DOI: 10.1111/jdv.18475 JEADV

ORIGINAL ARTICLE

The effect of risankizumab on achieving minimal clinically important differences in patient-reported outcomes in patients with psoriatic arthritis: results from KEEPsAKE 1 and 2

L.E. Kristensen,[1,*] A.M. Soliman,[2] K. Papp,[3] L. Barcomb,[2] A. Eldred,[2] A. Östör[4]

[1]The Parker Institute, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Copenhagen, Denmark
[2]AbbVie, Inc., North Chicago, IL, USA
[3]Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada
[4]Cabrini Hospital, Monash University & Emeritus Research, Melbourne, VIC., Australia
*Correspondence: L.E. Kristensen. E-mail: lars.erik.kristensen@regionh.dk

Abstract

Background Psoriatic arthritis (PsA) is a chronic inflammatory disease that reduces the quality of life. This study assessed the effects of risankizumab (RZB) on the achievement of minimal clinically important differences (MCID) in patient-reported outcomes (PROs).

Methods KEEPsAKE-1 and -2 are randomized, placebo-controlled Phase 3 clinical studies assessing RZB (150 mg) vs. placebo (PBO) in adult patients with PsA with inadequate response or intolerance to disease-modifying antirheumatic drugs and/or biologics. Patients were randomized 1:1 to receive RZB or PBO for 24 weeks; starting at Week 24, all patients received RZB 150 mg through Week 52. PROs assessed were Patient's Global Assessment of Disease Activity (PtGA), Patient's Assessment of Pain, Health Assessment Questionnaire—Disability Index (HAQ-DI), Short-Form 36 Physical and Mental Component Summary scores (PCS and MCS, respectively), 5-Level EQ-5D (EQ-5D-5L), Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-Fatigue), and Work Productivity and Activity Impairment (WPAI). The proportion of patients achieving MCID at Weeks 24 and 52 are reported. Odds ratios of achieving MCID with RZB treatment at Week 24, relative to PBO, were estimated by logistic regression controlling for baseline and stratification factors.

Results In KEEPsAKE-1, RZB- vs. PBO-treated patients were more likely to report MCID in all PROs at Week 24; similar results were obtained in KEEPsAKE-2, except for SF-36 MCS and WPAI presenteeism domain. In KEEPsAKE-1 and KEEPsAKE-2, 65% and 62% of RZB-treated patients, respectively, reported MCID in PtGA at Week 24, which increased to 74% and 68%, respectively, at Week 52. Approximately 48% of all PBO-treated patients reported MCID in PtGA at Week 24 and, after initiating RZB, >65% reported MCID at Week 52. Results were similar in the remaining PROs.

Conclusions These data demonstrate that patients with PsA receiving RZB treatment are more likely to report clinically important improvements in PROs compared with patients receiving PBO.

Received: 22 December 2021; Accepted: 11 July 2022

Conflict of interest

L.E. Kristensen has received fees for speaking from Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly and Janssen Pharmaceuticals, fees for consultancy from Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly and Janssen pharmaceuticals, and received IIT research grants from Pfizer, AbbVie, UCB, Gilead, Biogen, Novartis, Eli Lilly and Janssen pharmaceuticals. K. Papp has received honoraria or fees for serving on advisory boards, as a speaker or as a consultant and grants as an investigator from AbbVie, Amgen, Astellas, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, Eli Lilly, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa-Hakko Kirin, LEO Pharma, MedImmune, Merck-Serono, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Roche, Sanofi-Genzyme, Stiefel, Sun Pharma, Takeda, UCB and Valeant. A. Östör has received speaker and/or consulting fees and/or research grants from BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Eli Lilly and Novartis. A.M. Soliman, L. Barcomb and A. Eldred are full-time employees of AbbVie and may hold AbbVie stock and/or stock options.

Funding sources

AbbVie, Inc., funded this study and participated in the study design; study research; collection, analysis, and interpretation of data; writing, reviewing and approving of this publication. All authors had access to the data and participated in the development, review and approval, and in the decision to submit this publication. No honoraria or payments were made for authorship.

Introduction

Psoriatic arthritis (PsA) is a chronic, inflammatory disease characterized by articular and extra-articular joint pain and skin lesions, plaques, and patches.[1–3] As such, patients with PsA often experience reduced ability to participate in daily living activities, including general physical functioning and workability, thereby impacting the overall health-related quality of life (HRQoL).[4–7] PsA can be difficult to adequately treat, with many patients still experiencing persistent inflammation even after receiving treatment.[1,2]

When developing new therapies for chronic conditions, it is important that the patient's perspective be assessed. Studies have shown that patient satisfaction with treatment – including perceived efficacy and impact on daily living—influence medication adherence and treatment decisions.[8,9] Patient-reported outcome (PRO) measures are commonly used in clinical trials to capture the patient perspective on the impact of treatment on pain, physical functioning, fatigue, disease activity and workability.

Risankizumab (RZB) is an interleukin-23 inhibitor under evaluation for the treatment of PsA. Significant improvement in PsA disease activity, as determined by achievement of the American College of Rheumatology 20 (ACR20) composite measure, was shown in both Phase 2 and Phase 3 clinical studies.[10–12] Two Phase 3 studies, KEEPsAKE-1 and -2, also assessed the impact of RZB treatment on the mean change from baseline in several PROs after 24 weeks of RZB treatment.[11,12] The current analysis assessed the impact of RZB treatment on the likelihood of achieving minimal clinically important differences (MCID) at Week 24 relative to PBO-treated patients, as well as the proportion of patients reaching that milestone at Weeks 24 and 52.

Materials and methods

Study design and participants

KEEPsAKE-1 (NCT03675308) and KEEPsAKE-2 (NCT03671148) were double-blind, randomized, placebo-controlled Phase 3 clinical trials assessing the efficacy of RZB treatment in patients with PsA. The primary endpoint of the KEEPsAKE studies was the proportion of patients achieving ACR20 at Week 24. Eligible patients were ≥18 years old with a clinical diagnosis of PsA, defined as ≥5 tender joints (based on 68 joint counts) and ≥5 swollen joints (based on 66 joint counts), and active plaque or nail psoriasis. In KEEPsAKE-1 only, eligible patients also had ≥1 radiographic erosion based on central imaging view or high-sensitivity c-reactive protein levels ≥3.0 mg/L. All patients experienced symptom onset at least 6 months prior to the study screening visit and had no prior exposure to RZB. In KEEPsAKE-1, patients had an inadequate response or intolerance to, or contraindication for csDMARD therapy. In KEEPsAKE-2, patients had an inadequate response or intolerance to, or contraindication for csDMARD and/or 1 or 2 biologic therapies.[11,13]

Patients were randomized 1:1 to receive RZB (150 mg) or placebo (PBO) by subcutaneous injection at Weeks 0, 4, and 16. At Week 24, patients previously randomized to PBO received a blinded dose of RZB and patients randomized to RZB received a blinded dose of PBO. All patients received open-label RZB every 12 weeks from Week 28 to 52.

The protocol, informed consent form(s), and all participant materials were approved by appropriate ethics committees or institutional review boards at all study sites. All participants provided written, informed consent prior to enrollment. The clinical study was conducted in accordance with the ethical principles that have their origin in the current Declaration of Helsinki and is consistent with the International Conference on Harmonization Good Clinical Practice and Good Epidemiology Practices, and all applicable local regulatory requirements. All patient data were anonymized and complied with patient confidentiality requirements.

Patient-reported outcomes

This manuscript focuses on PROs used to assess the impact of RZB treatment on patient quality of life, physical functioning, pain and work productivity. PROs reported are Patient's Global Assessment of Disease Activity (PtGA), Patient's Assessment of Pain by visual analogue scale, Health Assessment Questionnaire—Disability Index (HAQ-DI), Short-Form 36 Physical and Mental Component Summary scores (PCS and MCS, respectively), 5-Level EQ-5D (EQ-5D-5L) index score, Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-Fatigue), and Work Productivity and Activity Impairment questionnaire (WPAI). Total scoring ranges and minimal clinically important differences (MCIDs), or the change from baseline values that denote clinically important improvements, are listed for each PRO in Table S1.

Statistical analysis of data

Data are reported as the observed percentage of patients achieving MCID at Weeks 24 and 52. Odds ratios of achieving MCID with RZB treatment, relative to PBO, at Week 24 were estimated

by logistic regression analysis of observed cases controlling for baseline PRO score and stratification factors of current csDMARD use (0 vs. ≥1), the number of prior biologic therapies (0 vs. ≥1), and extent of psoriasis (body surface area [BSA] <3% or ≥3%). Odds ratios were not calculated at Week 52 as all participants were receiving RZB treatment. Confidence intervals (CIs) were calculated for odds ratios. Data were further stratified by skin burden (BSA <3% or BSA ≥3%) and analysed by logistic regression analysis controlling for baseline score of the PRO and stratification factors (current csDMARD use [0 vs. ≥1] and the number of prior biologic therapies [0 vs. ≥1]).

Results

Patient demographics

Baseline patient clinical and demographic characteristics are published elsewhere.[11,13] Briefly, 50% of patients enrolled in KEEPsAKE-1 were male, with an average age of 51.3 ± 12.2 years; the mean duration of PsA was 7.1 ± 7.4 years. In KEEPsAKE-2, 55% of enrolled patients were female with an average age of 52.9 ± 12.6 years and the mean duration of PsA was 8.2 ± 8.3 years.

Proportion of patients achieving MCID in PROs: Results from KEEPsAKE-1

In KEEPsAKE-1, patients receiving RZB were significantly (OR [95%CI], $P < 0.001$) more likely to report MCID at Week 24 in PtGA (2.0 [1.5, 2.7]), pain (2.2 [1.6, 2.9]), and FACIT-Fatigue (1.9 [1.4, 2.5]) as compared with patients receiving PBO (Fig. 1). Amongst patients receiving RZB since the start of the study, most reported MCID in PtGA (64%; n/N: 289/449), pain (65%; n/N: 292/448), and FACIT-Fatigue (57%; n/N: 268/469) at Week 24; by Week 52, these values increased to 74% (n/N: 319/430), 73% (n/N: 312/429), and 66% (n/N: 295/446), respectively (Fig. 1). At Week 24, fewer patients receiving PBO had reported MCID in PtGA (48%; n/N: 215/445), pain (48%; n/N: 216/448) and FACIT-Fatigue (44%; n/N: 204/467) than with RZB. However, PBO patients initiated RZB treatment at Week 24 and, by Week 52, the

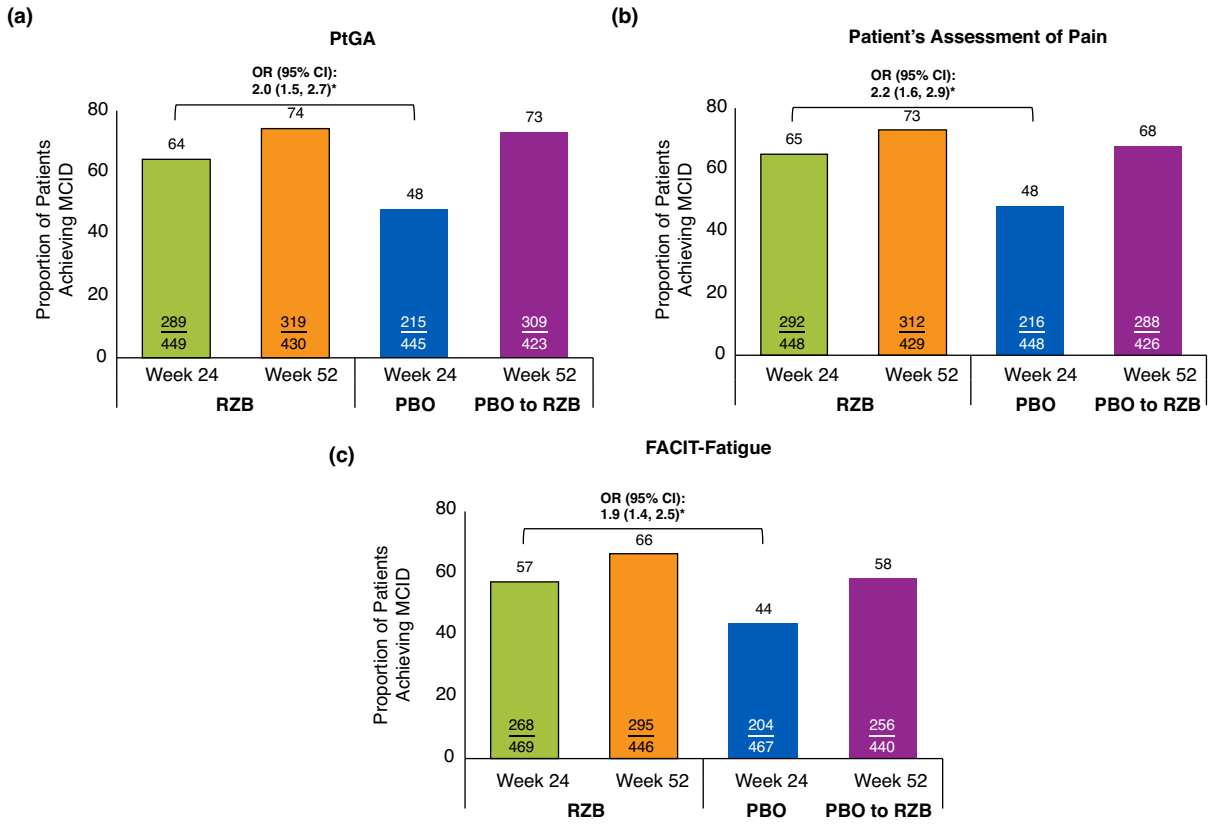

Figure 1 Proportion of patients reporting MCID in PtGA, Pain and FACIT—Fatigue*: Results* from KEEPsAKE-1. All patients had PtGA and Pain scores ≥1 at baseline. CI, confidence interval; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy—Fatigue; MCID, minimal clinically important difference; OR, odds ratio; PBO, placebo; PtGA, Patient's Assessment of Global Disease Activity; RZB, risankizumab. *$P < 0.001$.

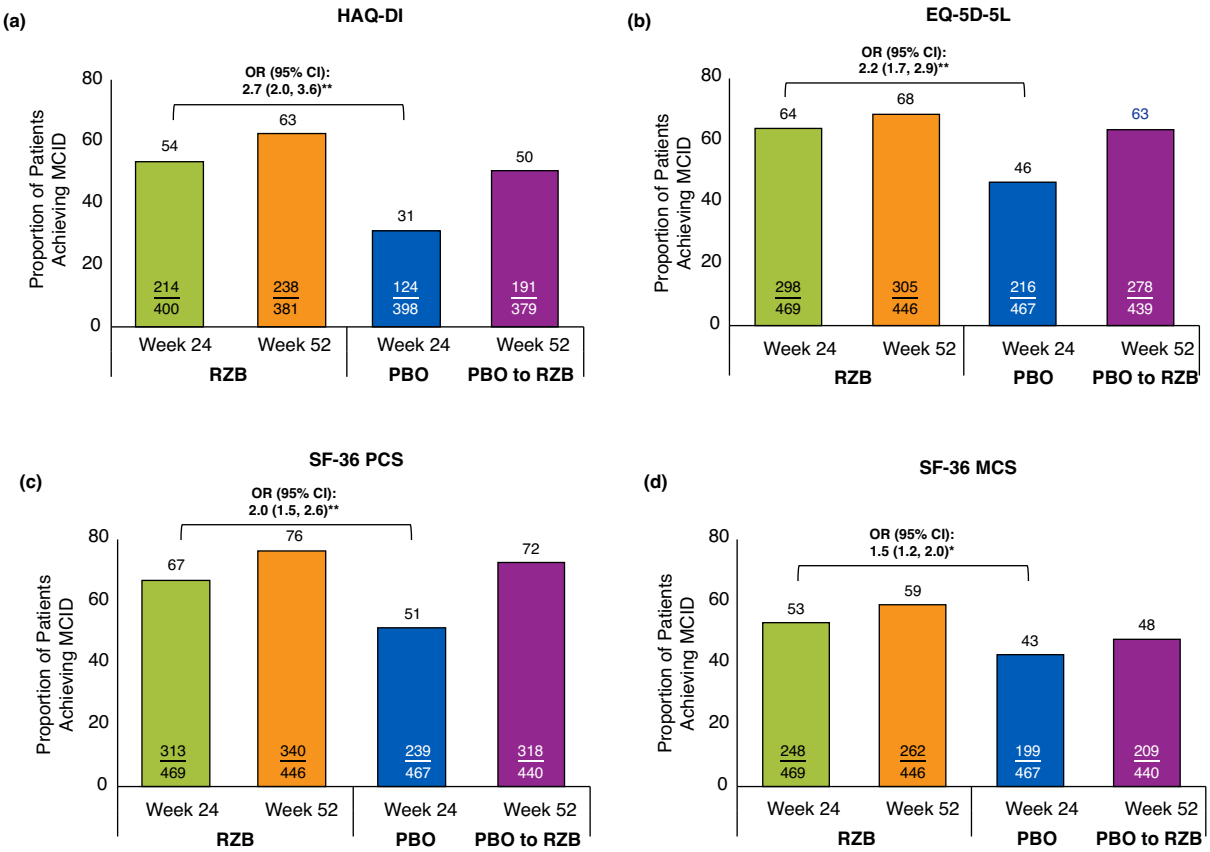

Figure 2 Proportion of patients reporting MCID in HAQ-DI, EQ-5D-5L and SF-36 PCS and MCS: Results from KEEPsAKE-1. All patients had HAQ-DI ≥0.35 at baseline. CI, confidence interval; EQ-5D-5L, 5-Level EQ-5D; HAQ-DI, Health Assessment Questionnaire—Disability Index; MCID, minimal clinically important difference; MCS, Mental Component Summary; OR, odds ratio; PBO, placebo; PCS, Physical Component Summary; RZB, risankizumab; SF-36, Short-Form 36 Questionnaire. *$P < 0.01$; **$P < 0.001$.

number of patients achieving MCID in PtGA (73%; n/N: 309/423), pain (68%; n/N: 288/426) and FACIT-Fatigue (58%; n/N: 256/440) increased and were similar to the trajectory of improvement seen in patients who received RZB for the duration of the study.

At Week 24, RZB- vs. PBO-treated patients were significantly more likely (OR [95% CI]) to report clinically important improvements in overall quality of life and physical functioning, as determined by the HAQ-DI (2.7 [2.0, 3.6], $P < 0.001$), EQ-5D-5L (2.2 [1.7, 2.9], $P < 0.001$), and SF-36 PCS (2.0 [1.5, 2.6], $P < 0.001$) and MCS (1.5 [1.2, 2.0], $P < 0.01$) questionnaires (Fig. 2). Moreover, 54—67% of RZB-treated patients reported MCID in these measures (HAQ-DI: 214/400, 54%; EQ-5D-5L: 298/469, 64%; SF-36 PCS: 313/469, 67%; SF-36 MCS: 248/469, 53%) at Week 24; by Week 52, 59—76% of RZB-treated patients reported MCID at Week 52 (HAQ-DI: 238/381, 63%; EQ-5D-5L: 305/446, 68%; SF-36 PCS: 340/446, 76%; SF-36 MCS: 262/446, 59%). In PBO-treated patients, only 31—51% of patients reported MCID at Week 24 (HAQ-DI: 124/398, 31%; EQ-5D-5L: 216/467, 46%; SF-36 PCS: 239/467, 51%; SF-36 MCS: 199/467, 43%). However, once initiating RZB treatment, 48—72% of these patients reported clinically important improvement at Week 52 (HAQ-DI: 191/379, 50%; EQ-5D-5L: 278/439, 63%; SF-36 PCS: 318/440, 72%; SF-36 MCS: 209/440, 48%). Patients receiving RZB were also significantly more likely to achieve MCID in all 8 SF-36 domains at Week 24 when compared with PBO-treated patients (Table S2).

The impact of RZB-treatment on WPAI domains presenteeism, work productivity loss, and activity impairment was also measured. Patients receiving RZB were significantly more likely (OR [95%CI]) to report MCID in all domains (presenteeism: 2.4 [1.5, 3.8], $P < 0.001$; work productivity loss: 1.9 [1.2, 2.9], $P = 0.005$; activity impairment: 1.8 [1.4, 2.4], $P < 0.001$; Fig. 3). At Week 24, 55% of RZB-treated patients reported MCID in presenteeism (n/N: 95/173), 51% in work productivity impairment (n/N: 97/190), and 54% (n/N: 229/428) in activity impairment. By Week 52, these proportions increased to 62% (n/N:

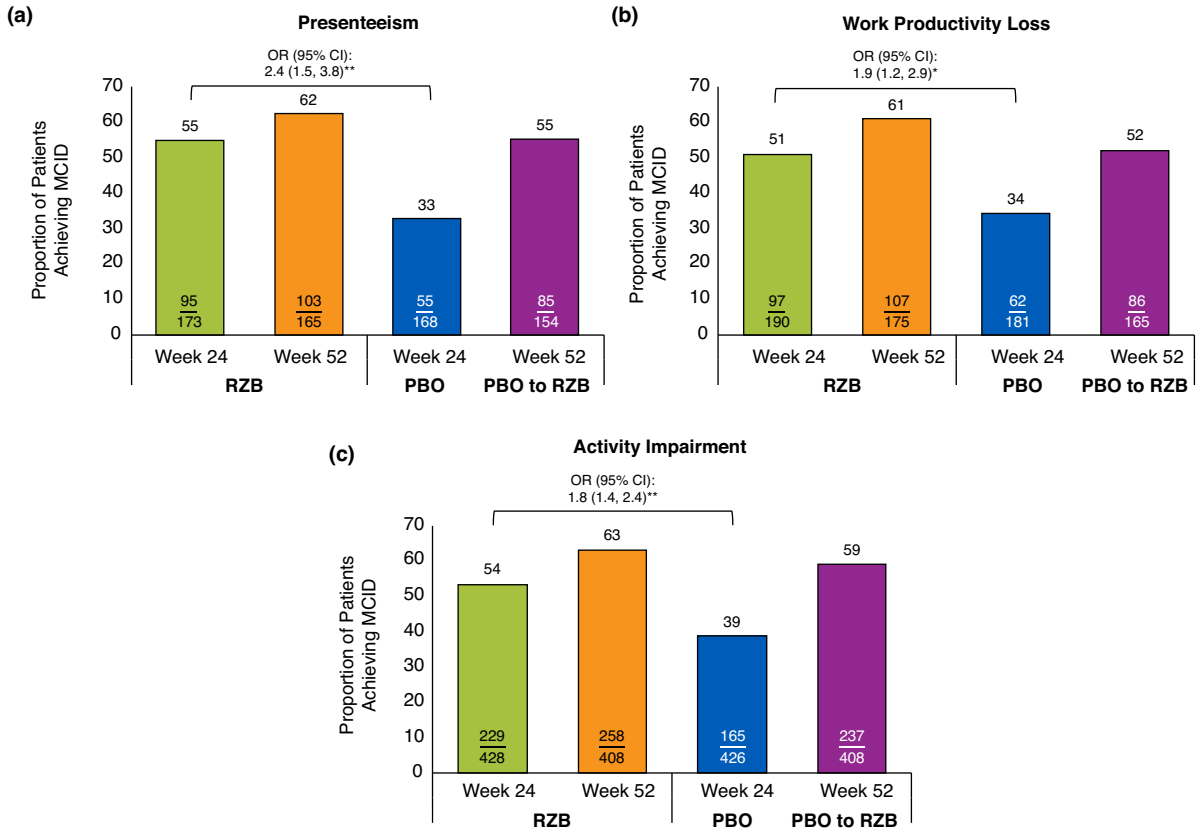

Figure 3 Proportion of patients reporting MCID in WPAI domains: Results from KEEPsAKE-1. Presenteeism and work productivity loss were only assessed amongst patients reporting active employment at baseline. Only patients with presenteeism ≥20%, work productivity loss ≥15%, and activity impairment ≥20% were included in the respective analyses. CI, confidence interval; MCID, minimal clinically important difference; OR, odds ratio; PBO, placebo; RZB, risankizumab; WPAI, Work Productivity and Activity Impairment. *$P < 0.01$; **$P < 0.001$.

103/165), 61% (n/N: 107/175), and 63% (n/N: 258/408), respectively. Fewer patients receiving PBO vs. RZB treatment reported MCID at Week 24 (presenteeism: 33% [n/N: 55/168]; work productivity loss: 34% [n/N: 62/181]; activity impairment: 39% [n/N: 165/426]) but showed notable increases at Week 52 after initiating RZB treatment (55% for presenteeism [n/N: 85/154]; work productivity loss: 52% [n/N: 86/165]; activity impairment: 59% [n/N: 237/401]).

When stratified by baseline skin burden (high: ≥3% BSA or low: <3% BSA), patients with a high skin burden who were receiving RZB were significantly more likely to report MCIDs in all PROs at Week 24 compared with those with a high skin burden receiving PBO (Table S3); outcomes amongst patients with a low skin burden were similar to the overall cohort.

Proportion of patients achieving MCID in PROs: Results from KEEPsAKE-2

In KEEPsAKE-2, patients receiving RZB were again significantly more likely (OR [95%CI]) to report MCID at Week 24 in PtGA (1.9 [1.2, 2.8], $P < 0.01$), pain (2.5 [1.6, 3.8], $P < 0.001$), and FACIT-Fatigue (1.9 [1.3, 2.9], $P < 0.01$) as compared with patients receiving PBO (Fig. 4). Patients receiving RZB since the study start reported MCID in PtGA (62%; n/N: 128/208), pain (60%; n/N: 125/208), and FACIT-Fatigue (53%; n/N: 113/215) at Week 24, which increased to 68% (n/N: 128/188), 64% (n/N: 121/188), and 59% (n/N: 115/195), respectively, at Week 52 (Fig. 4). Fewer patients receiving PBO had reported MCID in PtGA (47%; n/N: 89/189), pain (41%; n/N: 77/190), and FACIT-Fatigue (38%; n/N: 76/198) than with RZB at Week 24. However, after initiating RZB treatment at Week 24, these values increased to 66% (n/N: 117/177), 67% (n/N: 119/177), and 60% (n/N: 110/184), respectively, at Week 52.

RZB vs. PBO-treated patients were significantly more likely (OR [95% CI]) to have clinically important improvements in overall HRQoL and physical functioning at Week 24, as determined by the HAQ-DI (1.7 [1.1, 2.7], $P < 0.05$), EQ-5D-5L (1.7 [1.2, 2.6], $P < 0.05$), and SF-36 PCS (2.4 [1.6, 3.6], $P < 0.001$) questionnaires, but not for SF-36 MCS (1.5 [0.9, 2.3]; Fig. 5).

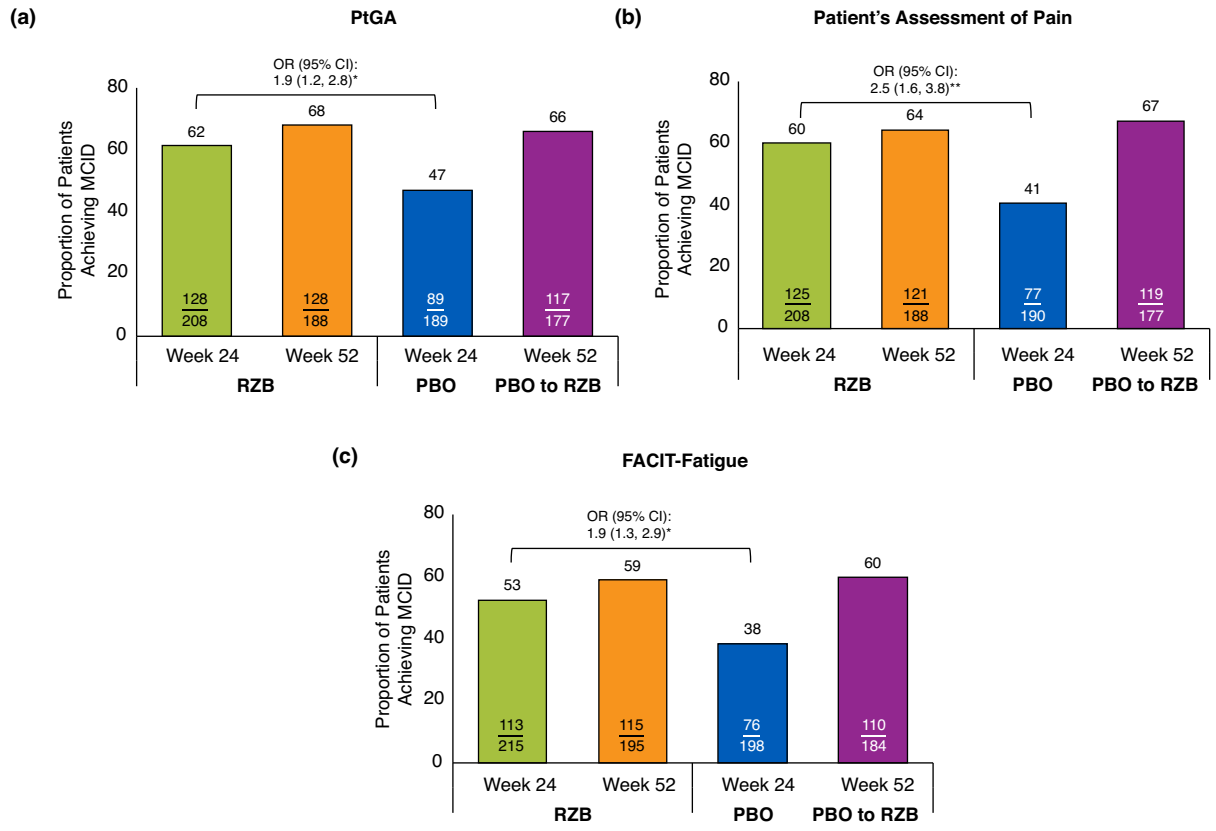

Figure 4 Proportion of patients reporting MCID in PtGA, Pain and FACIT—Fatigue: Results from KEEPsAKE-2. All patients had PtGA and Pain scores ≥1 at baseline. CI, confidence interval; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy – Fatigue; MCID, minimal clinically important difference; OR, odds ratio; PBO, placebo; PtGA, Patient's Assessment of Global Disease Activity; RZB, risankizumab. *$P < 0.01$; **$P < 0.001$.

Most RZB-treated patients reported MCID in EQ-5D-5L (52%; n/N: 112/215), and SF-36 PCS (66%; n/N: 142/215), with only 44% of patients reporting MCID in HAQ-DI (n/N: 81/186) and SF-36 MCS (n/N: 94/215). Between 52 and 68% of RZB-treated patients reported MCID at Week 52 (HAQ-DI: 84/169, 50%; EQ-5D-5L: 126/194, 65%; SF-36 PCS: 132/195, 68%; SF-36 MCS: 102/195, 52%). In PBO-treated patients, only 33—46% of patients reported MCID at Week 24 (HAQ-DI: 54/165, 33%; EQ-5D-5L: 78/197, 40%; SF-36 PCS: 91/198, 46%; SF-36 MCS: 72/198, 36%). However, once initiating RZB treatment, 51—68% of these patients reported clinically important improvement at Week 52 (HAQ-DI: 91/154, 59%; EQ-5D-5L: 117/183, 64%; SF-36 PCS: 125/184, 68%; SF-36 MCS: 94/184, 51%). Patients receiving RZB were also significantly more likely to achieve MCID in the SF-36 domains (except for vitality [$P = 0.053$] or role emotional [$P = 0.092$]) at Week 24 when compared with PBO-treated patients (Table S2).

Patients receiving RZB were significantly more likely (OR [95%CI], $P < 0.05$) to report MCID in the WPAI activity impairment domain (1.8 [1.1, 2.7]); OR was not significant for work productivity loss or presenteeism (1.5 [0.8, 2.9] and 1.5 [0.8, 2.9], respectively; Fig. 6). At Week 24, 46% of RZB-treated patients reported MCID in presenteeism (n/N: 37/81), 44% in work productivity impairment (n/N: 38/86), and 49% (n/N: 93/189) in activity impairment and was maintained through Week 52 (presenteeism: 51% [n/N: 35/69]; work productivity impairment: 48% [n/N: 36/75]; activity impairment 54% [n/N: 92/170], respectively). Fewer patients receiving PBO vs. RZB treatment reported MCID at Week 24 (presenteeism: 37% [n/N: 29/79]; work productivity loss: 35% [n/N: 29/84]; activity impairment: 36% [n/N: 63/175]) but showed notable increases at Week 52 after initiating RZB treatment (presenteeism: 59% [n/N: 42/71]; work productivity loss: 55% [n/N: 41/75]; activity impairment: 58% [n/N: 95/164]).

When stratified by baseline skin burden (high: ≥3% BSA or low: <3% BSA), patients with a high skin burden who were receiving RZB were significantly more likely to report MCIDs in most PROs at Week 24 (excluding HAQ-DI [$P = 0.265$], SF-36

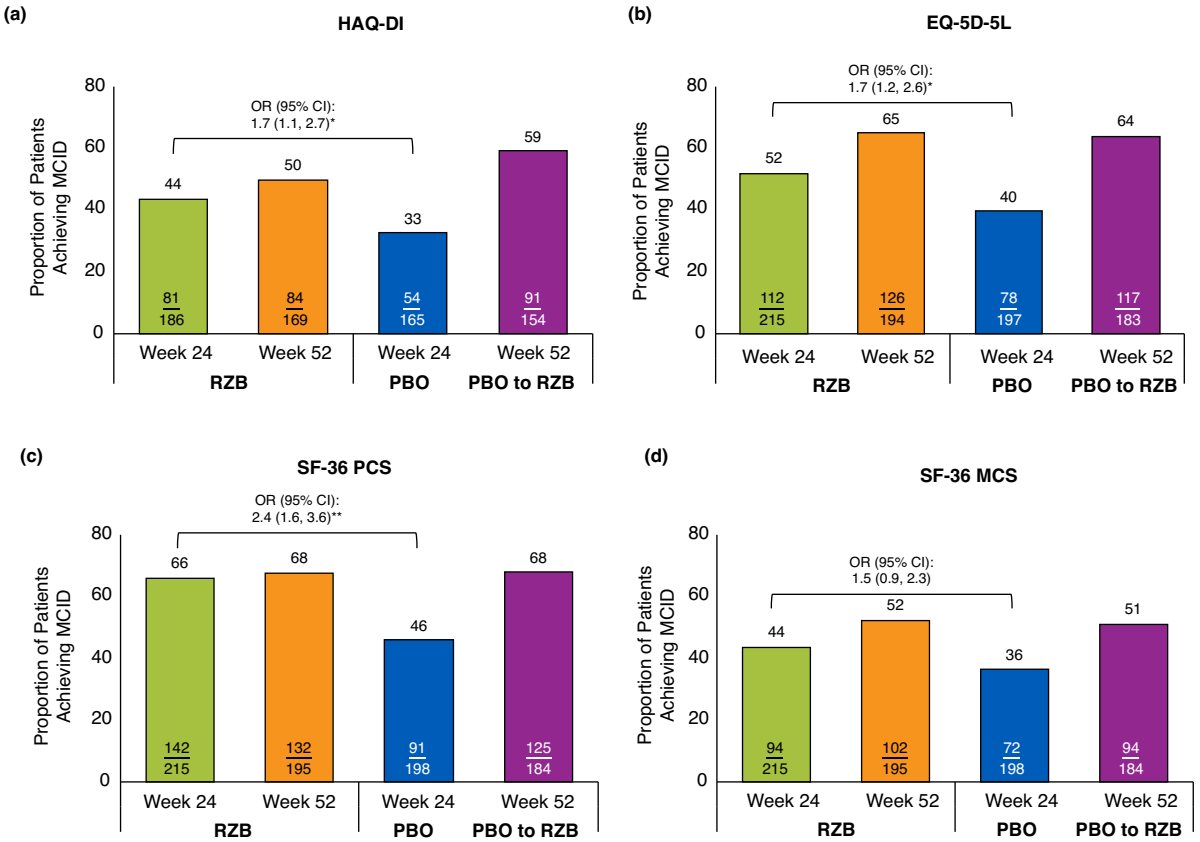

Figure 5 Proportion of patients reporting MCID in HAQ-DI, EQ-5D-5L and SF-36 PCS and MCS: Results from KEEPsAKE-2. All patients had HAQ-DI ≥0.35 at baseline. CI, confidence interval; EQ-5D-5L, 5-Level EQ-5D; HAQ-DI, Health Assessment Questionnaire—Disability Index; MCID, minimal clinically important difference; MCS, Mental Component Summary; OR, odds ratio; PBO, placebo; PCS, Physical Component Summary; RZB, risankizumab; SF-36, Short-Form 36 Questionnaire. *$P \leq 0.01$; **$P < 0.001$.

role emotional [$P = 0.281$], and all 3 WPAI domains) compared with those with a high skin burden receiving PBO (Table S3). The likelihood of achieving MCIDs in PROs amongst patients with a low skin burden who were receiving RZB compared with those receiving PBO was similar to that of the whole cohort.

Discussion

Results from KEEPsAKE-1 and -2 demonstrated that, after 24 weeks, patients receiving RZB treatment were generally more likely than patients receiving PBO to report clinically important improvements in PROs in the key domains of HRQoL, physical functioning, xz and activity impairment. Moreover, the proportion of RZB-treated patients achieving MCID was maintained and, in some cases, increased with continued treatment through Week 52. Fewer patients receiving PBO reported MCID at Week 24; after initiating RZB treatment, however, these values notably increased, matching the trajectory of improvement seen in patients who received RZB for the entire study, thereby highlighting the therapeutic benefit of RZB.

As mentioned previously, PROs are great tools for assessing patient perspectives on drug efficacy, both in terms of disease activity and HRQoL. Studies have shown that patients are less likely to adhere to therapies they deem ineffective.[8,9,14] As such, there may be patients who present with physician-rated clinical improvement of diseases, such as reduced tender or swollen joint counts, but who still experience pain or impaired physical functioning and thus feel as though their disease is inadequately controlled.[15] This analysis focused on patients achieving MCID in PROs, as well as the maintenance of that measure over time. Improvements that can be sustained over a long period of time are important to patients and critical to meaningful improvement in patient HRQoL. The achievement of MCID is an important clinical endpoint as it not only demonstrates that improvement has occurred, but that it is clinically meaningful and, most importantly, an improvement perceptible to the patient.[16] The MCIDs used in this manuscript have been validated elsewhere and have been shown to correspond to tangible improvement in patient-reported outcomes.[16–20] The PROs

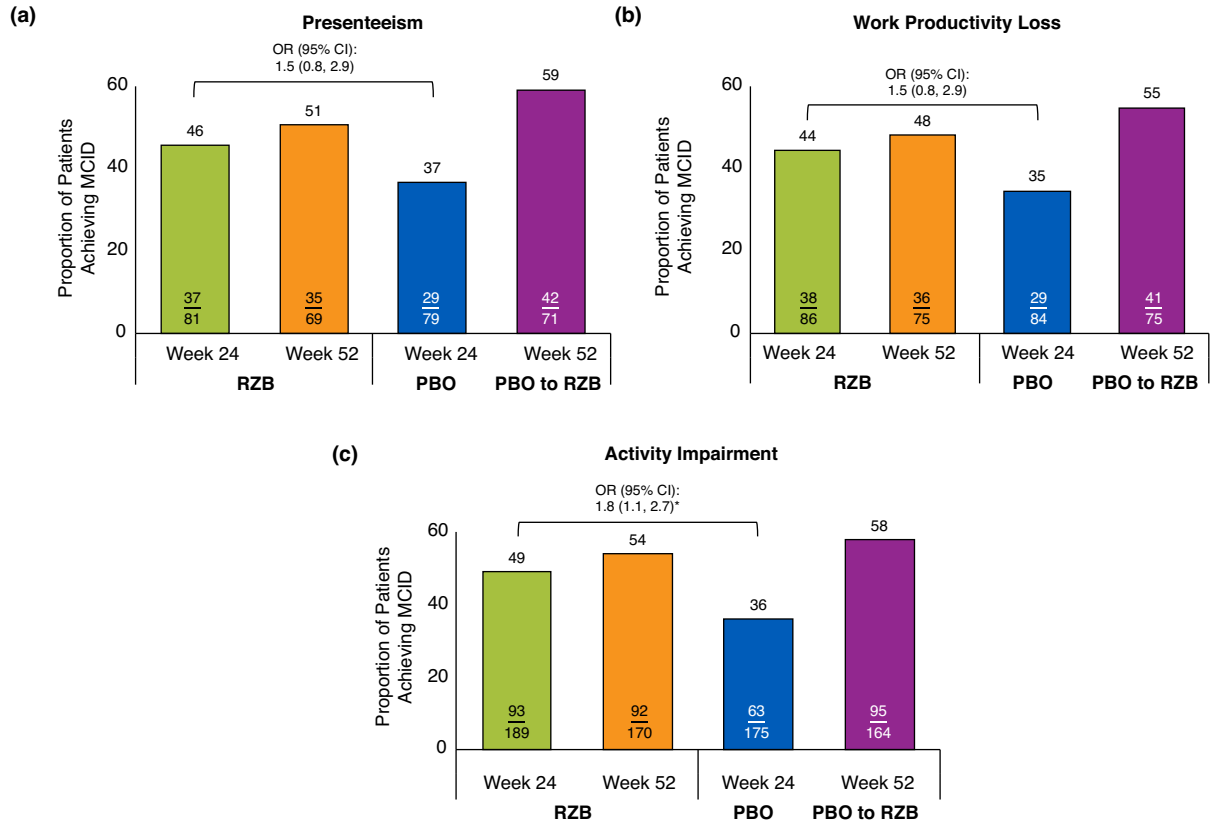

Figure 6 Proportion of patients reporting MCID in WPAI domains: Results from KEEPsAKE-2. Presenteeism and work productivity loss were only assessed amongst patients reporting active employment at baseline. Only patients with presenteeism ≥20%, work productivity loss ≥15%, and activity impairment ≥20% were included in the respective analyses. CI, confidence interval; MCID, minimal clinically important difference; OR, odds ratio; PBO, placebo; RZB, risankizumab; WPAI, Work Productivity and Activity Impairment. *$P < 0.05$.

measured in this study cover most of the domains recognized as important by the GRAPPA-OMERACT working group, which measured the impact of disease on patients with PsA.

These studies are not the first clinical trials to show significant improvement in PROs. Indeed, several studies have shown improvement in PROs, most commonly PtGA, pain, SF-36 domains and component summary scores, and WPAI, in patients with active PsA.[21–24] These studies assessed several different biologics, such as interleukin-17 inhibitors (secukinumab 10 mg; 24 Weeks[22]; ixekizumab 80 mg; 52 Weeks[24]), interleukin-12/23 inhibitors (ustekinumab 45 mg or 90 mg; 52 Weeks[23]), and tumour necrosis factor (TNF) inhibitors (adalimumab, etanercept, golimumab, infliximab, or certolizumab; 39 weeks[21]). Similarly, after 3 months of treatment with tofacitinib, a small-molecule JAK inhibitor, in patients with PsA with inadequate responses or intolerance to TNF inhibitors, patient-reported quality of life as measured by PtGA, Pain, SF-26 PCS, amongst others, was significantly improved compared with placebo.[25] Upadacitinib (UPA), also a JAK inhibitor, showed similar results at Weeks 12 and 24, with a greater proportion of patients achieving MCID in PROS, including PtGA, pain, HAQ-DI, and FACIT-Fatigue, in the UPA-treated groups, as compared with the PBO-treated group.[26,27] The current study, however, is one of the few to demonstrate clear, consistent improvement in such a wide array of PROs (PtGA, pain, FACIT-Fatigue, EQ-5D-5L, HAQ-DI, SF-36 domains and component summary scores, and WPAI). Likewise, this study also demonstrated that the difficult-to-treat population of patients with a high skin burden (≥3% BSA) were significantly more likely to report MCID in most of the PROs assessed. It is common to report mean change from baseline in PROs for a study cohort, however, it is not always intuitive how clinically meaningful such improvements are. Thus, this analysis reported data as the proportion and likelihood of patients achieving MCID. Presenting data in this way allows for a quick interpretation of how meaningful the improvements with RZB treatment are, as well as the likelihood that therapy may benefit a patient with PsA.

There are several strengths of these studies. Whilst a number of studies have assessed PROs in patients with PsA, few have assessed the impact of therapy on such a large array of PROs. The PROs assessed in this study addressed the full health-related patient experience – how the patient feels and functions—as well as disease activity measures. Moreover, the use of MCIDs strengthens the conclusions and provides insight into the clinically relevant improvements provided by RZB treatment. The open-label extension of this study also demonstrated the benefits of RZB treatment, as patients initially receiving PBO who then switched to RZB demonstrated a similar trajectory of improvement as the cohort of patients receiving RZB for the entire study. There are inherent limitations to using PROs. Many of the symptoms patients must recall are dynamic and may change from day-to-day. Thus, assessing PROs weeks apart may introduce recall bias that could affect the overall outcomes. In this study, we primarily assessed HRQoL outcomes and did not include socioeconomic status or regional political policies, both of which may greatly affect overall quality of life measures in populations with chronic disease. Likewise, whilst our assessments covered most of the GRAPPA-OMERACT guidelines, we did not assess all aspects of the guidelines and thus it is possible that significant changes occurred in other domains not covered here. This analysis only included observed cases and was not multiplicity controlled, thus all reported significance values are nominal.

Conclusions

These studies demonstrated the robust beneficial impact of RZB treatment in patients with active PsA. A majority of patients reported MCID in most PROs as early as Week 24 and continued improving through Week 52. Importantly, patients who initially received PBO showed a similar trajectory of improvement upon starting RZB treatment. Likewise, patients with a high skin burden, who are often more difficult to treat, were also more likely to report MCID when receiving RZB vs. PBO. These data, when complimented by primary efficacy data, support the use of RZB in patients with active PsA. Studies are ongoing to assess longer term impacts of RZB in this population and will provide insight into the durability of these results.

Acknowledgements

Medical writing services were provided by Samantha D. Francis Stuart, PhD of Fishawack Facilitate, Ltd., part of Fishawack Health, and funded by AbbVie, Inc. The patients in this manuscript have given written informed consent to the publication of their case details.

Data availability statement

AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. Access is provided to anonymized, patient and trial-level data (analysis data sets), as well as other information (eg, protocols and Clinical Study Reports) from AbbVie-sponsored Phase II-IV global interventional clinical trials conducted in patients (completed as of May 2004, for products and indications approved in either the United States or the European Union), 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. Access to this 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 (SAP) and execution of a Data Sharing Agreement (DSA). 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-and347informationsharing/data-and-information-sharing-with-qualified-researchers.html.

References

1 Ritchlin CT, Colbert RA, Gladman DD. Psoriatic Arthritis. *N Engl J Med* 2017; **376**: 957–970.
2 Carvalho AL, Hedrich CM. The molecular pathophysiology of psoriatic arthritis-the complex interplay between genetic predisposition, epigenetics factors, and the microbiome. *Front Mol Biosci* 2021; **8**: 662047.
3 Kishimoto M, Deshpande GA, Fukuoka K *et al*. Clinical features of psoriatic arthritis. *Best Pract Res Clin Rheumatol* 2021; **101670**: 101670.
4 Lee S, Mendelsohn A, Sarnes E. The burden of psoriatic arthritis: a literature review from a global health systems perspective. *Pharm Ther* 2010; **35**: 680.
5 Strand V, Sharp V, Koenig AS *et al*. Comparison of health-related quality of life in rheumatoid arthritis, psoriatic arthritis and psoriasis and effects of etanercept treatment. *Ann Rheum Dis* 2012; **71**: 1143–1150.
6 Salaffi F, Carotti M, Gasparini S, Intorcia M, Grassi W. The health-related quality of life in rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis: a comparison with a selected sample of healthy people. *Health Qual Life Outcomes* 2009; **7**: 1–12.
7 Gudu T, Gossec L. Quality of life in psoriatic arthritis [review]. *Expert Rev Clin Immunol* 2018; **14**: 405–417.
8 Lauck SB, Lewis KB, Borregaard B, de Sousa I. "What is the right decision for me?" Integrating patient perspectives through shared decision-making for valvular heart disease therapy. *Can J Cardiol.* 2021; **37**: 1054–1063.
9 Jin J, Sklar GE, Min Sen OV, Chuen LS. Factors affecting therapeutic compliance: A review from the patient's perspective. *Ther Clin Risk Manag* 2008; **4**: 269–286.
10 Mease P, Kellner H, Morita A *et al*. OP0307 Efficacy and safety of risankizumab, a selective il-23p19 inhibitor, in patients with active psoriatic arthritis over 24 weeks: results from a phase 2 trial. *Ann Rheum Dis* 2018; **77**: 200–201.
11 Kristensen L, Keiserman M, Papp K *et al*. 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* 2022; **81**: 225–231.
12 Ostor A, Van den Bosch F, Papp K *et al*. OP0228 Efficacy and safety of risankizumab for active psoriatic arthritis, including patients with inadequate response or intolerance to biologic therapies: 24-week results from the phase 3, randomized, double-blind, KEEPsAKE 2 trial. [abstract]. *Ann Rheum Dis* 2021; **80**: 138–139.
13 Ostor A, Van den Bosch F, Papp K *et al*. Efficacy and safety of risankizumab for active psoriatic arthritis: 24-week results from the randomised,

double-blind, phase 3 KEEPsAKE 2 trial. *Ann Rheum Dis* 2021; **80**: 138–139.
14 Volpicelli Leonard K, Robertson C, Bhowmick A, Herbert LB. Perceived Treatment Satisfaction and Effectiveness Facilitators Among Patients With Chronic Health Conditions: A Self-Reported Survey. *Interact J Med Res* 2020; **9**: e13029.
15 Eder L, Thavaneswaran A, Chandran V, Cook R, Gladman DD. Factors explaining the discrepancy between physician and patient global assessment of joint and skin disease activity in psoriatic arthritis patients. *Arthritis Care Res (Hoboken)* 2015; **67**: 264–272.
16 Strand V, Boers M, Idzerda L *et al*. It's good to feel better but it's better to feel good and even better to feel good as soon as possible for as long as possible. Response criteria and the importance of change at OMERACT 10. *J Rheumatol* 2011; **38**: 1720–1727.
17 Kitchen H, Hansen B, Abetz L. Patient-reported outcome measures for rheumatoid arthritis: minimal important differences review. *Arthritis Rheum* 2013; **65**(Suppl 10): Abstract 2268.
18 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**: 2461–2465.
19 Marra CA, Woolcott JC, Kopec JA *et al*. A comparison of generic, indirect utility measures (the HUI2, HUI3, SF-6D, and the EQ-5D) and disease-specific instruments (the RAQoL and the HAQ) in rheumatoid arthritis. *Soc Sci Med* 2005; **60**: 1571–1582.
20 Tillett W, Lin CY, Zbrozek A, Sprabery AT, Birt J. A threshold of meaning for work disability improvement in psoriatic arthritis measured by the work productivity and activity impairment questionnaire. *Rheumatol Ther.* 2019; **6**: 379–391.
21 Karadag O, Dalkilic E, Ayan G *et al*. Real-world data on change in work productivity, activity impairment, and quality of life in patients with psoriatic arthritis under anti-TNF therapy: a postmarketing, noninterventional, observational study. *Clin Rheumatol* 2021; **41**: 85–94.
22 Strand V, Mease P, Gossec L *et al*. Secukinumab improves patient-reported outcomes in subjects with active psoriatic arthritis: results from a randomised phase III trial (FUTURE 1). *Ann Rheum Dis* 2017; **76**: 203–207.
23 Rahman P, Puig L, Gottlieb AB *et al*. Ustekinumab treatment and improvement of physical function and health-related quality of life in patients with psoriatic arthritis. *Arthritis Care Res (Hoboken)*. 2016; **68**: 1812–1822.
24 Kavanaugh A, Marzo-Ortega H, Vender R *et al*. Ixekizumab improves patient-reported outcomes in patients with active psoriatic arthritis and inadequate response to tumour necrosis factor inhibitors: SPIRIT-P2 results to 52 weeks. *Clin Exp Rheumatol* 2019; **37**: 566–574.
25 Strand V, de Vlam K, Covarrubias-Cobos JA *et al*. Effect of tofacitinib on patient-reported outcomes in patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors in the phase III, randomised controlled trial: OPAL Beyond. *RMD Open* 2019; **5**: e000808.
26 Strand V, Mease PJ, Soriano ER *et al*. Improvement in patient-reported outcomes in patients with psoriatic arthritis treated with upadacitinib versus placebo or adalimumab: results from SELECT-PsA 1. *Rheumatol Ther* 2021; **8**: 1789–1808.
27 Strand V, Van den Bosch F, Ranza R *et al*. Patient-reported outcomes in psoriatic arthritis patients with an inadequate response to biologic disease-modifying antirheumatic drugs: SELECT-PsA 2. *Rheumatol Ther.* 2021; **8**: 1827–1844.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. MCIDs of PROs.
Table S2. Proportion of patients reporting MCIDs in SF-36 Domains.
Table S3. Proportion of patients reporting MCIDs stratified by baseline BSA.

