Figure. Mean PROMIS-29 T-scores at Baseline, W24, and W52 (Observed Data)* **Table 1. Mean Change and Effect Size of Change From Baseline in PROMIS-29 Domain Scores at W24 and W52 (Observed)**

	Mean Change From Baseline [Effect Size]					
	GUS Q4W		GUS Q8W		PBO W0-24	GUS Q4W W24-52
	W24	W52	W24	W52	W24	W52
Anxiety	-3.1 [-0.3]	-3.1 [-0.3]	-3.7 [-0.4]	-4.3 [-0.5]	-1.5 [-0.2]	-3.6 [-0.4]
Depression	-2.7 [-0.3]	-3.0 [-0.4]	-4.0 [-0.4]	-4.0 [-0.4]	-0.6 [-0.1]	-2.5 [-0.3]
Fatigue	-4.8 [-0.5]	-5.6 [-0.6]	-4.8 [-0.5]	-6.8 [-0.7]	-2.1 [-0.2]	-5.7 [-0.6]
Pain interference	-5.4 [-0.8]	-6.2 [-1.0]	-5.8 [-1.0]	-7.0 [-1.1]	-2.8 [-0.4]	-6.3 [-1.0]
Physical function	5.0 [0.8]	5.9 [0.9]	4.1 [0.6]	5.0 [0.7]	1.7 [0.2]	4.2 [0.6]
Sleep disturbance	-2.5 [-0.4]	-3.9 [-0.6]	-3.8 [-0.6]	-4.4 [-0.6]	-1.5 [-0.2]	-3.3 [-0.5]
Social participation	4.2 [0.5]	5.3 [0.7]	5.3 [0.6]	6.6 [0.8]	1.7 [0.2]	4.9 [0.6]
Pain intensity*	-2.3 [-1.2]	-2.8 [-1.5]	-2.1 [-1.1]	-2.7 [-1.4]	-0.7 [-0.4]	-2.5 [-1.3]

*Raw score; all other domains reported as T-score.

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POS1030

EFFICACY OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS STRATIFIED BY BASELINE SKIN SEVERITY: A SUBGROUP ANALYSIS OF TWO PHASE III TRIALS

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Background: In the SELECT-PsA 1 and 2 clinical trials, upadacitinib (UPA) demonstrated efficacy and safety in patients (pts) with active psoriatic arthritis (PsA).^{1,2} PsA is associated with varying degrees of psoriatic symptoms; however, the impact of skin severity on treatment outcomes is not well understood.

Objectives: This post-hoc analysis assessed the effects of baseline skin severity on UPA efficacy.

Methods: SELECT-PsA 1 and SELECT-PsA 2 enrolled pts with PsA and prior inadequate response (IR) or intolerance to ≥1 non-biologic disease-modifying antirheumatic drug (DMARD)¹ or ≥1 biologic DMARD², respectively. In both trials, pts received once daily UPA 15 mg or UPA 30 mg or placebo (switched at Wk 24 to either UPA 15 mg or 30 mg); SELECT-PsA 1 also included the active comparator adalimumab (ADA). Only continuous UPA 15 mg and ADA are presented here. In this analysis, pts were divided into subgroups based on the extent of psoriasis at baseline (body surface area [BSA] of ≥3%–<10% or BSA ≥10%); efficacy endpoints were analyzed at Wk 56. Results for binary endpoints are based on non-responder imputation; continuous endpoints are based on mixed model repeated measures analysis with as-observed data.

Results: In the UPA 15 mg and ADA groups, respectively, 32% (138/429) and 31% (132/429) of pts had a BSA ≥3%–<10% at baseline in SELECT-PsA 1; 18% (76/429) in each treatment group had a BSA ≥10%. In SELECT-PsA 2, 38% (80/211) had a BSA ≥3%–<10% and 24% (50/211) had a BSA ≥10% at baseline in the UPA 15 mg group. Across pt populations (non-biologic DMARD-IR and biologic DMARD-IR), generally consistent results were observed between patients in both skin severity subgroups (Figure 1). In non-biologic DMARD-IR pts, a numerically greater proportion of UPA 15 mg pts with lower skin involvement compared with higher skin involvement achieved PASI100 and PASI≤1, two more stringent

Figure. Efficacy Outcomes at Week 56 Stratified by the Severity of Skin Involvement at Baseline

MDA was determined by fulfilling 5 of 7: TJC ≤1; SJC ≤1; PASI ≤1 or BSA-psoriasis ≤3; patient assessment of pain ≤1.5 (0-10 NRS); PGA disease activity ≤2 (0-10 NRS); HAQ-DI score ≤0.5, and LEI ≤1.

ADA, adalimumab; BL, baseline; BSA, body surface area; CI, confidence interval; EOW, every other week; HAQ-DI, Health Assessment Questionnaire-Disability Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; NRS, numeric rating scale; PASI75/90/100, ≥75%/90%/100% improvement in Psoriasis Area Severity Index; QD, once daily; SAPS, Self-Assessment of Psoriasis Symptoms; SJC, swollen joint count; TJC, tender joint count; UPA, upadacitinib.

Table 1. Additional Efficacy Outcomes at Week 56 Stratified by Severity of Skin Involvement at Baseline

SELECT-PsA 1		
n/N (%) [95% CI]	UPA 15 mg	ADA
sIGA 0/1 w/at least 2 point improvement from BL ^a		
≥3%–<10%	71/128 (55.5) [46.9, 64.1]	53/124 (42.7) [34.0, 51.4]
≥10%	29/76 (38.2) [27.2, 49.1]	33/77 (42.9) [31.8, 53.9]
MDA + skin ^b		
≥3%–<10%	58/138 (42.0) [33.8, 50.3]	56/132 (42.4) [34.0, 50.9]
≥10%	19/76 (25.0) [15.3, 34.7]	28/79 (35.4) [24.9, 46.0]
SELECT-PsA 2		
n/N (%) [95% CI]	UPA 15 mg	
sIGA 0/1 w/at least 2 point improvement from BL ^a		
≥3%–<10%	24/71 (33.8) [22.8, 44.8]	
≥10%	18/50 (36.0) [22.7, 49.3]	
MDA + skin ^b		
≥3%–<10%	22/80 (27.5) [17.7, 37.3]	
≥10%	9/50 (18.0) [7.4, 28.6]	

^a defined as achieving an sIGA score of 0 or 1 and at least a 2 point improvement from BL, evaluated in pts with BL sIGA ≥2.

^b defined as achieving 5 of the 7 criteria, with PASI ≤1 or BSA-psoriasis ≤3 as a required component.

ADA, adalimumab; BL, baseline; CI, confidence interval; MDA, minimal disease activity; sIGA, Static Investigator Global Assessment of psoriasis; UPA, upadacitinib

skin endpoints. The achievement of MDA was generally consistent across skin severity subgroups; when pts were required to achieve the skin component of MDA, results were numerically better in the ≥3%–<10% skin severity group (Table 1). In non-biologic DMARD-IR pts, results were similar between UPA 15 mg and ADA. **Conclusion:** UPA is a viable treatment option for pts with active PsA regardless of the extent of psoriasis at baseline. Although these results are of interest and hypothesis-generating, they should be interpreted with caution due to low sample size.

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POS1031

LOW INCIDENCE OF GASTROINTESTINAL-RELATED AND OVERALL SERIOUS ADVERSE EVENTS AMONG GUSELKUMAB-TREATED PATIENTS: POOLED ANALYSES OF VOYAGE 1 & 2 AND DISCOVER 1 & 2 THROUGH 1-YEAR

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Background: Guselkumab (GUS), a human monoclonal antibody that specifically binds to the p19-subunit of interleukin (IL)-23, demonstrated efficacy in the Phase 3 VOYAGE 1&2 trials of patients (pts) with moderate to severe plaque psoriasis (PsO)^{1,2} and in the DISCOVER 1&2 trials of pts with active psoriatic arthritis (PsA).^{3,4} IL-17 inhibitors used to treat PsO and PsA have been associated with exacerbation or new onset of inflammatory bowel disease (IBD) (e.g., Crohn's disease or ulcerative colitis).⁵

Objectives: Evaluate the incidence of gastrointestinal (GI)-related and overall serious adverse events (SAEs) from pooled safety data through 1-year of GUS 100 mg treatment from the VOYAGE 1&2 and DISCOVER 1&2 trials.

Methods: Using pooled safety data from the VOYAGE 1&2 PsO trials and DISCOVER 1&2 PsA trials, SAEs related to GI disorders were identified using the Medical Dictionary for Regulatory Activities (MedDRA) system-organ class "GI disorders". Pts with a previous history of IBD were not excluded in these trials; medical history of IBD was collected at baseline in DISCOVER 1&2. Rates of overall SAEs and GI-related SAEs were calculated as the number of SAEs per 100 pt-years (PY) of follow-up (95% confidence intervals). Data are presented for the placebo (PBO)-controlled period (Weeks 0-16 for VOYAGE 1&2; Weeks 0-24 for DISCOVER 1&2) and through 1-year (defined as through Week 48 for VOYAGE 1&2; through Week 60 for DISCOVER 1, and through Week 52 for DISCOVER 2). Events of uveitis and opportunistic infections were also analyzed. **Results:** Through the PBO-controlled period, the overall rates of GI-related SAEs per 100 PY for pooled VOYAGE 1&2 were: PBO 0.78 (0.02, 4.34), GUS q8w 0; and for pooled DISCOVER 1&2: PBO 0.58 (0.01, 3.23), GUS q8w 0.58 (0.01, 3.21), GUS q4w 0. The GI-related SAEs included: gastrointestinal hemorrhage (PBO; n=1) for pooled VOYAGE 1&2; and inflammatory bowel disease (PBO; n=1) and mechanical ileus (GUS q8w; n=1) for pooled DISCOVER 1&2. Through 1-year, the overall rates of GI-related SAEs for pooled VOYAGE 1&2 were: Combined GUS group (GUS q8w and PBO→GUS groups) 0.51 (0.17, 1.20); and for pooled DISCOVER 1&2: GUS q8w 0.52 (0.06, 1.88), GUS q4w 0, Combined GUS group (GUS q8w, GUS q4w, and PBO→GUS groups) 0.21 (0.02, 0.74). The GI-related SAEs in the Combined GUS group for pooled VOYAGE 1&2 included: gastritis, hemorrhoids, inguinal hernia, pancreatitis, and umbilical hernia (0.10/100PY [0.00, 0.57]; n=1 for each); and in the Combined GUS group for pooled DISCOVER 1&2: mechanical ileus and pancreatitis chronic (0.10/100PY [0.00, 0.57]; n=1 for each). Overall, no cases of exacerbation or new onset of IBD were reported in GUS-treated pts, including 2 pts with a prior history of IBD in DISCOVER 1&2 (total PY of follow-up for the Combined GUS groups in VOYAGE and DISCOVER were 974 and 973, respectively). Through the PBO-controlled period, rates of overall SAEs for GUS-treated pts were comparable to PBO-pts and SAE rates remained low through 1-year of follow-up in the VOYAGE 1&2 and DISCOVER 1&2 trials. There were no reported cases of uveitis, opportunistic infections, or tuberculosis in GUS-treated pts through 1-year.

Conclusion: Through 1-year of follow-up with GUS treatment in pooled VOYAGE 1&2 and DISCOVER 1&2, GI-related SAE rates were low. There were no reported cases of uveitis, opportunistic infections, or new onset/exacerbation of IBD in GUS-treated pts. No new safety concerns were identified through 1-year.

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