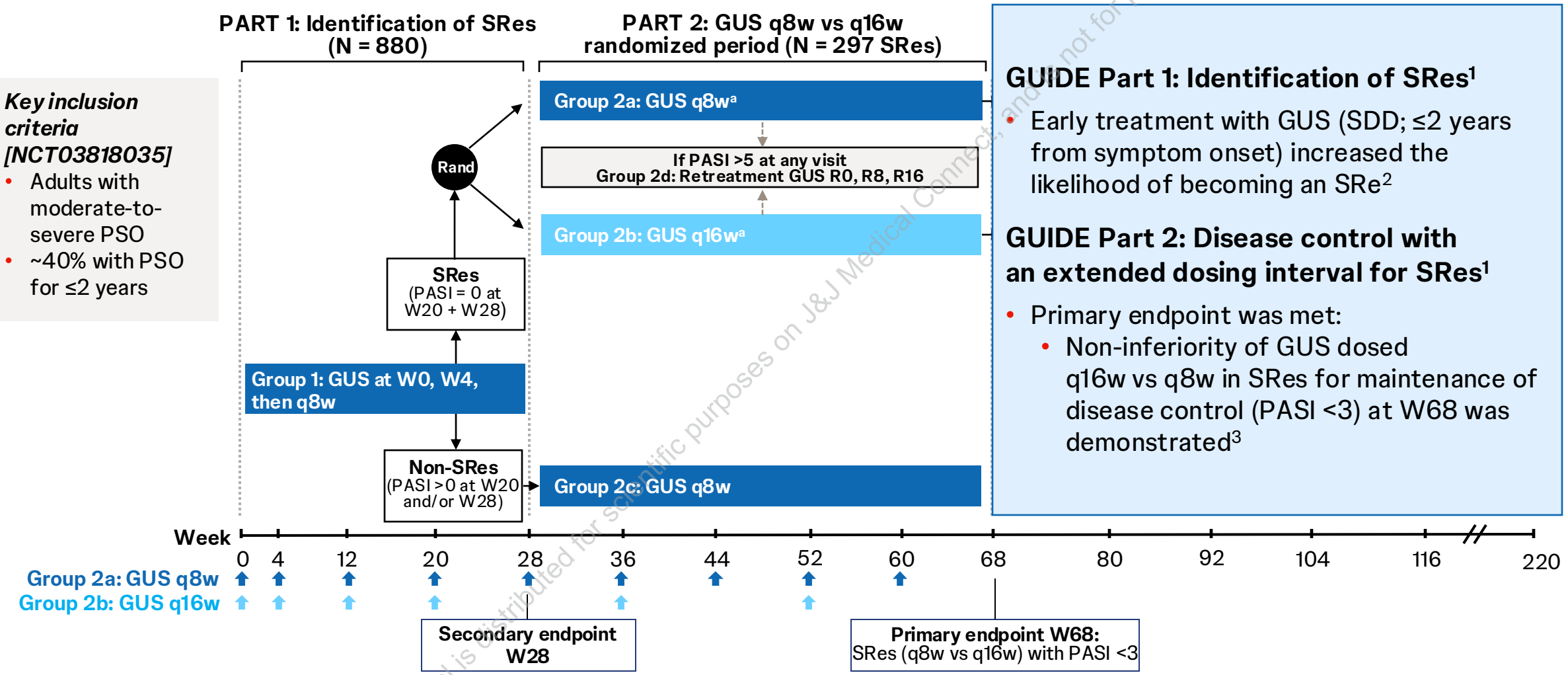


GUIDE Part 1: Identification of SRes[1]

- Early treatment with GUS (SDD; ≤2 years from symptom onset) increased the likelihood of becoming an SRe[2]

GUIDE Part 2: Disease control with an extended dosing interval for SRes[1]

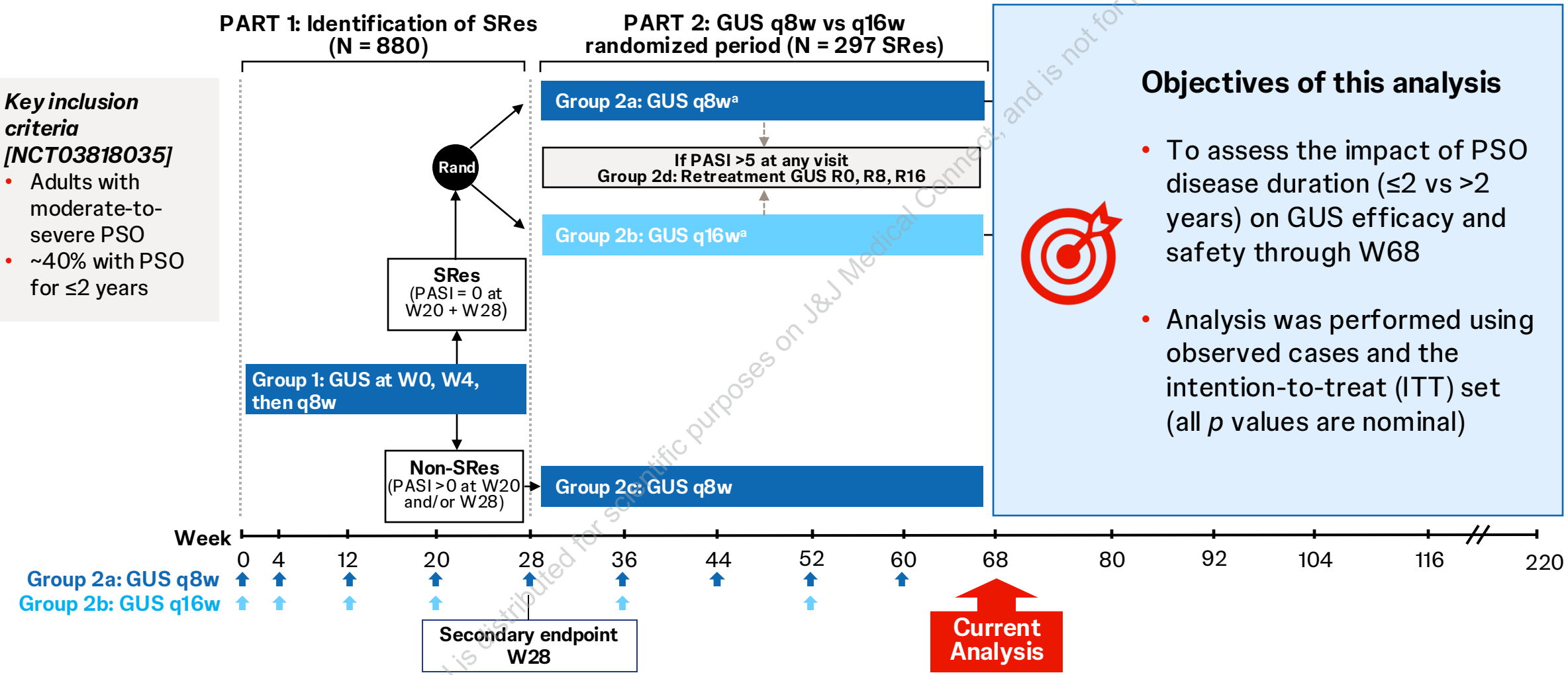
- Primary endpoint was met:
  - Non-inferiority of GUS dosed q16w vs q8w in SRes for maintenance of disease control (PASI <3) at W68 was demonstrated[3]

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;e242463. [a]Blinded treatment. **GUS**=guselkumab, **non-SRe**=non super responder, **PASI**=Psoriasis Area and Severity Index, **PSO**=psoriasis, **q8w**=every 8 weeks, **q16w**=every 16 weeks, **R**=retreatment, **Rand**=randomization, **SRe**=super responder, **W**=week.

Outcomes and Analyses

Key inclusion criteria [NCT03818035]

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



Objectives of this analysis

- To assess the impact of PSO disease duration (≤2 vs >2 years) on GUS efficacy and safety through W68
- Analysis was performed using observed cases and the intention-to-treat (ITT) set (all *p* values are nominal)

[a]Blinded treatment. **GUS**=guselkumab, **Non-SRe**=non super responder, **PASI**=Psoriasis Area and Severity Index, **PSO**=psoriasis, **q8w**=every 8 weeks, **q16w**=every 16 weeks, **R**=retreatment, **Rand**=randomization, **SRe**=super responder, **W**=week.

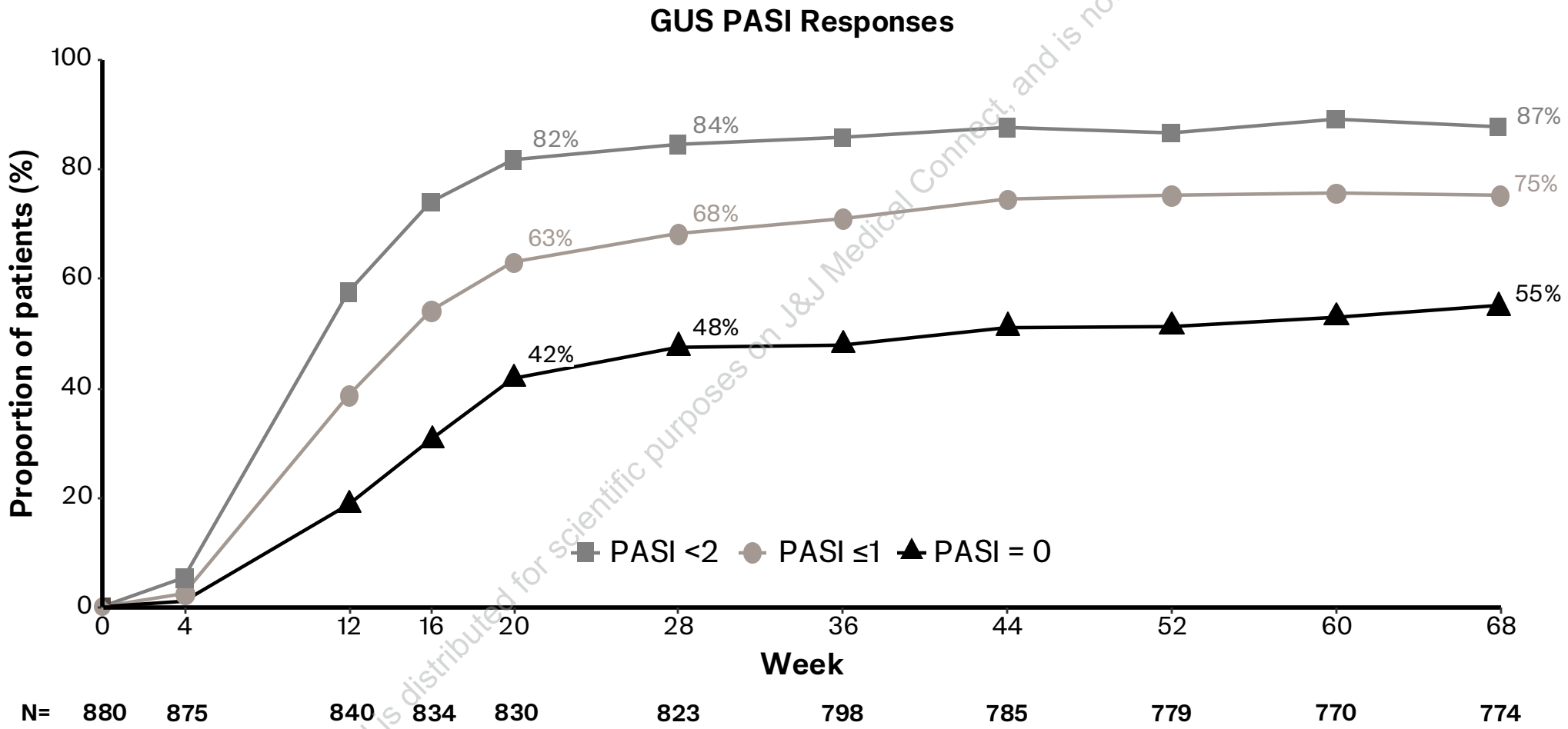
Results

Disease severity at baseline was comparable for patients with SDD (≤2 years) vs LDD (>2 years)

Baseline Characteristics of GUIDE Patients with SDD and LDD	SDD (N = 357)	LDD (N = 523)	Overall (N = 880)
Demographics			
Mean age, years (SD)	40.3 (16.0)	44.1 (13.5)	42.5 (14.7)
Female, n (%)	114 (31.9)	146 (27.9)	260 (29.5)
Mean BMI, kg/m^2 (SD)	27.8 (6.0)	28.7 (6.0)	28.3 (6.0)
Disease Characteristics			
Mean PSO duration, years (SD)	1.2 (0.6)	20.2 (13.1)	12.5 (13.8)
Mean BSA with PSO, % (SD)	25.8 (15.3)	26.8 (15.0)	26.4 (15.1)
Mean PASI (0-72) (SD)	18.7 (8.1)	19.4 (7.8)	19.1 (7.9)
PSO Medication Use			
Any prior PSO therapy, n (%)	341 (95.5)	523 (100)	864 (98.2)
Systemic therapy/biologic-naïve, n (%)	269 (75.4)	166 (31.8)	435 (49.4)
Prior systemic/biologic therapy, n (%)	88 (24.6)	357 (68.2)	445 (50.6)
≥1 biologic therapy, n (%)	5 (1.4)	118 (22.6)	123 (14.0)
SRes[a], n (%)	156 (43.7)	147 (28.1)	303 (34.4)
GUS Dosing in Part 2			
q8w, n	75	73	148
q16w, n	76	73	149

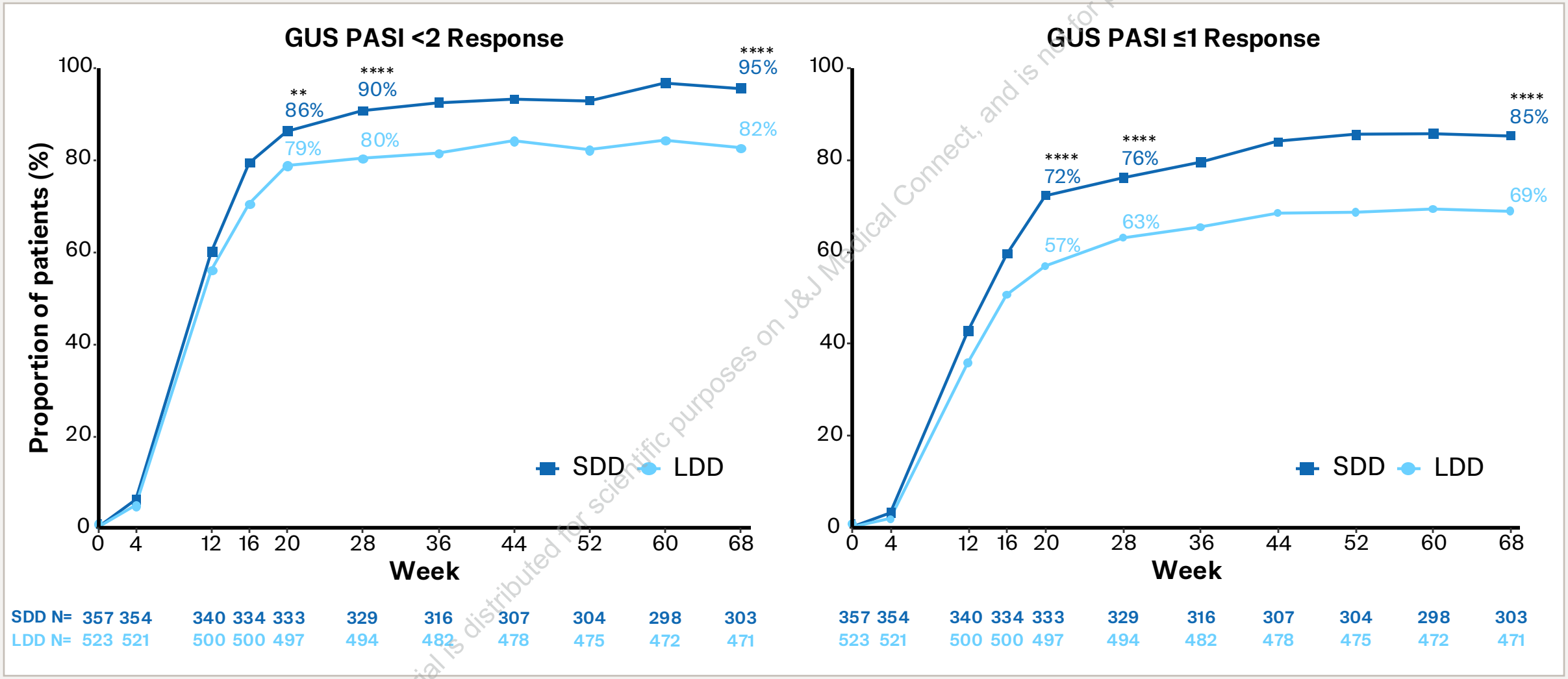
[a]SRes were randomized to q8W and q16W stratified by disease duration. **BMI**=body mass index, **BSA**=body surface area, **GUS**=guselkumab, **LDD**=long disease duration, **PASI**=Psoriasis Area and Severity Index, **PSO**=psoriasis, **q8w**=every 8 weeks; **q16w**=every 16 weeks, **SD**=standard deviation, **SDD**=short disease duration, **SRe**=super responder.

GUS demonstrated complete skin clearance in >50% of the overall study population at W68



GUS=guselkumab, **PASI**=Psoriasis Area and Severity Index, **W**=Week.

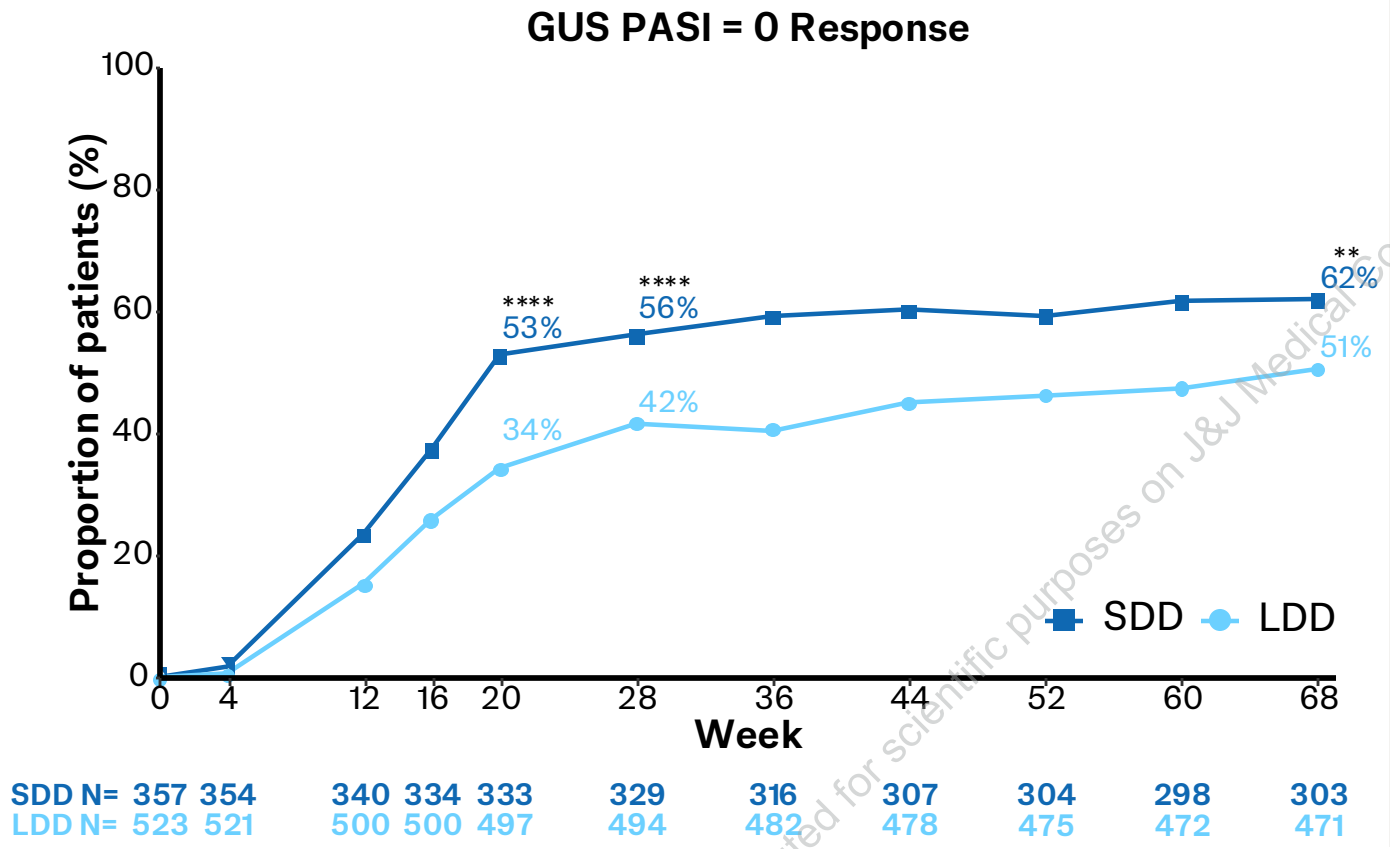
Substantially higher PASI <2 and PASI ≤1 response rates in SDD (≤2 years) vs LDD (>2 years) patients were seen with GUS through W68



Nominal **$p<0.01$, ****$p<0.0001$ vs LDD[a]

[a]Two-sided two-group normal approximation unadjusted Wald Z test (SDD vs LDD). **GUS**=guselkumab, **LDD**=long disease duration, **PASI**=Psoriasis Area and Severity Index, **SDD**=short disease duration, **W**=week.

GUS-treated SDD patients achieved complete skin clearance earlier and at substantially higher rates vs LDD patients through W68



- Patients with SDD demonstrated higher rates of complete skin clearance (PASI = 0)
- This trend was consistent among both SRes and Non-SRes

	SRes		Non-SRes	
W68 PASI = 0	**SDD**	**LDD**	**SDD**	**LDD**
	83.6%	75.7%	43.6%	40.2%

Nominal **$p<0.01$, ****$p<0.0001$ vs LDD[a]

Patients with SDD were more likely to maintain PASI = 0 between W36 and 68 (OR 1.43, 95% CI: 1.05-1.94)

[a]Two-sided two-group normal approximation unadjusted Wald Z test [SDD vs LDD]. **CI**=confidence interval, **GUS**=guselkumab, **LDD**=long disease duration, **Non-SRe**=non-super responder, **OR**=odds ratio, **PASI**=Psoriasis Area and Severity Index, **SDD**=short disease duration, **SRe**=super responder, **W**=week.

No new safety signals were identified for GUS through W68 among SDD (≤2 years) and LDD (>2 years) patients

Safety Through W68	SDD (N = 357)	LDD (N = 523)	Overall (N = 880)
Patients with TEAEs	310 (86.8)	453 (86.6)	763 (86.7)
Common TEAEs			
Nasopharyngitis	104 (29.1)	188 (35.9)	292 (33.2)
Headache	46 (12.9)	63 (12.0)	109 (12.4)
Hypertension	27 (7.6)	56 (10.7)	83 (9.4)
Arthralgia	20 (5.6)	49 (9.4)	69 (7.8)
Back pain	22 (6.2)	27 (5.2)	49 (5.6)
Death	1 (0.3)[a]	1 (0.2)[b]	2 (0.2)
MACE	4 (1.1)[c]	2 (0.4)[c]	6 (0.7)[c]
TEAE of interest	4 (1.1)	2 (0.4)	6 (0.7)
Acute TB or reactivation	0	0	0
Non-melanoma skin cancer[d]	4 (1.1)	0	4 (0.5)
Transitional cell carcinoma	1 (0.3)	1 (0.2)	2 (0.2)
IBD	0	0	0

[a]Unknown. [b]Accidental asphyxiation. [c]Only myocardial infarction was reported. [d]Includes basal cell carcinoma and squamous cell carcinoma. **GUS**=guselkumab, **IBD**=inflammatory bowel disease, **LDD**=long disease duration, **MACE**=major adverse cardiac event, **SDD**=short disease duration, **TB**=tuberculosis, **TEAE**=treatment-emergent adverse event, **W**=week.

Key Takeaways

- Post-hoc analysis of data from the GUIDE study in PSO demonstrated **sustained GUS efficacy in the overall population through W68**
- **Patients with SDD treated with GUS achieved earlier and substantially higher rates of complete skin clearance** compared to those with LDD through W68
- The advantage of SDD was evident for patients in both the SRe and Non-SRe populations, **reinforcing the benefits of early treatment with GUS**

GUS=guselkumab, **LDD**=long disease duration, **Non-SRe**=non super responder, **PSO**=psoriasis, **SDD**=short disease duration, **SRe**=super responder, **W**=week.

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