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ORIGINAL RESEARCH

Improvement in Patient-Reported Outcomes in Patients with Psoriatic Arthritis Treated with Upadacitinib Versus Placebo or Adalimumab: Results from SELECT-PsA 1

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ABSTRACT

Introduction: The aim of this work is to assess the effect of upadacitinib versus adalimumab and placebo on patient-reported outcomes (PROs) in psoriatic arthritis (PsA) patients with inadequate responses to ≥ 1 non-biologic disease-modifying anti-rheumatic drugs (non-bDMARD-IR) in SELECT PsA-1.

Methods: In this placebo- and active comparator, phase 3 randomized, controlled trial, patients received daily upadacitinib 15 or 30 mg, placebo, or adalimumab 40 mg every other week through 56 weeks. At week 24, placebo-assigned patients were rerandomized to upadacitinib 15 or 30 mg. PROs included Patient Global Assessment of Disease Activity (PtGA), pain, Health Assessment Questionnaire Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Short Form 36 Health Survey (SF-36), EQ-5D-5L index score, Bath Ankylosing Spondylitis Disease Activity Index, morning stiffness, Self-Assessment of Psoriasis Symptoms, and Work Productivity and Activity Impairment. Mean changes from baseline in PROs, improvements ≥ minimum clinically important differences (MCID), scores ≥ normative values, and sustained clinically meaningful responses were compared between treatment groups.

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Results: At weeks 12 and 24, upadacitinib treatment resulted in improvements from baseline versus placebo across all PROs as well as improvements versus adalimumab in HAQ-DI and SF-36 Physical Component Summary score (nominal $p < 0.05$). Improvements in PtGA, pain, and HAQ-DI were reported as early as week 2. At week 12, significantly (nominal $p < 0.05$) more upadacitinib- versus placebo-treated patients reported improvements ≥ MCID across all PROs including seven SF-36 domains. The proportions of upadacitinib-treated patients reporting clinically meaningful improvements at week 12 were similar to or greater than with adalimumab and sustained through week 56. Significantly (nominal $p < 0.05$) more upadacitinib-treated (both doses) patients reported scores ≥ normative values at week 12 versus placebo, and scores were generally similar to or greater than adalimumab.
Conclusions: Upadacitinib treatment provides rapid, sustained, and clinically meaningful improvements in PROs in non-bDMARD-IR patients with PsA.SELECT-PsA 1 ClinicalTrials.gov number, NCT03104400.

Keywords: Adalimumab; 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 is a multifaceted disease with substantial negative impact on health-related quality of life.

Despite various current treatment options, not all patients achieve disease control, demonstrating a need for new treatment options.

This trial provides a head-to-head comparison of patient-reported outcomes in patients treated with upadacitinib, an oral, Janus kinase inhibitor and adalimumab, a well-characterized tumor necrosis factor inhibitor commonly used to treat moderate and severe psoriatic arthritis.

What was learned from the study?

In patients with psoriatic arthritis and inadequate responses to non-biologic disease-modifying anti-rheumatic drugs, treatment with upadacitinib for 12 weeks resulted in clinically meaningful improvements in patient-reported outcomes that were maintained or further improved at weeks 24 and 56.

Overall, improvements with upadacitinib were similar to or greater than those reported with adalimumab.

INTRODUCTION

Psoriatic arthritis (PsA) is a heterogenous, inflammatory musculoskeletal disease characterized by peripheral arthritis, dactylitis, enthesitis, and axial arthritis, as well as skin and nail disease [1]. PsA is associated with significant psychosocial burden that negatively impacts work productivity, health-related quality of life (HRQoL), [2] and activities of daily living [3].

Treatment goals are to alleviate disease symptoms, prevent structural damage, and maximize HRQoL. Non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and non-biologic disease-modifying anti-rheumatic drugs (non-bDMARDs) are often used to treat mild disease [4–6]. bDMARDs and targeted synthetic DMARDs (tsDMARDs) are recommended in patients with severe disease or refractory disease and tumor necrosis factor (TNF) inhibitors are often used as first-line therapy [4–6]. In patients with inadequate responses to non-bDMARDs (non-bDMARD-IR) or TNF inhibitors (TNFi), other treatment options include interleukin (IL)-12/23, IL-17A,

and recently, IL-23 inhibitors, and tsDMARDs: Janus kinase inhibitors [4–6].

Upadacitinib is an oral reversible Janus kinase inhibitor [7] with demonstrated efficacy in the treatment of rheumatoid arthritis [8–12]. Adalimumab is a TNFi indicated for treatment of multiple diseases, including PsA [5, 6, 13]. Head-to-head comparisons of the effects of upadacitinib versus adalimumab on the multiple clinical aspects of PsA provide physicians with important information to guide their decisions regarding the treatment of this disease.

SELECT-PsA 1 was a phase 3 randomized controlled trial (RCT) comparing upadacitinib 15 mg once daily (QD), upadacitinib 30 mg QD, placebo QD, or adalimumab 40 mg every other week (EOW) in non-bDMARD-IR PsA patients. Key findings from the SELECT-PsA 1 study included significant improvements in the clinical manifestations of PsA, such as musculoskeletal outcomes, psoriasis severity, axial symptoms, as well as resolution of dactylitis and enthesitis [14]. Since PsA significantly impacts HRQoL, it is important to assess the effect of upadacitinib on patient-reported outcomes (PROs) when evaluating treatment benefits in PsA [15]. This report presents an evaluation of the attainment and maintenance of clinically meaningful improvements in PROs in PsA patients receiving upadacitinib versus placebo or adalimumab in the SELECT-PsA 1 trial.

METHODS

Study Design and Patients

The design and primary results from the SELECT-PsA 1 RCT have previously been reported [14]. The RCT was conducted at 281 sites in 45 countries. Key inclusion criteria in SELECT-PsA 1 were patients ≥ 18 years of age, fulfillment of the ClASsification criteria for Psoriatic ARthritis (CASPAR) [16], active or documented history of plaque psoriasis, and inadequate responses to ≥ 1 non-bDMARD. Major exclusion criteria were prior exposure to any bDMARDs, prior exposure to any JAK inhibitor, current treatment with ≥ 2 non-bDMARDs, current or past history of infection, and underlying medical diseases or problems.

Patients were randomly assigned in a 1:1:1:1 ratio to upadacitinib 15 mg QD, upadacitinib 30 mg QD, placebo followed by upadacitinib 15 mg QD or 30 mg QD (1:1) at week 24, or adalimumab 40 mg EOW. Study drug (upadacitinib, adalimumab, and placebo) was provided by AbbVie. The trial consisted of 24 weeks of randomized, blinded, placebo- and active comparator-controlled treatment followed by 32 weeks of active-comparator-controlled treatment. Stable treatment with nonsteroidal anti-inflammatory drugs (NSAID), corticosteroids, and ≤ 2 non-bDMARDs was permitted, but not required. Rescue therapy was permitted for non-responders at week 16.

The SELECT-PSA 1 RCT was conducted according to the International Conference on Harmonization guidelines and the principles of the Declaration of Helsinki. All patients provided written informed consent. The trial protocol was approved by independent ethics committees and institutional review boards (ESM Table S1).

Outcomes

Multiplicity-controlled secondary PRO endpoints included changes from baseline at week 12 in Health Assessment Questionnaire Disability Index (HAQ-DI; minimum clinically important difference [MCID]: ≥ 0.35 unit decrease; normative value: ≤ 0.25 units) [17, 18], Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F; MCID: ≥ 4-point increase; normative value: ≥ 40.1 points) [19, 20], Short Form 36 Health Survey (SF-36) Physical Component Summary (PCS) score (MCID: ≥ 2.5 increase; normative value ≥ 50 points) [21–23] and changes from baseline at week 16 in Self-Assessment of Psoriasis Symptoms (SAPS) (an 11-item patient self-assessment of psoriasis symptoms, which included 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; range 0–110, with higher scores indicating worse patient-reported

psoriasis symptoms) [24]. Additional PROs evaluated included Patient Global Assessment of Disease Activity (PtGA) and pain (0–10 NRS; MCID: ≥ 1-point decrease; normative value: ≤ 2 points; pain was a multiplicity-controlled secondary PRO) [23, 25, 26], SF-36 Mental Component Summary (MCS; MCID: ≥ 2.5-point increase; normative value: ≥ 50 points) and individual SF-36 domain scores (MCID: ≥ five-point increase) [21–23], EuroQoL 5-Dimension 5-Level index score (EQ-5D-5L; MCID: ≥ 0.05-unit increase; normative value: ≥ 0.915) [27, 28], Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; MCID: ≥ 1.1-point decrease), morning stiffness (mean of BASDAI questions 5 and 6) [29], BASDAI 50, Work Productivity and Activity Impairment (WPAI) [30, 31], and itch (SAPS question 2; 0–10 NRS, with higher scores indicating worse itch).

PtGA, pain, and HAQ-DI were assessed starting at week 2 while other PROs were assessed at week 12, except SAPS at week 16. SF-36 PCS and MCS are 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 [21, 22]. Age- and gender-matched US normative SF-36 domain scores were based on the protocol population [32]. BASDAI was assessed in patients who had investigator-determined psoriatic spondylitis at baseline. The WPAI activity impairment domain was evaluated in all patients while presenteeism, overall work impairment, and absenteeism domains were assessed in those employed at baseline [31].

Statistical Analyses

All analyses were conducted on the full analysis set of randomized patients who received ≥ 1 dose of trial drug. As previously described [14], the RCT was powered to detect a difference between placebo and upadacitinib for the primary endpoint (ACR 20 response), most key secondary endpoints, and evaluating noninferiority and superiority of each upadacitinib dose compared with adalimumab for ACR20 response at week 12. The study was not powered to detect differences between the upadacitinib groups nor to detect differences between upadacitinib and adalimumab with respect to the change from baseline in pain or HAQ-DI score. Demographic and baseline characteristics are summarized with descriptive statistics (mean, standard deviation for continuous endpoints, and *n* [%] for categoric endpoints). Least squares (LS) mean changes from baseline through weeks 12, 24, and 56 along with 95% confidence intervals (CIs) and nominal *p* values were based on mixed-effects repeated measures models (MMRM) analysis using an unstructured variance–covariance matrix, including treatment, visit, treatment-by-visit interaction, the stratification factor, current non-bDMARD use (yes/no) as fixed factors and the continuous fixed covariate of baseline measurement. MMRM analysis used observed longitudinal data up to the respective time point prior to premature study drug discontinuation. Spidergrams were used to illustrate changes from baseline in SF-36 domain scores in each treatment group against a combined baseline US normative population [32]. No formal comparisons of adalimumab versus placebo were performed.

The proportions of patients reporting BASDAI 50, improvements ≥ MCID, and ≥ normative values (age- and gender-matched for SF-36 domains) at weeks 12 and 24 were evaluated between both doses of upadacitinib and placebo or between both doses of upadacitinib and adalimumab using nonresponder imputation for missing responses. As-observed data were used to determine maintenance of clinically meaningful improvements ≥ MCID from weeks 12 to 56. The proportions of patients reporting scores ≥ normative values in respective PROs including SF-36 domains through week 24 were determined with missing responses imputed using nonresponder imputation.

The number needed to treat (NNT) to achieve one additional MCID improvement at weeks 12 and 24 for each upadacitinib dose compared with placebo or adalimumab 40 mg was defined as the reciprocal of the response rate difference between upadacitinib and placebo or adalimumab, with missing PRO responses imputed using nonresponder imputation. *P* values were calculated using

Cochran–Mantel–Haenszel test adjusting for the main stratification factor of current non-bDMARD use (yes/no). Statistical significance defined as $p < 0.05$ was nominal for non-multiplicity-controlled endpoints.

RESULTS

A total of 1705 patients in SELECT-PsA 1 were randomized with 1704 receiving ≥ 1 dose of study drug (placebo: $n = 423$; upadacitinib 15 mg: $n = 429$; upadacitinib 30 mg: $n = 423$; adalimumab 40 mg: $n = 429$) with approximately 58% of the patients employed. Demographics, disease characteristics, disease activity, and PRO scores at baseline were similar across the treatment groups (Table 1).

Improvements from Baseline in PROs

Significant improvements in LS mean changes from baseline to week 12 and 24 were reported with upadacitinib 15 mg and upadacitinib 30 mg compared with placebo across all PROs (Table 2). Improvements from baseline in PtGA, pain, HAQ-DI, and FACIT-F with both doses of upadacitinib differentiated from placebo as early as 2 weeks (Fig. 1).

As shown in Fig. 2, decrements from age- and gender-adjusted norms indicated that patients had substantial impairments in HRQoL at baseline. All eight SF-36 domain scores were significantly improved with upadacitinib versus placebo with scores approaching normative values at week 12 (Fig. 2). Improvements in PROs reported at week 12 with upadacitinib continued or further increased at week 24 (Table 2; ESM Fig. S1). BASDAI 50 response was reported by significantly more patients with upadacitinib 15 mg or 30 mg at weeks 12 (37% and 51%) and 24 (59% and 53%) than placebo (15% and 27%) (nominal $p < 0.001$).

Compared with adalimumab, both upadacitinib doses resulted in significant improvements in HAQ-DI and SF-36 PCS scores, and SF-36 physical function (PF) domain with upadacitinib 15 mg and PF, role physical (RP), bodily pain (BP), and general health (GH) domains with upadacitinib 30 mg at weeks 12 and 24; and in SAPS and itch response at weeks 16 and 24 (Table 2). Improvements in PROs with both doses of upadacitinib were maintained or further improved at 56 weeks of treatment (Table 3).

Patients receiving placebo who switched to upadacitinib 15 mg or upadacitinib 30 mg at week 24 reported improvements in PtGA, pain, HAQ-DI, and FACIT-F similar to those who initially received either upadacitinib dose. These improvements were maintained through week 56 (Fig. 1).

LS mean changes in SAPS score were significantly greater in patients treated with both doses of upadacitinib compared with placebo and indicative of important improvements in the signs and symptoms of psoriasis (Table 2). The itch response rate (derived from SAPS question 2) was greater in both upadacitinib groups compared with placebo at week 16 (33.8% for upadacitinib 15 mg, 48.3% for upadacitinib 30 mg versus 9.6–13.5% for placebo; ESM, Fig. S2). With upadacitinib 15 mg and 30 mg, itch responses improved to 45.5% and 54.3% at week 56, respectively. In patients who switched from placebo to upadacitinib at week 24, itch responses approached those reported by patients who initially received upadacitinib.

Clinically Meaningful Improvements in PROs

As early as week 2, significantly (nominal $p < 0.01$) more patients treated with upadacitinib 15 mg and 30 mg reported clinically meaningful improvements ≥ MCID in PtGA (15 mg: 67.8%, 30 mg: 73.5% versus placebo: 54.1%), pain (15 mg: 64.2%, 30 mg: 74.6%% versus placebo: 51.7%), and HAQ-DI (15 mg: 31.0%, 30 mg: 37.4% versus placebo: 21.7%) compared with placebo.

At week 12, the proportions of patients reporting improvements ≥ MCID were significantly greater with upadacitinib 15 mg and 30 mg compared with placebo in PtGA, pain HAQ-DI, FACIT-F, EQ-5D-5L, BASDAI, morning stiffness, and SF-36 PCS scores, as well as seven of eight SF-36 domains (Fig. 3) and maintained

Table 1 Baseline characteristics and PRO scores

	Placebo (*N* = 423)	Upadacitinib 15 mg QD (*N* = 429)	Upadacitinib 30 mg QD (*N* = 423)	Adalimumab 40 mg EOW (*N* = 429)
Female, %	49.9	55.5	55.8	51.7
Age (years), mean (SD)	50.4 (12.2)	51.6 (12.2)	49.9 (12.4)	51.4 (12.0)
White race, %	89.1	90.0	89.1	87.4
Duration since PsA diagnosis (years), mean (SD)	6.2 (7.0)	6.2 (7.4)	5.9 (6.4)	5.9 (7.1)
Body mass index (kg/m^2), mean	30.4 (6.8)	30.1 (6.4)	30.1 (6.8)	30.7 (7.2)
Use of $\geq$ 1 non-bDMARD at baseline, %	82.0	82.3	81.8	80.9
Presence of dactylitis,[a] %	29.8	31.7	30.0	29.6
Presence of enthesitis,[b] %	57.0	62.9	63.1	61.8
TJC (68 joints), mean (SD)	20.0 (14.3)	20.4 (14.7)	19.4 (13.3)	20.1 (13.8)
SJC (66 joints), mean	11.0 (8.2)	11.6 (9.3)	10.6 (7.1)	11.6 (8.8)
BSA-PsO $\geq$ 3%, %	49.9	49.9	49.6	49.2
PtGA 0–10, NRS, mean (SD)	6.3 (2.0)	6.6 (2.0)	6.4 (2.1)	6.3 (2.0)
Pain 0–10, NRS, mean (SD)	6.1 (2.1)	6.2 (2.1)	5.9 (2.1)	6.0 (2.1)
HAQ-DI, mean (SD)	1.12 (0.64)	1.15 (0.65)	1.09 (0.63)	1.12 (0.63)
FACIT-F, mean (SD)	30.0 (11.2)	29.0 (11.9)	29.8 (11.6)	29.5 (11.5)
SF-36 PCS, mean (SD)	35.1 (8.4)	34.8 (7.7)	35.8 (8.2)	35.8 (8.1)
SF-36 MCS, mean (SD)	45.6 (11.3)	44.7 (11.7)	45.6 (11.5)	45.0 (11.0)
SF-36 domains, mean (SD)				
PF	42.7 (25.6)	43.7 (24.3)	46.0 (25.2)	45.2 (25.5)
RP	42.6 (24.0)	41.2 (22.6)	46.4 (24.0)	44.2 (24.7)
BP	36.3 (17.6)	34.8 (17.0)	36.8 (17.6)	37.1 (17.8)
GH	42.5 (19.1)	41.2 (18.3)	41.4 (18.6)	41.8 (17.3)
VT	42.4 (20.0)	40.2 (20.5)	42.3 (20.7)	41.9 (19.6)
SF	60.3 (25.0)	57.3 (26.3)	60.2 (26.4)	60.6 (24.9)
RE	64.8 (27.9)	64.4 (26.6)	66.5 (26.6)	63.9 (27.8)
MH	60.5 (19.2)	59.9 (20.7)	61.3 (20.8)	60.1 (20.2)
EQ-5D-5L, mean (SD)	0.61 (0.24)	0.60 (0.25)	0.61 (0.24)	0.62 (0.25)
BASDAI,[c] mean (SD)	5.4 (2.1)	5.6 (2.2)	5.4 (2.2)	5.4 (2.2)
Morning stiffness,[c,d] mean (SD)	5.3 (2.5)	5.7 (2.6)	5.3 (2.6)	5.2 (2.6)

Table 1 continued

	Placebo (*N* = 423)	Upadacitinib 15 mg QD (*N* = 429)	Upadacitinib 30 mg QD (*N* = 423)	Adalimumab 40 mg EOW (*N* = 429)
SAPS, mean (SD)	44.0 (26.6)	44.3 (26.9)	43.2 (26.2)	42.7 (25.3)
Itch,[e] mean (SD)	4.6 (3.1)	4.5 (3.1)	4.5 (3.1)	4.5 (3.0)
WPAI AI, mean (SD)	49.6 (25.0)	52.0 (25.2)	46.5 (26.2)	49.3 (25.9)
WPAI presenteeism,[f] mean (SD)	43.6 (24.8)	43.0 (25.6)	38.3 (26.1)	38.3 (24.4)
WPAI OWI,[f] mean (SD)	50.8 (29.0)	48.3 (29.0)	44.8 (30.2)	44.8 (28.8)
WPAI absenteeism,[f] mean (SD)	16.3 (28.2)	11.7 (24.5)	12.9 (25.4)	12.8 (26.4)

AI activity impairment, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BP* bodily pain, *BSA* body surface area, *bDMARD* biologic disease-modifying anti-rheumatic drug, *EOW* every other week, *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, *PsO* 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 count, *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 questions 5 and 6

[e] SAPS question 2

[f] Reported only for patients who were employed. N for presenteeism, OWI, and absenteeism: placebo: 230, 241, and 241; upadacitinib 15 mg QD: 240, 251, and 251; upadacitinib 30 mg QD: 242, 251, and 251; adalimumab 40 mg EOW: 230, 243, and 243

or further improved at week 24 (ESM Fig. S3). At week 12, the proportions of upadacitinib-treated patients reporting clinically meaningful improvements were similar or greater than with adalimumab 40 mg, with exception of SF-36 role emotional (RE) domain. Of note, significantly more patients treated with upadacitinib 30 mg versus adalimumab 40 mg reported clinically meaningful improvements in pain as early as week 2 (74.6% versus 67.1%, nominal $p = 0.017$); sustained to week 56. Clinically meaningful improvements reported at week 12 continued or were further improved at week 56 with upadacitinib and adalimumab across all PROs (ESM Fig. S4).

At baseline, less than 11% of patients reported scores within the normative range in PtGA, EQ-5D-5L, SF-36 PCS, and four SF-36 domain scores (Fig. 4). At week 12, significantly (nominal $p < 0.05$) more patients receiving both doses of upadacitinib reported scores ≥ normative values in PtGA, HAQ-DI, FACIT-F, EQ-5D-5L, SF-36 PCS, and matched normative values in seven SF-36 domains compared with placebo (Fig. 4); scores were maintained or improved to week 24 (ESM Fig. S5) and were generally similar to or greater than with adalimumab (Fig. 4 and ESM Fig. S5).

NNTs for upadacitinib 15 mg and upadacitinib 30 mg ranged from 3.0 to 13.2 across all PROs at week 12 with NNTs ≤ 10 considered

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

	Placebo		Upadacitinib 15 mg QD		Upadacitinib 30 mg QD		Adalimumab 40 mg EOW	
	Week 12 (*N* = 394)	Week 24 (*N* = 367)	Week 12 (*N* = 405)	Week 24 (*N* = 390)	Week 12 (*N* = 398)	Week 24 (*N* = 376)	Week 12 (*N* = 410)	Week 24 (*N* = 391)
PtGA 0–10, NRS	− 1.2 (− 1.4,− 1.0)	− 1.6 (− 1.8,− 1.4)	− 2.7[‡] (− 2.9,− 2.4)	− 3.4[‡¶] (− 3.6,− 3.2)	− 3.1[‡¶] (− 3.3,− 2.9)	− 3.6[‡¶] (− 3.9,− 3.4)	− 2.6 (− 2.8,− 2.4)	− 2.9 (− 3.1,− 2.6)
Pain 0–10, NRS	− 0.9 (− 1.2,− 0.7)	− 1.4 (− 1.6,− 1.2)	− 2.3[‡] (− 2.5,− 2.0)	− 3.0[‡‖] (− 3.3,− 2.8)	− 2.7[‡‖] (− 2.9,− 2.5)	− 3.2[‡¶] (− 3.4,− 3.0)	− 2.3 (− 2.5,− 2.1)	− 2.6 (− 2.8, 2.4)
HAQ-DI	− 0.13 (− 0.18,− 0.09)	− 0.19 (− 0.24,− 0.13)	− 0.42[‡§] (− 0.47,− 0.37)	− 0.51[‡¶] (− 0.56,− 0.46)	− 0.47[‡¶] (− 0.52,− 0.42)	− 0.51[‡‖] (− 0.56,− 0.46)	− 0.34 (− 0.38,− 0.29)	− 0.39 (− 0.45,− 0.34)
FACIT-F	2.8 (1.9, 3.7)	3.8 (2.8, 4.7)	6.3[‡] (5.5, 7.2)	7.9[‡] (7.0, 8.8)	7.1[‡§] (6.2, 8.0)	8.0[‡] (7.1, 8.9)	5.7 (4.8, 6.6)	6.8 (5.9, 7.7)
SF-36 PCS	3.3 (2.5, 4.0)	4.3 (3.4, 5.1)	7.9[‡§] (7.2, 8.7)	9.8[‡¶] (9.0, 10.6)	9.0[‡¶] (8.2, 9.8)	9.9[‡¶] (9.0, 10.7)	6.9 (6.2, 7.7)	7.8 (7.0, 8.6)
SF-36 MCS	2.2 (1.4, 3.1)	2.4 (1.5, 3.4)	3.9[†] (3.1, 4.8)	4.7[‡] (3.8, 5.6)	3.4[*] (2.6, 4.3)	4.3[†] (3.4, 5.2)	3.6 (2.8, 4.4)	4.1 (3.2, 4.9)
SF-36 domains								
PF	8.4 (6.3, 10.5)	10.0 (7.8, 12.2)	18.9[‡§] (16.8, 20.9)	23.0[‡¶] (20.8, 25.1)	20.7[‡¶] (18.6, 22.8)	23.3[‡¶] (21.1, 25.5)	15.8 (13.8, 17.8)	17.9 (15.8, 20.1)
RP	8.7 (6.5, 10.8)	10.1 (7.8, 12.4)	17.8[‡] (15.7, 19.9)	22.3[‡§] (20.0, 24.5)	19.0[‡§] (16.9, 21.1)	22.9[‡§] (20.6, 25.2)	15.6 (13.5, 17.6)	19.0 (16.7, 21.2)
BP	9.1 (7.1, 11.2)	12.0 (9.8, 14.2)	21.3[‡] (19.3, 23.3)	26.0[‡‖] (23.9, 28.2)	24.4[‡¶] (22.4, 26.4)	26.3[‡‖] (24.1, 28.4)	19.8 (17.8, 21.7)	21.5 (19.4, 23.7)
GH	5.1 (3.5, 6.6)	6.9 (5.2, 8.7)	12.5[‡] (10.9, 14.0)	15.9[‡] (14.2, 17.6)	14.5[‡§] (12.9, 16.1)	16.0[‡] (14.2, 17.7)	12.1 (10.6, 13.7)	13.8 (12.1, 15.5)
VT	5.7 (4.0, 7.5)	8.5 (6.6, 10.3)	13.8[‡] (12.1, 15.5)	17.5[‡¶] (15.7, 19.4)	14.7[‡] (12.9, 16.4)	16.4[‡§] (14.6, 18.3)	12.7 (11.0, 14.4)	13.3 (11.4, 15.1)
SF	6.3 (4.3, 8.4)	8.3 (6.1, 10.5)	13.9[‡] (11.8, 15.9)	16.6[‡§] (14.4, 18.7)	14.1[‡] (12.1, 16.2)	15.6[‡] (13.4, 17.7)	12.0 (10.0, 14.0)	13.2 (11.1, 15.4)
RE	5.8 (3.7, 7.9)	6.0 (3.8, 8.2)	10.1[†] (8.1, 12.2)	12.2[‡] (10.1, 14.4)	9.3[*] (7.2, 11.4)	12.3[‡] (10.1, 14.5)	10.0 (8.0, 12.1)	12.6 (10.5, 14.8)
MH	5.2 (3.7, 6.8)	5.3 (3.6, 7.0)	9.2[‡] (7.6, 10.8)	10.9[‡] (9.3, 12.6)	9.1[‡] (7.5, 10.7)	11.1[‡§] (9.4, 12.8)	7.9 (6.3, 9.5)	8.8 (7.1, 10.4)
EQ-5D-5L	0.08 (0.06, 0.10)	0.10 (0.08, 0.12)	0.16[‡] (0.15, 0.18)	0.18[‡§] (0.17, 0.20)	0.18[‡] (0.16, 0.20)	0.19[‡§] (0.17, 0.21)	0.16 (0.15, 0.18)	0.16 (0.14, 0.18)
BASDAI[a]	− 1.0 (− 1.4,− 0.6)	− 1.7 (− 2.1,− 1.3)	− 2.2[‡] (− 2.6,− 1.8)	− 3.1[‡§] (− 3.5,− 2.7)	− 2.6[‡] (− 3.0,− 2.2)	− 3.2[‡§] (− 3.6,− 2.8)	− 2.4 (− 2.7,− 2.0)	− 2.6 (− 3.0,− 2.1)
BASDAI 50[a,b]	15.4 (9.2, 21.6)	26.9 (19.3, 34.5)	37.4[‡] (29.4, 45.5)	59.0[‡] (50.8, 67.2)	50.7[‡] (42.4, 59.1)	52.9[‡§] (44.6, 61.2)	42.5 (33.9, 51.1)	44.1 (35.5, 52.7)
Morning stiffness[a,c]	− 1.0 (− 1.2,− 0.8)	− 1.4 (− 1.6,− 1.2)	− 2.4[‡] (− 2.6,− 2.2)	− 3.0[‡¶] (− 3.3,− 2.8)	− 2.7[‡¶] (− 2.9,− 2.4)	− 3.1[‡¶] (− 3.3,− 2.8)	− 2.1 (− 2.4,− 1.9)	− 2.5 (− 2.7,− 2.3)
SAPS[d]	− 8.3 (− 10.2,− 6.3)	− 9.7 (− 11.7,− 7.7)	− 25.3[‡§] (− 27.2,− 23.4)	− 28.3[‡‖] (− 30.3,− 26.3)	− 28.0[‡¶] (− 30.0,− 26.1)	− 29.4[‡¶] (− 31.4,− 27.4)	− 22.8 (− 24.7,− 20.9)	− 24.4 (− 26.3,− 22.4)

Table 2 continued

	Placebo		Upadacitinib 15 mg QD		Upadacitinib 30 mg QD		Adalimumab 40 mg EOW	
	Week 12 (*N* = 394)	Week 24 (*N* = 367)	Week 12 (*N* = 405)	Week 24 (*N* = 390)	Week 12 (*N* = 398)	Week 24 (*N* = 376)	Week 12 (*N* = 410)	Week 24 (*N* = 391)
Itch[d,e]	− 0.9 (− 1.1,− 0.6)	− 1.2 (− 1.4,− 0.9)	− 2.7[‖] (− 2.9,− 2.4)	− 3.0[¶] (− 3.2,− 2.8)	− 3.1[‖] (− 3.3,− 2.9)	− 3.1[¶] (− 3.3,− 2.9)	− 2.3 (− 2.5,− 2.0)	− 2.5 (− 2.7,− 2.3)
WPAI AI	− 7.6 (− 9.8,− 5.4)	− 11.2 (− 13.6,− 8.8)	− 19.2[‡] (− 21.4,− 17.0)	− 24.3[‡§] (− 26.6,− 22.0)	− 21.2[‡‖] (− 23.5,− 19.0)	− 24.7[‡‖] (− 27.0,− 22.3)	− 17.0 (− 19.2,− 14.8)	− 20.4 (− 22.7,− 18.0)
WPAI presenteeism[f]	− 5.1 (− 7.8,− 2.3)	− 8.9 (− 11.8,− 6.1)	− 18.4[‡] (− 21.1,− 15.7)	− 22.4[‡] (− 25.1,− 19.6)	− 17.9[‡] (− 20.5,− 15.2)	− 21.7[‡] (− 24.4,− 18.9)	− 17.8 (− 20.5,− 15.0)	− 19.9 (− 22.7,− 17.1)
WPAI OWI[f]	− 5.0 (− 8.4,− 1.7)	− 8.3 (− 11.8,− 4.8)	− 20.1[‡] (− 23.4,− 16.9)	− 23.2[‡] (− 26.6,− 19.8)	− 19.5[‡] (− 22.7,− 16.3)	− 22.6[‡] (− 26.0,− 19.2)	− 17.1 (− 20.4,− 13.8)	− 20.3 (− 23.8,− 16.9)
WPAI absenteeism[f]	− 0.6 (− 3.4, 2.2)	− 0.2 (− 3.0, 2.6)	− 6.2[†] (− 9.0,− 3.5)	− 5.2[†] (− 7.9,− 2.5)	− 5.8[†] (− 8.6,− 3.1)	− 5.2[†] (− 7.9,− 2.5)	− 2.7 (− 5.5, 0.1)	− 5.5 (− 8.2,− 2.7)

AI activity impairment, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BP* bodily pain, *CI* confidence interval, *EOW* every other week, *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-effects model repeated measurement, *NRS* numerical rating scale, *OWI* overall work impairment, *PCS* Physical Component Summary, *PF* physical functioning, *PRO* patient-reported outcome, *PtGA* 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

[*] $p < 0.05$, [†] $P \leq 0.01$, and [‡] $P \leq 0.001$ for upadacitinib versus placebo and [§] $p < 0.05$, [‖] $P \leq 0.01$, and [¶] $p \leq 0.001$ for upadacitinib versus adalimumab. *P* values nominal except for week 12 multiplicity-controlled endpoints of HAQ-DI, FACIT-F, SF-36 PCS, and SAPS

[a] Reported only for patients with investigator-determined psoriatic spondylitis at baseline

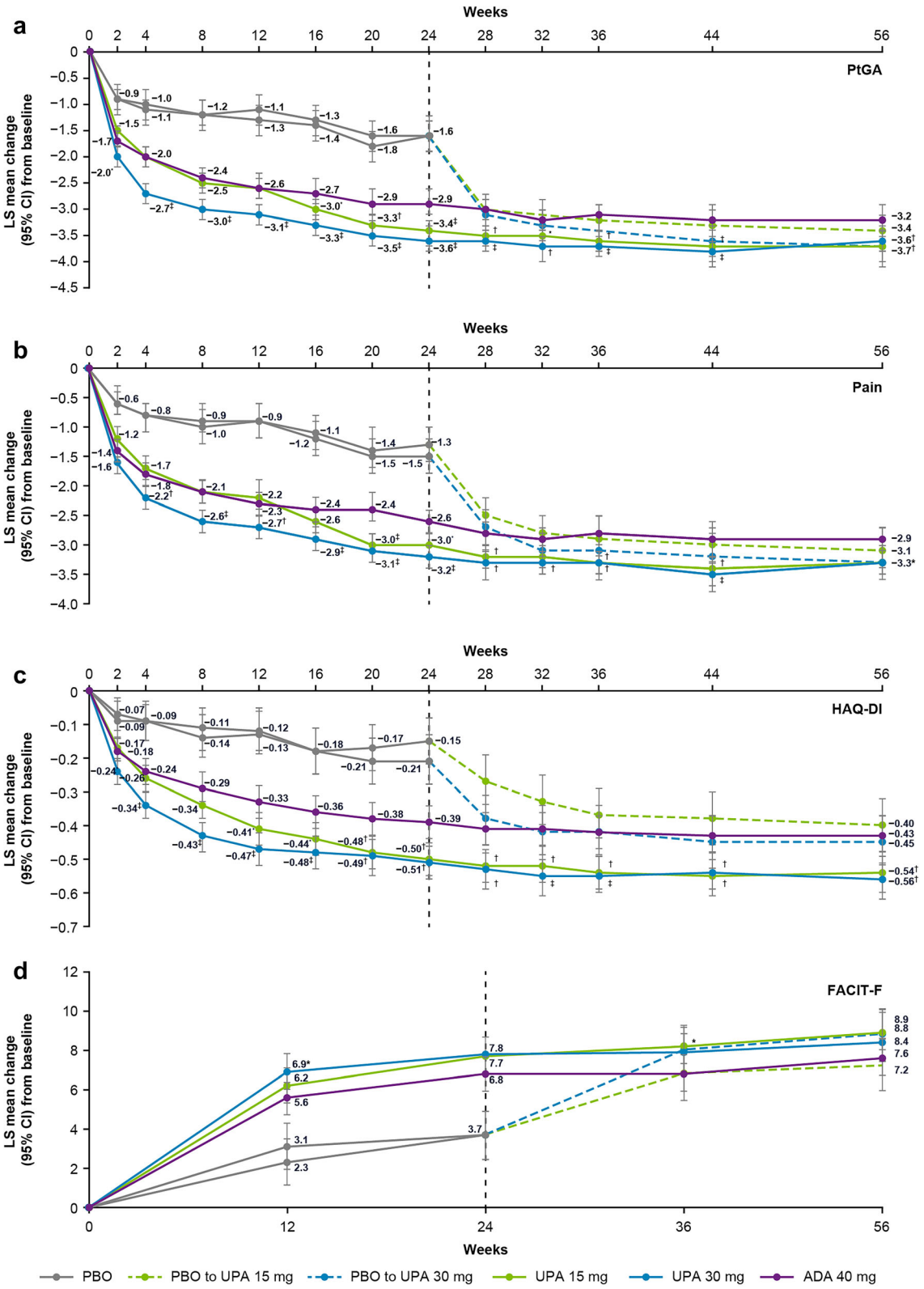
[b] Presented as response rate (95% CI). NRI. N: placebo: 130, upadacitinib 15 mg QD: 139, upadacitinib 30 mg QD: 138; and adalimumab 40 mg, 127

[c] Mean of BASDAI questions 5 and 6

[d] Assessed at week 16 instead of 12

[e] SAPS question 2

[f] Reported only for patients who were employed


a
Weeks
PtGA
LS mean change (95% CI) from baseline
b
Pain
c
HAQ-DI
d
FACIT-F
PBO
PBO to UPA 15 mg
PBO to UPA 30 mg
UPA 15 mg
UPA 30 mg
ADA 40 mg

◀**Fig. 1** Change from baseline through Week 56 in PtGA, pain, HAQ-DI, and FACIT-F over time (MMRM). **a** PtGA, **b** Pain, **c** HAQ-DI, **d** FACIT-F. $^{*}p < 0.05$, $^{\dagger}p \leq 0.01$, and $^{\ddagger}p \leq 0.001$ for UPA versus ADA. ADA adalimumab, CI confidence interval, FACIT-F Functional Assessment of Chronic Illness Therapy-Fatigue, HAQ-DI Health Assessment Questionnaire Disability Index, LS least squares, MMRM mixed-effects model repeated measurement, PBO placebo, PtGA Patient Global Assessment of Disease Activity, UPA upadacitinib

clinically meaningful (Fig. 3). The range of NNTs with upadacitinib 15 mg and 30 mg versus placebo was generally lower than for adalimumab 40 mg versus placebo at both 12 and 24 weeks (Fig. 3 and ESM Fig. S3).

DISCUSSION

The SELECT-PsA 1 RCT compared upadacitinib 15 and 30 mg with placebo and adalimumab as an active comparator in non-bDMARD-IR patients with PsA [14]. In this post hoc analysis of the SELECT-PsA 1 trial, patients receiving upadacitinib 15 and 30 mg reported significant and clinically meaningful improvements across a broad variety of PROs evaluating disease activity, pain, physical function, fatigue, psoriasis symptom severity, HRQoL, and work productivity at weeks 12 and 24 compared with placebo. Significant improvements in PtGA, pain, and HAQ-DI with upadacitinib were reported as early as week 2 suggesting rapid

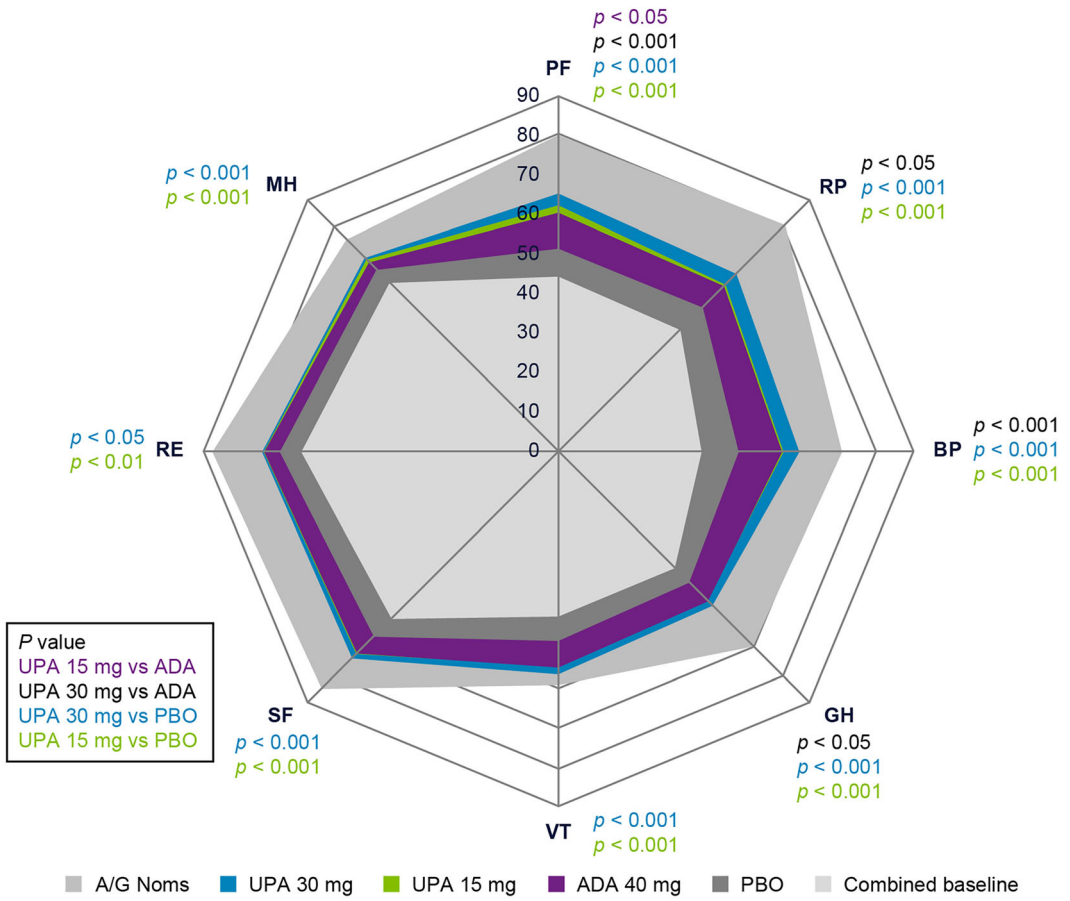


Fig. 2 SF-36 domain scores at Week 12 relative to age- and gender-adjusted normative values (MMRM). *ADA* adalimumab, *A/G norms* age- and gender-matched normative values, *BL* baseline, *BP* bodily pain, *GH* general health, *MH* mental health, *MMRM* mixed-effects model repeated measurement, *PBO* placebo, *PF* physical functioning, *RE* role emotional, *RP* role physical, *SF* social functioning, *SF-36* 36-Item Short Form Health Survey, *UPA* upadacitinib, *US* United States, *VT* vitality

Table 3 LS mean change (95% CI) from baseline in PRO scores at week 56 (MMRM)

	Upadacitinib 15 mg QD (*N* = 371)	**Upadacitinib 30 mg QD (*N* = 362)**	**Adalimumab 40 mg EOW (*N* = 364)**
PtGA 0–10, NRS	− 3.7 (− 3.9,− 3.4)†	− 3.6 (− 3.9,− 3.4)†	− 3.2 (− 3.4,− 2.9)
Pain 0–10, NRS	− 3.3 (− 3.6,− 3.1)*	− 3.3 (− 3.6,− 3.1)*	− 2.9 (− 3.1,− 2.7)
HAQ-DI	− 0.54 (− 0.59,− 0.48)†	− 0.56 (− 0.61,− 0.50)†	− 0.43 (− 0.49,− 0.38)
FACIT-F	8.9 (8.0, 9.9)	8.4 (7.4, 9.4)	7.6 (6.7, 8.6)
SF-36 PCS	10.8 (10.0, 11.7)†	10.5 (9.6, 11.4)†	8.9 (8.0, 9.8)
SF-36 MCS	5.2 (4.2, 6.1)	4.4 (3.4, 5.3)	4.3 (3.4, 5.2)
SF-36 domains			
PF	25.6 (23.2, 27.9)†	24.9 (22.5, 27.2)†	20.5 (18.2, 22.8)
RP	25.2 (22.9, 27.5)*	24.6 (22.3, 27.0)	21.6 (19.3, 23.9)
BP	28.6 (26.2, 30.9)†	28.8 (26.4, 31.2)†	24.1 (21.7, 26.4)
GH	17.4 (15.6, 19.3)	15.5 (13.6, 17.3)	15.3 (13.5, 17.2)
VT	19.9 (17.9, 21.9)‡	16.4 (14.4, 18.4)	15.0 (13.0, 17.0)
SF	17.9 (15.6, 20.1)	17.7 (15.5, 19.9)	14.9 (12.7, 17.2)
RE	14.2 (12.0, 16.4)	13.1 (10.9, 15.3)	13.4 (11.3, 15.6)
MH	12.1 (10.4, 13.8)*	11.1 (9.4, 12.8)	9.6 (7.9, 11.4)
EQ-5D-5L	0.20 (0.18, 0.22)	0.19 (0.18, 0.21)	0.18 (0.16, 0.20)
BASDAI[a]	− 3.3 (− 3.7,− 2.9)	− 3.2 (− 3.6,− 2.8)	− 2.8 (− 3.2,− 2.4)
BASDAI 50[a,b]	69.8 (61.5, 78.2)	68.1 (59.7, 76.4)	56.1 (46.7, 65.5)
Morning stiffness[a,c]	− 3.2 (− 3.4,− 3.0)†	− 3.3 (− 3.5,− 3.0)†	− 2.8 (− 3.0,− 2.6)
SAPS[d]	− 29.6 (− 31.4,− 27.9)†	− 30.4 (− 32.2,− 28.7)‡	− 25.8 (− 27.6,− 24.1)
Itch[d,e]	− 3.1 (− 3.3,− 2.9)†	− 3.2 (− 3.4,− 3.0)‡	− 2.7 (− 2.9,− 2.5)
WPAI AI	− 28.2 (− 30.5,− 25.9)†	− 26.8 (− 29.1,− 24.4)*	− 23.2 (− 25.5,− 20.9)
WPAI presenteeism[f]	− 25.5 (− 28.4,− 22.7)*	− 24.0 (− 26.8,− 21.1)	− 20.8 (− 23.7,− 17.9)
WPAI OWI[f]	− 24.5 (− 28.1,− 20.9)	− 22.9 (− 26.5,− 19.3)	− 20.8 (− 24.5,− 17.1)

Table 3 continued

	Upadacitinib 15 mg QD (*N* = 371)	Upadacitinib 30 mg QD (*N* = 362)	Adalimumab 40 mg EOW (*N* = 364)
WPAI absenteeism[f]	− 3.0 (− 5.8,− 0.1)	− 2.7 (− 5.5, 0.2)	− 4.9 (− 7.8,− 2.0)

AI activity impairment, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BP* bodily pain, *CI* confidence interval, *EOW* every other week, *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-effects model repeated measurement, NRS numerical rating scale, *OWI* overall work impairment, *PCS* Physical Component Summary, *PF* physical functioning, *PRO* patient-reported outcome, *PtGA* 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

* $p < 0.05$, † $P \leq 0.01$, and ‡ $p \leq 0.001$ for upadacitinib versus adalimumab

[a] Reported only for patients with investigator-determined psoriatic spondylitis at baseline

[b] Presented as response rate (95% CI). NRI. N: upadacitinib 15 mg QD: 116; upadacitinib 30 mg QD: 119; and adalimumab 40 mg, 107

[c] Mean of BASDAI questions 5 and 6

[d] Assessed at week 16 instead of 12

[e] SAPS question 2

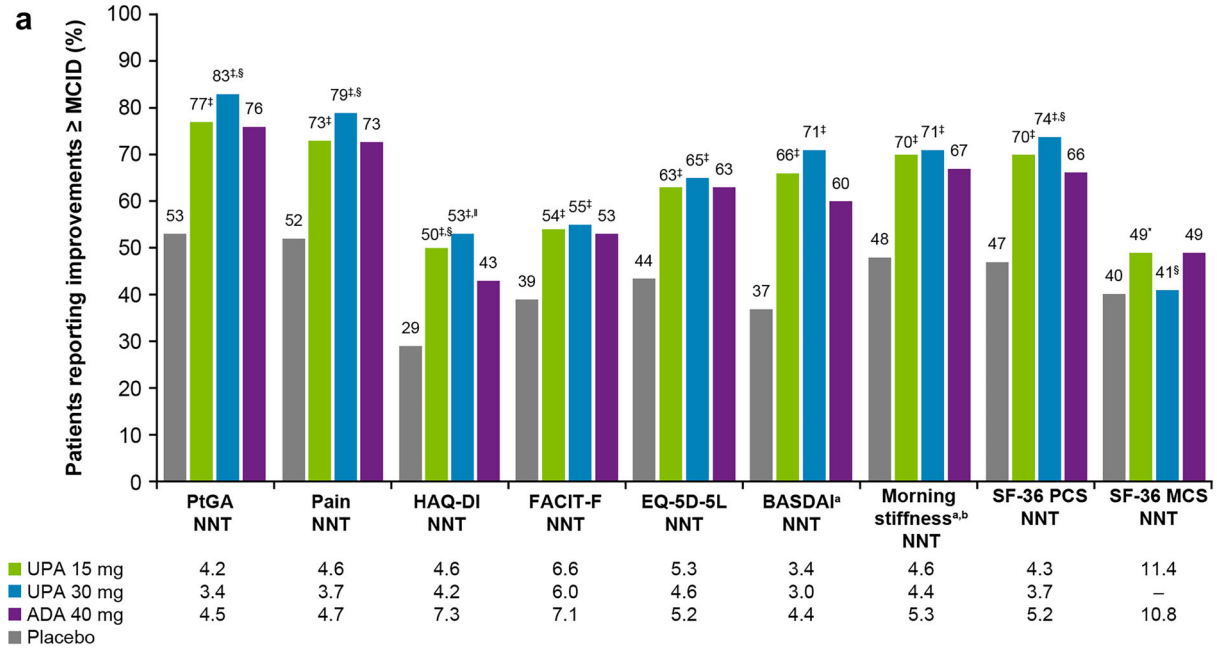
[f] Reported only for patients who were employed

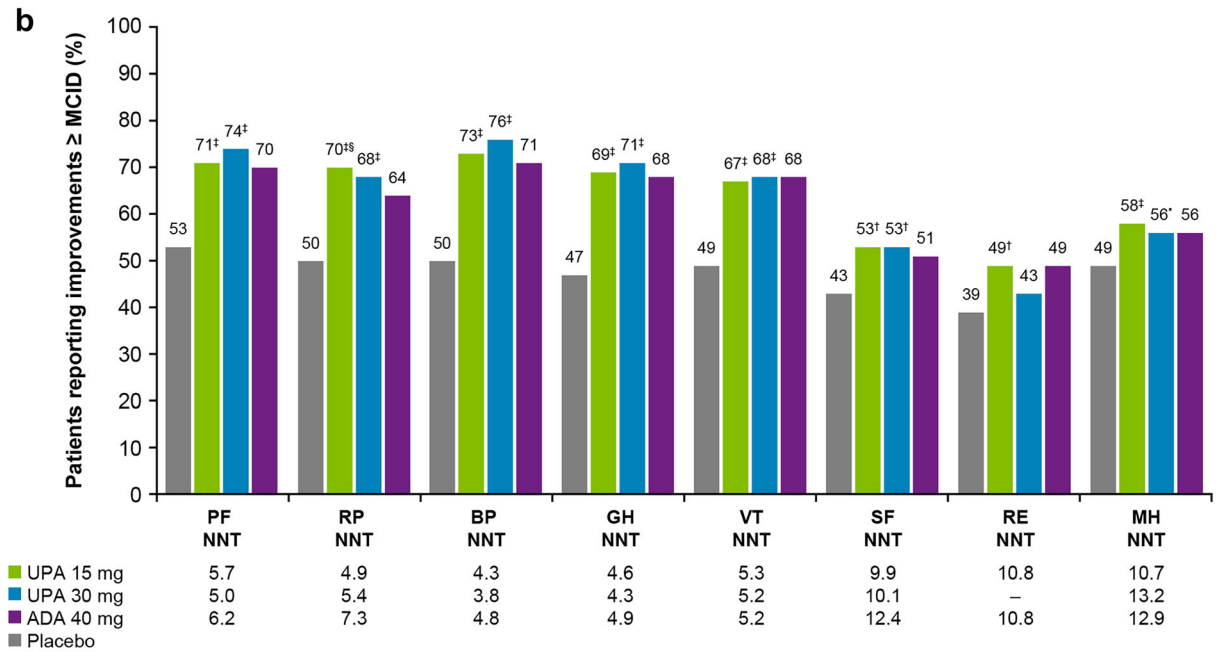
onset of effect in both pain and function. Significant sustained improvements with upadacitinib treatment in SF-36 PCS, MCS, all eight domains and FACIT-F scores at 24 and 56 weeks indicate a substantial positive impact on HRQoL. This is of particular importance because PsA negatively impacts many aspects of life including patients' psychological and psychosocial well-being, ability to perform daily activities, participation in social activities, as well as the physical and emotional aspects of life [33–37]. At 12 weeks, significantly more patients treated with both doses of upadacitinib reported PtGA, HAQ-DI, FACIT-F, EQ-5D-5L, SF-36 PCS, and 6–7 domain scores ≥ normative values, indicative of the healthy general population compared with placebo, despite ≤ 11% having such scores at baseline. These improvements continued to week 56 with the majority reporting scores as if they did not have an inflammatory arthritis such as PsA.

Sustained improvements in WPAI domains with upadacitinib treatment compared with placebo were also reported, and are noteworthy because approximately one-third of respondents in a multinational survey [38] reported that they missed work because of PsA and that their PsA impacted their ability to work full time.

At week 12, improvements in HAQ-DI, SAPS, and SF-36 PCS and PF domain scores with upadacitinib (15 mg: PF or 30 mg: PF, RP, BP and GH) were statistically greater than with adalimumab 40 mg and continued through week 56. Through week 24, NNTs were ≤ 10 across most PROs with both doses of upadacitinib and the range of NNTs generally lower than with adalimumab 40 mg.

At week 12, reported improvements in PROs were generally numerically greater with upadacitinib 30 mg compared with 15 mg. By week 24; however, improvements with both doses of upadacitinib were similar and sustained to week 56. It is important to contextualize the findings of this RCT with other JAK inhibitors indicated for the treatment of PsA such as tofacitinib. In the OPAL Broaden trial [39], significant improvements in PROs at week 12 were reported with tofacitinib (5 or 10 mg twice daily) treatment in DMARD-IR PsA patients. Three of eight SF-36 domain scores [PF, BP, and vitality (VT)] were significantly improved with


a
Patients reporting improvements ≥ MCID (%)
100
90
80
70
60
50
40
30
20
10
0
53
77‡
83‡,§
76
52
73‡
79‡,§
73
29
50‡,§
53‡,‖
43
39
54‡
55‡
53
44
63‡
65‡
63
37
66‡
71‡
60
48
70‡
71‡
67
47
70‡
74‡,§
66
40
49*
41§
49
PtGA NNT
Pain NNT
HAQ-DI NNT
FACIT-F NNT
EQ-5D-5L NNT
BASDAI[a] NNT
Morning stiffness[a,b] NNT
SF-36 PCS NNT
SF-36 MCS NNT
UPA 15 mg 4.2 4.6 4.6 6.6 5.3 3.4 4.6 4.3 11.4
UPA 30 mg 3.4 3.7 4.2 6.0 4.6 3.0 4.4 3.7 –
ADA 40 mg 4.5 4.7 7.3 7.1 5.2 4.4 5.3 5.2 10.8
Placebo


b
Patients reporting improvements ≥ MCID (%)
100
90
80
70
60
50
40
30
20
10
0
53
71‡
74‡
70
50
70‡§
68‡
64
50
73‡
76‡
71
47
69‡
71‡
68
49
67‡
68‡
68
43
53†
53†
51
39
49†
43
49
49
58‡
56*
56
PF NNT
RP NNT
BP NNT
GH NNT
VT NNT
SF NNT
RE NNT
MH NNT
UPA 15 mg 5.7 4.9 4.3 4.6 5.3 9.9 10.8 10.7
UPA 30 mg 5.0 5.4 3.8 4.3 5.2 10.1 – 13.2
ADA 40 mg 6.2 7.3 4.8 4.9 5.2 12.4 10.8 12.9
Placebo

◀**Fig. 3** Proportion of patients reporting improvements ≥ MCID and NNTs in PROs at Week 12 (NRI). **a** PROs, **b** SF-36 domains. $^{*}p < 0.05$, $^{\dagger}p \leq 0.01$, and $^{\ddagger}p \leq 0.001$ UPA versus placebo and $^{\S}p < 0.05$ and $^{\|}p \leq 0.01$ for UPA versus ADA. aReported only for patients with investigator-determined psoriatic spondylitis at baseline. bMean of BASDAI questions 5 and 6. NNTs were calculated for UPA versus PBO and for ADA versus PBO. NNT for UPA 30 mg was not calculated for MCS and RE because the proportion of patients reporting improvement was not significantly different for UPA 30 mg versus PBO. 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). *ADA* adalimumab, *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, *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

both doses of tofacitinib and additionally, the social functioning domain with 5 mg versus placebo at week 12 and were similar to those with adalimumab versus placebo in PF, BP, and GH domains. In contrast, improvements in HAQ-DI, SAPS, and SF-36 PCS scores following 12 weeks of upadacitinib treatment were greater than adalimumab. Similarly, all eight SF-36 domain scores were significantly improved with upadacitinib treatment versus placebo and exceeded those reported with adalimumab in one (15 mg) and four (30 mg) domains at week 12 in SELECT-PsA 1. Future comparative studies are needed to elucidate the comparative efficacy of JAK inhibitors in PsA patients.

The following limitations should be kept in mind when interpreting the results of this trial. The RCT was not powered to detect differences between the upadacitinib groups. There was no placebo group available for comparison after week 24. Finally, results may not be generalizable beyond the trial patient population.

CONCLUSIONS

Treatment with upadacitinib 15 or 30 mg resulted in clinically meaningful improvements in PROs compared with placebo at 12 weeks in non-bDMARD-IR patients with active PsA which were maintained or further improved at weeks 24 and 56. Clinically meaningful improvements in PtGA, pain, and HAQ-DI were evident as early as week 2 with upadacitinib (15 and 30 mg) and adalimumab 40 mg. Overall, improvements were similar between upadacitinib 15 mg QD and adalimumab 40 mg EOW with numerically better results for upadacitinib

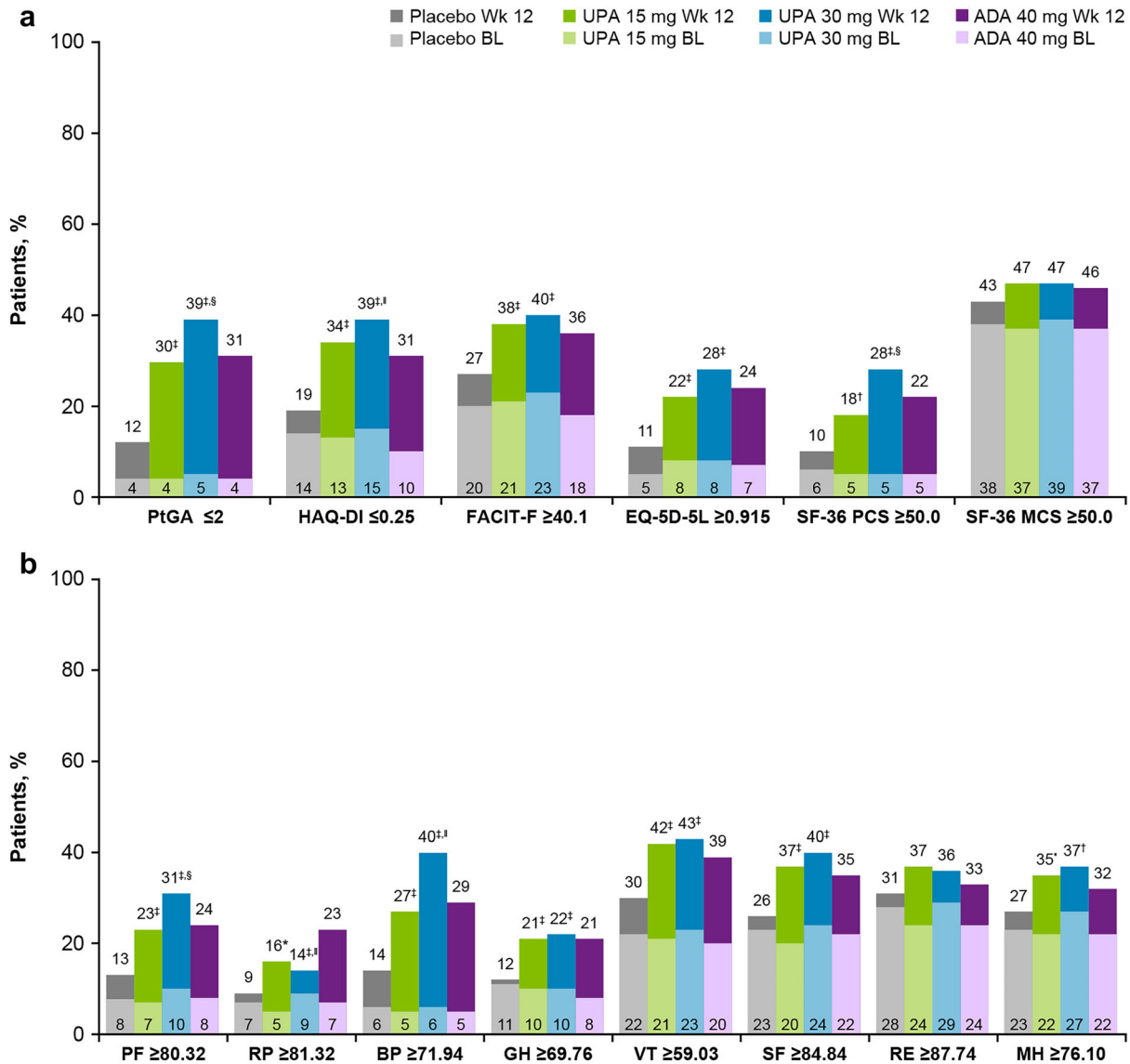


Fig. 4 Proportion of patients reporting PRO scores ≥ normative values at baseline and Week 12 (NRI) and age- and gender-matched normative values in SF-36 domains. **a** PROs, **b** SF-36 domains. $^{*}p < 0.05$, $^{\dagger}p \leq 0.01$, and $^{\ddagger}p \leq 0.001$ UPA versus PBO and $^{\S}p < 0.05$ and $^{\|}p \leq 0.01$ for UPA versus ADA. The percentages at 12 weeks may or may not include the same patients that achieved that outcome at baseline. *ADA* adalimumab, *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, *MCID* minimal clinically important difference, *MCS* Mental Component Summary, *MH* mental health, *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

30 mg QD in many PROs. Overall, findings from this study demonstrate the potential of upadacitinib treatment to provide significant and clinically meaningful improvements in HRQoL and other outcomes most important to patients with PsA.

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Compliance with Ethics Guidelines. The SELECT-PSA 1 study was conducted according to the International Conference on Harmonization guidelines and the principles of the Declaration of Helsinki. All patients provided written informed consent. The trial protocol was approved by independent ethics committees and institutional review boards (ESM Table S1).

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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