

# 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

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## Background

GUIDE is a Phase 3b, randomized, double-blind trial examining early intervention with guselkumab (GUS) in patients with moderate-to-severe plaque psoriasis (PSO)<sup>1,2</sup>

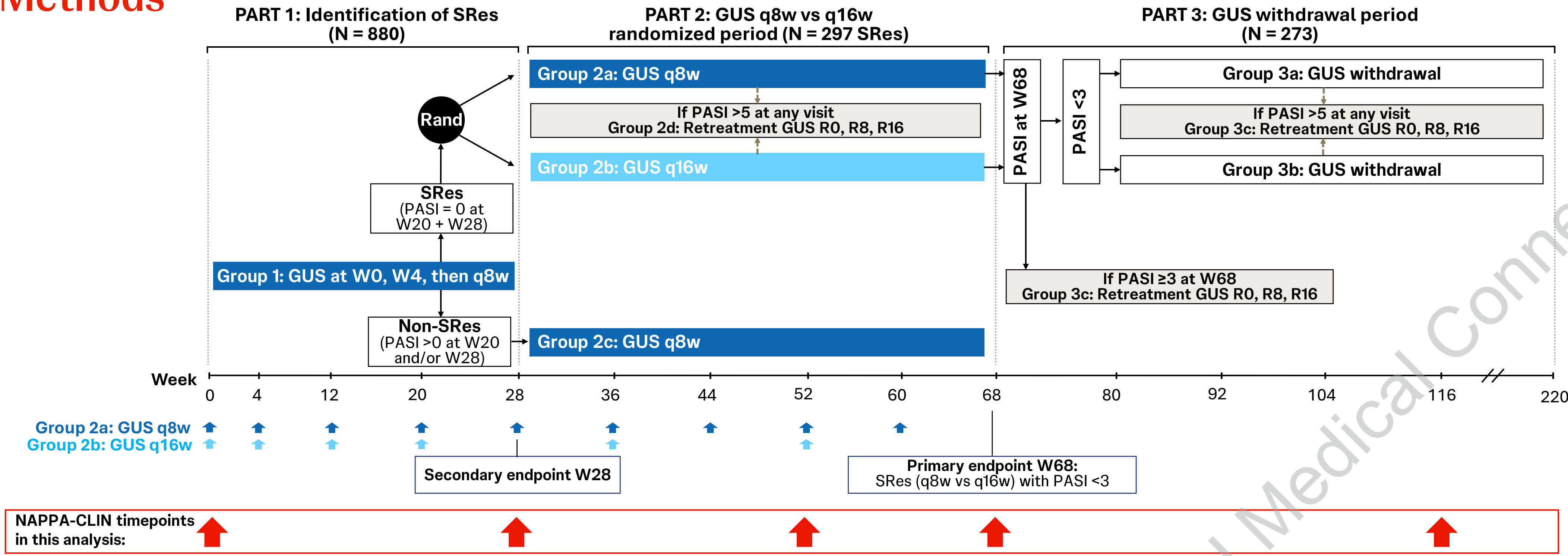
Previously, we demonstrated the benefit of early intervention with GUS for achieving super-responder (SRe) status (defined as Psoriasis Area and Severity Index [PASI] = 0 at week [W] 20 and W28),<sup>2</sup> and showed non-inferiority of a GUS every 16W (q16w) vs q8w dosing interval in SRes for maintenance of disease control (PASI <3) at W68, thereby meeting the primary endpoint<sup>3</sup>

Nail PSO, a distinct manifestation of PSO that is difficult to treat, can have a substantial impact on a patient's appearance and quality of life. It is considered a predictor of disease progression and psoriatic arthritis (PsA) development.<sup>4</sup> PSO management guidelines consider nail PSO as an upgrade criterion for defining PSO severity<sup>5,6</sup>

## Objectives

In this analysis of GUIDE, we evaluate the impact of SRe status and disease duration (short disease duration [SDD]: ≤2 years; long disease duration [LDD]: >2 years) on fingernail PSO among patients treated with GUS (up to W68), and on maintenance of fingernail PSO response following treatment withdrawal for >1 year (W116)

## Methods



### GUIDE Key Inclusion Criteria [NCT03818035]

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

### Study Design

- In Part 1 of GUIDE (W0–W28), 880 patients were enrolled and received GUS 100 mg at W0, W4, W12, and W20 to identify SRes
- In Part 2 (W28–W68), SRes were randomized to receive either GUS 100 mg q8w (five injections) or q16w (two injections). Non-SRes continued treatment with GUS q8w until W68
- In Part 3 (W68–W220), SRes with PASI<sup>a</sup> <3 at W68 were withdrawn from GUS (N=273).<sup>b</sup> Patients who worsened to PASI >5 after W68 received GUS q8w dosing at R0, R8, and R16

### Current Analysis

- We report observed NAPPA-CLIN<sup>c</sup> outcomes 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).<sup>7</sup> All P values are nominal

<sup>a</sup>PASI evaluates the extent and severity of PSO and ranges from 0 (no PSO) to 72 (severe). <sup>b</sup>Patients entering Part 3 from the q8w and q16w arms of Part 2 received their last GUS dose at W68 and W52, respectively. <sup>c</sup>A shortened version of the Nail PSO Severity Index that evaluates only four digits. ITT=intent-to-treat; NAPPA-CLIN=Nail Assessment in PSO and Psoriatic Arthritis–Clinical; Rand=Randomization; R=retreatment.

## Results

### Baseline characteristics were generally comparable across GUIDE patients with and without fingernail PSO

- Approximately half of GUIDE patients had fingernail PSO at baseline (48.0% vs 52.0%)
- Patients with fingernail PSO were more likely to be male (81.3% vs 60.5%), have LDD (70.4% vs 49.3%), and have longer mean disease duration (15.1 vs 10.1 years) compared with those without fingernail PSO (Table 1)

Table 1. Patient characteristics at baseline

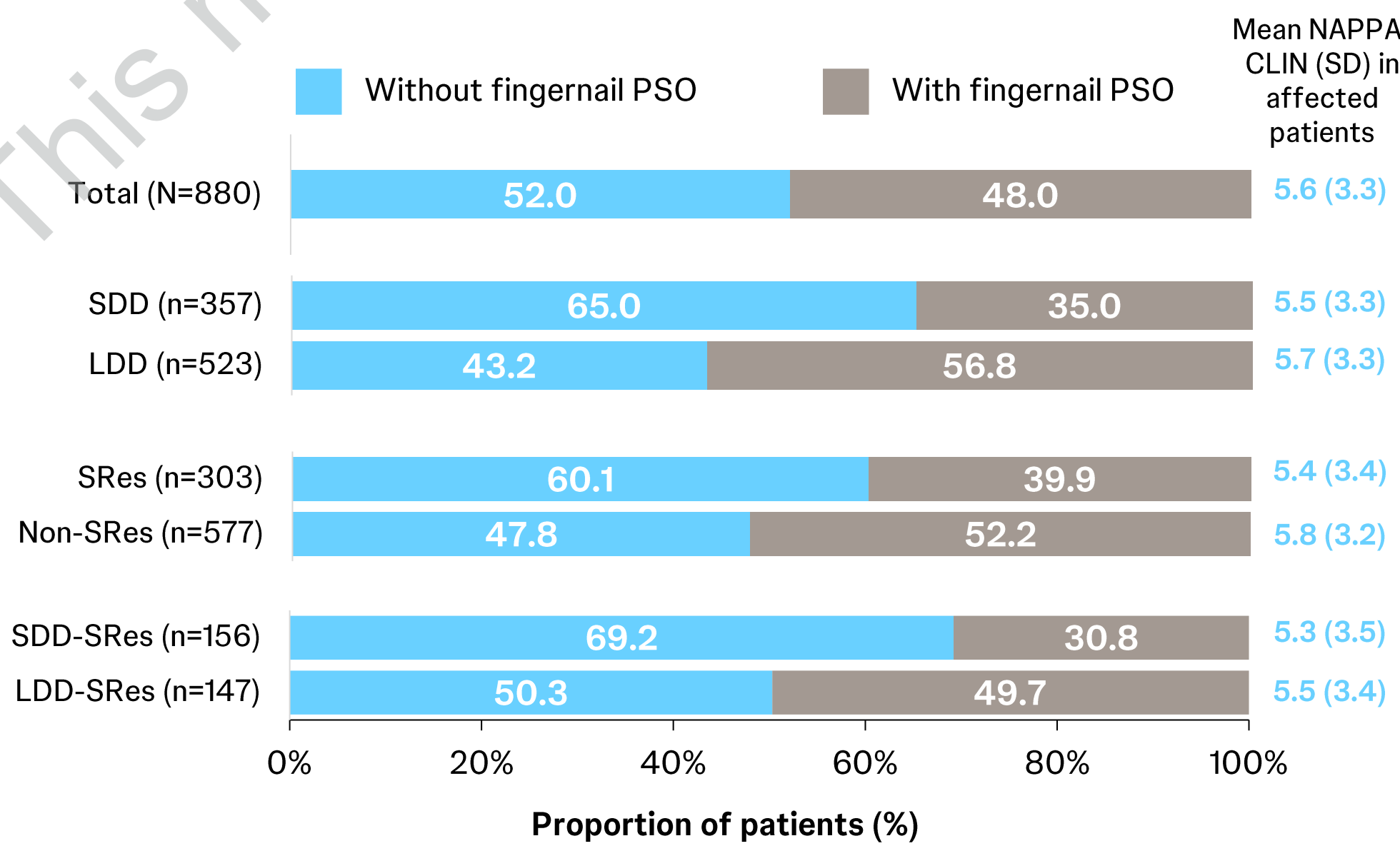
GUIDE Patient Characteristics	Without fingernail PSO (n=458)	With fingernail PSO (n=422)	Total (N=880)
Mean age, years (SD)	41.1 (15.5)	44.0 (13.7)	42.5 (14.7)
Sex, n (%)			
Male	277 (60.5)	343 (81.3)	620 (70.5)
Mean BMI, kg/m <sup>2</sup> (SD)	27.8 (6.1) <sup>a</sup>	28.9 (6.0)	28.3 (6.0) <sup>b</sup>
Duration of PSO			
Mean, years (SD)	10.1 (12.9)	15.1 (14.2)	12.5 (13.8)
≤2 years (SDD), n (%)	232 (50.7)	125 (29.6)	357 (40.6)
>2 years (LDD), n (%)	226 (49.3)	297 (70.4)	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)

<sup>a</sup>n=457. <sup>b</sup>n=879. BMI=body mass index; DLQI=Dermatology Life Quality Index.

### Fingernail PSO was less prevalent in patients with SDD vs LDD

- A lower proportion of SDD patients had fingernail PSO vs LDD patients (35.0% [125/357] vs 56.8% [297/523]), the mean NAPPA-CLIN score was similar among those affected (5.5 vs 5.7; Figure 1)
- Patients achieved SRes status irrespective of their fingernail PSO status at baseline
- Rates of fingernail PSO were slightly lower among SRes compared with non-SRes (39.9% [121/303] vs 52.2% [301/577])

Figure 1. Fingernail involvement at baseline by patient group



### GUS demonstrated high complete fingernail PSO clearance rates and significant fingernail improvements through W68

- Of those with fingernail involvement at baseline, 53.5% (200/374) achieved complete fingernail PSO clearance (NAPPA-CLIN=0) after 68W of GUS (39.8% at W28; 51.3% at W52); mean NAPPA-CLIN score decreased significantly from 5.6 at baseline to 1.5 at W68 (2.3 at W28; 1.7 at W52; all timepoints P<0.001<sup>a</sup>)
- Similar improvements were observed among GUS q8w-treated patients, with mean NAPPA-CLIN score decreasing significantly from baseline through W68 (all timepoints P<0.001<sup>a</sup>; Table 2)

Table 2. Mean NAPPA-CLIN scores through W68 among GUS q8w-treated patients with fingernail PSO at baseline

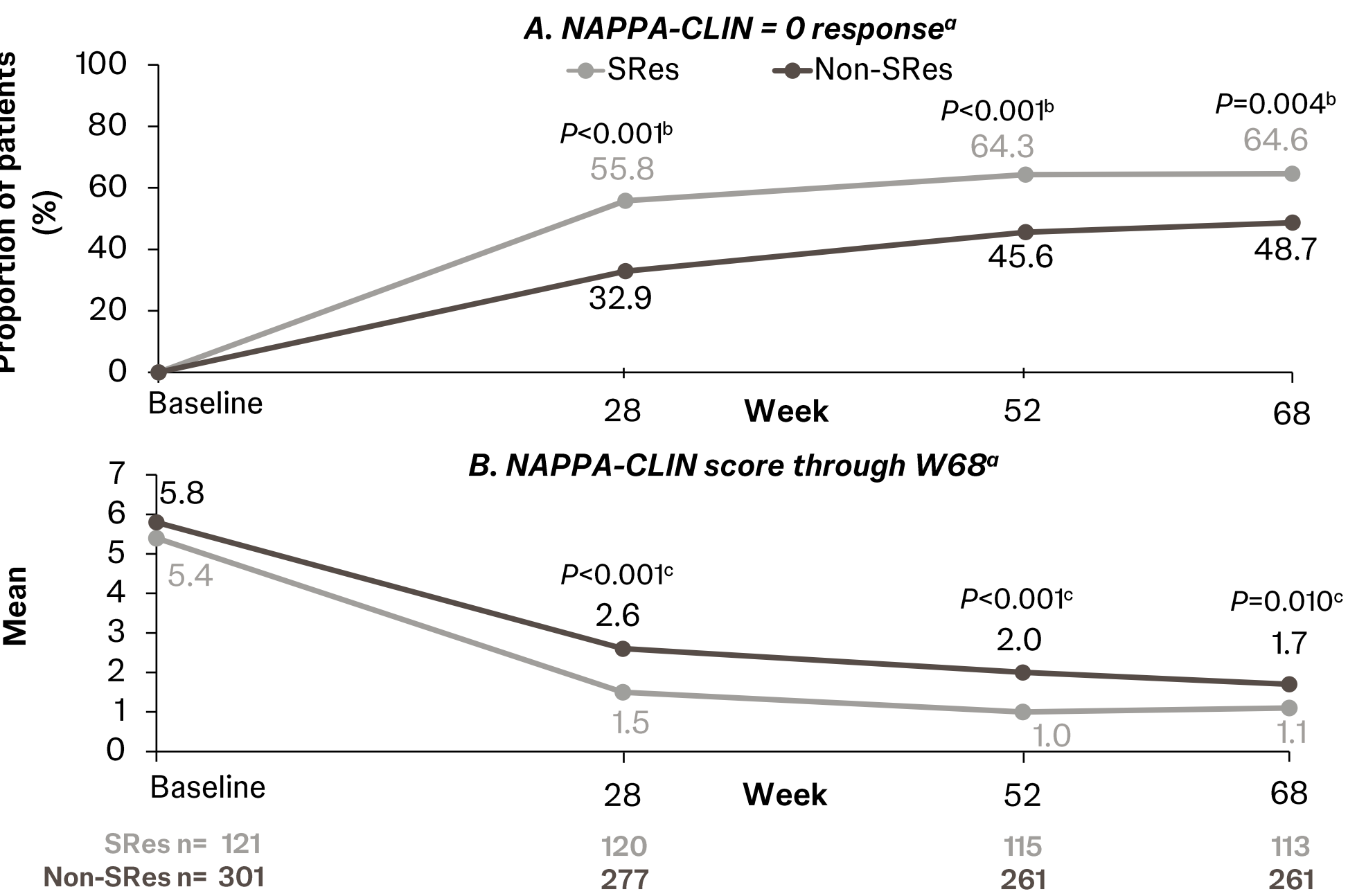
Week	Total	Score vs baseline <sup>a</sup>
0	5.7 (n=337)	–
28	2.5 (n=335)	P<0.001
52	1.8 (n=318)	P<0.001
68	1.7 (n=316)	P<0.001

<sup>a</sup>Paired t-test without adjustments for covariates (each visit W vs baseline).

### SRes had higher rates of complete fingernail PSO clearance and greater fingernail improvements vs non-SRes through W68 with GUS

- SRes achieved a higher rate of complete fingernail PSO clearance and a lower mean NAPPA-CLIN score than Non-SRes at W68 (64.6% [73/113] and 1.1 vs 48.7% [127/261] and 1.7, respectively; Figures 2A and 2B)
- 51.7% (30/58) of GUS q8w- and 78.2% (43/55) of q16w-treated SRes achieved NAPPA-CLIN=0 at W68

Figure 2. Fingernail PSO through W68 by SRe status

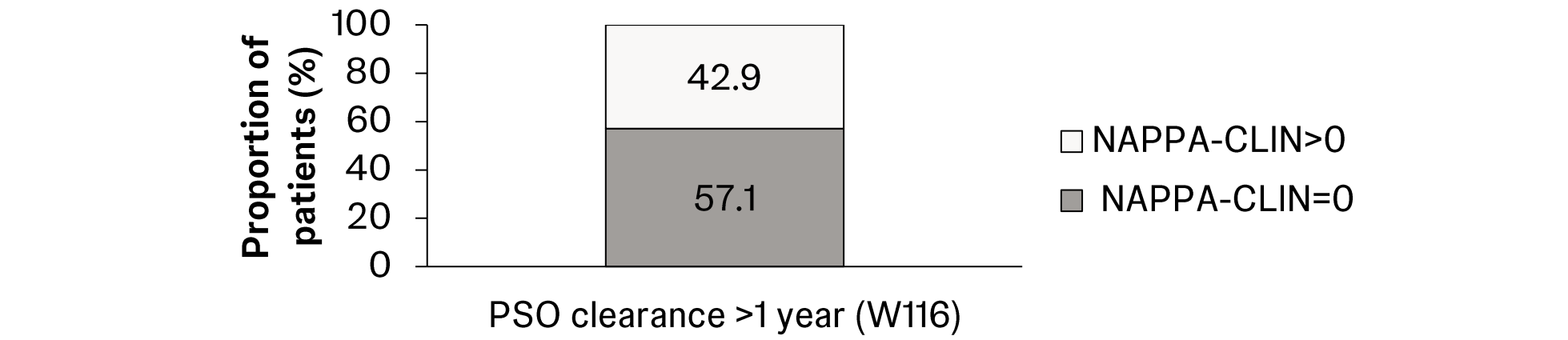


<sup>a</sup>Among patients with fingernail involvement at baseline. <sup>b</sup>Two-sided two-group normal approximation Wald Z-test (SRes vs Non-SRes). <sup>c</sup>Two-sided non-adjusted two-group t-test (SRes vs Non-SRes).

### Almost 60% of SRes had complete fingernail PSO clearance >1 year (W116) after GUS withdrawal

- Among 74 SRes who remained treatment free for >1 year after GUS withdrawal, 21 had fingernail PSO at baseline
- Of these SRes, mean NAPPA-CLIN score was 2.1 and 57.1% (12/21) had completely clear fingernails >1 year after withdrawal (W116; Figure 3)

Figure 3. Fingernail PSO response >1 year after withdrawal (n=21)



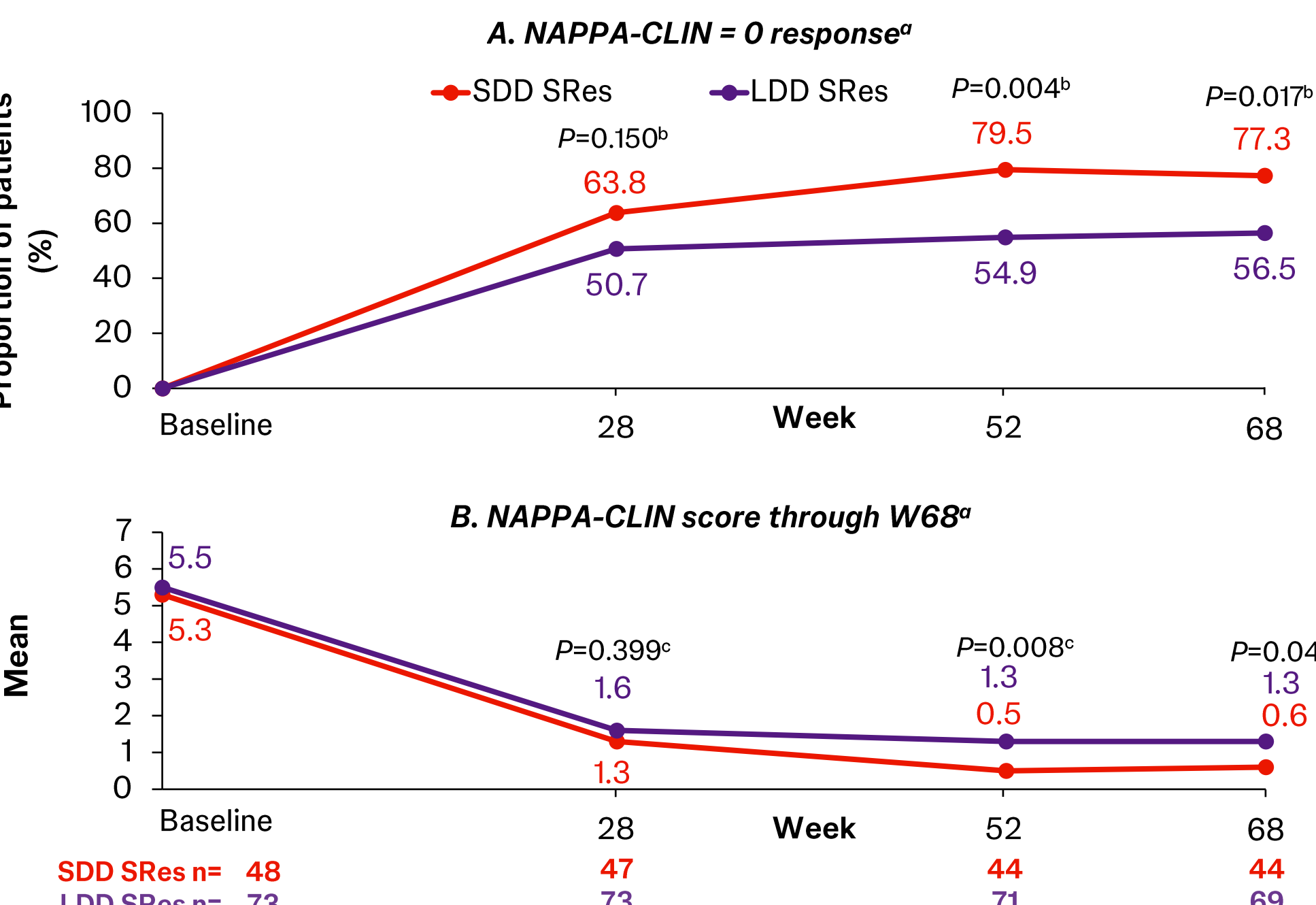
### SDD is associated with a higher rate of complete fingernail PSO clearance in SRes

- At W68 of GUS treatment, a higher proportion of SDD SRes achieved clear fingernails compared with LDD SRes (77.3% [34/44] vs 56.5% [39/69], respectively; Figure 4A)
- Among SRes who received GUS q8w/q16w during Part 2 of the study, 73.9% (17/23)/81.0% (17/21) of SDD and 51.6% (16/31)/60.5% (23/38) of LDD patients achieved clear fingernails at W68
- SDD SRes had a lower mean NAPPA-CLIN score at W68 compared with LDD SRes (0.6 vs 1.3; Figure 4B)
- Among GUS q8w-treated SRes, SDD associated with a lower mean NAPPA-CLIN score (Table 3)

Table 3. Mean NAPPA-CLIN scores among GUS q8w-treated SRes with fingernail PSO at baseline

Week	SDD	LDD	SDD vs LDD <sup>c</sup>	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)

Figure 4. Fingernail PSO through W68 in SRes by disease duration



<sup>a</sup>Among patients with fingernail involvement at baseline. <sup>b</sup>Two-sided two-group normal approximation Wald Z-test (SDD SRes vs LDD SRes). <sup>c</sup>Two-sided non-adjusted two-group t-test (SDD SRes vs LDD SRes).

### Almost 75% of SDD SRes had complete fingernail clearance >1 year (W116) after GUS withdrawal

- 49 SDD and 25 LDD SRes remained treatment free for >1 year after GUS withdrawal. Of these, 11 SDD and 10 LDD SRes had fingernail PSO at baseline
- >1 year after withdrawal (W116), SDD SRes had a higher rate of complete fingernail PSO clearance (72.7% vs 40.0%; Figure 5) and a lower mean NAPPA-CLIN score (0.7 vs 3.6) compared with LDD SRes

Figure 5. Fingernail response at W116 by disease duration

