Upadacitinib response rates in patients with psoriatic arthritis enrolled in the SELECT-PsA-1 and SELECT-PsA-2 trials assessed according to modified PsARC

Laura C. Coates[1*], Toby Garrood[2], Nicola Gullick[3], Philip Helliwell[4], Toby Kent[5], Jonathan Marks[6], William Tillett[7], Daljit Kaur-Papadakis[5], Hasan Tahir[8], Stijn van Haaren[5], Iain McInnes[9]

[1]NDORMS, University of Oxford, Oxford, UK;

[2]Guy's and St. Thomas' Foundation Trust, London, UK;

[3]University Hospitals Coventry and Warwickshire, Coventry, UK;

[4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK;

[5]Abbvie Ltd, Maidenhead, UK;

[6]Christchurch Hospital, University Hospitals Dorset NHS Foundation Trust, Christchurch, UK;

[7]Royal National Hospital for Rheumatic Diseases, University of Bath, Bath, UK;

[8]Barnet Hospital, Royal Free London NHS Trust, Barnet, UK;

[9]University of Glasgow College of Medical Veterinary Sciences, Glasgow, UK

**Corresponding author:*

Postal address

Botnar Research Centre, Windmill Road, Oxford, OX3 7LD, UK

Email laura.coates@ndorms.ox.ac.uk

Key message: Upadacitinib efficacy can be effectively assessed according to the modified PsARC at 12 weeks.

Dear Editor,

Upadacitinib (UPA), an oral Janus kinase inhibitor approved for the treatment of moderate to severe rheumatoid arthritis (RA), is being introduced as a new treatment option for psoriatic arthritis (PsA) (1) and has recently received marketing approval in Europe and the UK. Two recent randomised controlled trials, SELECT-PsA-1 and SELECT-PsA-2 have demonstrated positive results regarding the efficacy and safety of UPA in patients with PsA and prior inadequate response or intolerance to ≥1 disease-modifying antirheumatic drugs (DMARDs). SELECT-PsA-1 evaluated UPA versus placebo versus adalimumab (ADA) in patients with an intolerance or inadequate response to ≥1 non-biologic DMARDs (1). SELECT-PsA-2 assessed UPA versus placebo in patients with an intolerance or inadequate response to ≥1 biologic DMARDs (2).

In both trials, the primary efficacy outcome was the percentage of patients achieving the American College of Rheumatology 20% improvement score (ACR20) at Week 12. However, the UK National Institute for Health and Care Excellence recommends that response to PsA treatment is assessed according to the modified Psoriatic Arthritis Response Criteria (PsARC) at Week 12, 16, or 24, depending on the mode of action. The modified PsARC response is based on four components: tender joint count (TJC) of 68 joints, swollen joint count (SJC) of 66 joints, patient global self-assessment (PtGA) and physician global assessment (PGA). A modified PsARC response is achieved if no component has worsened and at least two of the following four criteria for improvement apply: TJC or SJC improvement of ≥30% (at least one of these is required) and/or PtGA and/or PGA improvement of ≥1 point (on a five-point Likert scale) (3).

The purpose of the present analysis was to assess modified PsARC responses from Week 2 to Week 24 post-initiation for patients enrolled in SELECT-PsA-1 (treatment arms: UPA-15 mg once-daily [UPA-15mg], placebo and ADA-40 mg every other week) and SELECT-PsA-2 (treatment arms: UPA-15mg and placebo) (Supplementary Figure S1, available at *Rheumatology* online).

Despite relatively high placebo response rates, UPA-15mg response rates were significantly higher than for placebo ($P<0.05$) at all assessments between Week 2 and Week 24 in the SELECT-PsA-1 and SELECT-PsA-2 trials (see Table 1) (4). UPA-15mg response rates were also higher than for ADA ($P<0.05$) at Week 20 and Week 24 in SELECT-PsA-1 (Supplementary Figure S1, available at *Rheumatology* online). The outcomes assessed using PsARC were consistent with previously published ACR20 responses (Week 12 ACR20 response rate was significantly higher with UPA-15mg versus placebo in both SELECT-PsA-1 (70.6% versus 36.2%; $P<0.0001$) (5) and SELECT-PsA-2 (56.9% versus 24.1%; $P<0.0001$) (6)).

Further, UPA-15mg rates for improvement in the individual modified PsARC components between Week 12 and Week 24 were consistent and, at Week 24, response rates for individual components ranged between 81.6% (PtGA) and 89.7% (PGA) in SELECT-PsA-1 and between 69.2% (PtGA) and 79.6% (PGA) in SELECT-PsA-2 (Supplementary Table S1, available at *Rheumatology* online). Additionally, baseline characteristics (including sex, PsA duration, body mass index (BMI), tobacco use, body surface area (BSA) ≥3%, enthesitis and dactylitis) were generally balanced between Week 24 modified PsARC responders and non-responders in each trial treatment arm (not shown; data available upon request).

Lastly, modified PsARC response rate differences between treatment arms at Week 24 for UPA-15mg versus placebo (according to pooled SELECT-PsA-1 and SELECT-PsA-2 data) and for UPA-15mg versus ADA (SELECT-PsA-1 data) were similar in patients when stratified by baseline characteristics and in patients receiving UPA-15mg monotherapy versus combination therapy (not shown; data available upon request).

From these results, we can conclude that patients treated with UPA-15mg demonstrated higher modified PsARC response rates compared to placebo (P<0.05), with improvements observed as early as Week 2 and stable response rates observed from Week 12 in both SELECT-PsA-1 and SELECT-PsA-2 (Table 1). The observed response rates for improvement in individual modified PsARC components were consistent, including at Week 24 in both trials (Supplementary Table S1, available at *Rheumatology* online). In addition, higher modified PsARC response rates for UPA-15mg versus ADA (P<0.05) were observed at Week 20 and Week 24 in SELECT-PsA-1 (Table 1) and differences in Week 24 modified PsARC responses versus placebo and versus ADA were generally consistent across baseline characteristics and UPA-15mg mono/combination therapy (not shown; data available upon request). A previous integrated analysis of pooled safety data from SELECT-PsA-1 and SELECT-PsA-2, reported a generally consistent safety profile between UPA-15mg and ADA (not shown; data available upon request) from long-term exposure to UPA-15mg (7).

These results suggest that UPA efficacy can be effectively assessed according to the modified PsARC.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Table 1. Modified PsARC response rate differences between treatment arms in SELECT-PsA-1 and SELECT-PsA-2

Week of assessment	Modified PsARC response rate differences between treatment arms % (95% CI)		
	SELECT-PsA-1		SELECT-PsA-2
	UPA-15mg minus placebo	UPA-15mg minus ADA	UPA-15mg minus placebo
Week 2	14.8 (8.5–21.1)*	−2.3 (−9.0, 4.3)	22.4 (13.5, 31.3)*
Week 12	23.7 (17.6–29.9)*	2.8 (−2.8, 8.4)	34.3 (25.4, 43.2)*
Week 16	24.4 (18.3–30.5)*	1.9 (−3.6, 7.4)	31.4 (22.4, 40.5)*
Week 20	21.3 (15.5–27.1)*	6.3 (1.0, 11.6)*	28.6 (19.6, 37.7)*
Week 24	24.3 (18.5–30.2)*	7.0 (1.7, 12.3)*	31.9 (22.9, 40.9)*

*Difference between treatment arms statistically significant at 0.05 level.
The table was adapted from Coates et al., 2021 (4).