



Patient-Reported Outcomes in Psoriatic Arthritis Patients with an Inadequate Response to Biologic Disease-Modifying Antirheumatic Drugs: SELECT-PsA 2

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ABSTRACT

Introduction: Psoriatic arthritis (PsA) has a major impact on health-related quality of life (HRQOL) and other patient-reported outcomes (PROs), important components in the assessment of therapeutic efficacy. We evaluated the impact of upadacitinib on PROs in PsA patients with inadequate responses or intolerance to

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biologic disease-modifying anti-rheumatic drugs (bDMARD-IR).

Methods: Patients enrolled in the phase 3 SELECT-PsA 2 randomized controlled trial (RCT) received 56 weeks of oral upadacitinib 15 mg QD, upadacitinib 30 mg QD, or placebo switched to either dose of upadacitinib at week 24. PROs included patient global assessment of disease activity (PtGA), pain, physical function (HAQ-DI), health-related quality of life (SF-36 physical (PCS) and mental (MCS) component summary and domain scores), fatigue (FACIT-F), psoriasis symptom severity (SAPS), and work productivity (WPAI). Mean changes from baseline in PROs, improvements \geq minimum clinically important differences (MCID) and scores \geq normative values, and maintenance of improvements were assessed.

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Results: At weeks 12 and 24, patients treated with either upadacitinib dose reported statistically and nominally significant improvements from baseline across all PROs versus placebo ($p \leq 0.05$), except the WPAI absenteeism domain, which were maintained or further improved to week 56. A significantly greater proportion of patients receiving either upadacitinib dose reported improvements \geq MCID and scores \geq normative values versus placebo (nominal $p \leq 0.01$) in most PROs at weeks 12 and 24, with clinically meaningful improvements continuing to week 56. Improvements \geq MCID were reported as early as week 2 in PtGA, pain, and HAQ-DI.

Conclusions: Upadacitinib provides rapid, clinically meaningful, and sustained improvements in PROs reported by bDMARD-IR PsA patients. SELECT-PsA 2 ClinicalTrials.gov number, NCT03104374.

Keywords: Activity; Biologic disease-modifying anti-rheumatic drugs; Pain; Patient-reported outcomes; Physical function; Psoriatic arthritis; Quality of life; Work productivity; Upadacitinib

Key Summary Points

Why carry out this study?

Psoriatic arthritis (PsA) has a major impact on a patient's health-related quality of life, an important component when evaluating treatment response.

We evaluated whether the Janus kinase inhibitor upadacitinib improved patient-reported outcomes (PROs) in PsA patients with inadequate responses to biologic disease-modifying anti-rheumatic drugs from the phase 3 SELECT-PsA 2 trial.

What was learned from the study?

Significant and clinically meaningful (e.g., improvements \geq minimal clinically important difference) in PROs were reported with upadacitinib at 12 weeks, which were maintained through 56 weeks.

PRO scores \geq normative values were reported with upadacitinib, indicating that such a goal is achievable in this patient population.

INTRODUCTION

Psoriatic arthritis (PsA) is a multisystem, heterogeneous inflammatory disease that may present with multiple clinical manifestations, including plaque psoriasis, arthritis, dactylitis, enthesitis, and axial skeleton involvement [1]. The burden of disease is substantial, with significant negative impacts on health-related quality of life (HRQOL), physical and emotional functioning, ability to perform daily activities, and work productivity [2, 3]. Current treatment options for PsA include disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate; biologic DMARDs (bDMARDs), including tumor necrosis factor (TNF), Interleukin (IL)-12/23, IL-23, and IL-17A inhibitors; and targeted synthetic DMARDs, such as Janus kinase (JAK) inhibitors [4–6]. Despite the recent increase in available advanced therapies for PsA, a significant number of patients still fail to achieve adequate disease control, resulting in substantial HRQOL impairments, which are reported in patient surveys, and highlighting a continued need for novel and effective treatment options.

Upadacitinib is an oral, reversible JAK inhibitor engineered for increased selectivity for JAK1 over other members of the JAK family (JAK2, JAK3, and tyrosine kinase 2 [TYK2]) [7]. Upadacitinib is approved in Europe for patients with PsA and ankylosing spondylitis with inadequate responses or intolerance to DMARDs and conventional therapy, respectively, and in the United States and Europe for patients with moderate-to-severe rheumatoid arthritis with inadequate responses or intolerance to methotrexate, based on the findings from eight separate phase 3 clinical trials [8–17]. In the phase 3 SELECT-PsA 2 trial, upadacitinib 15 or 30 mg once daily (QD) provided significant improvements in clinical manifestations of PsA, such as musculoskeletal (peripheral

arthritis, enthesitis, dactylitis, and axial) symptoms and psoriasis, in patients who were refractory to bDMARDs compared with placebo [15].

Patient-reported outcomes (PROs) assess the impact of disease from a patient perspective and are recommended as one of the core components in the evaluation of treatment responses in randomized controlled trials (RCTs) in PsA [18]. We present here analyses from the SELECT-PsA 2 RCT that compare reported improvements in PROs with both doses of upadacitinib versus placebo, which are clinically meaningful as well as scores that meet or exceed normative values.

METHODS

Study design and patients

Detailed study information has been previously reported [15]. SELECT-PsA 2 (NCT03104374) is a phase 3, placebo-controlled, multicenter RCT in patients ≥ 18 years of age with a clinical diagnosis of PsA with symptom onset ≥ 6 months prior to screening and active disease at baseline who fulfilled the Classification Criteria for PsA (CASPAR), and had a diagnosis or documented history of plaque psoriasis, and inadequate responses or intolerance to ≥ 1 bDMARD treatment (bDMARD-IR). Patients were excluded if they had prior exposure to JAK inhibitors or current treatment with ≥ 2 non-bDMARDs.

Patients were randomized 2:2:1:1 to receive oral upadacitinib 15 mg QD, upadacitinib 30 mg QD, or placebo switched to either upadacitinib 15 mg once daily (QD) or upadacitinib 30 mg QD at week 24. Treatment in the randomized controlled portion of the trial was 24 weeks, with blinding to 56 weeks and an open-label extension up to 5 years. Background treatment with nonsteroidal anti-inflammatory drugs, corticosteroids, and ≤ 2 non-bDMARDs was allowed, but not required, with rescue therapy permitted at week 16 and optimization of background therapy after week 36.

The trial was approved by the independent ethics committees or institutional review boards at all study sites and conducted in accordance

with the Declaration of Helsinki and consistent with International Conference on Harmonisation Good Clinical Practice and Good Epidemiology Practices, along with all applicable local regulatory requirements. All patients provided written approval before enrollment, and patient data were de-identified and complied with patient confidentiality requirements.

Outcomes

Multiplicity-controlled secondary PRO endpoints included changes from baseline at week 12 in Health Assessment Questionnaire-Disability Index (HAQ-DI; minimal clinically important difference [MCID]: ≥ 0.35 -unit decrease; normative value: ≤ 0.25 units) [19, 20], Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F; MCID: ≥ 4 -point increase; normative value: ≥ 40.1 points) [21, 22], 36-Item Short Form Health Survey (SF-36) physical component summary (PCS) score (MCID: ≥ 2.5 -point increase; normative value: ≥ 50 points) [23–25], and change from baseline at week 16 in Self-Assessment of Psoriasis Symptoms (SAPS) (range: 0–110, with higher scores indicating worse patient-reported psoriasis symptoms) [26]. Additional PROs evaluated included Patient Global Assessment of Disease Activity (PtGA) and patient pain (0–10 numerical rating scale [NRS]; MCID: ≥ 1 -point decrease; normative value: ≤ 2 points [PtGA]) [27–29], SF-36 mental component summary (MCS; MCID: ≥ 2.5 -point increase; normative value: ≥ 50 points) [23–25] and domains (MCID: ≥ 5 -point increase) [23, 24], EuroQoL 5-Dimension 5-Level index score (EQ-5D-5L; MCID: ≥ 0.05 -unit increase; normative value: ≥ 0.915) [30, 31], Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; MCID: ≥ 1.1 -point decrease) and morning stiffness (mean of BASDAI questions 5 and 6; MCID: ≥ 1 -point decrease) [32], BASDAI 50, Work Productivity and Activity Impairment (WPAI) [33, 34], and itch (SAPS question 2; 0–10 NRS, with higher scores indicating worse itch).

SF-36 PCS and MCS scores were norm-based with a mean value of 50 and standard deviation of 10; SF-36 domains were scored from 0 to 100

with higher scores indicating better HRQOL [23–25]. BASDAI assessments were assessed in patients with presence of psoriatic spondylitis at baseline determined by the investigator (34% of total population). The WPAI activity impairment domain was assessed in all patients, while presenteeism, overall work impairment, and absenteeism domains only in those employed at baseline [33, 34]. SAPS consists of an 11-item patient self-assessment of psoriasis symptoms that includes questions on severity of pain, itching, redness, scaling, flaking, bleeding, burning, stinging, tenderness, pain due to skin cracking, and joint pain in the areas affected by psoriasis [26].

Following baseline assessments, PtGA, pain, and HAQ-DI were assessed starting at week 2; other PROs at week 12 (except SAPS, which started at week 16).

Statistical methods

Analyses were performed using the full analysis set population, including all randomized patients who received \geq one dose of study drug. Demographic and baseline characteristics are summarized with descriptive statistics (mean, standard deviation for continuous endpoints, and n [%] for categorical endpoints). For analysis of changes from baseline, within-group least squares (LS) means and 95% confidence intervals (CI) at weeks 12, 24, and 56; and between-group nominal p values at weeks 12 and 24 were based on mixed-effect model repeated measurement (MMRM) analysis using an unstructured variance–covariance matrix, including treatment, visit, treatment-by-visit interaction, and the stratification factor current DMARD use (yes/no) as fixed factors and baseline measurement as a continuous fixed covariate. MMRM analysis used observed longitudinal data up to the respective time point prior to study drug premature discontinuation, with as-observed data reported. Spidergrams were used to illustrate changes from baseline in SF-36 domain scores from 0 to 100 for each treatment group against a combined baseline population and US normative values age- and

gender-matched matched to the protocol population [35].

The proportions of patients reporting BASDAI 50, improvements \geq MCID and scores \geq normative values at weeks 12 and 24 were evaluated using non-responder imputation for missing responses. Persistence of improvements \geq MCID from weeks 12 to 56 was determined using as-observed data. The number needed to treat (NNT) to obtain 1 additional MCID response at weeks 12 and 24 for each upadacitinib dose compared with placebo was defined as the reciprocal of the response rate difference between upadacitinib and placebo, with missing responses imputed using non-responder imputation. p values were calculated using Cochran–Mantel–Haenszel test adjusting for the main stratification factor of current DMARD use (yes/no). Statistical significance defined as $p < 0.05$ was nominal for non-multiplicity-controlled endpoints.

RESULTS

A total of 642 patients were randomized; 641 patients received at least one dose of study drug (placebo, $n = 212$; upadacitinib 15 mg, $n = 211$; upadacitinib 30 mg, $n = 218$) [15]. Baseline PROs, demographics, disease characteristics, and disease severity were generally similar across treatment arms (Table 1).

Improvement from baseline in PROs

Compared with placebo, significant improvements from baseline to weeks 12 and 24 were reported with upadacitinib 15 and 30 mg across all PROs ($p < 0.05$, nominal except for week 12 multiplicity controlled endpoints of HAQ-DI, FACIT-F, SF-36 PCS, and SAPS, Table 2), with exception of WPAI absenteeism, assessed only in those patients working outside the home ($n = 100$ [placebo], 120 [upadacitinib 15 mg], and 119 [upadacitinib 30 mg]; $p \geq 0.08$). Mean improvements were maintained or further improved through week 56 (Table 2). Greater improvements from baseline in PtGA, pain, and HAQ-DI were reported as early as week 2 with both doses of upadacitinib compared with

Table 1 Baseline demographics and characteristics

	Placebo (N = 212)	Upadacitinib 15 mg QD (N = 211)	Upadacitinib 30 mg QD (N = 218)
Female, %	56.6	53.6	52.8
Age (years), mean (SD)	54.1 (11.5)	53.0 (12.0)	53.0 (11.9)
White race, %	87.7	86.7	89.9
Duration since PsA diagnosis (years), mean (SD)	11.0 (10.3)	9.6 (8.4)	9.7 (8.7)
Body mass index (kg/m ²), mean (SD)	31.8 (7.5)	31.5 (7.4)	30.8 (7.0)
Number of prior failed bDMARDs, %			
0	8.5	7.6	7.8
1	63.7	59.7	59.6
2	16.5	16.6	21.1
≥ 3	11.3	16.1	11.5
Current use of ≥ 1 non-bDMARD at baseline, %	47.2	46.4	45.0
Presence of dactylitis ^a , %	30.2	26.1	22.9
Presence of enthesitis ^b , %	67.9	63.0	69.7
TJC (68 joints), mean (SD)	25.3 (17.6)	24.9 (17.3)	24.2 (15.9)
SJC (66 joints), mean (SD)	12.0 (8.9)	11.3 (8.2)	12.9 (9.4)
% BSA-PsO ≥ 3%, %	61.8	61.6	60.1
PtGA 0–10, NRS, mean (SD)	6.8 (2.0)	6.8 (1.9)	6.7 (2.2)
Pain 0–10, NRS, mean (SD)	6.6 (2.1)	6.4 (2.1)	6.2 (2.2)
HAQ-DI, mean (SD)	1.23 (0.69)	1.10 (0.61)	1.19 (0.66)
FACIT-F, mean (SD)	26.6 (12.7)	27.6 (11.9)	28.8 (12.3)
SF-36 PCS, mean (SD)	34.5 (9.3)	35.0 (8.5)	34.8 (8.7)
SF-36 MCS, mean (SD)	43.9 (12.2)	44.7 (11.2)	46.0 (12.2)
SF-36 domains, mean (SD)			
PF	40.4 (27.3)	43.7 (26.6)	42.4 (26.4)
RP	40.6 (26.9)	44.1 (26.0)	43.7 (25.6)
BP	34.3 (19.6)	35.2 (18.0)	35.4 (18.3)
GH	43.0 (19.5)	40.7 (18.8)	42.8 (19.5)
VT	34.6 (21.1)	37.4 (20.1)	39.9 (21.4)
SF	55.7 (29.0)	56.9 (26.2)	59.8 (28.2)
RE	61.5 (31.6)	65.0 (28.2)	65.5 (29.1)

Table 1 continued

	Placebo (<i>N</i> = 212)	Upadacitinib 15 mg QD (<i>N</i> = 211)	Upadacitinib 30 mg QD (<i>N</i> = 218)
MH	60.2 (21.0)	60.9 (21.1)	62.8 (21.7)
EQ-5D-5L, mean (SD)	0.59 (0.26)	0.61 (0.24)	0.61 (0.24)
BASDAI ^c , mean (SD)	6.1 (2.2)	5.9 (2.1)	5.8 (2.3)
Morning stiffness ^{c,d} , mean (SD)	5.8 (2.5)	6.0 (2.5)	5.7 (2.7)
SAPS, mean (SD)	52.9 (29.2)	50.4 (27.4)	47.1 (29.2)
Itch ^c , mean (SD)	5.4 (3.2)	5.3 (3.1)	4.7 (3.2)
WPAI AI, mean (SD)	55.1 (26.5)	52.0 (26.1)	50.2 (28.3)
WPAI presenteeism ^f , mean (SD)	41.9 (27.3)	41.1 (24.4)	39.9 (24.4)
WPAI OWI ^f , mean (SD)	49.4 (31.5)	48.5 (29.6)	44.9 (27.2)
WPAI absenteeism ^f , mean (SD)	16.3 (27.5)	15.8 (29.1)	9.6 (21.1)

AI activity impairment, BASDAI Bath Ankylosing Spondylitis Disease Activity Index, BP bodily pain, BSA body surface area, bDMARD biologic DMARD, DMARD disease-modifying anti-rheumatic drug, EQ-5D-5L EuroQoL 5-Dimension 5-Level index score, FACIT-F Functional Assessment of Chronic Illness Therapy-Fatigue, GH general health, HAQ-DI Health Assessment Questionnaire-Disability Index, MCS mental component summary, MH mental health, NRS numerical rating scale, OWI overall work impairment, PCS physical component summary, PF physical functioning, Ps psoriasis, PsA psoriatic arthritis, PtGA Patient Global Assessment of Disease Activity, QD once daily, RE role-emotional, RP role-physical, SAPS Self-Assessment of Psoriasis Symptoms, SD standard deviation, SF social functioning, SF-36 36-Item Short Form Health Survey, SJC swollen joint pain, TJC tender joint count, VT vitality, WPAI Work Productivity and Activity Impairment

^a Defined as Leeds Dactylitis Index > 0

^b Defined as Leeds Enthesitis Index > 0

^c Reported only for patients with investigator-determined psoriatic spondylitis at baseline

^d Mean of BASDAI Q5 and Q6

^e SAPS question 2

^f Reported only for patients who were employed at baseline. *N* at baseline for presenteeism

OWI, absenteeism: placebo: 95, 100, and 100; upadacitinib 15 mg QD: 113, 120, and 120; upadacitinib 30 mg QD: 116, 119, and 119

placebo, with statistically significant improvements based on nominal *p* values (Fig. 1). In patients receiving placebo who were switched to upadacitinib 15 or 30 mg at week 24, rapid improvements in PtGA, pain, HAQ-DI, and FACIT-F were reported with similar responses at week 56 to those originally randomized to upadacitinib (Fig. 1).

Significant improvements from baseline in all SF-36 domain scores were reported with both doses of upadacitinib compared to placebo at week 12 (nominal $p \leq 0.01$ for all domains),

which continued to week 24 (Table 2, Fig. 2, and Fig. S1 in the electronic supplementary material). BASDAI 50 responses were reported by significantly more patients receiving upadacitinib 15 or 30 mg at weeks 12 (20 and 29%) and 24 (32 and 35%) than placebo (7 and 4%) (nominal $p < 0.05$). Additionally, a greater percentage of patients reported resolution of itch with both doses of upadacitinib versus placebo at weeks 16 and 24, with 31 and 47% of patients reporting itch resolution at week 24 with upadacitinib 15 and 30 mg, respectively,

Table 2 LS mean change (95% CI) from baseline in PRO scores at weeks 12, 24, and 56 (MMRM)

	Placebo		Upadacitinib 15 mg QD			Upadacitinib 30 mg QD		
	Week 12 (N = 185)	Week 24 (N = 169)	Week 12 (N = 201)	Week 24 (N = 183)	Week 56 (N = 164)	Week 12 (N = 206)	Week 24 (N = 191)	Week 56 (N = 171)
PtGA	− 0.6 (− 0.9, − 0.3)	− 0.8 (− 1.2, − 0.5)	− 2.3 [†] (− 2.6, − 2.0)	− 2.6 [†] (− 2.9, − 2.3)	− 2.8 (− 3.2, − 2.5)	− 2.9 [†] (− 3.2, − 2.6)	− 3.1 [†] (− 3.5, − 2.8)	− 3.2 (− 3.5, − 2.8)
Pain	− 0.5 (− 0.8, − 0.2)	− 0.7 (− 1.1, − 0.4)	− 1.9 [†] (− 2.2, − 1.6)	− 2.2 [†] (− 2.5, − 1.9)	− 2.6 (− 2.9, − 2.2)	− 2.6 [†] (− 2.8, − 2.3)	− 2.8 [†] (− 3.1, − 2.5)	− 2.8 (− 3.1, − 2.4)
HAQ-DI	− 0.10 (− 0.16, − 0.03)	− 0.08 (− 0.15, − 0.01)	− 0.3 [†] (− 0.37, − 0.24)	− 0.33 [†] (− 0.40, − 0.26)	− 0.35 (− 0.43, − 0.27)	− 0.41 [†] (− 0.47, − 0.35)	− 0.45 [†] (− 0.52, − 0.38)	− 0.49 (− 0.56, − 0.41)
FACIT-F	1.3 (0.1, 2.5)	1.4 (0.0, 2.7)	5.0 [†] (3.8, 6.1)	4.7 [†] (3.4, 6.0)	6.1 (4.7, 7.5)	6.1 [†] (4.9, 7.2)	6.9 [†] (5.6, 8.1)	6.8 (5.4, 8.1)
SF-36 PCS	1.6 (0.5, 2.6)	1.3 (0.2, 2.5)	5.1 [†] (4.1, 6.1)	6.4 [†] (5.3, 7.5)	7.2 (6.0, 8.4)	7.0 [†] (6.0, 8.0)	8.3 [†] (7.2, 9.4)	8.1 (6.9, 9.3)
SF-36 MCS	− 0.1 (− 1.3, 1.0)	0.4 (− 1.0, 1.7)	2.8 [†] (1.8, 3.9)	2.3 [†] (1.0, 3.5)	3.3 (2.0, 4.6)	3.1 [†] (2.1, 4.2)	2.7 [†] (1.4, 3.9)	3.3 (2.0, 4.5)
SF-36 domains								
PF	1.1 (− 1.8, 3.9)	1.9 (− 1.3, 5.0)	12.5 [†] (9.8, 15.2)	14.4 [†] (11.4, 17.4)	17.5 (14.3, 20.7)	16.5 [†] (13.8, 19.2)	19.0 [†] (16.1, 22.0)	19.6 (16.4, 22.7)
RP	4.0 (1.0, 7.0)	3.6 (0.2, 6.9)	11.5 [†] (8.6, 14.3)	13.0 [†] (9.8, 16.3)	17.4 (14.0, 20.8)	16.5 [†] (13.7, 19.3)	19.0 [†] (15.8, 22.2)	18.5 (15.2, 21.9)
BP	5.2 (2.4, 8.0)	5.8 (2.8, 8.8)	16.4 [†] (13.7, 19.0)	19.1 [†] (16.2, 22.0)	21.1 (17.8, 24.5)	20.7 [†] (18.1, 23.3)	23.1 [†] (20.3, 26.0)	23.7 (20.4, 26.9)
GH	1.3 (− 0.8, 3.5)	− 0.2 (− 2.5, 2.1)	6.3 [†] (4.2, 8.3)	8.1 [†] (5.9, 10.3)	8.6 (6.9, 11.0)	9.4 [†] (7.4, 11.4)	10.3 [†] (8.2, 12.5)	9.7 (7.3, 12.0)
VT	1.9 (− 0.4, 4.3)	3.0 (0.3, 5.7)	10.0 [†] (7.8, 12.2)	10.7 [†] (8.1, 13.2)	13.0 (10.3, 15.7)	10.4 [†] (8.2, 12.6)	12.6 [†] (10.1, 15.2)	13.4 (10.7, 16.0)
SF	1.0 (− 2.1, 4.1)	0.7 (− 2.5, 3.9)	10.8 [†] (7.8, 13.7)	12.3 [†] (9.2, 15.4)	13.0 (9.6, 16.3)	14.4 [†] (11.5, 17.3)	13.8 [†] (10.7, 16.8)	14.3 (11.0, 17.6)
RE	− 0.5 (− 3.3, 2.4)	1.5 (− 1.8, 4.8)	7.7 [†] (4.9, 10.4)	6.0 (2.9, 9.2)	8.9 (5.9, 12.0)	10.3 [†] (7.5, 13.0)	9.2 [†] (6.1, 12.3)	10.8 (7.8, 13.8)
MH	0.1 (− 2.0, 2.1)	0.7 (− 1.7, 3.2)	5.8 [†] (3.8, 7.8)	5.2 [†] (2.9, 7.5)	8.2 (5.8, 10.6)	6.6 [†] (4.7, 8.6)	6.6 [†] (4.3, 8.9)	7.8 (5.4, 10.1)
EQ-5D-5L	0.03 (0.01, 0.06)	0.03 (0.01, 0.06)	0.12 [†] (0.10, 0.15)	0.13 [†] (0.10, 0.16)	0.15 (0.12, 0.17)	0.15 [†] (0.12, 0.17)	0.16 [†] (0.13, 0.19)	0.16 (0.14, 0.19)
BASDAI ^a	− 0.3 (− 0.7, 0.2)	− 0.2 (− 0.7, 0.3)	− 1.4 [†] (− 1.8, − 0.9)	− 2.1 [†] (− 2.5, − 1.6)	− 2.2 (− 2.7, − 1.6)	− 2.0 [†] (− 2.5, − 1.6)	− 2.4 [†] (− 2.9, − 1.9)	− 2.4 (− 3.0, − 1.9)
BASDAI 50 ^{ab}	6.7 (1.0, 12.3)	4.0 (0.0, 8.4)	19.7 [†] (10.8, 28.7)	31.6 [†] (21.1, 42.0)	46.3 (33.0, 59.6)	29.4 [†] (18.6, 40.2)	35.3 [†] (23.9, 46.7)	41.2 (27.7, 54.7)
Morning stiffness ^{ac}	− 0.5 (− 0.8, − 0.1)	− 0.7 (− 1.1, − 0.4)	− 1.9 [†] (− 2.2, − 1.6)	− 2.3 [†] (− 2.6, − 2.0)	− 2.5 (− 2.9, − 2.2)	− 2.3 [†] (− 2.6, − 2.0)	− 2.8 [†] (− 3.1, − 2.5)	− 2.8 (− 3.1, − 2.5)
SAPS ^d	− 1.5 (− 4.7, 1.8)	− 6.2 (− 9.4, − 2.9)	− 24.4 [†] (− 27.5, − 21.2)	− 25.3 [†] (− 28.4, − 22.1)	− 27.7 (− 30.5, − 24.9)	− 29.7 [†] (− 32.8, − 26.6)	− 31.7 [†] (− 34.7, − 28.6)	− 32.2 (− 35.0, − 29.5)
Itch ^{de}	− 0.2 (− 0.5, 0.2)	− 0.5 (− 0.9, − 0.1)	− 2.6 [†] (− 2.9, − 2.2)	− 2.7 [†] (− 3.1, − 2.4)	− 2.8 (− 3.2, − 2.5)	− 3.0 [†] (− 3.4, − 2.7)	− 3.4 [†] (− 3.8, − 3.1)	− 3.4 (− 3.7, − 3.0)

Table 2 continued

	Upadacitinib 15 mg QD		Upadacitinib 30 mg QD		
	Week 12 (N = 185)	Week 24 (N = 169)	Week 12 (N = 201)	Week 24 (N = 183)	Week 56 (N = 164)
WP/Al AI	– 3.1 (– 6.4, 0.1)	– 2.3 (– 5.9, 1.3)	– 14.1 [†] (– 17.2, – 11.0)	– 18.5 [†] (– 21.9, – 15.1)	– 21.1 (– 24.7, – 17.5)
WP/Al presenteism ^f	1.7 (– 3.0, 6.5)	– 1.1 (– 6.0, 3.9)	– 11.1 [†] (– 15.3, – 6.9)	– 13.2 [†] (– 17.6, – 8.9)	– 17.7 (– 22.3, – 13.1)
WP/Al OWI ^f	– 0.5 (– 5.8, 4.8)	0.3 (– 5.5, 6.0)	– 12.0 [†] (– 16.6, – 7.5)	– 10.6 [†] (– 15.6, – 5.7)	– 15.6 (– 21.4, – 9.9)
WP/Al absenteism ^f	– 5.2 (– 9.0, – 1.4)	– 0.7 (– 5.4, 4.0)	– 2.5 (– 5.8, 0.8)	1.4 (– 2.6, 5.4)	– 0.9 (– 5.9, 4.0)

AI activity impairment, BASDAI Bath Ankylosing Spondylitis Disease Activity Index, BP bodily pain, CI confidence interval, DMARD disease-modifying anti-rheumatic drug, EQ-5D-5L EuroQoL 5-Dimension 5-Level index score, FACIT-F Functional Assessment of Chronic Illness Therapy-Fatigue, GH general health, HAQ-DI Health Assessment Questionnaire-Disability Index, LS least squares, MCS mental component summary, MH mental health, MMRM Mixed-Effect Model Repeated Measurement, NRI non-responder imputation, OWI overall work impairment, PCS physical component summary, PF physical functioning, PRO patient-reported outcome, PGA Patient Global Assessment of Disease Activity, QD once daily, RE role-emotional, RP role-physical, SAPS Self-Assessment of Psoriasis Symptoms, SF social functioning, SF-36 36-Item Short Form Health Survey, VT vitality, WPAI Work Productivity and Activity Impairment

^a $p < 0.05$, ^b $p \leq 0.01$ and ^c $p \leq 0.001$ versus placebo, p values nominal except for week 12 multiplicity controlled endpoints of HAQ-DI, FACIT-F, SF-36 PCS, and SAPS

^d Reported only for patients with investigator-determined psoriatic spondylitis at baseline

^e Presented as response rate (95% CI). NRI. N: placebo: 75; Upadacitinib 15 mg QD: 76 (54 for week 56); and upadacitinib 30 mg QD: 68 (51 for week 56)

^f Mean of BASDAI Q5 and Q6

^g Assessed at week 16 instead of 12

^h SAPS question 2

ⁱ Reported only for patients who were employed at baseline. N at baseline for presentism

OWI, absenteeism: placebo: 95, 100, and 100; upadacitinib 15 mg QD: 113, 120, and 120; upadacitinib 30 mg QD: 116, 119, and 119

compared with 6–9% with placebo (Fig. S2 in the electronic supplementary material). Improvements with upadacitinib were maintained through week 56.

Clinically meaningful improvements in PROs

At week 12, a significantly greater proportion of patients receiving either dose of upadacitinib compared with placebo reported improvements \geq MCID across all PROs (including all eight SF-36 domains) (all nominal $p \leq 0.01$) with exception of SF-36 MCS score with upadacitinib 30 mg, which numerically, but not statistically, exceeded placebo (Fig. 3). The highest proportion of patients reporting improvements \geq MCID with upadacitinib were in PtGA (71 and 77% with 15 and 30 mg, respectively, vs. 46% placebo) and pain (68 and 76%, respectively, vs. 46% placebo) (Fig. 3). A significantly greater proportion of patients reported clinically meaningful improvements at week 2 with both doses of upadacitinib versus placebo (nominal $p \leq 0.01$) in PtGA (15 mg: 70%, 30 mg: 72%, placebo: 52%), pain (15 mg: 67%, 30 mg: 69%, placebo: 50%), and HAQ-DI (15 mg: 32%, 30 mg: 42%, placebo: 19%). NNTs to achieve one additional response \geq MCID ranged from 3.2 to 7.3 and 2.6 to 6.9 with upadacitinib 15 mg and 30 mg, respectively, across evaluated PROs (Fig. 3). Similar results were reported at week 24 (Fig. S3 in the electronic supplementary material). Among patients receiving upadacitinib reporting improvements \geq MCID at week 12, $\geq 80\%$ reported continued or further improved responses at week 56 across most PROs (Fig. S4 in the electronic supplementary material).

Scores \geq normative values in most PROs were reported by a significantly greater proportion of patients with both doses of upadacitinib versus placebo at week 12 (nominal $p < 0.05$; Fig. 4), with responses maintained at week 24 (Fig. S5 in the electronic supplementary material). At week 12, the proportion of patients receiving upadacitinib 15 mg and 30 mg reporting scores \geq normative values were 25% and 32%, respectively, in PtGA versus 9% with

placebo; 28% and 31%, respectively, in HAQ-DI versus 12% with placebo; and 29% and 35%, respectively, in FACIT-F versus 17% with placebo (Fig. 4a).

DISCUSSION

In this post hoc analysis of the phase 3 SELECT-PsA 2 study of PsA patients refractory or intolerant to bDMARDs, upadacitinib treatment provided significant and clinically meaningful improvements across a broad range of PROs after 12 and 24 weeks compared with placebo. In PtGA, pain, and HAQ-DI, these were reported as early as 2 weeks after treatment initiation. With upadacitinib, significantly greater percentages of patients reported PRO scores \geq normative values, reflective of a population without inflammatory arthritis. Additionally, NNTs ≤ 10 , considered economically and clinically meaningful [36], were calculated based on improvements \geq MCID with upadacitinib at weeks 12 and 24 across all PROs. Improvements in these PROs were maintained through week 56.

PROs reflect many important issues that significantly impact patients with PsA, including challenges in mental, physical, and social functioning, pain, fatigue, work-related disability, in addition to psoriatic, axial, and skin disease symptoms. Many of these symptoms and sequelae of disease are represented by the core domains recommended by the GRAPPA-OMERACT working group to be measured in all RCTs to evaluate treatment efficacy [2, 3, 18, 37–40]. In a recent qualitative interview study of PsA patients recruited through the FORWARD databank, joint pain and stiffness, skin symptoms, fatigue, and physical disability were identified as some of the most salient PsA symptoms [39]. Similarly, pain, fatigue, and poor HRQOL have been identified as some of the highest-ranking outcomes that patients would want treatment to remedy [40]. In an international survey of 1268 patients with PsA, moderate-to-major impairment was reported in 78, 62, and 69% of patients in physical activity, work productivity, and emotional/mental well-being, respectively [37]. In a separate study,

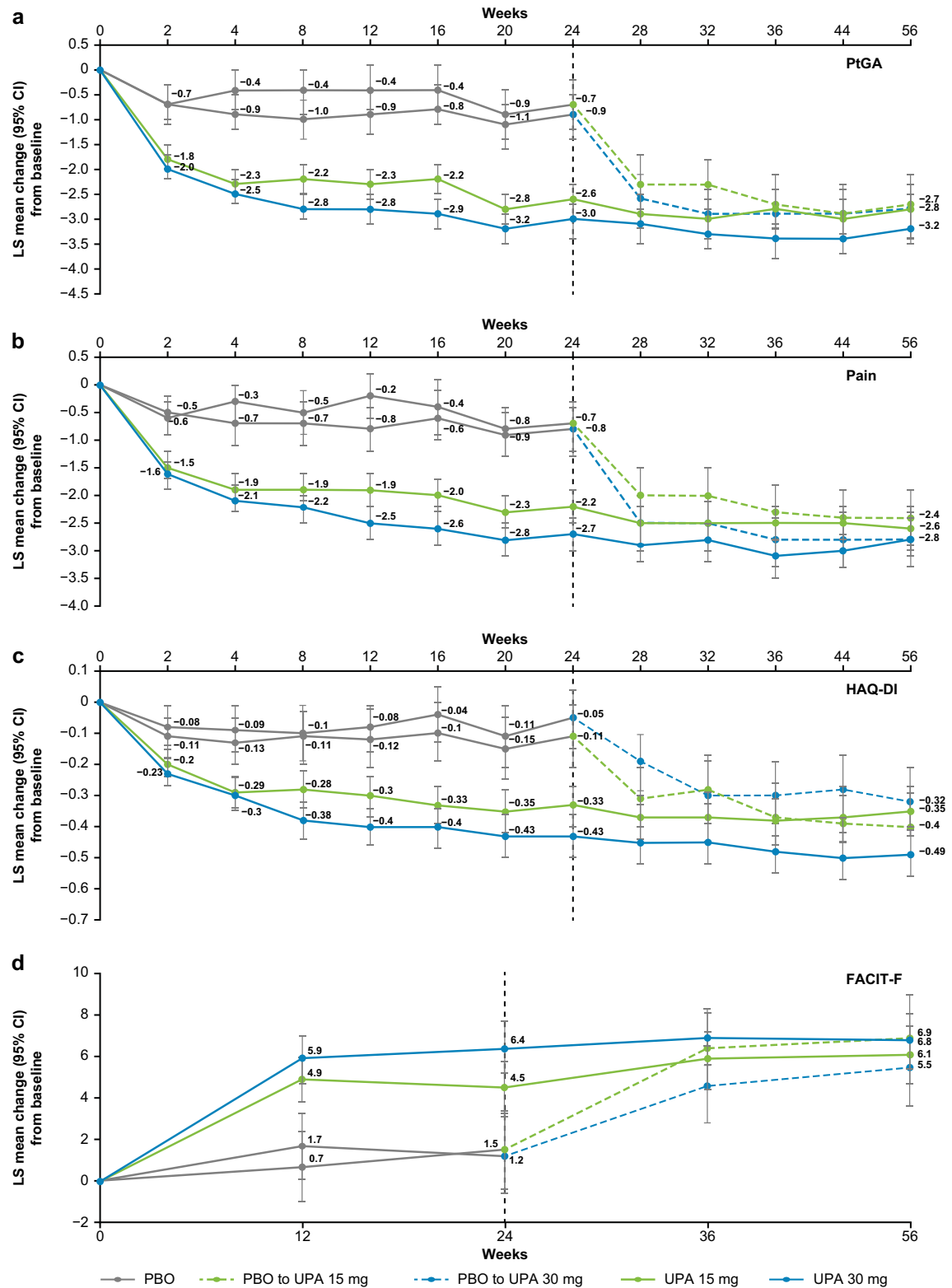


Fig. 1 Mean changes from baseline in PtGA, pain, HAQ-DI, and FACIT-F through 56 weeks (MMRM). **a** PtGA. **b** Pain. **c** HAQ-DI. **d** FACIT-F. *CI* confidence interval, *FACIT-F* Functional Assessment of Chronic Illness Therapy-Fatigue, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *LS* least squares, *MMRM* Mixed-Effect Model Repeated Measurement, *PBO* placebo, *PtGA* Patient Global Assessment of Disease Activity, *UPA* upadacitinib

approximately 50% of patients reported the social impact of PsA to include negative effects on personal relationships, relationships with

family and friends, and engagement in sports and recreational activities [37]. The results presented here demonstrate that upadacitinib has the potential to provide a substantial positive impact on symptoms, domains, and the impact of disease on HRQOL that most affect patients with PsA.

These results also complement the primary clinical findings from SELECT-PsA 2, where significant clinical improvements in musculoskeletal and psoriatic symptoms of PsA were observed with upadacitinib compared with placebo [15]. Additionally, the magnitude of improvements in PROs reported in this RCT in a

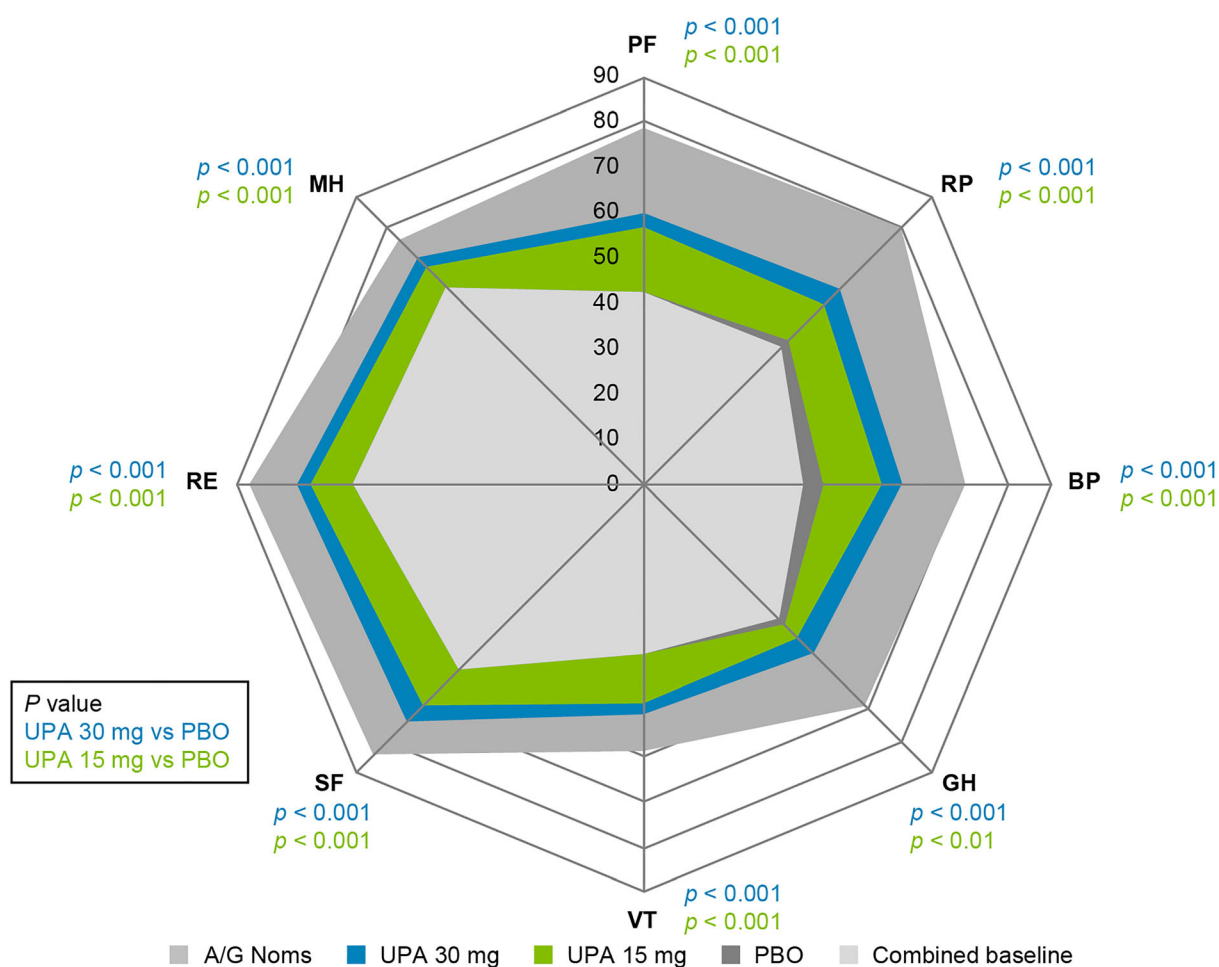
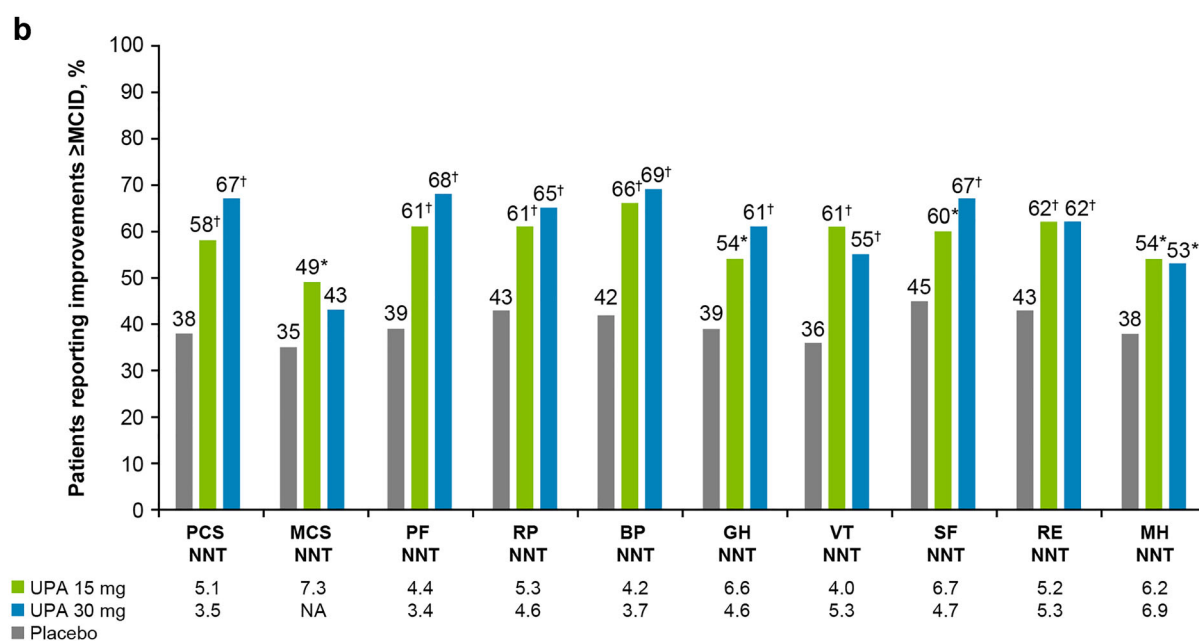
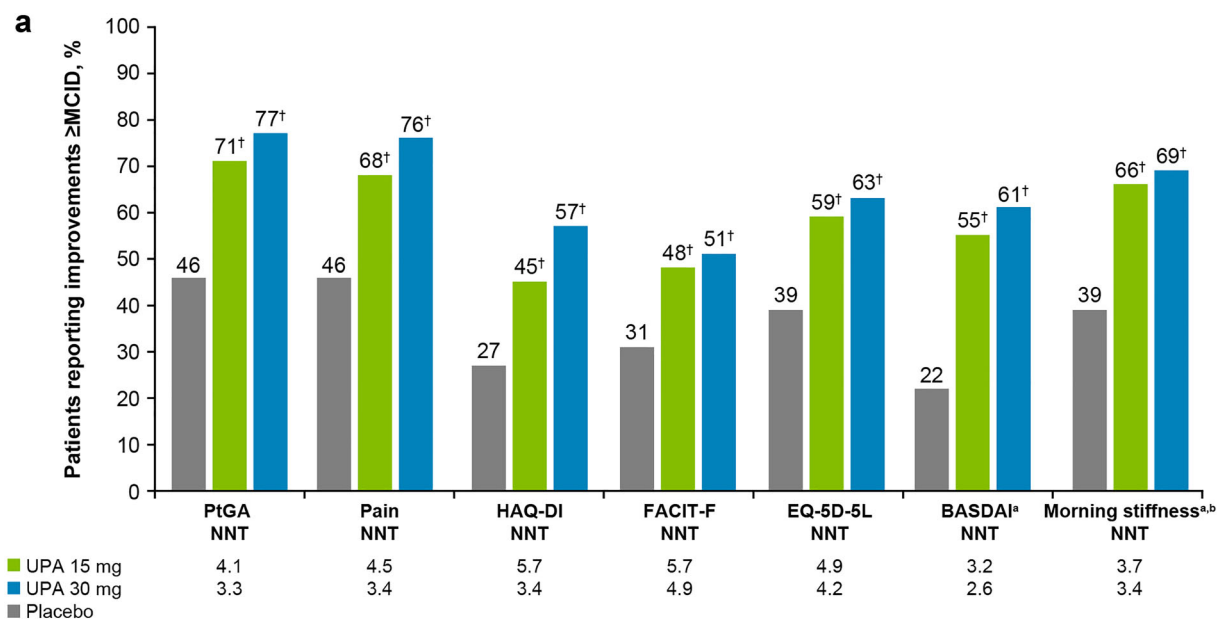


Fig. 2 Week 12 SF-36 domain scores in comparison to age- and gender-matched normative values (MMRM). *p* values nominal. *A/G* age-gender adjusted, *BL* baseline, *BP* bodily pain, *DMARD* disease-modifying anti-rheumatic drug, *GH* general health *MH* mental health,

MMRM Mixed-Effect Model Repeated Measurement, *PBO* placebo, *PF* physical functioning, *RE* role-emotional, *RP* role-physical, *SF* social functioning, *SF-36* 36-Item Short Form Health Survey, *UPA* upadacitinib, *VT* vitality



◀**Fig. 3** Proportion of patients reporting improvements \geq MCID and NNTs in PROs at week 12 (NRI). **a** PROs excluding SF-36. **b** SF-36 PCS, MCS, and domains. * $p \leq 0.01$ and $^{\dagger}p \leq 0.001$ versus placebo. p values nominal. ^aReported only for patients with investigator-determined psoriatic spondylitis at baseline. ^bMean of BASDAI questions 5 and 6. NNT not calculated for non-significant results for upadacitinib versus placebo. MCID definitions: ≥ 1 -point decrease (PtGA, pain, and morning stiffness), ≥ 0.35 -unit decrease (HAQ-DI), ≥ 4 -point increase (FACIT-F), ≥ 0.05 -unit increase (EQ-5D-5L), ≥ 1.1 -point decrease (BASDAI), ≥ 2.5 -point increase (SF-36 PCS and MCS), and ≥ 5 -point increase (SF-36 domains). *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BP* bodily pain, *EQ-5D-5L* EuroQoL 5-Dimension 5-Level index score, *FACIT-F* Functional Assessment of Chronic Illness Therapy-Fatigue, *GH* general health, *HAQ-DI* Health Assessment Questionnaire-Disability Index, *MCID* minimal clinically important difference, *MCS* mental component summary, *MH* mental health, *NA* not available, *NNT* number needed to treat, *NRI* non-responder imputation, *PBO* placebo, *PCS* physical component summary, *PF* physical functioning, *PRO* patient-reported outcome, *PtGA* Patient Global Assessment of Disease Activity, *RE* role-emotional, *RP* role-physical, *SF* social functioning, *SF-36* 36-Item Short Form Health Survey, *UPA* upadacitinib, *VT* vitality

more heavily treated bDMARD-IR population is similar to those reported by the biologic-naïve population in the parallel phase 3 RCT, SELECT-PsA 1 (NCT03104400) [16, 41]. Further, nominally significant improvements with both upadacitinib doses versus placebo at week 12 were more consistently reported in SELECT-PsA -2 than -1 [41].

Treatment options for patients with PsA who are refractory to bDMARDs are limited. The inhibitors for JAK (tofacitinib), IL-12/23 (ustekinumab), IL-23 (guselkumab), and IL-17A (secukinumab and ixekizumab) have demonstrated efficacy and HRQOL improvements in this patient population and are approved for treatment of PsA [42–46]. Although comparisons between these and the current RCT are difficult owing to differences in treatment mechanisms of action, study designs and patient populations, some observations can be made. Following 12 weeks of tofacitinib 5 or

10 mg BID treatment, statistically significant improvements versus placebo were similarly reported in PtGA, pain, HAQ-DI, SF-36 PCS, FACIT-F, and EQ-5D scores and 4 and 5 SF-36 domains, respectively [42]. NNTs were generally lower with upadacitinib than tofacitinib treatment, reflecting the percentages of patients reporting improvements \geq MCID with tofacitinib versus placebo did not statistically differ in FACIT-F and 4/8 SF-36 domains [42]. Further, with tofacitinib treatment, the percentages reporting scores \geq normative values were not significantly different from placebo across the majority of PROs, noting that all patients in the BEYOND protocol were required to have been receiving methotrexate [42]. With secukinumab and ixekizumab, significant improvements at weeks 16 and 24, respectively, were reported across most PROs compared with placebo, similar to upadacitinib [45, 46], and, like upadacitinib, ixekizumab was reported to resolve itch [46].

A limitation of this study was that it was not powered to detect differences between upadacitinib treatment arms and there was no placebo or active comparator after week 24. Additionally, results may not be generalizable beyond the trial patient population.

CONCLUSIONS

Patients with active PsA who had failed \geq one bDMARD reported significant and clinically meaningful improvements in PROs with upadacitinib 15 or 30 mg QD through 24 weeks, maintained or further improved through 56 weeks. Clinically meaningful responses in PtGA, pain, and HAQ-DI were reported as early as week 2 with both doses of upadacitinib with NNTs ≤ 10 at weeks 12 and 24. Further, significantly more patients receiving upadacitinib reported scores \geq normative values across all evaluated PROs. In summary, these results highlight the potential for upadacitinib to provide substantial improvement in HRQOL and other important patient-reported outcomes in patients with PsA.

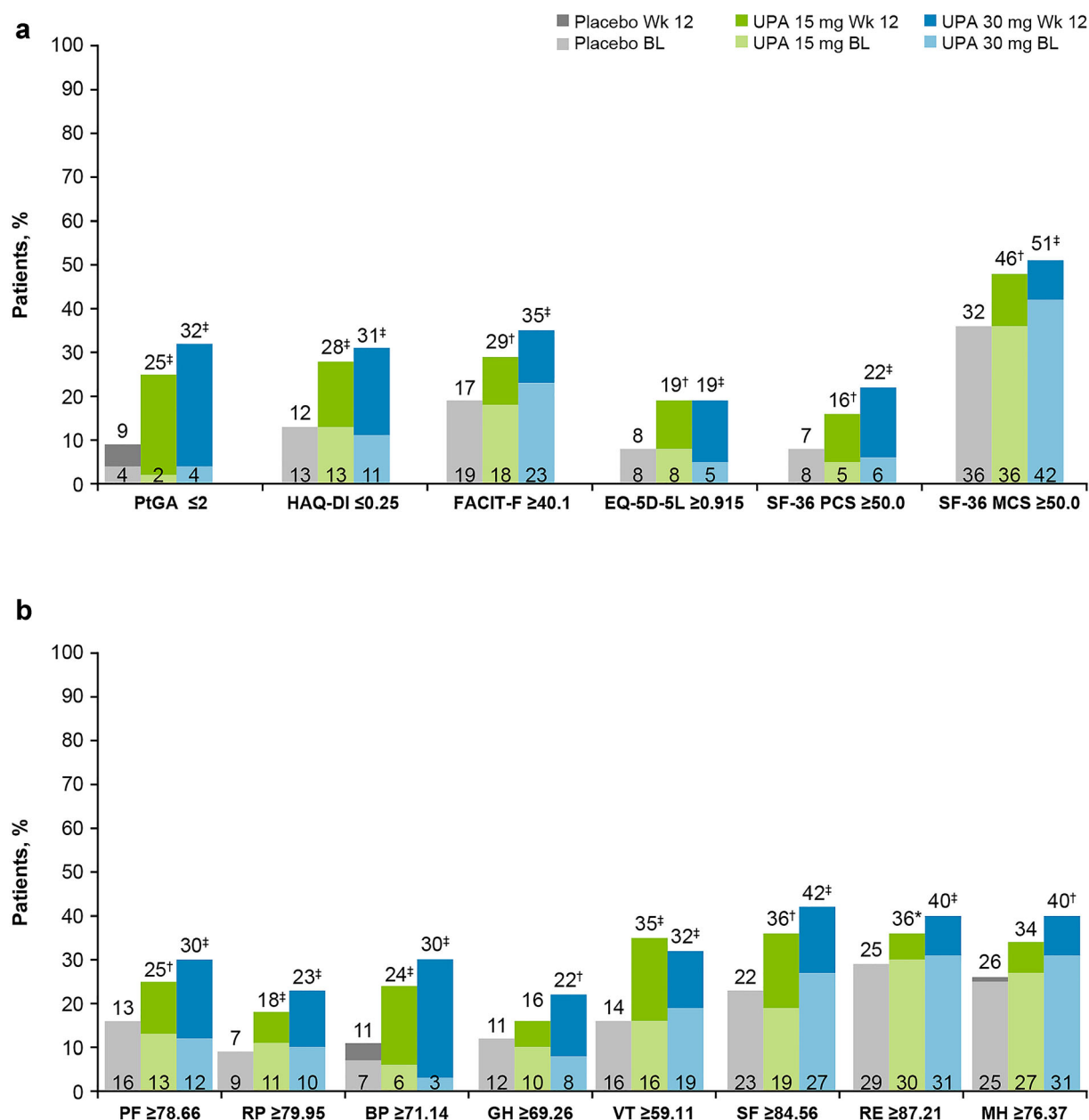


Fig. 4 Proportion of patients reporting PRO scores \geq normative values at baseline and week 12 and age- and gender-matched normative values in SF-36 domains (NRI). **a** PROs excluding SF-36 domains. **b** SF-36 domains. * $p < 0.05$, $^{\dagger}p \leq 0.01$, and $^{\ddagger}p \leq 0.001$ versus placebo. p values nominal. The percentage at 12 weeks might or might not include the same patients that achieved that outcome at baseline. BL baseline, BP bodily pain, EQ-5D-5L EuroQoL 5-Dimension 5-Level index score, FACIT-F Functional Assessment of Chronic Illness

Therapy-Fatigue, GH general health, HAQ-DI Health Assessment Questionnaire-Disability Index, MCS mental component summary, MH mental health, NRI non-responder imputation, PBO placebo, PCS physical component summary, PF physical functioning, PtGA Patient Global Assessment of Disease Activity, PRO patient-reported outcome, RE role-emotional, RP role-physical, SF social functioning, SF-36 36-Item Short Form Health Survey, UPA upadacitinib, VT vitality

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Compliance with Ethics Guidelines. The study was approved by the independent ethics committees or institutional review boards at all study sites and conducted in accordance with the Declaration of Helsinki and consistent with International Conference on Harmonisation Good Clinical Practice and Good Epidemiology Practices, along with all applicable local regulatory requirements. All patients provided written approval before enrollment, and patient data were de-identified and complied with patient confidentiality requirements.

Data Availability. The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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REFERENCES

- McGagh D, Coates LC. Assessment of the many faces of PsA: single and composite measures in PsA clinical trials. *Rheumatology* (Oxford). 2020;59(Supplement_1):i29–36.
- Husni ME, Merola JF, Davin S. The psychosocial burden of psoriatic arthritis. *Semin Arthritis Rheum*. 2017;47(3):351–60.
- Kavanaugh A, Helliwell P, Ritchlin CT. Psoriatic arthritis and burden of disease: patient perspectives from the population-based multinational assessment of psoriasis and psoriatic arthritis (MAPP) survey. *Rheumatol Ther*. 2016;3(1):91–102.
- Coates LC, Kavanaugh A, Mease PJ, et al. Group for research and assessment of psoriasis and psoriatic arthritis 2015 treatment recommendations for psoriatic arthritis. *Arthritis Rheumatol*. 2016;68(5):1060–71.
- Gossec L, Baraliakos X, Kerschbaumer A, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. *Ann Rheum Dis*. 2020;79(6):700–12.
- Singh JA, Guyatt G, Ogdie A, et al. Special article: 2018 American College of Rheumatology/National Psoriasis Foundation guideline for the treatment of psoriatic arthritis. *Arthritis Care Res (Hoboken)*. 2019;71(1):2–29.
- Parmentier JM, Voss J, Graff C, et al. In vitro and in vivo characterization of the JAK1 selectivity of upadacitinib (ABT-494). *BMC Rheumatol*. 2018;2:23.
- RINVOQ™ (upadacitinib) prescribing information (AbbVie, Inc, North Chicago, IL, USA). 2020 November 12, 2020. https://www.rxabbvie.com/pdf/rinvoq_pi.pdf. Accessed 12 Nov 2020.
- European Medicines Agency. Summary of product characteristics-RINVOQ™ 2021 March 11, 2021. https://www.ema.europa.eu/en/documents/product-information/rinvoq-epar-product-information_en.pdf. Accessed 11 Mar 2021.
- Burmester GR, Kremer JM, Van den Bosch F, et al. Safety and efficacy of upadacitinib in patients with rheumatoid arthritis and inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs (SELECT-NEXT): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*. 2018;391(10139):2503–12.
- Fleischmann R, Pangan AL, Song IH, et al. Upadacitinib versus placebo or adalimumab in patients with rheumatoid arthritis and an inadequate response to methotrexate: results of a phase III, double-blind, randomized controlled trial. *Arthritis Rheumatol*. 2019;71(11):1788–800.
- Genovese MC, Fleischmann R, Combe B, et al. Safety and efficacy of upadacitinib in patients with active rheumatoid arthritis refractory to biologic disease-modifying anti-rheumatic drugs (SELECT-BEYOND): a double-blind, randomised controlled phase 3 trial. *Lancet*. 2018;391(10139):2513–24.
- Smolen JS, Pangan AL, Emery P, et al. Upadacitinib as monotherapy in patients with active rheumatoid arthritis and inadequate response to methotrexate (SELECT-MONOTHERAPY): a randomised, placebo-controlled, double-blind phase 3 study. *Lancet*. 2019;393(10188):2303–11.
- van Vollenhoven R, Takeuchi T, Pangan AL, et al. Efficacy and safety of upadacitinib monotherapy in methotrexate-naïve patients with moderately to severely active rheumatoid arthritis (SELECT-EARLY): a randomized, double-blind, active-comparator, multi-center, multi-country trial. *Arthritis Rheum*. 2020;72(10):1607–20.
- Mease PJ, Lertratanakul A, Anderson JK, et al. Upadacitinib for psoriatic arthritis refractory to biologics: SELECT-PsA 2. *Ann Rheum Dis*. 2021;80:312–20.
- McInnes IB, Anderson JK, Magrey M, et al. Trial of upadacitinib and adalimumab for psoriatic arthritis. *N Engl J Med*. 2021;384(13):1227–39.
- van der Heijde D, Song IH, Pangan AL, et al. Efficacy and safety of upadacitinib in patients with active ankylosing spondylitis (SELECT-AXIS 1): a multi-centre, randomised, double-blind, placebo-controlled, phase 2/3 trial. *Lancet*. 2019;394(10214):2108–17.
- Ogdie A, de Wit M, Callis Duffin K, et al. Defining outcome measures for psoriatic arthritis: A report from the GRAPPA-OMERACT Working Group. *J Rheumatol*. 2017;44(5):697–700.
- Mease PJ, Woolley JM, Bitman B, et al. Minimally important difference of Health Assessment Questionnaire in psoriatic arthritis: relating thresholds of improvement in functional ability to patient-rated importance and satisfaction. *J Rheumatol*. 2011;38(11):2461–5.

20. Krishnan E, Sokka T, Hakkinen A, Hubert H, Han-nonen P. Normative values for the Health Assessment Questionnaire disability index: benchmarking disability in the general population. *Arthritis Rheum.* 2004;50(3):953–60.
21. Hewlett S, Dures E, Almeida C. Measures of fatigue: Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional Questionnaire (BRAFM-DQ), Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scales (BRAFNRS) for severity, effect, and coping, Chalder Fatigue Questionnaire (CFQ), Checklist Individual Strength (CIS20R and CIS8R), Fatigue Severity Scale (FSS), Functional Assessment Chronic Illness Therapy (Fatigue) (FACIT-F), Multi-Dimensional Assessment of Fatigue (MAF), Multi-Dimensional Fatigue Inventory (MFI), Pediatric Quality Of Life (PedsQL) Multi-Dimensional Fatigue Scale, Profile of Fatigue (ProF), Short Form 36 Vitality Subscale (SF-36 VT), and Visual Analog Scales (VAS). *Arthritis Care Res (Hoboken).* 2011;63(Suppl 11):S263–86.
22. Webster K, Cella D, Yost K. The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: properties, applications, and interpretation. *Health Qual Life Outcomes.* 2003;1:79.
23. Ware JE Jr, Kosinski M, Bjorner JB, et al. User's manual for the SF-36v2 health survey. 2nd ed. Lincoln: Quality Metric Incorporated; 2007.
24. Strand V. Clinically meaningful improvements may be interpreted in multiple ways. In: White Paper for OMERACT/Cochrane Pain Meeting.
25. Ware JE Jr, Kosinski M, Bayliss MS, et al. Comparison of methods for the scoring and statistical analysis of SF-36 health profile and summary measures: summary of results from the Medical Outcomes Study. *Med Care.* 1995;33(4 Suppl):AS264–79.
26. Armstrong AW, Banderas B, Foley C, et al. Development and psychometric evaluation of the self-assessment of psoriasis symptoms (SAPS)—clinical trial and the SAPS—real world patient-reported outcomes. *J Dermatol Treat.* 2017;28(6):505–14.
27. Strand V, Boers M, Idzerda L, et al. It's good to feel better but it's better to feel good and even better to feel good as soon as possible for as long as possible. Response criteria and the importance of change at OMERACT 10. *J Rheumatol.* 2011;38(8):1720–7.
28. Salaffi F, Stancati A, Silvestri CA, Ciapetti A, Grassi W. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain.* 2004;8(4):283–91.
29. Anderson JK, Zimmerman L, Caplan L, Michaud K. Measures of rheumatoid arthritis disease activity: Patient (PtGA) and Provider (PrGA) Global Assessment of Disease Activity, Disease Activity Score (DAS) and Disease Activity Score with 28-Joint Counts (DAS28), Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Patient Activity Score (PAS) and Patient Activity Score-II (PASII), Routine Assessment of Patient Index Data (RAPID), Rheumatoid Arthritis Disease Activity Index (RADAI) and Rheumatoid Arthritis Disease Activity Index-5 (RADAI-5), Chronic Arthritis Systemic Index (CASI), Patient-Based Disease Activity Score With ESR (PDAS1) and Patient-Based Disease Activity Score without ESR (PDAS2), and Mean Overall Index for Rheumatoid Arthritis (MOI-RA). *Arthritis Care Res (Hoboken).* 2011;63(Suppl 11):S14–36.
30. Dolan P. Modeling valuations for EuroQol health states. *Med Care.* 1997;35(11):1095–108.
31. Hinz A, Kohlmann T, Stobel-Richter Y, Zenger M, Brahler E. The quality of life questionnaire EQ-5D-5L: psychometric properties and normative values for the general German population. *Qual Life Res.* 2014;23(2):443–7.
32. Kviatkovsky MJ, Ramiro S, Landewe R, et al. The minimum clinically important improvement and patient-acceptable symptom state in the BASDAI and BASFI for patients with ankylosing spondylitis. *J Rheumatol.* 2016;43(9):1680–6.
33. Reilly Associates. Work productivity and activity questionnaire specific health problem V2.0 (WPAI-SHP) 2010.October 29, 2020. http://www.reillyassociates.net/WPAI_SHP.html. Accessed 29 Oct 2020.
34. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics.* 1993;4(5):353–65.
35. Strand V, Crawford B, Singh J, et al. Use of “spydergrams” to present and interpret SF-36 health-related quality of life data across rheumatic diseases. *Ann Rheum Dis.* 2009;68(12):1800–4.
36. Siwek J, Newman DH. Introducing medicine by the numbers: a collaboration of the NNT group and AFP. *Am Fam Physician.* 2015;91(7):434–5.
37. Coates LC, Orbai AM, Azevedo VF, et al. Results of a global, patient-based survey assessing the impact of psoriatic arthritis discussed in the context of the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire. *Health Qual Life Outcomes.* 2020;18(1):173.

38. Sunkureddi P, Doogan S, Heid J, et al. Evaluation of self-reported patient experiences: insights from digital patient communities in psoriatic arthritis. *J Rheumatol*. 2018;45(5):638–47.
39. Ogdie A, Michaud K, Nowak M, et al. Patient's experience of psoriatic arthritis: a conceptual model based on qualitative interviews. *RMD Open*. 2020;6(3):e001083.<https://doi.org/10.1136/rmdopen-2020-001321>.
40. Tillett W, Dures E, Hewlett S, et al. A Multicenter nominal group study to rank outcomes important to patients, and their representation in existing composite outcome measures for psoriatic arthritis. *J Rheumatol*. 2017;44(10):1445–52.
41. Strand V, Mease PJ, Soriano ER, et al. Improvement in patient-reported outcomes in patients with psoriatic arthritis treated with upadacitinib versus placebo or adalimumab: results from SELECT-PsA 1. *Rheumatol Ther*. 2021 [Epub ahead of print].
42. Strand V, de Vlam K, Covarrubias-Cobos JA, et al. Effect of tofacitinib on patient-reported outcomes in patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors in the phase III, randomised controlled trial: OPAL Beyond. *RMD Open*. 2019;5(1):e000808.
43. Ritchlin C, Rahman P, Kavanaugh A, et al. Efficacy and safety of the anti-IL-12/23 p40 monoclonal antibody, ustekinumab, in patients with active psoriatic arthritis despite conventional non-biological and biological anti-tumour necrosis factor therapy: 6-month and 1-year results of the phase 3, multicentre, double-blind, placebo-controlled, randomised PSUMMIT 2 trial. *Ann Rheum Dis*. 2014;73(6):990–9.
44. Deodhar A, Helliwell PS, Boehncke WH, et al. Guselkumab in patients with active psoriatic arthritis who were biologic-naïve or had previously received TNF α inhibitor treatment (DISCOVER-1): a double-blind, randomised, placebo-controlled phase 3 trial. *Lancet*. 2020;395(10230):1115–25.
45. Strand V, Kaeley G, Bergman M, et al. Efficacy of secukinumab on patient-reported outcomes in patients with active psoriatic arthritis stratified by prior tumor necrosis factor inhibitor use: post hoc analysis from a phase 3 trial. *Arthritis Rheumatol*. 2020;72(suppl 10):Abstract 1363.
46. Kavanaugh A, Marzo-Ortega H, Vender R, et al. Ixekizumab improves patient-reported outcomes in patients with active psoriatic arthritis and inadequate response to tumour necrosis factor inhibitors: SPIRIT-P2 results to 52 weeks. *Clin Exp Rheumatol*. 2019;37(4):566–74.