



OPEN ACCESS

## CLINICAL SCIENCE

# Efficacy and safety of risankizumab for active psoriatic arthritis: 24-week results from the randomised, double-blind, phase 3 KEEPsAKE 2 trial

Andrew Östör,<sup>1</sup> Filip Van den Bosch ,<sup>2</sup> Kim Papp,<sup>3</sup> Cecilia Asnal,<sup>4</sup> Ricardo Blanco ,<sup>5</sup> Jacob Aelion,<sup>6</sup> Gabriela Alperovich,<sup>7</sup> Wenjing Lu,<sup>7</sup> Zailong Wang,<sup>7</sup> Ahmed M Soliman,<sup>7</sup> Ann Eldred,<sup>7</sup> Lisa Barcomb,<sup>7</sup> Alan Kivitz<sup>8,9</sup>

Handling editor Josef S Smolen

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/annrheumdis-2021-221048>).

For numbered affiliations see end of article.

**Correspondence to**

Dr Andrew Östör, Emeritus Research, Level 2/1180 Toorak Rd, Camberwell, VIC 3124, Australia; [andrewostor@gmail.com](mailto:andrewostor@gmail.com)

This work was presented at the 2021 European League Against Rheumatism European Congress of Rheumatology Virtual Congress (Östör A, *et al.* *Ann Rheum Dis* 2021;80:138–9).

Received 24 June 2021

Accepted 12 October 2021



© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

**To cite:** Östör A, Van den Bosch F, Papp K, *et al.* *Ann Rheum Dis* Epub ahead of print: [please include Day Month Year]. doi:10.1136/annrheumdis-2021-221048

**ABSTRACT**

**Objectives** Risankizumab is an interleukin-23 inhibitor under study for the treatment of patients with psoriatic arthritis (PsA). The phase 3 KEEPsAKE 2 trial investigated the efficacy and safety of risankizumab versus placebo in patients with active PsA who had previous inadequate response or intolerance to  $\leq 2$  biological therapies (Bio-IR) and/or  $\geq 1$  conventional synthetic disease-modifying antirheumatic drug (csDMARD-IR). Results through week 24 are reported here.

**Methods** Adults with PsA who were Bio-IR and/or csDMARD-IR were randomised to receive subcutaneously administered risankizumab 150 mg or placebo at weeks 0, 4 and 16 during a 24-week, double-blind treatment period. The primary endpoint was the proportion of patients who achieved  $\geq 20\%$  improvement in American College of Rheumatology score (ACR20) at week 24. Secondary endpoints assessed key domains of PsA and patient-reported outcomes.

**Results** A total of 444 patients (median age 53 years, range 23–84 years) were randomised to risankizumab (n=224) or placebo (n=220); 206 patients (46.5%) were Bio-IR. At week 24, a significantly greater proportion of patients receiving risankizumab achieved the primary endpoint of ACR20 (51.3% vs 26.5%,  $p < 0.001$ ) and all secondary endpoints ( $p < 0.05$ ) compared with placebo. Serious adverse events were reported for 4.0% and 5.5% of risankizumab-treated and placebo-treated patients, respectively; serious infections were reported for 0.9% and 2.3%, respectively.

**Conclusion** Treatment with risankizumab resulted in significant improvements versus placebo in key disease outcomes and was well tolerated in patients with PsA who were Bio-IR and/or csDMARD-IR.

**Trial registration number** NCT03671148.

**INTRODUCTION**

Psoriatic arthritis (PsA) is a progressive, chronic, inflammatory condition that affects approximately 30% of patients with psoriasis.<sup>1,2</sup> Symptoms of PsA involve the synovium, tendons, entheses and bone in axial or peripheral joints, and progression is characterised by joint degeneration, leading to disability and increased risk of mortality.<sup>3–5</sup> Comorbid conditions such as cardiovascular disease, metabolic syndrome, obesity, diabetes and mood disorders are common among patients with PsA, contributing to functional impairment and decreased quality of

**Key messages****What is already known about this subject?**

► Many patients with psoriatic arthritis (PsA) do not achieve an adequate response or are intolerant to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) or biological agents, highlighting a need for additional effective treatments.

**What does this study add?**

► This study demonstrates the efficacy of the interleukin-23 inhibitor, risankizumab, across multiple domains of PsA, including patient-reported outcomes assessing disease burden in patients who had previous inadequate responses to csDMARDs or biological agents.  
► Risankizumab was well tolerated based on low rates of serious adverse events (AEs), severe AEs, serious and opportunistic infections, and discontinuation of treatment due to AEs by  $< 1\%$  of patients receiving risankizumab.

**How might this impact on clinical practice or future developments?**

► Results from the phase 3 KEEPsAKE 2 trial demonstrate that risankizumab is effective and well tolerated to treat active PsA.  
► Risankizumab may provide an additional treatment option for patients with PsA who have had an inadequate response or are intolerant to currently approved therapies.

life.<sup>3,6</sup> PsA is also associated with considerable individual, societal and economic burdens, including reduced employment and increased healthcare costs compared with the general population.<sup>7</sup>

The aim of PsA treatment is to reduce symptoms, structural damage and inflammation, while restoring overall function, with a goal of remission (REM) and/or reduced disease activity and increased long-term, health-related quality of life.<sup>8,9</sup> Initial recommended treatment for PsA is non-steroidal anti-inflammatory drugs (NSAIDs), which may be combined with local corticosteroid injections. Second-line treatment includes use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as methotrexate, followed by

therapy using antitumour necrosis factor medications, and/or other biological agents.<sup>8,9</sup>

Although biological agents are effective in treating PsA,<sup>10</sup> approximately 25%–40% of patients do not achieve at least 20% improvement in American College of Rheumatology score (ACR20), and clinical REM and minimal disease activity (MDA) are often short-lived.<sup>11–19</sup> Lack of efficacy frequently leads to treatment switching or discontinuation, which may negatively affect patients' clinical outcomes and increase treatment costs,<sup>20–24</sup> revealing a need for well-tolerated treatments with sustained efficacy.

Risankizumab is a humanised IgG1 monoclonal antibody that specifically inhibits interleukin (IL)-23 by binding to its p19 subunit.<sup>25–26</sup> IL-23 is a key component driving the release of IL-17 from Th17 cells, and overexpression of IL-23 has been reported in affected skin in psoriasis and in the synovial tissue of patients with PsA.<sup>26–28</sup> KEEPSAKE 2 is an ongoing clinical trial that is evaluating the efficacy and safety of risankizumab to treat PsA in patients with a history of inadequate response or intolerance to csDMARD and/or biological therapies. The results of the initial 24-week double-blind period of the KEEPSAKE 2 trial are reported here.

## METHODS

### Study design and treatment

This was a phase 3, global, multicentre study assessing the efficacy and safety of risankizumab 150 mg vs placebo to treat PsA in patients with inadequate response or intolerance to biological agents (Bio-IR) and/or inadequate response or intolerance to conventional synthetic disease-modifying antirheumatic drugs (csDMARD-IRs). During a screening period of approximately 35 days, patients were stratified by current csDMARD use (0 vs  $\geq 1$ ), number of prior biological therapies (0 vs  $\geq 1$ ) and extent of psoriasis ( $\geq 3\%$  vs  $< 3\%$  body surface area affected by psoriasis), then randomised using an interactive response technology system in a 1:1 ratio to receive double-blind treatment with risankizumab 150 mg or matched placebo for 24 weeks, administered subcutaneously at weeks 0, 4 and 16. Patients then received open-label risankizumab every 12 weeks through week 208. The current report presents results for the 24-week double-blind period only, which was from 7 March 2019 to 22 June 2020. Study modifications for the COVID-19 pandemic included out-of-window study visits, phone calls and/or at-home visits for patients unable to attend on-site visits due to travel restrictions, quarantine or COVID-19 infection. The study drug was not administered to patients with suspected or confirmed COVID-19 infection; study drug administration and study visits could be resumed after patients recovered from infection.

### Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

### Patient eligibility

Eligible patients were adults (aged 18 years or older) with a clinical diagnosis of active PsA defined as  $\geq 5$  tender joints and  $\geq 5$  swollen joints, meeting the Classification Criteria for Psoriatic Arthritis, with symptoms of  $\geq 6$  months before screening, and active plaque psoriasis with  $\geq 1$  psoriatic plaque of  $\geq 2$  cm in diameter or nail changes consistent with psoriasis at screening. Patients were also required to be Bio-IR and/or csDMARD-IR, as described further.

### Prior or concomitant medications

Stable treatment with  $\leq 2$  concomitant csDMARDs at study entry was permitted if treatment was started  $\geq 12$  weeks before baseline at protocol-approved doses. In addition, patients could remain taking stable doses of concomitant NSAIDs, oral corticosteroids (equivalent to prednisone  $\leq 10$  mg/day) and other analgesics if they were started  $\geq 1$  week before baseline. Patients with a demonstrated lack of efficacy after  $\geq 12$  weeks or those who experienced intolerance or had a contraindication to methotrexate, sulfasalazine, leflunomide, apremilast, bucillamine, iguratimod or ciclosporin A were defined as csDMARD-IR.

Patients previously treated with biologic agents, except for IL-23, IL-12/23 or IL-17 antagonists, were also eligible for enrolment. The discontinuation of biological agents was required for prespecified durations before the first study treatment ( $\geq 4$  weeks for etanercept;  $\geq 8$  weeks for adalimumab, infliximab, certolizumab, golimumab and abatacept;  $\geq 1$  year (or  $\geq 6$  months with normalisation of B cells) for rituximab; or  $\geq 5$  times the mean terminal elimination half-life for any other permitted biological agent). Patients with a demonstrated lack of efficacy after  $\geq 12$  weeks of treatment, or intolerance to one or two eligible biological agents, were defined as Bio-IR.

### Assessments

#### Efficacy

The primary endpoint was the proportion of patients who achieved ACR20 at week 24. Ranked secondary endpoints assessed at week 24, except where noted, were change from baseline in Health Assessment Questionnaire–Disability Index (HAQ-DI), proportion of patients who achieved  $\geq 90\%$  reduction in Psoriasis Area and Severity Index (PASI 90), proportion of patients who achieved ACR20 at week 16, proportion of patients who achieved MDA, change from baseline in 36-Item Short Form Health Survey Physical Component Summary (SF-36 PCS) score and change from baseline in Functional Assessment of Chronic Illness Therapy–Fatigue Questionnaire (FACIT-Fatigue) score.

Additional non-ranked secondary endpoints included the proportion of patients who achieved ACR50, ACR70, resolution of enthesitis (Leeds Enthesitis Index=0) and resolution of dactylitis (Leeds Dactylitis Index=0) at week 24. Post hoc analyses included the proportions of patients who achieved very low disease activity (VLDA), Disease Activity in Psoriatic Arthritis (DAPSA) REM (defined as DAPSA score  $\leq 4$ ), low disease activity (LDA) +REM (defined as DAPSA score  $\leq 14$ ),  $\geq 50\%$  and  $\geq 85\%$  reductions in DAPSA, HAQ-DI score  $\leq 0.5$ ,  $\geq 10\%$  and  $\geq 30\%$ , and  $\geq 50\%$  reductions in pain (as measured on a visual analogue scale (VAS)), and minimally clinically important difference (MCID) for PtGA (defined as a reduction of 10 mm or more from baseline as measured on a VAS).

#### Safety

Safety assessments were based on monitoring of treatment-emergent adverse events (TEAEs), which were defined as adverse events (AEs) with onset after the first dose of study drug and were summarised based on the Medical Dictionary for Regulatory Activities V.23.1. Findings from physical examinations, vital sign measurements and clinical laboratory tests (haematology and chemistry) were also assessed. Unblinded safety data were reviewed periodically by an external independent data monitoring committee through the week 24 interim analysis.

## Statistics

### Sample size determination

It was estimated that 210 patients per treatment group would have a 90% power to detect a mean difference of 0.24 for the changes from baseline in HAQ-DI between risankizumab and placebo, assuming a common SD of 0.72. This sample size would also ensure that analyses would have at least a 90% power to detect a 20% treatment difference in ACR20 at week 24, with an assumed placebo response rate of 35%, using a two-sided test at a significance level of 0.05 and accounting for a 10% dropout rate.

### Efficacy and safety analyses

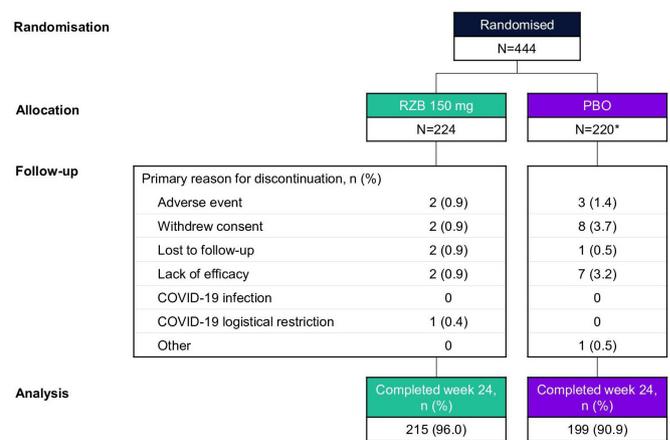
Efficacy and safety analyses were conducted based on the full analysis set, defined as all randomised patients who received one or more doses of the study drug. Patient demographic and medical characteristics were summarised using categorical variables or continuous variables as appropriate.

For the efficacy analyses, the Cochran-Mantel-Haenszel test adjusted for the stratification factors was used for categorical variables, and a mixed-effect model repeat-measurement method was used for continuous variables, each with a two-sided  $\alpha$  of 0.05. Due to the smaller number of patients with enthesitis and dactylitis at baseline, it was prespecified that data for the analyses of resolution of enthesitis and dactylitis were to be pooled from the companion study, KEEPsAKE 1 (NCT03675308), and KEEPsAKE 2 to increase sample size. Pooled data for these endpoints were analysed under the multiplicity control of KEEPsAKE 1 and are reported separately.<sup>29</sup> A multiple testing procedure was used to control the type I error rate by comparing risankizumab versus placebo in a fixed hypothesis testing procedure that began with the primary endpoint, proceeded through the ranked secondary endpoints in sequence, and continued until an endpoint did not achieve statistical significance. For categorical efficacy endpoints, missing data were handled by non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 (NRI-C). Missing data unrelated to COVID-19 were handled by non-responder imputation, and missing data due to COVID-19 (infection or logistical restrictions) were handled by multiple imputation. In addition, patients were considered non-responders after the initiation of rescue therapy or concomitant medications for PsA that could have meaningfully impacted efficacy assessments. For continuous efficacy endpoints, observations after the initiation of rescue therapy or concomitant medications for PsA that could have meaningfully impacted efficacy assessments were considered as missing and were excluded from the model. Safety results are summarised as the number and proportion of patients for whom TEAEs were reported within each treatment group.

## RESULTS

### Patients

A total of 444 patients at 99 sites in 23 countries were randomised to receive risankizumab (n=224) or placebo (n=220); of these patients, 215 (96.0%) and 199 (90.5%), respectively, completed the week 24 study visit (figure 1). One patient was randomised but never received the study drug and was excluded from the efficacy analyses; therefore, 443 patients were included in the full analysis set. Reasons for study discontinuation are summarised in figure 1. No patients discontinued from the study because of COVID-19 infection during the double-blind period; however, one patient discontinued because of COVID-19-related logistical restrictions. Less than 2.5% of patients had missing efficacy



**Figure 1** Patient disposition. \*One patient was randomised but never received study drug and was therefore excluded from the efficacy analyses, resulting in 219 patients included in the PBO group in the full analysis set. PBO, placebo; RZB, risankizumab.

data for any parameter in either treatment group because of COVID-19 (online supplemental table 1).

Demographics and baseline disease characteristics were generally balanced between treatment groups (table 1). The median age (range) was 53 (23–84) years and 55.1% were female. A total of 46.5% patients were Bio-IR. Demographics and baseline disease characteristics for the Bio-IR and csDMARD-IR subgroups are presented in online supplemental table 2. Baseline enthesitis and dactylitis were present for slightly greater proportions of patients in the placebo group compared with the risankizumab group.

### Efficacy assessments

The primary endpoint and all ranked secondary endpoints were met (table 2). For the primary endpoint, 51.3% of patients treated with risankizumab and 26.5% treated with placebo achieved ACR20 at week 24 ( $p<0.001$ ). Changes from baseline in each ACR component at week 24 are summarised in online supplemental table 3. Higher ACR20 response rates were observed for patients treated with risankizumab versus placebo, regardless of whether patients received concomitant csDMARDs (50.4% vs 33.9%) or risankizumab as monotherapy (53.0% vs 16.0%), and among the csDMARD-IR (56.3% vs 36.6%) and Bio-IR (45.7% vs 14.9%) patient populations (online supplemental table 4). For the full patient population, similar results favouring risankizumab were also observed for ACR50 (26.3% vs 9.3%, nominal  $p<0.001$ ) and ACR70 (12.0% vs 5.9%, nominal  $p<0.05$ ) (table 2).

At week 4 (after a single dose), a greater proportion of patients treated with risankizumab than placebo achieved ACR20 (nominal  $p=0.016$ ), and the improvement was sustained for all subsequent time points (figure 2A), including a significant difference for the secondary endpoint of ACR20 at week 16 (48.3% vs 25.3%,  $p<0.001$ ; table 2). Similar patterns occurred with ACR50 (figure 2B) and ACR70 (figure 2C) results.

At week 24, a greater proportion of patients treated with risankizumab versus placebo experienced resolution of enthesitis (42.9% vs 30.4%, nominal  $p<0.01$ ) and dactylitis (72.5% vs 42.1%, nominal  $p<0.001$ ; table 2). These results are consistent with the pooled results from KEEPsAKE 1 and 2 previously reported.<sup>29</sup> Additionally, a significantly greater proportion of patients treated with risankizumab versus placebo achieved PASI

**Table 1** Demographics and baseline characteristics

Characteristics	RZB 150 mg N=224	PBO N=219
Female, n (%)	124 (55.4)	120 (54.8)
Age (years), median (range)	53 (23–84)	52 (24 to 83)
Race, n (%)		
White	218 (97.3)	210 (95.9)
Black or African-American	2 (0.9)	3 (1.4)
Asian	2 (0.9)	3 (1.4)
Other	2 (0.9)	3 (1.4)
Not Hispanic/Latino, n (%)	182 (81.3)	176 (80.4)
BMI (kg/m <sup>2</sup> ), mean (SD)	31.5 (8.0)	31.2 (6.8)
PsA duration (years), mean (SD)	8.2 (8.2)	8.2 (8.3)
Swollen joint count,* mean (SD)	13.0 (8.7)	13.6 (9.0)
Tender joint count,† mean (SD)	22.8 (14.9)	22.3 (13.8)
Patient's assessment of pain,‡ mean (SD)	55.0 (23.5)	57.0 (23.1)
PtGA of disease activity,§ mean (SD)	56.2 (21.8)	56.2 (23.0)
PGA of disease activity,¶ mean (SD)	63.0 (17.0)	60.7 (16.4)
HAQ-DI, mean (SD)	1.10 (0.62)	1.13 (0.63)
hsCRP (mg/L),§ mean (SD)	7.5 (10.9)	8.2 (17.1)
Presence of psoriasis affecting ≥3% BSA, n (%)	123 (54.9)	119 (54.3)
BSA (%),¶ mean (SD)	12.5 (15.4)	11.7 (14.9)
PASI,¶ mean (SD)	7.7 (6.7)	8.4 (9.9)
MDA, n (%)	5 (2.2)	5 (2.3)
Presence of enthesitis,** n (%)	147 (65.6)	158 (72.1)
LEI,†† mean (SD)	3.0 (1.5)	3.0 (1.6)
Presence of dactylitis,‡‡ n (%)	40 (17.9)	57 (26.3)
LDI,§§ mean (SD)	78.9 (98.4)	109.8 (155.3)
SF-36 PCS score, mean (SD)	35.6 (8.8)	35.2 (9.1)
FACIT-Fatigue score, mean (SD)	28.2 (11.5)	27.7 (12.7)
Prior csDMARDs, n (%)		
0	12 (5.4)	11 (5.0)
1	88 (39.3)	81 (37.0)
2	60 (26.8)	60 (27.4)
≥3	64 (28.6)	67 (30.6)
Any prior biologic, n (%)	105 (46.9)	101 (46.1)
Prior failed biologics, n (%)		
0	137 (61.2)	132 (60.3)
1	72 (32.1)	64 (29.2)
≥2	15 (6.7)	23 (10.5)
Prior TNF antagonist, n (%)	103 (46.0)	100 (45.7)
Concomitant medication at baseline, n (%)		
MTX¶¶	110 (49.1)	99 (45.2)
csDMARD other than MTX***	31 (13.8)	30 (13.7)
MTX and another csDMARD	8 (3.6)	10 (4.6)
Oral corticosteroids	28 (12.5)	22 (10.0)
NSAIDs	141 (62.9)	145 (66.2)

\*Based on 66 joints.

†Based on 68 joints.

‡Scored as millimetres on a 100 mm horizontal visual analogue scale.

§Reference range: 0–10 mg/dL.

¶Among patients with ≥3% BSA affected by psoriasis (RZB, n=223; PBO, n=119).

\*\*LEI &gt;0.

††Among patients with LEI &gt;0 (RZB, n=147; PBO, n=158).

‡‡LDI &gt;0.

§§Among patients with LDI &gt;0 (RZB, n=40; PBO, n=57).

¶¶As monotherapy or in combination with another csDMARD.

\*\*\*Sulfasalazine, leflunomide or apremilast, without MTX.

BMI, body mass index; BSA, body surface area; csDMARD, conventional synthetic disease-modifying antirheumatic drug; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; hsCRP, high-sensitivity C reactive protein; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; MTX, methotrexate; NSAID, non-steroidal anti-inflammatory drug; PASI, Psoriasis Area and Severity Index; PBO, placebo; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary; PGA, physician's global assessment; PsA, psoriatic arthritis; PtGA, patient's global assessment; RZB, risankizumab; TNF, tumour necrosis factor.

90 at week 24 (55.0% vs 10.2%,  $p < 0.001$ ); a difference was observed as early as week 4 (figure 2D).

In the analysis of patient-reported outcomes, the change from baseline in HAQ-DI score was significantly greater in the risankizumab group compared with the placebo group ( $-0.22$  vs  $-0.05$ ,  $p < 0.001$ ; table 2). In a prespecified analysis of patients with HAQ-DI  $\geq 0.35$  at baseline, a greater proportion of patients treated with risankizumab achieved a clinically meaningful improvement in HAQ-DI ( $\geq 0.35$  from baseline<sup>30</sup>) at week 24 versus placebo (39.9% vs 23.6%, nominal  $p < 0.001$ ). Significantly greater changes from baseline were also observed for patients treated with risankizumab versus placebo for both SF-36 PCS score (5.9 vs 2.0,  $p < 0.001$ ) and FACIT-Fatigue score (4.9 vs 2.6,  $p < 0.01$ ). The proportion of patients achieving MDA was significantly greater for risankizumab versus placebo (25.6% vs 11.4%,  $p < 0.001$ ; table 2). Additional outcomes on VLDA, DAPSA REM and LDA+REM; percentage reductions in DAPSA and pain; HAQ-DI score  $\leq 0.5$ ; and MCID for PtGA are reported in online supplemental table 5.

### Safety

TEAEs were reported for 124 (55.4%) and 120 (54.8%) patients in the risankizumab and placebo groups, respectively (table 3). Most events reported in the risankizumab group were mild or moderate. The most frequently reported TEAE was upper respiratory tract infection (risankizumab, n=17 (7.6%); placebo, n=12 (5.5%); table 4); no other event was reported for  $\geq 5\%$  of patients in either treatment group. Frequencies of serious and severe TEAEs were similar between treatment groups, and, except for severe psoriatic arthropathy (risankizumab, n=1 (0.4%); placebo, n=2 (0.9%)), no severe TEAE was reported for more than one patient in either group. TEAEs leading to discontinuation of treatment were more frequent in the placebo group (n=5, 2.3%) than in the risankizumab group (n=2, 0.9%). No deaths occurred during the 24-week double-blind period.

Frequencies of AEs of safety interest were low and comparable between treatment groups (table 3). However, injection site reactions were more frequently reported in the risankizumab group (n=3, 1.3%) than the placebo group (n=1, 0.5%). None of the injection site reactions occurring in the risankizumab group were serious or resulted in patient discontinuation, and no anaphylactic reactions were reported. One (0.4%) patient in the risankizumab group with a history of hypertension experienced a non-fatal stroke adjudicated as a major adverse cardiac event. Serious infections were reported for two (0.9%) patients in the risankizumab group and for five (2.3%) patients in the placebo group. There were no reports of active tuberculosis or other opportunistic infection in either treatment group, and only one case of herpes zoster was reported for a patient receiving placebo. There was one reported AE of uveitis in a patient treated with risankizumab and no reported AEs of inflammatory bowel disease.

Mean changes in haematology and clinical chemistry values were small, not clinically meaningful, and comparable between the risankizumab and placebo groups. There were no grade 3 transaminase elevations (as judged by Common Terminology Criteria for Adverse Events V.4.03) reported in either treatment group. Shifts in transaminase levels from baseline are reported in online supplemental table 6.

### DISCUSSION

In this phase 3 study, treatment with the IL-23 p19 inhibitor, risankizumab, led to significant improvements in key efficacy measures for patients with active PsA who were csDMARD-IR or

**Table 2** Primary and secondary efficacy endpoints

	RZB 150 mg N=224	PBO N=219	Difference (95% CI)	P value
<b>Primary endpoint</b>				
ACR20 at week 24, n (%)	115 (51.3)	58 (26.5)	24.5 (15.9, 33.0)	<0.001*
<b>Ranked secondary endpoints</b>				
Change in HAQ-DI at week 24, mean (95% CI)	-0.22 (-0.28 to -0.15)	-0.05 (-0.12 to 0.02)	-0.16 (-0.26 to 0.07)	<0.001*
PASI 90 at week 24, † n (%)	68 (55.0)	12 (10.2)	44.3 (33.9 to 54.6)	<0.001*
ACR20 at week 16, n (%)	108 (48.3)	55 (25.3)	22.6 (13.9 to 31.2)	<0.001*
MDA at week 24, n (%)	57 (25.6)	25 (11.4)	14.0 (7.0 to 21.0)	<0.001*
Change in SF-36 PCS score at week 24, mean (95% CI)	5.9 (4.9 to 6.9)	2.0 (0.9 to 3.1)	3.9 (2.4 to 5.3)	<0.001*
Change in FACIT-Fatigue score at week 24, mean (95% CI)	4.9 (3.7 to 6.0)	2.6 (1.4 to 3.9)	2.2 (0.6 to 3.9)	<0.01*
<b>Non-ranked secondary endpoints</b>				
ACR50 at week 24, n (%)	59 (26.3)	20 (9.3)	16.6 (9.7 to 23.6)	<0.001
ACR70 at week 24, n (%)	27 (12.0)	13 (5.9)	6.0 (0.8 to 11.3)	<0.05
Resolution of enthesitis at week 24, ‡ n (%)	63 (42.9)	48 (30.4)	13.8 (3.5 to 24.2)	<0.01
Resolution of dactylitis at week 24, § n (%)	29 (72.5)	24 (42.1)	38.8 (22.9 to 54.8)	<0.001

All changes are LS mean changes from baseline.

Results for binary endpoints are based on non-responder imputation incorporating multiple imputation if there are missing data due to COVID-19 or non-responder imputation if there are no missing data due to COVID-19. Results for continuous endpoints are based on mixed models for repeated measures.

ACR20/50/70, ≥20/50/70% improvement in American College of Rheumatology score; BSA, body surface area; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy–Fatigue Questionnaire; HAQ-DI, Health Assessment Questionnaire–Disability Index; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; LS, least square; MDA, minimal disease activity; PASI 90, ≥90% reduction in Psoriasis Area and Severity Index; PBO, placebo; RZB, risankizumab; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary.

\*Statistically significant under overall type I error control.

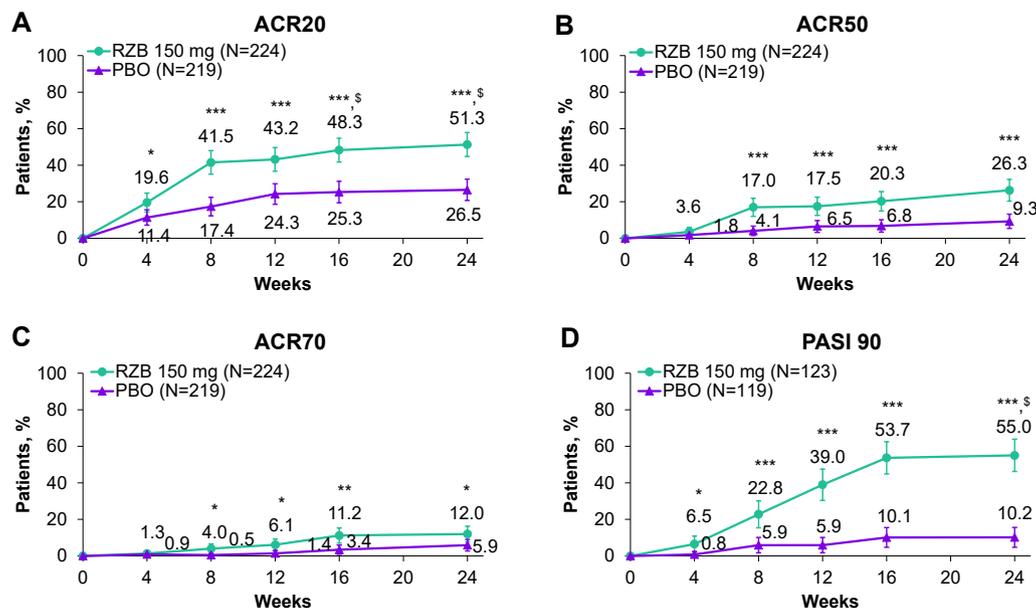
†Among patients with ≥3% BSA affected by psoriasis at baseline (RZB, n=123; PBO, n=119).

‡Defined as LEI=0 among patients with LEI >0 at baseline (RZB, n=147; PBO, n=158).

§Defined as LDI=0 among patients with LDI >0 at baseline (RZB, n=40; PBO, n=57).

Bio-IR. A significantly greater proportion of patients treated with risankizumab versus placebo achieved ACR20 at 24 weeks and all secondary endpoints, including assessments of disease activity in joints and skin, and patient-reported outcomes. Overall, the safety profile was consistent with that described in the UltIMMa-1, UltIMMa-2,<sup>31</sup> IMMvent,<sup>32</sup> IMMhance,<sup>33</sup> and IMMerge<sup>34</sup> studies of risankizumab in patients with moderate-to-severe

plaque psoriasis, and no new safety signals were observed. Of note, serious infections were reported for <1% of patients treated with risankizumab through week 24, and there were no cases of opportunistic infection, including herpes zoster, systemic candidiasis, or active tuberculosis. There was one major adverse cardiac event reported among patients receiving risankizumab (a non-fatal stroke in a patient with a history of hypertension



**Figure 2** ACR and PASI response rates over time. (A) ACR20, (B) ACR50, (C) ACR70 and (D) PASI 90 response rates for RZB 150 mg and PBO over the 24-week, double-blind treatment period. PASI 90 results are among patients with ≥3% body surface area affected by psoriasis at baseline. \*P≤0.05, \*\*P≤0.01, \*\*\*P≤0.001. †Statistically significant under overall type I error control. ACR20/50/70, ≥20/50/70% improvement in American College of Rheumatology criteria score; PASI 90, ≥90% reduction in Psoriasis Area and Severity Index; PBO, placebo; RZB, risankizumab.

Table 3 Safety summary

Patients, n (%)	RZB 150 mg N=224	PBO N=219
TEAE	124 (55.4)	120 (54.8)
COVID-19-related TEAE	1 (0.4)	0
Serious AE	9 (4.0)	12 (5.5)
Severe TEAE	6 (2.7)	7 (3.2)
TEAE leading to discontinuation of study drug	2 (0.9)	5 (2.3)
Death	0	0
Serious infections*	2 (0.9)	5 (2.3)
Active tuberculosis	0	0
Herpes zoster	0	1 (0.5)
Any other opportunistic infections	0	0
Malignancy†	1 (0.4)	1 (0.5)
Anaphylactic reactions	0	0
Injection site reactions	3 (1.3)‡	1 (0.5)
MACE	1 (0.4)	0

\*Serious infections reported in the RZB group were abscess and cellulitis (one patient) and gastroenteritis (one patient); in the placebo group, serious infections were erysipelas, gastroenteritis, postoperative abscess, upper respiratory tract infection and urinary tract infection (each reported for one patient).

†Both were non-melanoma skin cancer.

‡All were non-serious and did not result in discontinuation of the study drug.

AE, adverse event; MACE, major adverse cardiovascular event; PBO, placebo; RZB, risankizumab; TEAE, treatment-emergent adverse event.

that did not result in discontinuation of risankizumab). Additionally, only two patients (0.9%) in the risankizumab group discontinued the study due to AEs as the primary reason, which is comparable to the rate in the placebo group (three patients; 1.4%). Together, these results show that risankizumab 150 mg is effective and well-tolerated in patients with PsA.

Multiple agents that target IL-23 or its downstream pathway component, IL-17, are approved to treat PsA.<sup>10</sup> Data from the KEEPsAKE 1<sup>29</sup> and KEEPsAKE 2 trials provide further evidence that specifically targeting the p19 subunit of IL-23 is an effective therapeutic strategy to treat PsA. Notably, similar efficacy was observed with or without background csDMARDs or methotrexate for patients treated with risankizumab (ACR20 response rates, 48% for csDMARDs other than methotrexate and 51% for any methotrexate vs 53% for no csDMARD; online supplemental table 4). However, patients receiving placebo had higher ACR20 response rates when treated with concomitant csDMARDs or methotrexate than did those without any csDMARD or methotrexate use (27% for csDMARDs other than methotrexate and 36% for any methotrexate vs 16% for

Table 4 Frequently reported TEAEs

Patients, n (%)	RZB 150 mg N=224	PBO N=219
TEAEs reported in ≥2% of patients in either group		
Upper respiratory tract infection	17 (7.6)	12 (5.5)
Hypertension	10 (4.5)	6 (2.7)
Nasopharyngitis	9 (4.0)	8 (3.7)
Arthralgia	7 (3.1)	7 (3.2)
Nausea	6 (2.7)	4 (1.8)
Psoriatic arthropathy	6 (2.7)	9 (4.1)
Bronchitis	5 (2.2)	4 (1.8)
Diarrhoea	5 (2.2)	5 (2.3)
Headache	5 (2.2)	8 (3.7)

PBO, placebo; RZB, risankizumab; TEAE, treatment-emergent adverse event.

no csDMARD). The KEEPsAKE 2 study results also support the effectiveness of this mechanism of action for patients with a history of inadequate response to other biological therapies (ie, patients who are generally considered to be more treatment refractory as evidenced by higher rates of treatment discontinuation and switching).<sup>21 22 35</sup> As a larger proportion of patients who had failed prior biologics achieved ACR20 at week 24 when treated with risankizumab (45.7%) versus placebo (14.9%), risankizumab may provide an additional effective treatment option for these patients. Among patients who were not Bio-IR, 56.3% versus 36.6% in the risankizumab versus placebo groups achieved ACR20 at week 24. Overall, ACR20 response rates among patients receiving risankizumab were similar among patients who were Bio-IR and those who were csDMARD-IR (45.7% and 56.3%, respectively).

Greater improvement across key domains of PsA, including psoriasis, enthesitis (among the 69% of the study population who had LEI>0 at baseline) or dactylitis (among the 22% of the study population who had LDI>0 at baseline) was observed in patients treated with risankizumab versus placebo. Importantly, risankizumab treatment significantly improved physical function, fatigue and health-related quality of life as assessed by HAQ-DI, FACIT-Fatigue and SF-36 scores, respectively. Together, results from this study demonstrate the efficacy of risankizumab across key domains of PsA for not only musculoskeletal manifestations but also patient-reported outcomes.

This study enrolled a relatively large, representative population of patients with PsA and assessed a broad range of meaningful endpoints. However, there were some limitations. First, the study was performed during the COVID-19 pandemic, which introduced health-related and logistical challenges. These were addressed by implementing specific mechanisms to handle missing data resulting from the pandemic. Overall, less than 2.5% of patients had missing efficacy data because of COVID-19, and this did not affect the overall study results. In addition, no safety concerns attributed to COVID-19 were observed. Though the study is currently limited by the relatively brief assessment period of 24 weeks, the open-label portion of this study, which remains ongoing at the time of this report, will provide safety and efficacy data for risankizumab in this patient population over a 4-year period.

In conclusion, results from the 24-week, double-blind portion of this phase 3 clinical trial in patients with active PsA reveal that risankizumab was well tolerated and effective in treating patients who have experienced previous intolerance and/or inadequate response to csDMARDs or prior biological therapies. Overall, treatment with risankizumab demonstrated efficacy in key clinical PsA domains, providing additional evidence that targeting the p19 unit of IL-23 is a rational therapeutic approach to treat PsA.

#### Author affiliations

<sup>1</sup>Monash Medical School, Cabrini Hospital and Emertius Research, Melbourne, Victoria, Australia

<sup>2</sup>Department of Rheumatology, Ghent University, VIB Center for Inflammation Research, Ghent, Belgium

<sup>3</sup>Probit Medical Research—K Papp Clinical Research, Waterloo, Ontario, Canada

<sup>4</sup>DOM Centro de Reumatología, Buenos Aires, Argentina

<sup>5</sup>Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

<sup>6</sup>Arthritis Clinic and West Tennessee Research Institute, Jackson, Tennessee, USA

<sup>7</sup>AbbVie Inc, Madrid, Spain

<sup>8</sup>AbbVie Inc, North Chicago, Illinois, USA

<sup>9</sup>Altoona Center for Clinical Research, Pennsylvania, Duncansville, USA

**Acknowledgements** AbbVie Inc. participated in the study design; study research; collection, analysis and interpretation of data; and writing, reviewing and approving this manuscript. All authors had access to the data and participated in the development, review and approval, and in the decision to submit the manuscript

for publication. AbbVie and the authors thank all study investigators for their contributions and the patients who participated in this study. AbbVie funded the research for this study and provided writing support for this manuscript. Medical writing assistance, funded by AbbVie, was provided by Nate Connors, PhD, ISMPP CMPP, Jennifer C Jaworski, MS, and Lisa M Pitchford, PhD, of JB Ashtin, who developed the first draft based on an author-approved outline and assisted in implementing author revisions.

**Contributors** All authors critically reviewed this manuscript and provided the final approval for publication. AO participated in data acquisition and data interpretation. FEVD, KP, CA, RB, JA and AK participated in data acquisition. AMS, AE and LB participated in the study concept/design and data interpretation. GA participated in study conduct and data interpretation. WL and ZW participated in statistical analysis and data interpretation.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** AO received speaker or consulting fees and/or research grants from AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi and UCB. FEVD received speaker and/or consulting fees from AbbVie, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer and UCB. KP received honoraria or fees for serving on advisory boards, as a speaker and as a consultant. He has received grants for services as principal investigator from AbbVie, Amgen, Astellas, Bausch Health (Valeant), Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Kirin, LEO Pharma, Lilly, MedImmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Stiefel, Sun Pharma, Takeda and UCB. CA received research support and honoraria or fees for serving on advisory boards or as a speaker from AbbVie, Amgen, Genentech, Janssen, Lilly, Pfizer and Roche. RB received grants or research support from AbbVie, Merck and Roche. He has received consultation fees or honoraria for serving as a speaker for AbbVie, Bristol-Myers Squibb, Janssen, Lilly, Merck, Pfizer and Roche. JA received honoraria as a consultant, speaker or expert witness. He has received research support from AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Galapagos/Gilead, Genentech, GlaxoSmithKline, Lilly, Mallinckrodt, Nektar Therapeutics, Nichi-Iko, Novartis, Pfizer, Regeneron, Roche, Sanofi, Selecta Biosciences and UCB. WL, ZW, AMS, AE and LB are full-time employees of AbbVie, and may hold AbbVie stock or stock options. AMS is listed as an inventor on some AbbVie patents. GA was a full-time employee of AbbVie at the time of this study and may hold AbbVie stock or stock options. AK is a shareholder of Amgen, Gilead, GlaxoSmithKline, Novartis, Pfizer and Sanofi. He received consulting fees from AbbVie, Boehringer Ingelheim, Flexion, Gilead, Janssen, Pfizer, Regeneron, Sanofi and SUN Pharma, and has received speaker's fees or honoraria from AbbVie, Celgene, Flexion, Genzyme, GlaxoSmithKline, Lilly, Merck, Novartis, Pfizer, Sanofi and UCB.

**Patient consent for publication** Not applicable.

**Ethics approval** The study is being conducted in accord with International Council for Harmonisation guidelines. An independent ethics committee/institutional review board ensured the ethical, scientific and medical appropriateness of the study before it was conducted and approved all relevant documentation. All patients provided written, informed consent before enrolment.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. This includes access to anonymised, individual and trial-level data (analysis data sets), as well as other information (eg, protocols and clinical study reports), as long as the trials are not part of an ongoing or planned regulatory submission. This includes requests for clinical trial data for unlicensed products and indications. Clinical trial data can be requested by any qualified researchers who engage in rigorous, independent scientific research and will be provided following review and approval of a research proposal and statistical analysis plan and execution of a data sharing agreement. Data requests can be submitted at any time and the data will be accessible for 12 months, with possible extensions considered. For more information on the process, or to submit a request, visit the following link: <https://www.abbvie.com/our-science/clinical-trials/clinical-trials-data-and-information-sharing/data-and-information-sharing-with-qualified-researchers.html>.

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which

permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

#### ORCID iDs

Filip Van den Bosch <http://orcid.org/0000-0002-3561-5932>

Ricardo Blanco <http://orcid.org/0000-0003-2344-2285>

#### REFERENCES

- Ogdie A, Weiss P. The epidemiology of psoriatic arthritis. *Rheum Dis Clin North Am* 2015;41:545–68.
- Mease PJ, Gladman DD, Papp KA, et al. Prevalence of rheumatologist-diagnosed psoriatic arthritis in patients with psoriasis in European/North American dermatology clinics. *J Am Acad Dermatol* 2013;69:729–35.
- Lee S, Mendelsohn A, Sarnes E. The burden of psoriatic arthritis: a literature review from a global health systems perspective. *P T* 2010;35:680–9.
- Ritchlin CT, Colbert RA, Gladman DD. Psoriatic arthritis. *N Engl J Med* 2017;376:957–70.
- Elalouf O, Muntyanu A, Polachek A, et al. Mortality in psoriatic arthritis: risk, causes of death, predictors for death. *Semin Arthritis Rheum* 2020;50:571–5.
- Verhoeven F, Prati C, Demougeot C, et al. Cardiovascular risk in psoriatic arthritis, a narrative review. *Joint Bone Spine* 2020;87:413–8.
- Kristensen LE, Jørgensen TS, Christensen R, et al. Societal costs and patients' experience of health inequities before and after diagnosis of psoriatic arthritis: a Danish cohort study. *Ann Rheum Dis* 2017;76:1495–501.
- 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;79:700.1–12.
- 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;54:n/a–71.
- Yang K, Oak ASW, Elewski BE. Use of IL-23 inhibitors for the treatment of plaque psoriasis and psoriatic arthritis: a comprehensive review. *Am J Clin Dermatol* 2021;22:173–92.
- Combe B, Tsai T-F, Huffstutter JE, et al. Ixekizumab, with or without concomitant methotrexate, improves signs and symptoms of PSA: week 52 results from Spirit-P1 and Spirit-P2 studies. *Arthritis Res Ther* 2021;23:41.
- Mease PJ, Genovese MC, Weinblatt ME, et al. Phase II study of ABT-122, a tumor necrosis factor- and interleukin-17A-targeted dual variable domain immunoglobulin, in patients with psoriatic arthritis with an inadequate response to methotrexate. *Arthritis Rheumatol* 2018;70:1778–89.
- Mease PJ, Helliwell PS, Hjuler KF, et al. Brodalumab in psoriatic arthritis: results from the randomised phase III AMVISION-1 and AMVISION-2 trials. *Ann Rheum Dis* 2021;80:185–93.
- Mease PJ, Lertratanakul A, Anderson JK, et al. Upadacitinib for psoriatic arthritis refractory to biologics: SELECT-PsA 2. *Ann Rheum Dis* 2020;80:312–20.
- Smolen JS, Sebba A, Ruderman EM, et al. Efficacy and safety of ixekizumab with or without methotrexate in Biologic-Naive patients with psoriatic arthritis: 52-week results from SPIRIT-H2H study. *Rheumatol Ther* 2020;7:1021–35.
- Torres T, Barcelos A, Filipe P, et al. A systematic review with network meta-analysis of the available biologic therapies for psoriatic disease domains. *Front Med* 2020;7:618163.
- Saber TP, Ng CT, Renard G, et al. Remission in psoriatic arthritis: is it possible and how can it be predicted? *Arthritis Res Ther* 2010;12:R94.
- Perrotta FM, Lubrano E. Subcutaneous anti-TNF alpha induced sustained minimal disease activity and remission in psoriatic arthritis patients: a retrospective study. *Postgrad Med* 2016;128:693–6.
- Hagège B, Tan E, Gayraud M, et al. Remission and low disease activity in psoriatic arthritis publications: a systematic literature review with meta-analysis. *Rheumatology* 2020;59:1818–25.
- Walsh JA, Cai Q, Lin I, et al. Real-World 2-year treatment patterns among patients with psoriatic arthritis treated with injectable biologic therapies. *Curr Med Res Opin* 2020;36:1245–52.
- Costa L, Perricone C, Chimenti MS, et al. Switching between biological treatments in psoriatic arthritis: a review of the evidence. *Drugs R D* 2017;17:509–22.
- Mease PJ, Karki C, Liu M, et al. Discontinuation and switching patterns of tumour necrosis factor inhibitors (TNFi) in TNFi-naive and TNFi-experienced patients with psoriatic arthritis: an observational study from the US-based Corrona registry. *RMD Open* 2019;5:e000880.
- Song Y, Betts KA, Lu Y, et al. Economic burden of switching to different biologic therapies among tumour necrosis factor inhibitor-experienced patients with psoriatic arthritis. *Rheumatol Ther* 2019;6:285–97.
- Wu JJ, Pelletier C, Ung B, et al. Treatment patterns and healthcare costs among biologic-naive patients initiating apremilast or biologics for the treatment of psoriatic arthritis: results from a US claims analysis. *Curr Med Res Opin* 2020;36:169–76.

- 25 Papp KA, Blauvelt A, Bukhalo M, *et al.* Risankizumab versus ustekinumab for moderate-to-severe plaque psoriasis. *N Engl J Med* 2017;376:1551–60.
- 26 Singh S, Kroe-Barrett RR, Canada KA, *et al.* Selective targeting of the IL23 pathway: generation and characterization of a novel high-affinity humanized anti-IL23A antibody. *MAbs* 2015;7:778–91.
- 27 Krueger JG, Ferris LK, Menter A, *et al.* Anti-IL-23A mAb BI 655066 for treatment of moderate-to-severe psoriasis: safety, efficacy, pharmacokinetics, and biomarker results of a single-rising-dose, randomized, double-blind, placebo-controlled trial. *J Allergy Clin Immunol* 2015;136:116–24.
- 28 Nerviani A, Boutet M-A, Tan WSG, *et al.* IL-23 skin and joint profiling in psoriatic arthritis: novel perspectives in understanding clinical responses to IL-23 inhibitors. *Ann Rheum Dis* 2021;80:591–7.
- 29 Kristensen LE, Keiserman M, Papp K. Efficacy and safety of risankizumab for active psoriatic arthritis: 24-week results from the randomised, double-blind, phase 3 KEEPSAKE 1 trial. *Ann Rheum Dis* 2021;80:1315–6.
- 30 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;38:2461–5.
- 31 Gordon KB, Strober B, Lebwohl M, *et al.* Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials. *Lancet* 2018;392:650–61.
- 32 Reich K, Gooderham M, Thaçi D, *et al.* Risankizumab compared with adalimumab in patients with moderate-to-severe plaque psoriasis (IMMvent): a randomised, double-blind, active-comparator-controlled phase 3 trial. *Lancet* 2019;394:576–86.
- 33 Blauvelt A, Leonardi CL, Gooderham M, *et al.* Efficacy and safety of continuous Risankizumab therapy vs treatment withdrawal in patients with moderate to severe plaque psoriasis: a phase 3 randomized clinical trial. *JAMA Dermatol* 2020;156:649–58.
- 34 Warren RB, Blauvelt A, Poulin Y, *et al.* Efficacy and safety of risankizumab vs. secukinumab in patients with moderate-to-severe plaque psoriasis (IMMerge): results from a phase 3, randomized, open-label, efficacy-assessor-blinded clinical trial. *Br J Dermatol* 2021;184:50–9.
- 35 Reddy SM, Crean S, Martin AL, *et al.* Real-World effectiveness of anti-TNF switching in psoriatic arthritis: a systematic review of the literature. *Clin Rheumatol* 2016;35:2955–66.

**SUPPLEMENTARY MATERIAL**