Efficacy and safety of risankizumab for active psoriatic arthritis: 52-week results from the KEEPsAKE 2 study

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Abstract

Objective. Psoriatic arthritis (PsA) is a chronic inflammatory disease in which the skin and joints are affected. In this follow-up analysis, the 52-week efficacy and safety of risankizumab 150 mg in patients with active PsA who had previous inadequate response/intolerance to one or two biologic therapies (Bio-IR) or one or more conventional synthetic disease-modifying antirheumatic drug (csDMARD-IR) were evaluated.

Methods. In the ongoing, phase 3, KEEPsAKE 2 trial, patients with active PsA were randomized 1:1 to receive subcutaneous risankizumab 150 mg or placebo at weeks 0, 4 and 16 (period 1). At week 24 (period 2), patients who received placebo were switched to risankizumab, and all patients received risankizumab 150 mg every 12 weeks from weeks 28–208.

Results. At week 24, 51.3% of risankizumab-treated patients (N = 224) achieved ≥20% improvement in American College of Rheumatology criteria (ACR20) *vs* 26.5% of placebo-treated patients (N = 220; $P < 0.001$). At week 52, 58.5% of patients randomized to receive continuous risankizumab achieved ACR20, and 55.7% of patients who switched from placebo to risankizumab at week 24 achieved ACR20. Similar trends were observed for other efficacy measures. Rates of serious treatment-emergent adverse events (TEAEs) and TEAEs leading to discontinuation remained stable through week 52, and no deaths were reported.

Conclusion. Risankizumab was well tolerated and improved symptoms of PsA in Bio-IR/csDMARD-IR patients, with a consistent long-term safety profile from weeks 24–52.

Trial registration. United States National Library of Medicine clinical trials database www.clinicaltrials.gov; KEEPsAKE 2; NCT03671148

Key words: biologic agent, interleukin 23, disease-modifying antirheumatic drug, risankizumab, psoriatic arthritis

Rheumatology key messages

- Risankizumab demonstrated efficacy in patients who were csDMARD-IR or Bio-IR though 52 weeks.
- Risankizumab is generally well tolerated, with a safety profile consistent with risankizumab studies in psoriasis.
- Risankizumab provides long-term benefits in patients with PsA who were csDMARD-IR or Bio-IR.

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory disease that may impair physical function, emotional well-being and self-esteem, leading to long-term disruption of health-related quality of life (HRQoL) [1].

Current treatment guidelines for PsA recommend conventional synthetic disease-modifying antirheumatic drugs (csDMARDs; e.g. methotrexate) as first-line therapy for patients with polyarticular PsA [2]. However, methotrexate may induce liver toxicity in some patient populations, and some patients have an inadequate biologic response or intolerance (Bio-IR) to tumor necrosis factor inhibitors (or similar biologics) or csDMARDs (csDMARD-IR) [3].

Although there are several therapeutic options available to treat PsA, there is a need for additional efficacious and well-tolerated, long-term therapies that address the range of rheumatologic and dermatologic signs and symptoms of the disease for patients who are considered Bio-IR or csDMARD-IR. Risankizumab is a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits interleukin 23 by binding to its p19 subunit, which is approved in many countries to treat moderate-to-severe plaque psoriasis and active PsA [4].

KEEPsAKE 2 (NCT03671148) is an ongoing, global, multicenter, phase 3 study evaluating the efficacy and safety of risankizumab to treat active PsA in patients who were Bio-IR or csDMARD-IR [5]. In the 24-week primary analysis, 51.3% of patients who received risankizumab achieved ≥20% improvement in American College of Rheumatology criteria (ACR20) compared with 26.5% of patients who received placebo ($P < 0.001$). Risankizumab 150 mg significantly improved multiple domains of PsA, including patient-reported outcomes assessing disease burden, compared with placebo in patients who were Bio-IR or csDMARD-IR

($P < 0.05$). Achievement of ACR20 was similar for patients who were Bio-IR *vs* csDMARD-IR [5].

Risankizumab was well tolerated, with low rates of serious adverse events (AEs), severe AEs and serious and opportunistic infections; discontinuation of treatment owing to AEs was low (<1%) [5].The safety profile for risankizumab in patients with PsA was comparable to that of risankizumab in patients with psoriasis.[5]. Here we report results through 52 weeks of treatment (open-label extension after week 24).

Methods

A detailed description of the study design and patient population was previously reported [5]. Eligible patients were adults with a clinical diagnosis of active PsA defined as ≥5 tender joints (based on 68 joint counts) and ≥5 swollen joints (based on 66 joint counts), who fulfilled the Classification Criteria for Psoriatic Arthritis (CASPAR) with symptoms ≥6 months before screening, and active plaque psoriasis with ≥1 psoriatic plaque of ≥2-cm diameter or nail changes consistent with psoriasis at screening. Patients were also required to have demonstrated inadequate response or intolerance to 1 or 2 biologic therapies (i.e. Bio-IR) or to ≥1 csDMARDs (i.e. csDMARD-IR). See **Supplementary Table S1** for complete eligibility criteria.

This study consisted of a screening period; a 24-week double-blind, placebo-controlled, parallel-group period (period 1); an open-label extension period after week 24 to week 208 (period 2) and a follow-up period consisting of a completion visit 12 weeks after the last dose and a follow-up phone call 20 weeks after the last dose. Patients were randomized 1:1 to receive subcutaneous administration of risankizumab 150 mg or placebo at weeks 0, 4 and 16 To maintain blinding of treatment in period 1, at week 24, patients who were randomized to

risankizumab received blinded placebo, and patients who were randomized to placebo received the first dose of blinded risankizumab**.** All patients received open-label risankizumab 150 mg at week 28 and every 12 weeks thereafter until week 208. Treatment with risankizumab was discontinued for patients classified as non-responders (i.e. those achieving <20% improvement in tender joint count and/or swollen joint count at two consecutive visits) starting at week 36.

Assessments

Efficacy

Efficacy assessments included the proportion of patients who achieved ≥20%/50%/70% improvement in American College of Rheumatology criteria (ACR20/ACR50/ACR70), the change from baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI), the proportion of patients who achieved ≥90% reduction in Psoriasis Area and Severity Index (PASI 90) in patients with an affected body surface area ≥3% at baseline, the proportion of patients who achieved minimal disease activity (MDA), the change from baseline in 36-Item Short Form Health Survey Physical Component Summary score (SF-36 PCS), the change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue Questionnaire score (FACIT-Fatigue), the resolution of enthesitis (Leeds Enthesitis Index [LEI] = 0, among patients with LEI >0 at baseline), the resolution of dactylitis (Leeds Dactylitis Index [LDI] = 0, among patients with LDI >0 at baseline) and the proportion of patients achieving a clinically meaningful improvement in the HAQ-DI (change −0.35 or less) in patients with ≥0.35 HAQ--DI at baseline. All efficacy outcomes were assessed at weeks 24 and 52.

Safety

Safety assessments were based on AE monitoring. Physical examinations, vital sign measurements and laboratory values were also assessed throughout the study. Safety results

are described at week 24 and at the week 52 long-term data cut-off date (defined as safety data reported through the 19 April 2021 cut-off date) for all patients who received any dose of risankizumab 150 mg.

Statistical analysis

Efficacy and safety were assessed up to the week 52 data cutoff (19 April 2021). All efficacy analyses were conducted in the full analysis set (all patients who received ≥1 dose of risankizumab). The primary analysis (up to week 24) used non-responder imputation (NRI) incorporating multiple imputation to handle missing data due to COVID-19 (NRI-C), where 1) missing data due to COVID-19 were handled by multiple imputation and 2) patients with data missing due to reasons other than COVID-19 or after intercurrent events (i.e. initiation of rescue medication or concomitant medications that could meaningfully impact efficacy assessment) were imputed as non-responders. and a mixed-effect model for repeated measures considering intercurrent events. Long-term analysis (weeks 24–52) used NRI (as observed with imputation) for categorical variables and mixed-effect model for repeated measures for continuous variables based on as-observed data. Safety was assessed in all patients who received ≥1 dose of risankizumab. AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 23.0 or higher, and COVID-19–related treatment-emergent adverse events (TEAEs) were identified using relevant COVID-19 terms available in MedDRA. TEAEs were summarized using exposure-adjusted event rates (EAERs, events[E]/100 patient-years [PYs]). Post-baseline grades for select liver function tests were summarized using exposure-adjusted incidence rates. Laboratory abnormalities were classified by National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03.

Ethics

The study is being conducted in accord with International Council for Harmonisation guidelines. The Bellberry Limited Human Research Ethics Committee (Eastwood, Australia) 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 enrollment.

Results

Patients

Of 443 patients who were randomized and received ≥1 dose of study drug, 414 (93.5%) completed the placebo-controlled period and entered the open-label extension period. Patients randomized to receive continuous risankizumab (190/224 [84.8%]) and patients randomized to receive placebo and switch to risankizumab at week 24 (176/219 [80.4%]) continued the study through the end of the 52-week data cut-off date (19 April 2021). The most frequent reason for study discontinuation in period 2 was withdrawal of consent (2.7%; **Supplementary Fig. S1**). Twenty-four patients (5.4%) discontinued risankizumab treatment because of non-response (i.e. <20% improvement in tender joint count/swollen joint count compared with baseline at two consecutive visits, as required by the protocol) after week 36. Demographics and baseline characteristics (previously reported) were generally balanced between groups; 206 patients (46.5%) were Bio-IR at baseline [5].

Efficacy

As previously reported, 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 were met ($P < 0.05$) compared with placebo at week 24 [5]. In patients randomized to receive continuous risankizumab, the proportion achieving ACR20 increased from week 24 (51.3% [115/224]) to week 52 (58.5% [131/224]; **Table 1**; **Fig. 1A**). Similarly, the proportion of patients achieving ACR50 and ACR70 increased from week 24 (26.3% [59/224] and 12.0% [27/224]) to week 52 (32.1% [72/224] and 16.5% [37/224]; **Fig. 1C, 1E**). The observed ACR20/50/70 responses over time are shown in **Fig. 1B, 1D and 1F**.

Among patients with enthesitis (LEI >0) at baseline, 42.9% (63/147) of patients randomized to receive continuous risankizumab achieved resolution of enthesitis at week 24, with a similar proportion of patients achieving resolution of enthesitis at week 52 (43.5% [64/147]). Similarly, among patients with dactylitis (LDI >0) at baseline, 72.5% (29/40) of patients randomized to receive continuous risankizumab achieved resolution of dactylitis at week 24, with 67.5% (27/40) achieving resolution of dactylitis at week 52 (**Table 1**).

Among patients with ≥3% body surface area affected by psoriasis at baseline, 55.0% (68/123) of patients randomized to receive continuous risankizumab achieved PASI 90 at week 24, and by week 52, 64.2% (79/123) achieved PASI 90 response (**Table 1**, **Fig. 2A**). The observed PASI 90 response rates over time are shown in **Fig. 2B**.

Patients randomized to receive continuous risankizumab also reported additional improvement in physical function from week 24 (**Table 1**). The 24-week least square mean (95% CI) change in HAQ-DI was −0.22 (−0.28, −0.15); these improvements were maintained at week 52 (−0.26 [−0.32, −0.20]; mixed-model repeated measures analysis, **Table 1**; as observed, **Supplementary Table S2**). Among patients with a baseline HAQ-DI ≥0.35, 39.9% (78/224) of patients randomized to receive continuous risankizumab achieved a clinically meaningful improvement in HAQ-DI, defined as ≥0.35 change from baseline, at week 24, which increased to 42.9% (84/224) by week 52 (**Table 1**).

Patients treated with continuous risankizumab also reported numerical improvement in HRQoL and fatigue, as assessed by SF-36 PCS and FACIT-Fatigue, respectively. From week 24 to week 52, the least squares mean (95% CI) change in SF-36 PCS scores increased from 5.9 (4.9, 6.9) to 6.3 (5.2, 7.3). Similarly, from week 24 to week 52, the least squares mean (95% CI) change in FACIT-Fatigue scores increased from 4.9 (3.7, 6.0) to 5.7 (4.5, 6.9) (**Table 1**).

Patients randomized to receive continuous risankizumab also reported improvement in achieving MDA. At week 24, 25.6% (57/224) achieved MDA, which increased to 27.2% (61/224) by week 52 (**Table 1**).

Improvements in efficacy were also observed among patients who were initially randomized to receive placebo in period 1 and then switch to risankizumab in period 2. At week 52, 55.7% (122/219) of patients in this group achieved ACR20; ACR50 and ACR70 were achieved by 32.0% (70/219) and 21.0% (46/219) of patients (**Table 1**). Similarly, resolution of enthesitis and dactylitis increased to 52.5% (83/158) and 70.2% (40/57), respectively, at week 52. Improvements in PASI 90 were also observed, and by week 52, 59.7% (71/119) achieved PASI 90 (**Table 1**). The least square mean (95% CI) change in HAQ-DI improved by week 52 (−0.34 [−0.41, −0.28]), as did the proportion of patients with a baseline HAQ-DI ≥0.35 who achieved a clinically meaningful improvement in HAQ-DI (48.7% [91/187] by week 52; **Table 1**). From week 24 to week 52, the least square mean (95% CI) change in SF-36 PCS increased to 7.3 (6.2, 8.4; **Table 1**), and the least square mean (95% CI) change in FACIT-Fatigue increased to 7.0 (5.8, 8.2; **Table 1**) by week 52. Finally, 33.8% (74/219) of patients achieved MDA by week 52 (**Table 1**).

Generally consistent response patterns were observed among patients who were Bio-IR. At week 24, 45.7% (48/105) of patients treated with risankizumab achieved ACR20. Efficacy was maintained through week 52, and 49.1% (52/106; note, one patient was reclassified as Bio-IR

after week 24) of patients achieved ACR20 at week 52. Similar patterns were observed for other efficacy outcomes (**Supplementary Table S3**).

Safety

As of the data cutoff for the week 52 analysis (19 April 2021), the EAER for any TEAE was 184.2 E/100 PYs for patients receiving risankizumab (including those who switched from placebo at week 24). The EAERs for serious TEAEs (9.4 E/100 PYs) and TEAEs leading to treatment discontinuation (1.6 E/100 PYs) were consistent with the rates reported at week 24 (13.4 E/100 PYs and 1.9 E/100 PYs, respectively). By the long-term data cutoff, 38 (7.5 E/100 PYs) COVID-19–related TEAEs were reported, up from one reported event at week 24. The EAER for serious infections was 2.0 E/100 PYs, which was consistent with the week 24 rate. By the long-term data cutoff, there was one (0.2 E/100 PYs) opportunistic infection not including tuberculosis or herpes zoster (an oral fungal infection) and three (0.6 E/100 PY) herpes zoster infections reported; all these events were reported after week 24. Candidiasis was reported for three patients (seven events, all nonserious); events included one event (0.2 E/100 PY) of anal candidiasis, four events (0.8 E/100 PY) of oral candidiasis and two events (0.4 E/100 PY) of vulvovaginal candidiasis. Furthermore, 11 (2.2 E/100 PYs) malignancies (nine events of non-melanoma skin cancer [NMSC], one event of acral lentiginous melanoma and one event of papillary thyroid cancer) were reported by the long-term data cutoff. Except for one event of NMSC, all events of malignancies were reported after week 24 (**Table 2**).

A total of three (0.6 E/100 PYs) major adverse cardiovascular events were reported through the data cutoff, including two newly reported after week 24. One patient with a history of hypertension experienced a non-fatal stroke, and two patients (one with a history of previous myocardial infarctions with coronary artery stents, and one who is an active smoker with

dyslipidemia) experienced non-fatal myocardial infarctions. Consistent with the week 24 data [5], the most commonly reported TEAEs were upper respiratory tract infections (5.9 E/100 PYs), nasopharyngitis (5.1 E/100 PYs), hypertension (4.9 E/100 PYs) and psoriatic arthropathy (4.7 E/100 PYs) Uveitis was reported for two patients (0.4 E/100 PYs). No worsening of inflammatory bowel disease (i.e. ulcerative colitis or Crohn's disease) was reported. No instances of active tuberculosis or deaths were reported (**Table 2**).

Through the data cut-off date, one patient (0.2 n/100 PYs) experienced an elevation in aspartate aminotransferase (AST) level that was grade 3 or higher (i.e. >5 times the upper limit of normal [× ULN]) as rated by Common Terminology Criteria for Adverse Events. There were no grade 3 elevations in alanine aminotransferase (ALT) or bilirubin levels reported and no grade 4 elevations in ALT, AST or bilirubin were observed. There were no elevated levels in liver function tests that met the criteria for biochemical Hy's Law (total bilirubin >2 × ULN and ALT or AST ≥3 × ULN; **Supplementary Table S4**).

Discussion

These efficacy and safety data from the ongoing phase 3 KEEPsAKE 2 study in patients who experienced Bio-IR or csDMARD-IR demonstrate robust and durable long-term efficacy of risankizumab through 52 weeks of treatment. Patients randomized to receive continuous treatment with risankizumab experienced improvements in multiple measures of the clinical signs and symptoms of PsA (e.g. joint and skin), as well as HRQoL and fatigue, with efficacy responses maintained through 52 weeks of treatment. Notably, efficacy was maintained with administration of risankizumab every 12 weeks, while similar IL-23 inhibitors are administered every eight weeks. By the long-term data cutoff (19 April 2021), 84.8% of patients randomized to receive continuous risankizumab continued on the study.

Among patients randomized to continuous risankizumab, the proportions of patients achieving ACR20/50/70 were generally maintained from week 24 to week 52. Additionally, some numerical improvements were observed from week 24 to week 52 in the proportions of patients achieving PASI 90 and MDA and in HAQ-DI, SF-36 PCS and FACIT-Fatigue scores.

Resolution of enthesitis and resolution of dactylitis were maintained from week 24 to week 52 in patients randomized to receive continuous risankizumab. In KEEPsAKE 1 (NCT03675308), a parallel study that evaluated the efficacy and safety of risankizumab in patients with active PsA who were csDMARD-IR, resolution of enthesitis and dactylitis were also reported. In a pooled analysis of the KEEPsAKE 1 and KEEPsAKE 2 studies, 55.0% (244/444) and 76.1% (143/188) of patients with enthesitis and dactylitis, respectively, at baseline who received continuous risankizumab achieved resolution of enthesitis and dactylitis, respectively, at week 52 [6].

As anticipated, patients initially randomized to receive placebo and then switched to risankizumab at week 24 experienced a similar trajectory of improvements in the signs and symptoms of PsA from week 24 through week 52.

Furthermore, risankizumab was efficacious in patients who were considered Bio-IR. In this study, nearly half of the patients were Bio-IR. Although patients who are Bio-IR are generally more refractory to treatment, improvements in PsA signs and symptoms were observed at week 24, and responses were maintained or continued to improve through week 52 in the Bio-IR cohort who received continuous risankizumab.

Risankizumab was generally well tolerated. No new safety signals were identified, and the safety profile observed with long-term treatment was generally consistent with previously reported 24-week results. The rise in COVID-19–related TEAEs during period 2 of the study coincided with the peak of the COVID-19 pandemic. By the long-term data cutoff, no cases of active tuberculosis or inflammatory bowel disease were reported. Patients with psoriasis are at increased risk of developing NMSC, especially if they have received prior systemic therapy or phototherapy [7]. All events of NMSC occurred in patients who had received previous therapy for psoriasis, and three of the seven patients had a history of NMSC. The low rates of opportunistic infections and herpes zoster through 52 weeks of treatment were consistent with the safety profile observed in patients with psoriasis that were treated with Risankizumab [4, 8, 9].

This study was not without limitations. First, the relatively homogeneous study population may limit generalizability to global populations. Second, the study was performed during the COVID-19 pandemic, which introduced logistical challenges during the placebo-controlled portion of the study, though this was addressed by using multiple imputation. Due to the study design, placebo safety data were only recorded for 24-weeks, though this was mitigated by reporting

events/100 PYs. Similarly, after week 24, patients were no longer blinded (as all patients received open-label risankizumab), and the open-label extension period is biased toward patients who responded to risankizumab (starting at week 36, non-responders were required to discontinue treatment). These limitations are mitigated by using non-responder imputation in the efficacy analyses. Finally, this ongoing study will provide safety and efficacy data over a 4-year period, so the 52-week analysis detailed here is somewhat brief.

In conclusion, results from this 52-week follow-up analysis of the phase 3 KEEPsAKE 2 clinical trial demonstrated long-term, durable efficacy of risankizumab in improving symptom control, physical function and quality of life in patients with active PsA who were csDMARD-IR or Bio-IR. Risankizumab was well tolerated, and the long-term safety profile was generally consistent with that observed at week 24. The KEEPsAKE 2 trial is ongoing, and the long-term efficacy and safety of risankizumab in PsA will continue to be evaluated.

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Collaborators

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Data availability statement

AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. This includes access to anonymized, individual, and trial-level data (analysis data sets), as well as other information (e.g. 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. 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-and-information-sharing/data-and-information-sharing-with-qualified-researchers.html.

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Table 1 Efficacy results

Parameter	Week 24[a] (Period 1)		Week 52 (Period 1 and 2)	
	RZB 150 mg *N* = 224	PBO *N* = 219	RZB 150 mg *N* = 224	PBO to RZB 150 mg *N* = 219
ACR20, *n* (%) (95% CI)	115 (51.3)***,† (44.8, 57.9)	58 (26.5) (20.7, 32.4)	131 (58.5) (52.0, 64.9)	122 (55.7) (49.1, 62.3)
ACR50, *n* (%) (95% CI)	59 (26.3)*** (20.3, 32.3)	20 (9.3) (5.4, 13.2)	72 (32.1) (26.0, 38.3)	70 (32.0) (25.8, 38.1)
ACR70, *n* (%) (95% CI)	27 (12.0)* (7.7, 16.3)	13 (5.9) (2.7, 9.0)	37 (16.5) (11.7, 21.4)	46 (21.0) (15.6, 26.4)
Resolution of enthesitis,[b, d] *n/N* (%) (95% CI)	63/147 (42.9)** (34.9, 50.9)	48/158 (30.4) (23.2, 37.6)	64/147 (43.5) (35.5, 51.6)	83/158 (52.5) (44.7, 60.3)
Resolution of dactylitis,[c, d] *n/N* (%) (95% CI)	29/40 (72.5)*** (58.7, 86.3)	24/57 (42.1) (29.3, 54.9)	27/40 (67.5) (53.0, 82.0)	40/57 (70.2) (58.3, 82.1)
PASI 90,[e] *n/N* (%) (95% CI)	68/123 (55.0)***,† (46.2, 63.9)	12/119 (10.2) (4.7, 15.6)	79/123 (64.2) (55.8, 72.7)	71/119 (59.7) (50.8, 68.5)
Change in HAQ-DI, mean (95% CI)	−0.22***,† (−0.28, −0.15)	−0.05 (−0.12, 0.02)	−0.26 (−0.32, −0.20)	−0.34 (−0.41, −0.28)
Clinically meaningful improvement in HAQ-DI,[f] *n (%)* (95% CI)	78 (39.9)*** (33.0, 46.8)	44 (23.6) (17.5, 29.7)	84 (42.9) (35.9, 49.8)	91 (48.7) (41.5, 55.8)
Change in SF-36 PCS, mean (95% CI)	5.9***,† (4.9 6.9)	2.0 (0.9, 3.1)	6.3 (5.2, 7.3)	7.3 (6.2, 8.4)
Change in FACIT-Fatigue, mean (95% CI)	4.9**,† (3.7, 6.0)	2.6 (1.4, 3.9)	5.7 (4.5, 6.9)	7.0 (5.8, 8.2)
MDA, *n (%)* (95% CI)	57 (25.6)***,† (19.9, 31.4)	25 (11.4) (7.2, 15.6)	61 (27.2) (21.4, 33.1)	74 (33.8) (27.5, 40.1)

All changes data are presented as least square mean changes from baseline.
Results based on full analysis set; NRI-C (week 24 binary endpoints), NRI (as observed with imputation; week 52 binary endpoints), or MMRM (continuous endpoints).
***Nominal $P < 0.001$, **nominal $P < 0.01$ *nominal $P < 0.05$.
†Statistically significant under overall type I error control.
[a]24-week results previously reported [1].
[b]Defined as Leeds Enthesitis Index = 0.
[c]Defined as Leeds Dactylitis Index = 0.
[d]Among patients with enthesitis or dactylitis at baseline.

[e]Among patients with ≥3% body surface area affected by psoriasis.
[f]Improvement of HAQ-DI ≥0.35 in patients with baseline HAQ-DI ≥0.35.
ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology score; 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; MDA: minimal disease activity; MMRM: mixed-effect model repeated measurement; NRI: non-responder imputation; NRI-C: NRI incorporating multiple imputation to handle missing data due to COVID-19; 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.

Table 2 Summary of safety during risankizumab treatment through week 52

Events (E/100 PYs)	Week 24 *N* = 224 PYs = 104.3	Long Term[a] *N* = 419 PYs = 509.7
Any TEAE	286 (274.2)	939 (184.2)
Serious TEAE	14 (13.4)	48 (9.4)
TEAE leading to discontinuation of study drug	2 (1.9)	8 (1.6)
COVID-19–related TEAE[b]	1 (1.0)	38 (7.5)
MACE	1 (1.0)	3 (0.6)
Serious infections	3 (2.9)	10 (2.0)
Opportunistic infections excluding TB and herpes zoster	0	1 (0.2)
Active TB	0	0
Herpes zoster	0	3 (0.6)
Malignant tumors		
Including NMSC	1 (1.0)	11 (2.2)
Excluding NMSC	0	2 (0.4)
All deaths	0	0

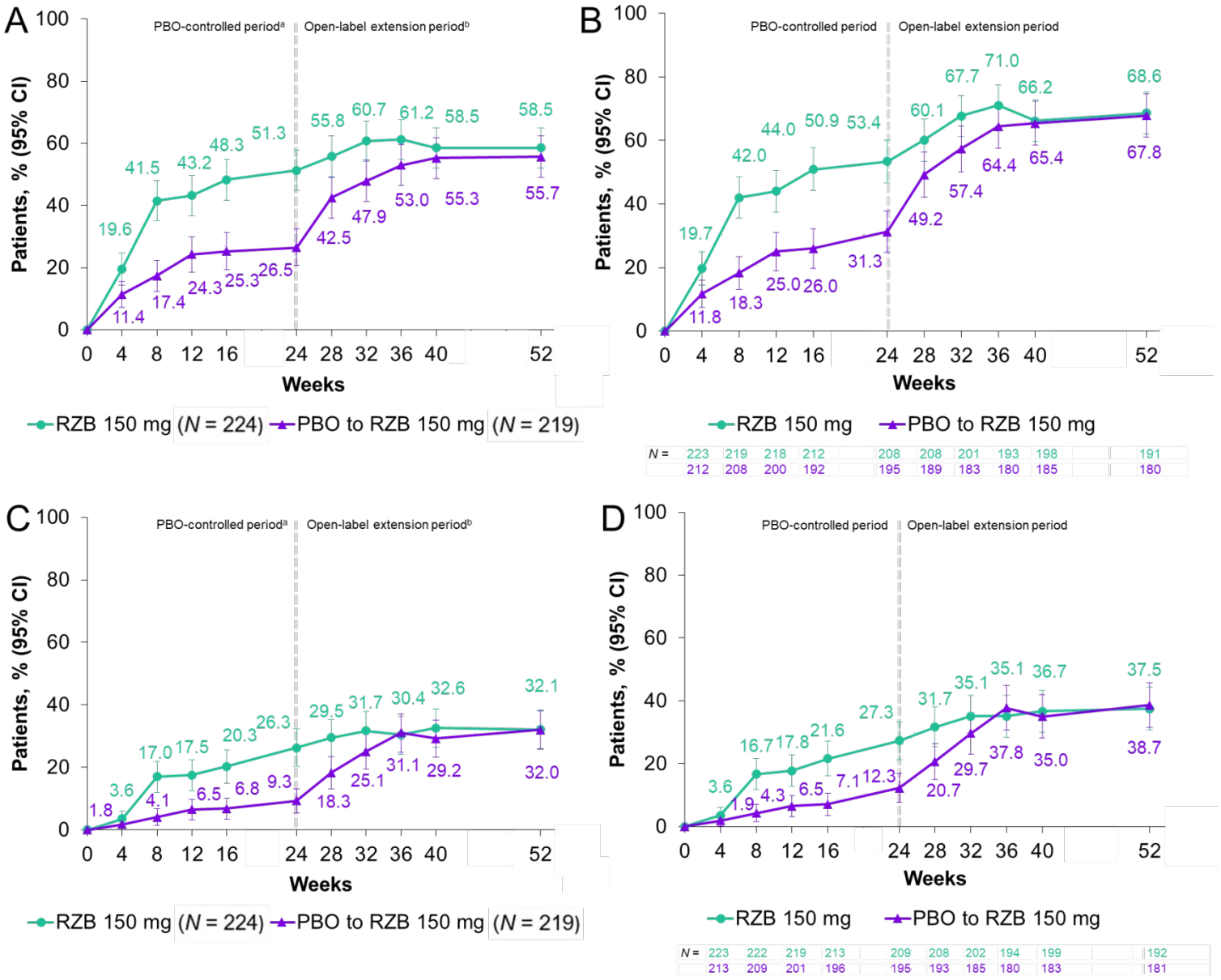
[a]Safety reported through data cut-off date (19 April 2021), which includes data through week 52 and all patients who received RZB 150 mg, including those who started on RZB 150 mg at randomization and who switched from placebo to RZB 150 mg after week 24.

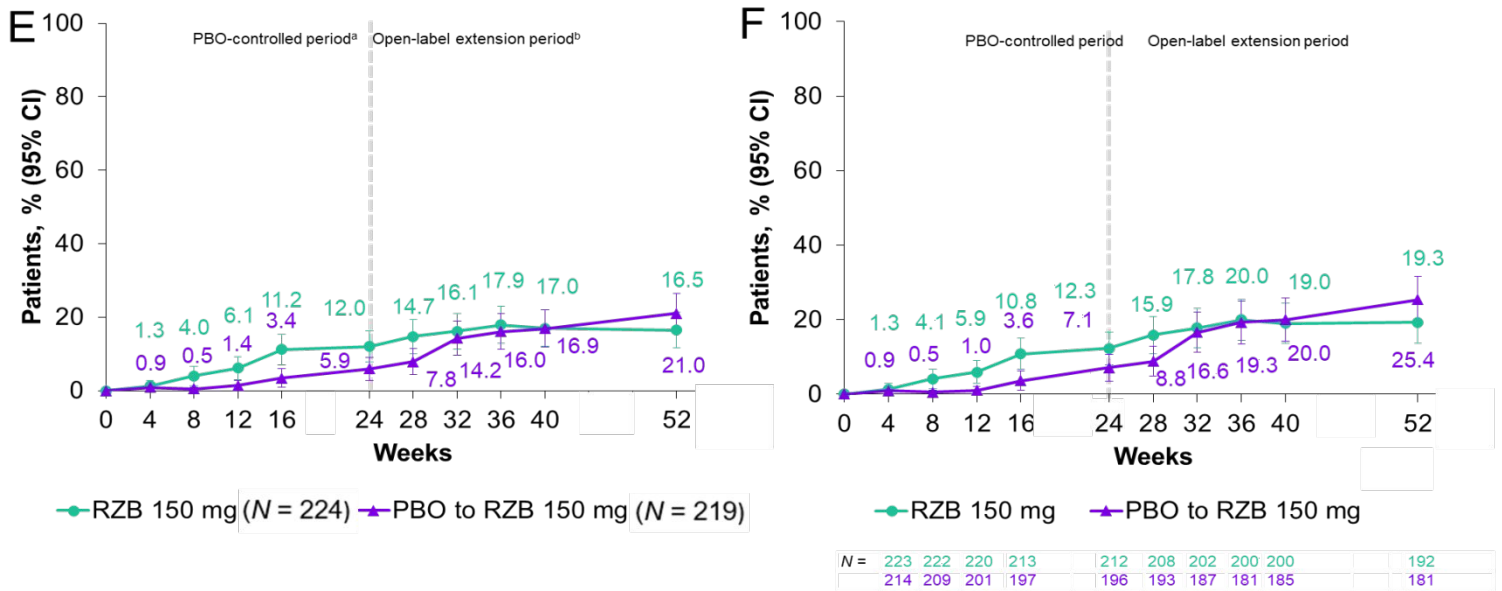
[b]One event of COVID-19 was reported during the placebo-controlled period. The 38 COVID-19–related TEAEs reported through data cut-off date included two events (0.4 E/100 PY) of asymptomatic COVID-19, 35 events (6.9 E/100 PY) of COVID-19 and one event (0.2 E/100 PY) of COVID-19 pneumonia.

TEAEs were defined as an adverse event with an onset date on or after the first dose of RZB and up to 140 days after the last dose of RZB if the patient discontinued study drug prematurely.

E: events; MACE: major adverse cardiovascular events; NMSC: non-melanoma skin cancer; PYs: patient-years; RZB: risankizumab; TB: tuberculosis; TEAE: treatment-emergent adverse events.

Fig 1 ACR responses over time.





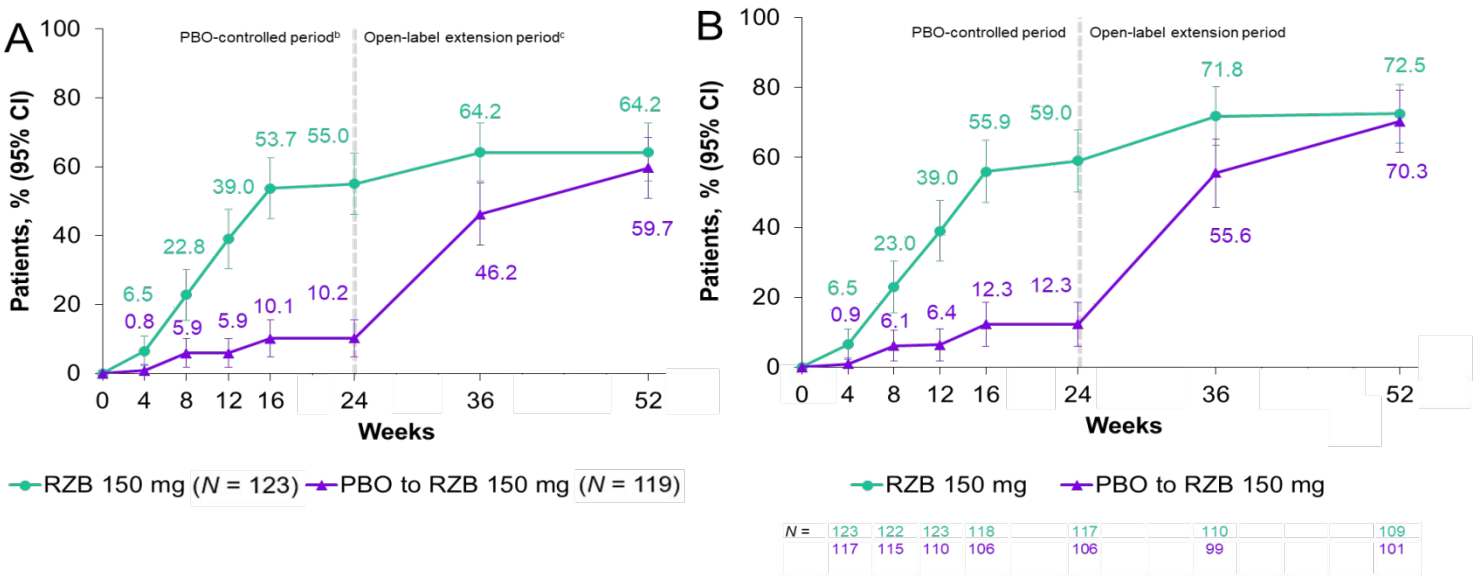
(A) ACR20 (NRI-C/NRI), (B) ACR20 (AO), (C) ACR50 (NRI-C/NRI), (D) ACR50 (AO), (E) ACR70 (NRI-C/NRI) and (F) ACR70 (AO) response rates for risankizumab 150 mg and placebo over the 24-week, double-blind treatment period and for open-label risankizumab 150 mg from weeks 24 through 52.

[a]Based on full analysis set, NRI-C was used.

[b]Based on full analysis set, NRI (as observed with imputation) was used.

ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology criteria; AO: as observed; NRI: non-responder imputation; NRI-C: NRI incorporating multiple imputation to handle missing data due to COVID-19; PBO: placebo; RZB: risankizumab.

Fig. 2 PASI 90 response over time[a].



(A) PASI 90 (NRI-C/NRI) and (B) PASI 90 (AO) response rates over the 24-week, double-blind treatment period for risankizumab 150 mg and placebo and response rates for open-label risankizumab 150-mg treatment from weeks 24 through 52.

[a]Among patients with ≥3% body surface area affected by psoriasis at baseline.

[b]Based on full analysis set, NRI-C was used.

[c]Based on full analysis set, NRI (as observed with imputation) was used.

AO: as observed; NRI: non-responder imputation; NRI-C: NRI incorporating multiple imputation to handle missing data due to COVID-19; PASI 90: ≥90% reduction in Psoriasis Area and Severity Index; PBO: placebo; RZB: risankizumab.