Supplementary Material

Efficacy of Guselkumab in Treating Nails, Scalp, Hands and Feet in Patients with Psoriasis and Selfreported Psoriatic Arthritis

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Methods

Assessments. The fingernail Physician's Global Assessment (f-PGA) score rates fingernail involvement with psoriasis on a 5-point scale, with a score of 0 indicating no involvement of nail psoriasis and a score of 4 indicating severe disease. The Nail Psoriasis Area and Severity Index (NAPSI) evaluates psoriasis of the nail matrix (pitting, leukonychia, red spots in the lunula, and nail plate crumbling) and nail bed (onycholysis, splinter hemorrhages, oil drop discoloration, and nail bed hyperkeratosis) on a scale of 0 to 4 (total nail score: 0 to 8) with higher scores indicative of more extensive nail disease. The scalp-specific Investigator's Global Assessment (ss-IGA) graded scalp psoriasis from 0 (clear) to 4 (severe disease). Severity of psoriasis of the palms and/or soles was evaluated using the hand and/or foot PGA (hf-PGA; 0 indicates clear palms and/or soles; 4 indicates severe disease). A Dermatology Life Quality Index (DLQI) score of 0 or 1 indicates no effect of psoriasis or its treatment on health-related quality of life (HRQoL).

Safety. Adverse events (AEs) were summarized by actual treatment received. Rates of serious AEs (SAEs), AEs leading to discontinuation, infections (including *Candida* infections), serious infections, nonmelanoma skin cancer (NMSC) and other malignancies, and major adverse cardiovascular events (MACE) were reported.

Statistical methods. The proportions of patients in each treatment group achieving scores of 0/1 for ss-IGA, hf-PGA, and f-PGA were determined among patients with baseline scores ≥2. The proportions of patients achieving a NAPSI score of 0 (100% improvement) as well as the mean (standard deviation [SD]) percent improvement in NAPSI scores were determined in patients with a baseline NAPSI score >0. The proportions of patients achieving a Dermatology Life Quality Index (DLQI) score of 0/1 were determined among patients with baseline DLQI scores >1.

Data analysis. Patients who discontinued study agent due to lack of efficacy or an AE of worsening of psoriasis, or who initiated a protocol-prohibited psoriasis treatment (topical therapies, phototherapy or systemic therapies) during the study period, were considered non-responders or have no change in score from that point onward. Specifically, baseline values were assigned regardless of the observed data for continuous endpoints, zero was assigned to improvement and percent improvement, and non-responder status was assigned to binary response variables. After these treatment failure rules were applied, remaining missing data were imputed as non-response for binary endpoints, and last observation carried forward was applied for continuous variables. Treatment group comparisons at Weeks 16 and 24 employed the Cochran-Mantel-Haenszel χ^2 test stratified by study for binary endpoints or a nonparametric analysis of variance test with study as a covariate for continuous variables. As all p-values reported herein are nominal, statistical significance has not been established. Treatment group comparisons were not performed at Week 48. Analyses were performed using the statistical software package SAS 9.4 (Statistical Analysis System, SAS-Institute, Cary, NC, USA).

Results

Baseline characteristics/Disposition. Through Week 28, among VOYAGE-1 and -2 patients with self-reported PsA, 7 (9.2%), 13 (8.5%), and 15 (14.2%) patients in the pooled placebo, guselkumab, and adalimumab groups, respectively, discontinued study agent. In VOYAGE-1, of patients with self-reported PsA, 1 (3.4%), 5 (7.8%), and 10 (16.1%) patients in the placebo-to-guselkumab crossover, guselkumab, and adalimumab groups, respectively, discontinued the study agent through Week 48.

Safety. During the 16-week placebo-controlled period, 40.8%, 45.1%, and 50.0% of VOYAGE-1 and -2 patients with self-reported PsA in the pooled placebo, guselkumab, and adalimumab groups reported ≥1 AE. SAEs occurred in 1 (1.3%), 3 (2.0%), and 4 (3.8%) patients in the placebo, guselkumab and adalimumab groups, respectively, while 2 (2.6%), 6 (3.9%), and 2 (1.9%) patients, respectively, discontinued study agent due to an AE. Infections occurred in 21.1% of placebo, 19.0% of guselkumab, and 27.4% of adalimumab patients; the one serious infection (injection site abscess) occurred in a patient receiving adalimumab. No deaths or cases of active tuberculosis, *Candida* infections, NMSC or other malignancies were reported. One MACE occurred in the adalimumab group.

SUPPLEMENTAL TABLES AND FIGURES

Table S1. Baseline demographics and clinical characteristics for patients with self-reported PsA in pooled VOYAGE-1 and -2.

	Placebo (N=76)	**Guselkumab** (N=153)	**Adalimumab** (N=106)	**Total** (N=335)
Age (years), mean (SD)	47.9 (11.1)	47.5 (11.0)	43.4 (10.8)	46.3 (11.1)
Male	55 (72.4)	100 (65.4)	72 (67.9)	227 (67.8)
Race				
White	61 (80.3)	134 (87.6)	88 (83.0)	283 (84.5)
Black or African American	4 (5.3)	0	2 (1.9)	6 (1.8)
Asian	9 (11.8)	16 (10.5)	13 (12.3)	38 (11.3)
Other	2 (2.6)	3 (2.0)	3 (2.8)	8 (2.4)
BMI (kg/m^2), mean (SD)	28.6 (5.4)	30.0 (6.0)	30.6 (7.5)†	29.9 (6.4)
Normal (<25)	18 (23.7)	29 (19.0)	24 (22.9)	71 (21.3)
Overweight (25 to <30)	34 (44.7)	60 (39.2)	28 (26.7)	122 (36.5)
Obese (≥30)	24 (31.6)	64 (41.8)	53 (50.5)	141 (42.2)
Clinical characteristics				
BSA (0-100%), mean (SD)	31.0 (18. 7)	33.6 (20.1)	32.4 (17.7)	32.7 (19.0)
PASI score (0-72), mean (SD)	22.7 (9.5)	25.1 (11.3)	24.2 (10.0)	24.3 (10.5)
NAPSI score (0-8), N	50	111	74	235
Mean (SD)	5.4 (1.8)	5.0 (1.9)	5.2 (2.0)	5.2 (1.9)
IGA score (0-4)				
Cleared (0)	0	0	0	0
Minimal (1)	0	0	0	0
Mild (2)	0	0	0	0
Moderate (3)	57 (75.0)	108 (70.6)	77 (72.6)	242 (72.2)
Severe (4)	19 (25.0)	45 (29.4)	29 (27.4)	93 (27.8)
ss-IGA score (0-4), N	67	135	95	297
Cleared (0)	0	0	0	0
Very mild (1)	1 (1.5)	6 (4.4)	1 (1.1)	8 (2.7)
Mild (2)	7 (10.4)	22 (16.3)	20 (21.1)	49 (16.5)
Moderate (3)	48 (71.6)	87 (64.4)	59 (62.1)	194 (65.3)
Severe (4)	11 (16.4)	20 (14.8)	15 (15.8)	46 (15.5)
hf-PGA score (0-4), N	28	47	32	107
Cleared (0)	0	0	0	0
Almost Cleared (1)	1 (3.6)	2 (4.3)	1 (3.1)	4 (3.7)
Mild (2)	9 (32.1)	15 (31.9)	7 (21.9)	31 (29.0)
Moderate (3)	14 (50.0)	26 (55.3)	19 (59.4)	59 (55.1)
Severe (4)	4 (14.3)	4 (8.5)	5 (15.6)	13 (12.1)
f-PGA score (0-4), N	50	113	74	237
Cleared (0)	0	0	0	0

Minimal (1)	3 (6.0)	10 (8.8)	5 (6.8)	18 (7.6)
Mild (2)	15 (30.0)	28 (24.8)	19 (25.7)	62 (26.2)
Moderate (3)	22 (44.0)	57 (50.4)	39 (52.7)	118 (49.8)
Severe (4)	10 (20.0)	18 (15.9)	11 (14.9)	39 (16.5)
Prior treatments				
Phototherapy (PUVA or UVB)	41 (53.9)	78 (51.3)‡	55 (51.9)	174 (52.1)
Methotrexate	49 (64.5)	108 (70.6)	65 (61.3)	222 (66.3)
Non-biologics¶	57 (75.0)	120 (78.4)	81 (76.4)	258 (77.0)
Biologics§	19 (25.0)	46 (30.1)	29 (27.4)	94 (28.1)

BMI body mass index, *BSA* body surface area, *f-PGA* fingernail-Physician's Global Assessment, *hf-PGA* hand and/or foot-Physician's Global Assessment, *NAPSI* Nail Psoriasis Severity Index, *PASI* Psoriasis Area and Severity Index, *PsA* psoriatic arthritis, *PUVA* Psoralen and Ultraviolet A, *SD* standard deviation, *ss-IGA* scalp specific-Investigator's Global Assessment, *UVB* Ultraviolet B

Data presented as n (%) unless otherwise noted.

†The number of patients with available BMI for adalimumab was 105.

‡The number of patients with available phototherapy (PUVA or UVB) for guselkumab was 152.

¶Non-biologics included PUVA, methotrexate, cyclosporine, acitretin, apremilast, or tofacitinib.

§Biologics included etanercept, infliximab, alefacept, efalizumab, ustekinumab, briakinumab, secukinumab, ixekizumab, or brodalumab.

Table S2. Baseline demographics and clinical characteristics for patients with self-reported PsA in VOYAGE-1.

	Placebo (N=30)	**Guselkumab** (N=64)	**Adalimumab** (N=62)	**Total** (N=156)
Age (years), mean (SD)	49.6 (12.5)	48.4 (12.1)	44.2 (11.6)	47.0 (12.1)
Male	22 (73.3)	40 (62.5)	46 (74.2)	108 (69.2)
Race				
White	24 (80.0)	52 (81.3)	51 (82.3)	127 (81.4)
Black or African American	1 (3.3)	0	1 (1.6)	2 (1.3)
Asian	5 (16.7)	10 (15.6)	9 (14.5)	24 (15.4)
Other	0	1 (1.6)	1 (1.6)	2 (1.3)
BMI (kg/m^2), mean (SD)	28.3 (6.3)	28.8 (5.4)	30.0 (7.0)	29.2 (6.3)
Normal (<25)	8 (26.7)	15 (23.4)	15 (24.2)	38 (24.4)
Overweight (25 to <30)	15 (50.0)	29 (45.3)	18 (29.0)	62 (39.7)
Obese (≥30)	7 (23.3)	20 (31.3)	29 (46.8)	56 (35.9)
Clinical characteristics				
BSA (0-100%), mean (SD)	31.5 (18.2)	35.0 (21.5)	30.5 (16.0)	32.6 (18.8)
PASI score (0-72), mean (SD)	23.6 (10.3)	26.2 (12.3)	23.9 (9.1)	24.8 (10.8)
NAPSI score (0-8), N	21	46	42	109
Mean (SD)	5.0 (1.9)	4.7 (2.0)	5.0 (2.1)	4.9 (2.0)
IGA score (0-4)				
Cleared (0)	0	0	0	0
Minimal (1)	0	0	0	0
Mild (2)	0	0	0	0
Moderate (3)	21 (70.0)	49 (76.6)	41 (66.1)	111 (71.2)
Severe (4)	9 (30.0)	15 (23.4)	21 (33.9)	45 (28.8)
ss-IGA score (0-4), N	27	57	59	143
Cleared (0)	0	0	0	0
Very mild (1)	0	2 (3.5)	0	2 (1.4)
Mild (2)	3 (11.1)	11 (19.3)	16 (27.1)	30 (21.0)
Moderate (3)	19 (70.4)	36 (63.2)	35 (59.3)	90 (62.9)
Severe (4)	5 (18.5)	8 (14.0)	8 (13.6)	21 (14.7)
hf-PGA score (0-4), N	12	24	22	58
Cleared (0)	0	0	0	0
Almost cleared (1)	1 (8.3)	2 (8.3)	1 (4.5)	4 (6.9)
Mild (2)	3 (25.0)	8 (33.3)	7 (31.8)	18 (31.0)
Moderate (3)	5 (41.7)	12 (50.0)	11 (50.0)	28 (48.3)
Severe (4)	3 (25.0)	2 (8.3)	3 (13.6)	8 (13.8)
f-PGA score (0-4), N	21	46	42	109
Cleared (0)	0	0	0	0
Minimal (1)	0	6 (13.0)	2 (4.8)	8 (7.3)

Mild (2)	7 (33.3)	11 (23.9)	11 (26.2)	29 (26.6)
Moderate (3)	11 (52.4)	21 (45.7)	24 (57.1)	56 (51.4)
Severe (4)	3 (14.3)	8 (17.4)	5 (11.9)	16 (14.7)
Prior treatments				
Phototherapy (PUVA or UVB)	14 (46.7)	35 (54.7)	33 (53.2)	82 (52.6)
Methotrexate	21 (70.0)	45 (70.3)	40 (64.5)	106 (67.9)
Non-biologics†	22 (73.3)	50 (78.1)	48 (77.4)	120 (76.9)
Biologics‡	8 (26.7)	21 (32.8)	19 (30.6)	48 (30.8)

BMI Body mass index, *BSA* body surface area, *f-PGA* fingernail-Physician's Global Assessment, *hf-PGA* hand and/or foot-Physician's Global Assessment, *NAPSI* Nail Psoriasis Severity Index, *PASI* Psoriasis Area and Severity Index, *PsA* psoriatic arthritis, *PUVA* Psoralen and Ultraviolet A, *SD* Standard deviation, *ss-IGA* scalp specific-Investigator's Global Assessment, *UVB* Ultraviolet B

Data presented as n (%) unless otherwise noted.

†Non-biologics included PUVA, methotrexate, cyclosporine, acitretin, apremilast, or tofacitinib.

‡Biologics included etanercept, infliximab, alefacept, efalizumab, ustekinumab, briakinumab, secukinumab, ixekizumab, or brodalumab.

Table S3. Summary of adverse events through Week 28 in VOYAGE-1 and -2 patients with moderate-to-severe psoriasis and self-reported PsA.

	Placebo-controlled period (Weeks 0-16)			Active comparator-controlled period (Weeks 0-28)	
	Placebo	**Guselkumab**	**Adalimumab**	**Guselkumab**	**Adalimumab**
	N=76	N=153	N=106	N=153	N=106
Mean duration of follow-up (weeks)	15.7	16.1	16.0	27.4	27.4
≥1 AE	31 (40.8)	69 (45.1)	53 (50.0)	87 (56.9)	69 (65.1)
≥1 SAE	1 (1.3)	3 (2.0)	4 (3.8)	5 (3.3)	6 (5.7)
Discontinued due to AE	2 (2.6)	6 (3.9)	2 (1.9)	6 (3.9)	3 (2.8)
≥1 infections	16 (21.1)	29 (19.0)	29 (27.4)	40 (26.1)	40 (37.7)
Serious infections	0	0	1 (0.9)	1 (0.7)	1 (0.9)
Candida infection	0	0	0	0	0
TB	0	0	0	0	0
NMSC	0	0	0	0	0
Malignancies (excluding NMSC)	0	0	0	0	0
MACE*	0	0	1 (0.9)	0	1 (0.9)
Deaths	0	0	0	0	0

Data presented as n (%).
AE adverse event, *MACE* major adverse cardiovascular event, *NMSC* nonmelanoma skin cancer, *PsA* psoriatic arthritis, *SAE* serious adverse event, *TB* tuberculosis
*Includes sudden cardiac death, myocardial infarction, and stroke.

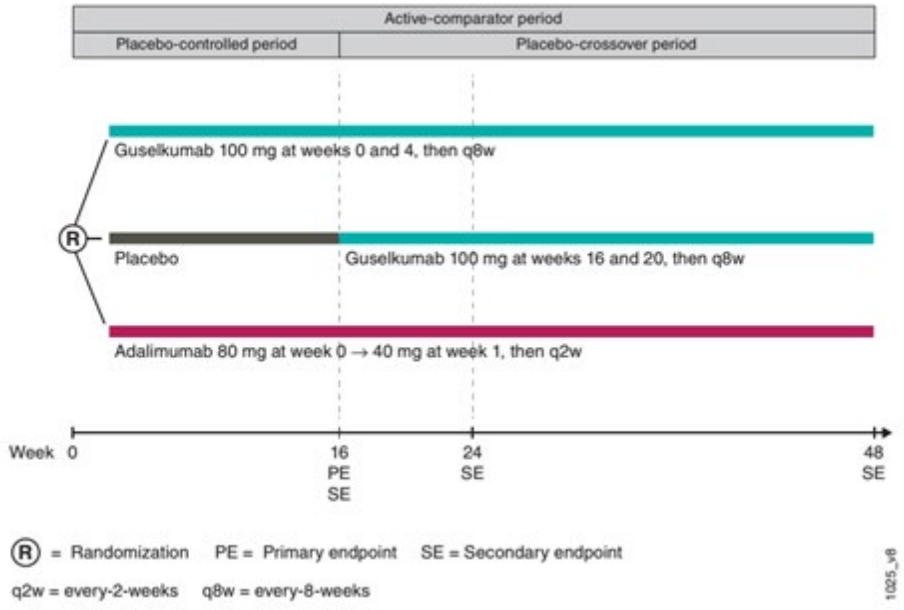
Table S4. Summary of adverse events through Week 48 in VOYAGE-1 patients with moderate-to-severe psoriasis and self-reported PsA

	Guselkumab N=64	**Adalimumab** N=62
Mean duration of follow-up (weeks)	46.5	45.0
≥1 AE	46 (71.9)	46 (74.2)
≥1 SAE	1 (1.6)	5 (8.1)
Discontinued due to AE	4 (6.3)	4 (6.5)
≥1 infections		
Serious infections	0	0
Candida infection	0	1 (1.6)
TB	0	0
NMSC	0	0
Malignancies (excluding NMSC)	1 (1.6)	0
MACE*	0	1 (1.6)
Deaths	0	0

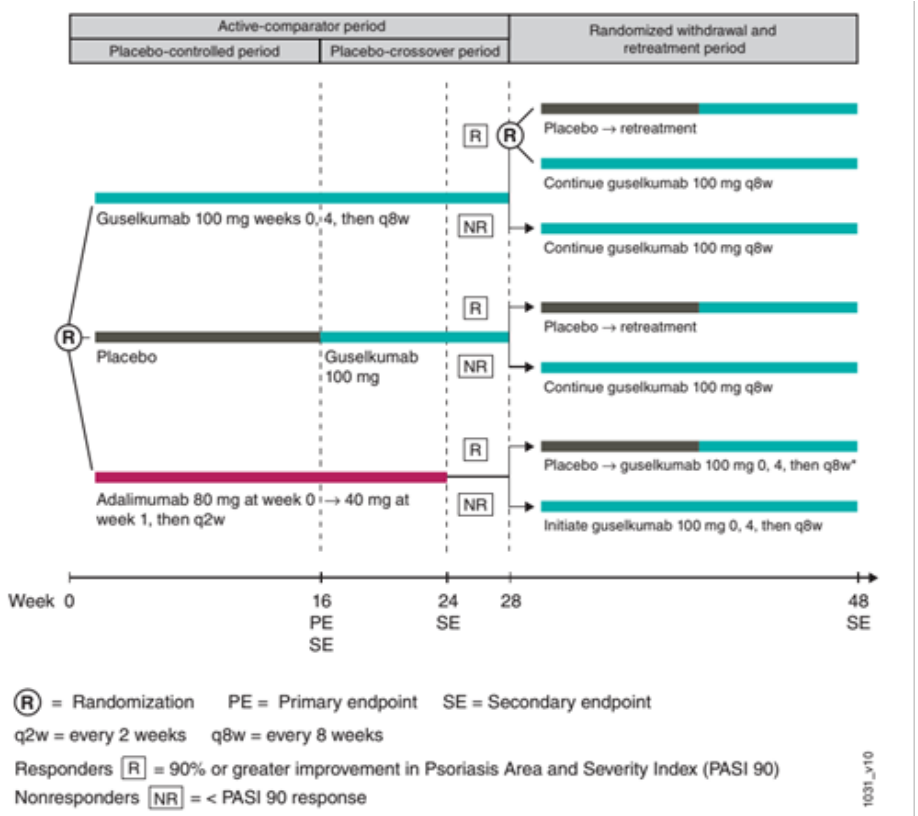
Data presented as n (%).
AE adverse event, *MACE* major adverse cardiovascular event, *NMSC* nonmelanoma skin cancer, *PsA* psoriatic arthritis, *SAE* serious adverse event, *TB* tuberculosis
*Includes sudden cardiac death, myocardial infarction, and stroke.

Figure S1. Study design for VOYAGE-1 (A) and VOYAGE-2 (B).

A.



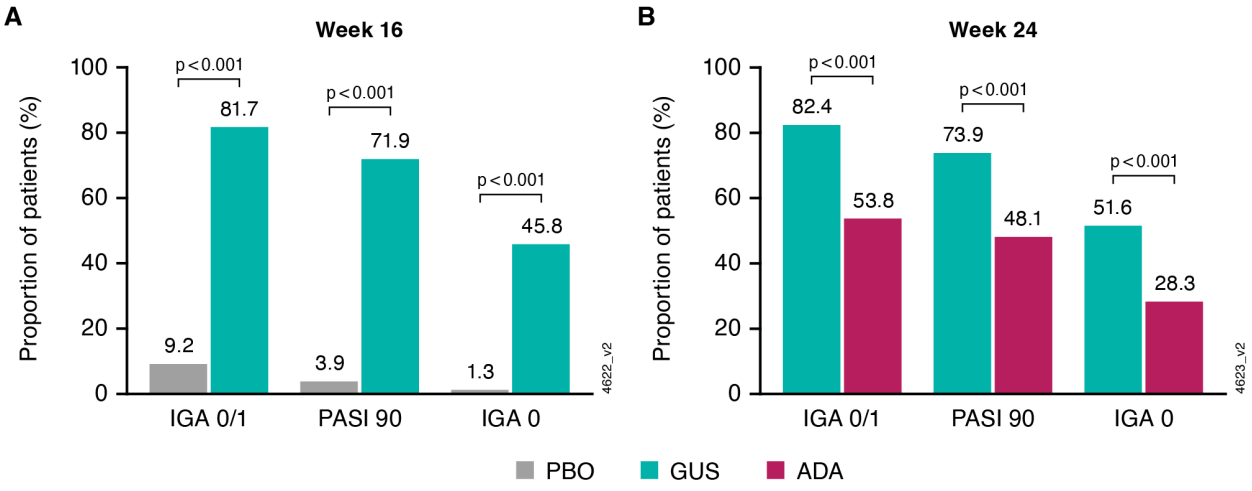
B.



*Patients initiated guselkumab upon loss of ≥50% of week 28 Psoriasis Area and Severity Index (PASI) response.

Figure adapted from [8, 9]

Figure S2. Proportions of patients achieving an IGA of 0 (clear) or 1 (minimal), PASI 90, and IGA of 0 (clear) at Week 16 (A) and Week 24 (B) in VOYAGE-1 and VOYAGE-2 patients with self-reported PsA. Treatment group comparisons employed the Cochran-Mantel-Haenszel $\chi 2$ test stratified by study. All p-values are nominal. *ADA* adalimumab, *GUS* guselkumab, *IGA* Investigator's Global Assessment, *PASI 90* ≥90% improvement in Psoriasis Area and Severity Index, *PsA* psoriatic arthritis



IGA 0/1 and PASI 90 indicate cleared or minimal psoriasis. IGA 0 indicates cleared psoriasis.

Figure S3. Proportions of patients achieving an f-PGA score of 0 (clear) or 1 (minimal) (A), f-PGA score of 0 (B), ss-IGA score of 0 (clear) or 1 (very mild) (C), ss-IGA score of 0 (D), hf-PGA score of 0 or 1 (almost clear) (E), and hf-PGA score of 0 (F) at Week 48 in VOYAGE-1 patients with self-reported PsA, among those with baseline scores ≥2. *ADA* adalimumab, *f-PGA* fingernail Physician's Global Assessment, *GUS* guselkumab, *hf-PGA* hand and/or foot PGA, *PsA* psoriatic arthritis, *ss-IGA* scalp-specific Investigator's Global Assessment

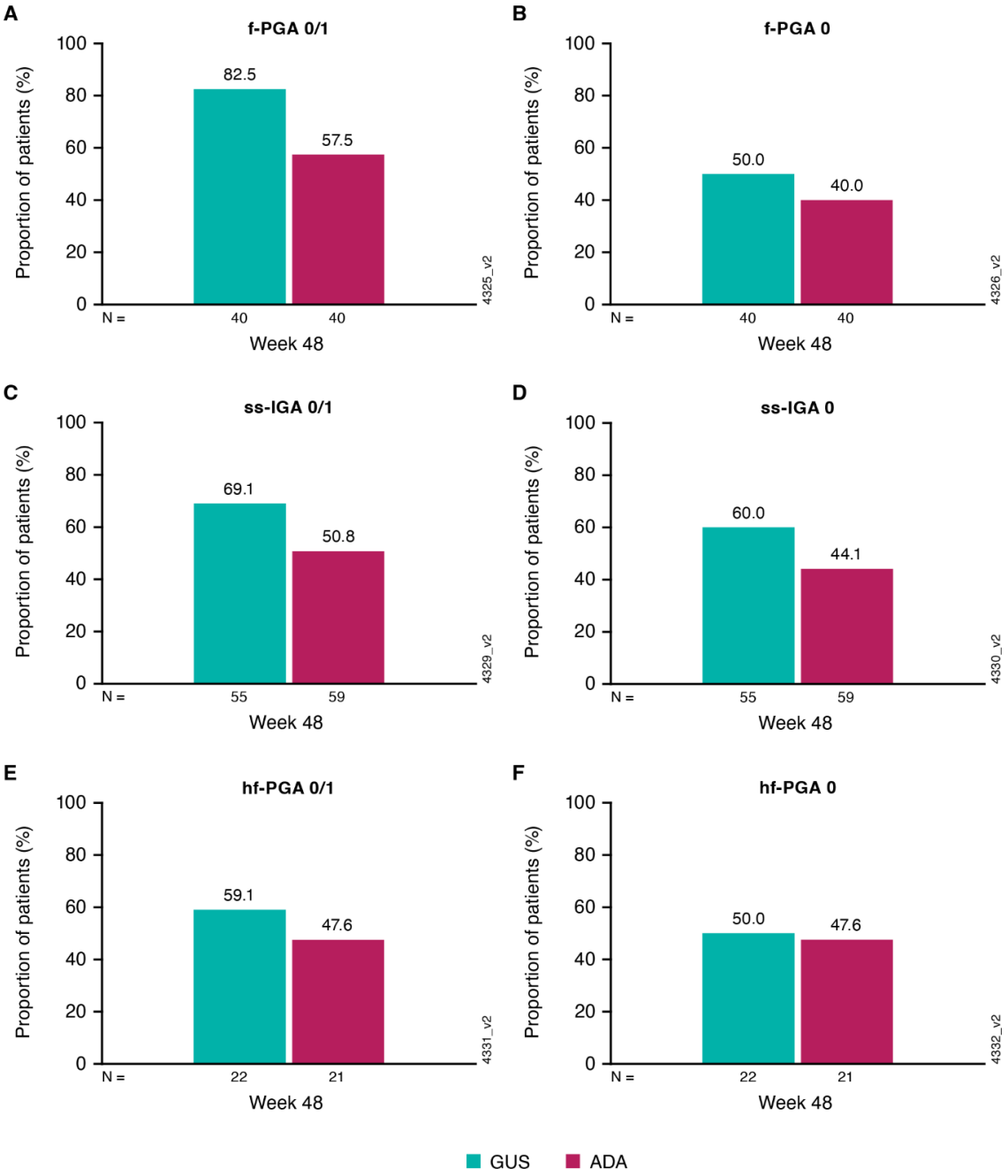


Figure S4. NAPSI assessment at Week 48 in VOYAGE-1 patients with self-reported PsA. Proportion of patients achieving NAPSI score of 0 among those with baseline NAPSI score >0 (A), mean percent improvement from baseline in NAPSI score among those with baseline NAPSI score >0 (B), mean NAPSI nail bed psoriasis score (C), and nail matrix psoriasis score (D). *ADA* adalimumab, *GUS* guselkumab, *NAPSI* Nail Psoriasis Severity Index, *PsA* psoriatic arthritis

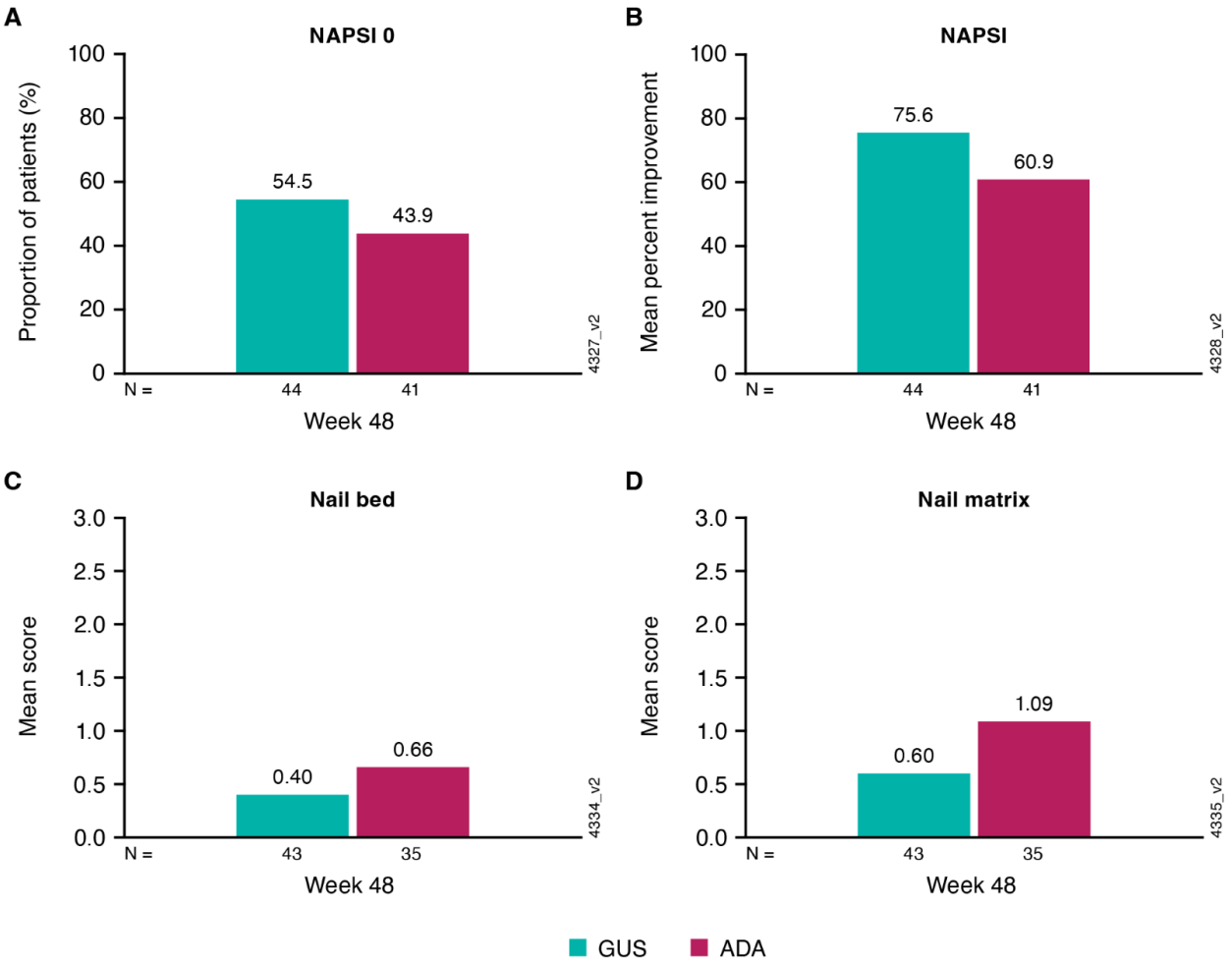


Figure S5. Proportion of patients achieving a DLQI score of 0 or 1 (no effect on HRQoL) at Week 48 in VOYAGE-1 patients with self-reported PsA, among those with baseline DLQI score >1. *ADA* adalimumab, *DLQI* Dermatology Life Quality Index, *GUS* guselkumab, *HRQoL* health-related quality of life, *PsA* psoriatic arthritis