Table 1. PsAID-12 scores by BL characteristic subgroup

Mean (95% CI)	UST		TNFi	
	BL	Unadjusted change from BL at 1 year (LOCF)	BL	Unadjusted change from BL at 1 year (LOCF)
Biologic line				
1st	5.51	-2.14	5.44	-2.41
	(5.19; 5.82)	(-2.49; -1.79)	(5.15; 5.72)	(-2.72; -2.09)
2nd	6.05	-2.14	5.57	-2.37
	(5.69; 6.41)	(-2.55; -1.72)	(5.19; 5.95)	(-2.79; -1.94)
3rd	5.84	-1.81	5.34	-1.89
	(5.33; 6.35)	(-2.45; -1.17)	(4.52; 6.15)	(-2.62; -1.16)
Sex*				
Male	5.27	-2.35	4.89	-2.49
	(4.95; 5.59)	(-2.70; -1.99)	(4.56; 5.23)	(-2.83; -2.15)
Female	6.14	-1.86	5.95	-2.20
	(5.86; 6.43)	(-2.20; -1.52)	(5.67; 6.23)	(-2.53; -1.87)
Enthesitis				
Yes	5.95	-2.19	5.89	-2.65
	(5.66; 6.24)	(-2.51; -1.86)	(5.61; 6.17)	(-2.98; -2.31)
No	5.51	-1.98	4.99	-2.02
	(5.19; 5.83)	(-2.36; -1.59)	(4.65; 5.32)	(-2.35; -1.68)
Psoriasis BSA, %				
<3	5.66	-1.60	4.97	-1.89
	(5.32; 6.00)	(-2.03; -1.18)	(4.63; 5.31)	(-2.25; -1.52)
3–10	5.44	-2.16	5.78	-2.99
	(5.05; 5.83)	(-2.59; -1.74)	(5.43; 6.14)	(-3.38; -2.59)
>10	6.15	-2.93	6.13	-2.86
	(5.70; 6.60)	(-3.43; -2.43)	(5.55; 6.71)	(-3.49; -2.23)
Joint involvement†				
Mono/oligoarticular	5.07	-1.96	4.82	-2.18
	(4.56; 5.58)	(-2.47; -1.45)	(4.38; 5.25)	(-2.66; -1.70)
Polyarticular	5.98	-2.21	5.78	-2.47
	(5.75; 6.22)	(-2.51; -1.92)	(5.52; 6.04)	(-2.75; -2.18)
FIRST score*				
<5	5.15	-2.18	5.10	-2.44
	(4.87; 5.44)	(-2.50; -1.87)	(4.83; 5.36)	(-2.71; -2.16)
≥5	6.72	-1.95	6.49	-2.09
	(6.43; 7.00)	(-2.38; -1.53)	(6.15; 6.83)	(-2.57; -1.61)

*At BL, female pts and pts with FIRST score ≥5 (chronic widespread pain) were significantly more impacted than male pts and pts with FIRST score <5, and remained significantly more impacted at 1 year. †Polyarticular pts were significantly more impacted at BL, but not 1 year. BSA, body surface area; CI, confidence interval; FIRST, Fibromyalgia Rapid Screening Tool; LOCF, last observation carried forward

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POS1047

IMPACT OF UPADACITINIB ON REDUCING PAIN IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM TWO PHASE 3 TRIALS IN PATIENTS WITH INADEQUATE RESPONSE TO NON-BIOLOGIC OR BIOLOGIC DMARDs

L. McInnes¹, W. Tillett², P. J. Mease³, K. De Vlam⁴, L. Bessette⁵, R. Lippe⁶, A. Maniccia⁷, P. Zueger⁷, D. Feng⁷, K. Kato⁷, A. Ostor⁸. ¹University of Glasgow, Rheumatology, Glasgow, United Kingdom; ²Royal National Hospital, Rheumatic Diseases, Bath, United Kingdom; ³Swedish Medical Center, Providence St Joseph Health and University of Washington, Seattle, United States of America; ⁴University Hospitals Leuven, Rheumatology, Leuven, Belgium; ⁵Laval University, Rheumatology, Québec City, Canada; ⁶AbbVie Deutschland, GmbH & Co. KG, Wiesbaden, Germany; ⁷AbbVie Inc., Rheumatology, North Chicago, United States of America; ⁸Cabrini Hospital, Monash University & Emeritus Research, Melbourne, Australia

Background: Pain is a dominant symptom of psoriatic arthritis (PsA), and pain reduction is a priority for patients (pts) that is often assessed in clinical trials. Upadacitinib (UPA), a Janus kinase (JAK) inhibitor engineered for increased selectivity for JAK1 over JAK2, JAK3, and tyrosine kinase2, has demonstrated safety and efficacy in pts with active PsA in the SELECT-PsA 1 and 2 studies.^{1,2}

Objectives: The objective of this analysis was to compare the efficacy of UPA vs placebo (PBO) and adalimumab (ADA) on pain using different assessments through 24 weeks (wks).

Methods: The SELECT-PsA program enrolled adult pts with active PsA with prior inadequate response (IR) or intolerance to ≥1 non-biologic DMARD (SELECT-PsA 1; NCT03104400) or prior IR or intolerance to ≥1 biologic DMARD (SELECT-PsA 2; NCT03104374). Concomitant background therapy with ≤2 non-biologic DMARDs was allowed but not required. Pts were randomized to UPA 15 mg or UPA 30 mg once daily (QD) or PBO (both studies), or ADA 40 mg every other week (EOW; SELECT-PsA 1 only). Pain was assessed as proportion of pts achieving ≥30%, ≥50%, or ≥70% reduction from baseline (BL) in Pt's global assessment (PGA) of pain numeric rating scale (NRS) score (0–10), proportion of pts achieving minimal clinically important difference (MCID) in pain (defined as ≥1 point reduction or 15% reduction from BL on a 0–10 NRS)^{3,4} and change from baseline in pain NRS (0–10) at all time points. In addition, change from BL in BASDAI questions 2 (spinal pain) and 3 (joint pain/swelling) and 36-Item Short Form Survey (SF-36) questions 7 (bodily pain) and 8 (pain interference) at weeks 12 and 24 were assessed. Non-responder imputation was used for binary endpoints and mixed-effects model for repeated measurements for continuous endpoints. The statistical significance defined as $P < 0.05$ was exploratory in nature.

Results: In both studies, a significantly higher proportion of pts receiving UPA 15 mg QD and UPA 30 mg QD vs PBO achieved improvements in most pain endpoints as early as wk 2, and improvements were generally either sustained or increased through wk 24 (nominal $P < 0.05$). A significant improvement with UPA vs PBO was also observed for change from BL in PGA of pain NRS scores over time, as well as in BASDAI spinal pain and joint pain/swelling and SF-36 bodily pain and pain interference at weeks 12 and 24. In SELECT-PsA 1 significantly higher proportions of pts receiving UPA 30 mg QD vs ADA 40 mg EOW achieved improvements in most pain assessments as early as wk 2 which were sustained through wk 24; improvements in several assessments were also significantly greater with UPA 15 mg QD vs ADA 40 mg EOW at wk 24 (nominal $P < 0.05$; **Data will be presented**).

Conclusion: In pts with active PsA who had inadequate response to non-biologic or biologic DMARDs, a greater proportion of pts treated with UPA vs PBO achieved rapid, significant, and clinically meaningful reductions in pain across multiple pain assessments. The reductions in pain were sustained over 24 wks.

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POS1048

IN PHASE-3 TRIALS DISCOVER 1 & 2, GUSELKUMAB REDUCED FATIGUE OVER 52 WEEKS IN PATIENTS WITH PSORIATIC ARTHRITIS AND DEMONSTRATED INDEPENDENT TREATMENT EFFECTS ON FATIGUE AFTER ADJUSTMENT FOR CLINICAL RESPONSE (ACR20)

P. Rahman¹, P. Helliwell², A. Deodhar³, A. Kollmeier⁴, E. C. Hsia^{4,5}, B. Zhou⁶, X. Lin⁷, C. Han⁸, P. J. Mease⁹. ¹Memorial University of Newfoundland, Discipline of Medicine, Faculty of Medicine, St. Johns, Canada; ²University of Leeds, Clinical Rheumatology, Leeds, United Kingdom; ³Oregon Health & Science University, Division of Arthritis & Rheumatic Diseases, Oregon, United States of America; ⁴Janssen Research & Development, LJ IMMUNOLOGY, Spring House, United States of America; ⁵University of Pennsylvania School of Medicine, Division of Rheumatology, Philadelphia, United States of America; ⁶Janssen Research & Development, CLINICAL BIOSTATS PA, Spring House, United States of America; ⁷Janssen Research & Development, SMM-PA, Spring House, United States of America; ⁸Janssen Research & Development, STRATEGIC MKT ACCESS, Spring House, United States of America; ⁹Swedish Medical Center/Providence St Joseph Health and University of Washington School of Medicine, Department of Internal Medicine, Seattle, United States of America

Background: DISCOVER 1 & 2 are phase-3 trials of guselkumab (GUS, an IL-23 inhibitor) in patients with psoriatic arthritis (PsA). In both trials, treatment with GUS led to significantly more improvement than placebo (PBO) in the primary endpoint (American College of Rheumatology 20% improvement criteria [ACR20]) and in other measures of arthritis and psoriasis at week (w) 24,^{1,2} and these improvements were maintained through 1 year of active treatment.^{3,4}

Objectives: To evaluate the effect of GUS on fatigue in DISCOVER 1 & 2 using the patient reported outcome (PRO) FACIT-Fatigue, which has demonstrated content validity and strong psychometric properties in clinical trials.⁵

Methods: DISCOVER 1 & 2 enrolled patients with active PsA, despite non-biologic DMARDs or NSAIDs, who were biologic naïve except ~30% of patients in DISCOVER 1 who had received 1-2 TNFi. Patients were randomized (1:1:1) in a blinded fashion to subcutaneous GUS 100 mg at w0, w4, then every (q) 8w; GUS 100 mg q4w; or matching PBO. At w24, PBO patients were switched to GUS q4w. Concomitant treatment with select non-biologic DMARDs, oral corticosteroids, and NSAIDs was allowed. The FACIT-Fatigue is a 13-item PRO assessing fatigue and its impact on daily activities and function over the past 7 days, total score ranging from 0 to 52, higher score denoting less fatigue. A change of ≥4 points is considered clinically meaningful.⁵ The change from baseline in FACIT-Fatigue presented below is based on observed data. Mediation analysis⁶ was applied to the treatment effect of GUS on FACIT-Fatigue to estimate the natural direct and indirect effects, after adjusting for ACR20 response (Table 1).

Results: At baseline in DISCOVER 1 & 2, the mean FACIT-fatigue scores (SD) were 30.4 (10.4) and 29.7 (9.7), respectively, indicating that patients with PsA experienced fatigue worse than the general population. At w24 in the DISCOVER trials, treatment with GUS led to significant improvements in FACIT-Fatigue scores compared with PBO, as early as w16 in DISCOVER 1 and w8 in DISCOVER 2. Improvements in fatigue were similar between GUS q4w and q8w

doses, and the improvements at w24 were maintained through w52 (Figure 1). After a switch to GUS q4w at w24, PBO patients achieved FACIT-Fatigue scores that were comparable to those of GUS patients (Figure 1). 54%-63% of GUS patients compared with 35%-46% of PBO patients achieved clinically meaningful improvement (≥4 points) in FACIT-Fatigue at w24 (P≤0.003). At w52, 61%-70% of both GUS and PBO to GUS groups reached this improvement. As evaluated by mediation analysis at w24, GUS had independent positive treatment effects on fatigue (12%-36% in the q8w GUS dosing group and 69%-70% in the q4w GUS group) after adjustment for ACR20 response (Table 1).

Conclusion: In 2 phase-3 trials, GUS treatment improved fatigue when compared to PBO during PBO-controlled periods and maintained improvements through 1 year of active treatment. Substantial proportions of those effects were independent of the effects on ACR20, especially for the q4w dosing group.

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Table 1. Mediation Analysis: Guselkumab Has Direct Effects and Indirect Effects (Mediated through ACR20) on Fatigue in PsA

	Effect	GUS 100 mg q8w vs. PBO (95% CI)	GUS 100 mg q4w vs. PBO (95% CI)
DISCOVER-1	Total Effect	3.1 (1.0, 5.2)	3.8 (1.9, 5.4)
	% Direct Effect	(p<0.02) 11.7%	(p<0.02) 68.5%
	% Indirect effect mediated by ACR20	88.3%	31.5%
DISCOVER-2	Total Effect	4.0 (2.4, 5.5)	3.6 (2.1, 5.0)
	% Direct Effect	(p<0.02) 36.3%	(p<0.02) 69.7%
	% Indirect effect mediated by ACR20	63.7%	30.3%

ACR, American College of Rheumatology; CI, confidence interval; GUS, guselkumab; PBO, placebo; PsA, psoriatic arthritis; q4w, every 4 weeks; q8w, every 8 weeks

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POS1049

EFFECT OF FILGOTINIB ON PASDAS: DRIVERS OF LOW AND VERY LOW ACTIVITY UP TO WEEK 100

L. C. Coates¹, P. J. Mease^{2,3}, P. Helliwell⁴, F. Van den Bosch⁵, M. Trivedi⁶, M. Alani^{6,7}, F. O. Le Brun⁸, R. Besuyen⁹, L. Gheyle¹⁰, E. Gvozdenovic¹¹, D. D. Gladman¹². ¹University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom;