

# Long-Term Efficacy and Safety of Risankizumab for csDMARD-IR Patients With Active Psoriatic Arthritis: 244-Week Results From the KEEPSAKE 1 Trial

Mauro Keiserman,<sup>1</sup> Kim Papp,<sup>2,3</sup> Douglas White,<sup>4,5</sup> Angela Crowley,<sup>6</sup> Joseph F Merola,<sup>7</sup> Hayley Barnard,<sup>8</sup> Ana Biljan,<sup>8</sup> Thomas Iyile,<sup>8</sup> Lingfeng Luo,<sup>8</sup> Douglas Ashley,<sup>8</sup> Arathi R Setty,<sup>8</sup> Hayato Yamazaki,<sup>8</sup> and Frank Behrens<sup>9,10</sup>

<sup>1</sup>Rheumatology Section, Pontifical Catholic University, School of Medicine, Porto Alegre, Brazil; <sup>2</sup>Probit Medical Research and Alliance Clinical Trials, Waterloo, Ontario, Canada; <sup>3</sup>Division of Dermatology, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada; <sup>4</sup>Rheumatology Department, Waikato Hospital, Hamilton, New Zealand; <sup>5</sup>Waikato Clinical School, University of Auckland, Auckland, New Zealand; <sup>6</sup>Willow Rheumatology and Wellness, Willowbrook, IL, United States; <sup>7</sup>Department of Dermatology and Division of Rheumatology, UT Southwestern Medical Center, Dallas, TX, United States; <sup>8</sup>AbbVie Inc., North Chicago, IL, United States; <sup>9</sup>Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Frankfurt, Germany; <sup>10</sup>Department of Rheumatology, Immunology – Inflammation Medicine, University Hospital Goethe University, Frankfurt, Germany

Modified Presentation from the American College of Rheumatology Convergence (ACR), October 24-29, 2025, Chicago, IL

## OBJECTIVE

- To report the long-term efficacy and safety of risankizumab through 244 weeks in adult patients with PsA and an inadequate response or intolerance to csDMARDs

## INTRODUCTION

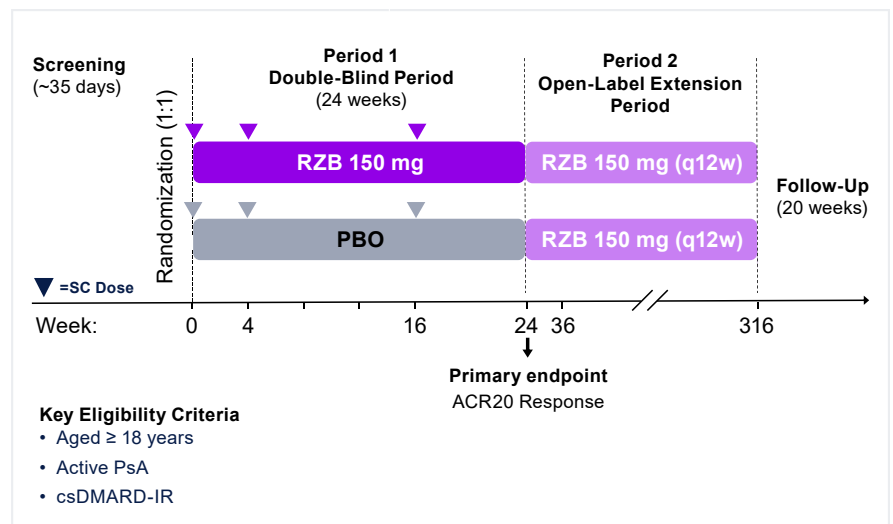
- Risankizumab (RZB) is a humanized immunoglobulin G1 monoclonal antibody that inhibits interleukin-23 by targeting its p19 subunit with high affinity and specificity, and is approved for the treatment of adult patients with psoriatic arthritis (PsA)
- KEEPSAKE 1 (NCT03675308) is an ongoing, global, phase 3, multicenter clinical trial to evaluate the efficacy and safety of RZB versus placebo (PBO) in adults with moderately to severely active PsA
  - Eligible patients were ≥ 18 years old, naïve to biologic therapy, and had a history of inadequate response or intolerance to ≥ 1 conventional synthetic DMARD (csDMARD-IR)
- In the KEEPSAKE 1 trial, more patients randomized to RZB compared with PBO achieved the primary endpoint of ≥ 20% improvement in American College of Rheumatology (ACR20) score at week 24, and the trial has demonstrated efficacy of treatment with continuous RZB 150 mg across several PsA disease domains<sup>1</sup>
- Here, we report the long-term efficacy and safety of RZB through week 244

## METHODS

### Study Design

- Following a 24-week double-blind, PBO-controlled, parallel-group treatment period (period 1), patients entered an open-label extension treatment period from week 24 up to week 316 (period 2)
  - Radiographic endpoints were collected only to week 244
- In period 1, patients were randomized 1:1 to receive subcutaneous RZB 150 mg or PBO at weeks 0, 4, and 16
- Starting at week 28, all patients received open-label RZB 150 mg every 12 weeks through week 316
- Data are reported as observed (AO); missing data for categorical endpoints were imputed using nonresponder imputation, except for data missing due to the COVID-19 pandemic or the geopolitical conflict in Ukraine and Russia, which were imputed using multiple imputation; results for continuous endpoints are reported using a mixed-effect model for repeated measurement

Figure 1. KEEPSAKE 1 Study Design

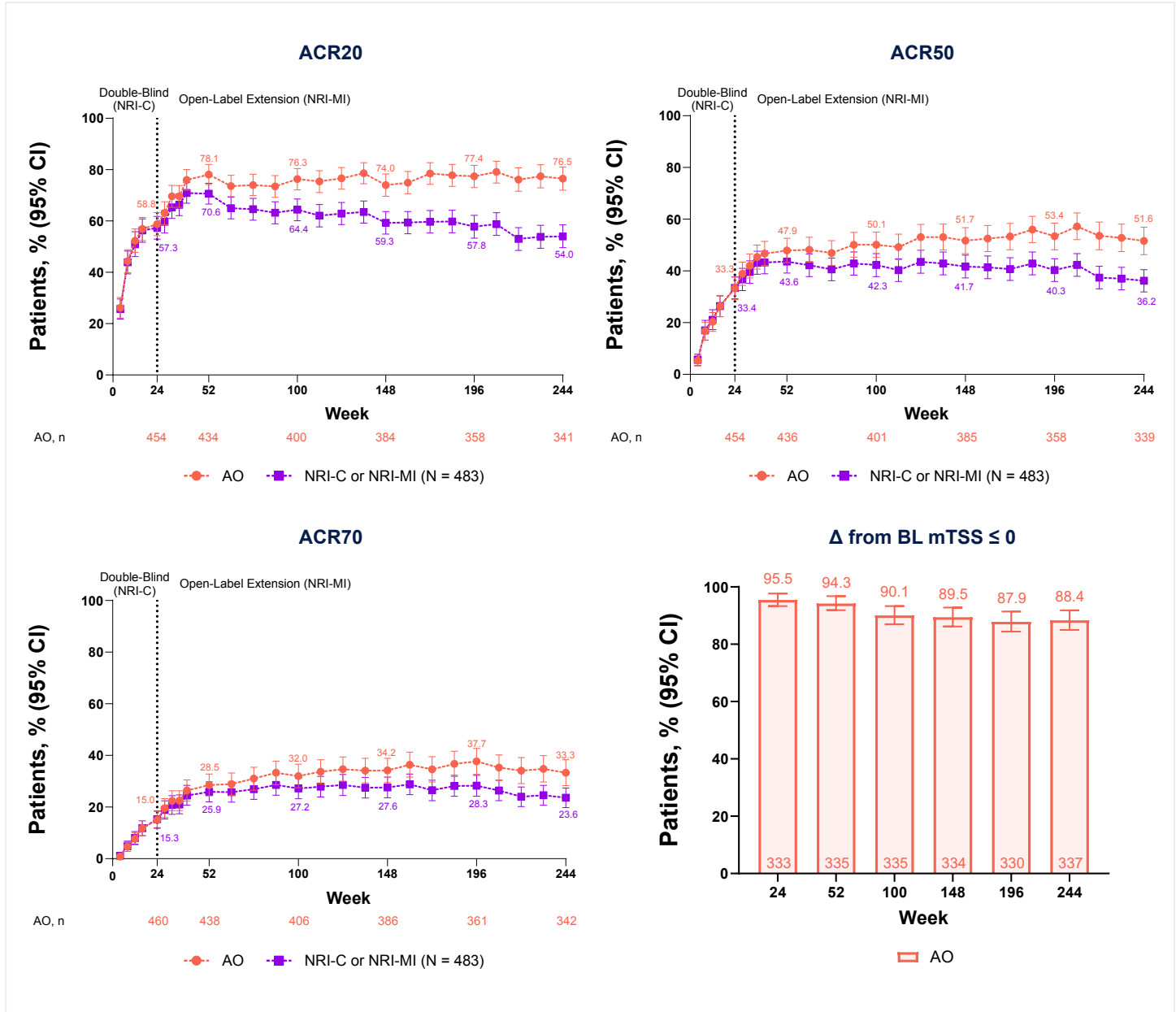


ACR20, ≥ 20% improvement in American College of Rheumatology; csDMARD-IR, conventional synthetic disease modifying anti-rheumatic drug-inadequate responder; PBO, placebo; PsA, psoriatic arthritis; RZB, risankizumab; SC, subcutaneous.

# RESULTS

- Patients treated with RZB through week 244 showed durable, long-term improvement in key signs and symptoms of PsA, including:
  - Achievement of ACR20, ACR50, ACR70, and inhibition of radiographic progression (as defined by change from baseline in modified Total Sharp Score [mTSS]  $\leq 0$ )<sup>a</sup> (Figure 2)
  - Resolution of enthesitis and dactylitis (Figure 3)
  - Achievement of minimal disease activity (MDA) and  $\geq 90\%$  reduction in Psoriasis Area Severity Index (PASI90) (Figure 4)
- The overall rates of treatment-emergent adverse events (TEAEs; 119.0 E/100 patient-years [PY]), serious TEAEs (7.6 E/100 PY), and AEs leading to discontinuation of study drug (1.8 E/100 PY) have remained stable and generally consistent with those reported during the 24-week, PBO-controlled period 1 (Table 1)

**Figure 2. Achievement of ACR Responses and  $\leq 0$  Change From Baseline in mTSS<sup>a</sup> in Patients Originally Randomized to RZB**

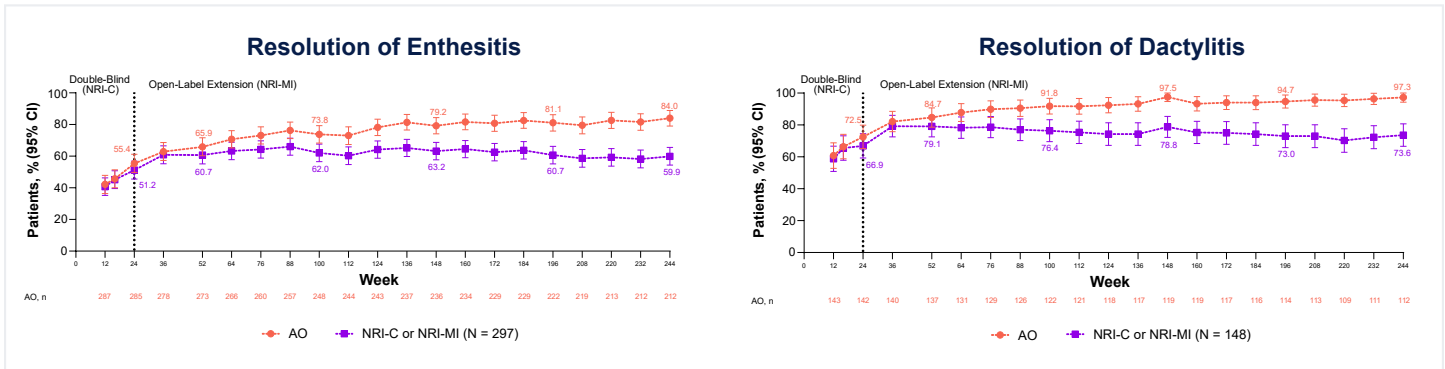


ACR20/50/70,  $\geq 20/50/70\%$  improvement in American College of Rheumatology score; AO, as observed; NRI-C, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; NRI-MI, missing data imputed as non-responders, except those missing due to COVID-19 or geopolitical conflict in Ukraine, Russia, or Israel, which are imputed by multiple imputations; RZB, risankizumab.

<sup>a</sup>Change from baseline in mTSS was not statistically different between patients treated with risankizumab versus placebo at week 24, which was a ranked, secondary endpoint in KEEPSAKE 1. The proportion of patients with no radiographic progression (as defined by change from baseline in mTSS  $\leq 0$ ) was a prespecified, but nonranked, endpoint; therefore, no statistical conclusions can be drawn.

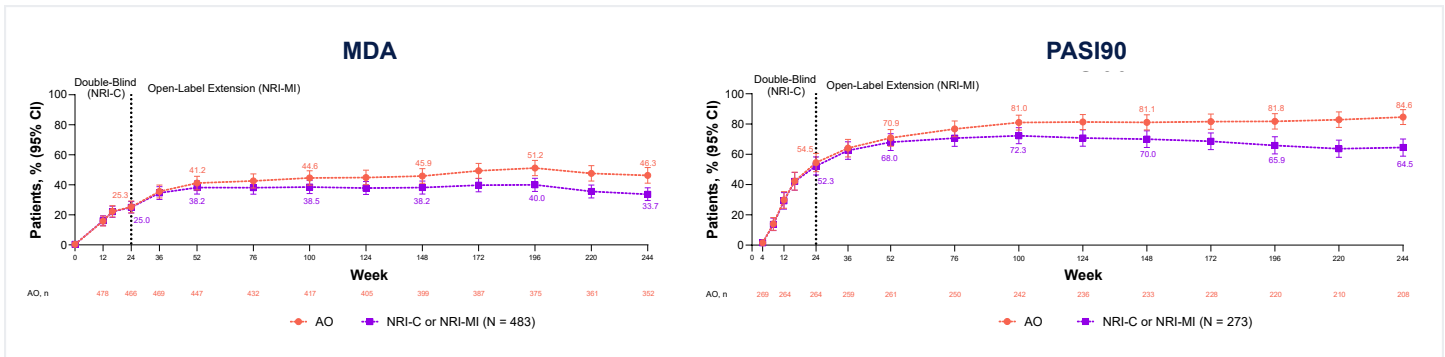
## RESULTS (CONTINUED)

**Figure 3. Resolution of Enthesitis and Dactylitis in Patients Originally Randomized to RZB**



ACR20/50/70,  $\geq 20/50/70\%$  improvement in American College of Rheumatology score; AO, as observed; BL; baseline; E/100 PY; events per 100 patient-years; mTSS, modified Total Sharp Score; NRI-C, nonresponder imputation incorporating multiple imputation to handle missing data due to COVID-19; NRI-MI, missing data imputed as nonresponders, except those missing due to COVID-19 or the geopolitical conflict in Ukraine, Russia, or Israel, which are imputed by multiple imputations; RZB, risankizumab.

**Figure 4. Achievement of MDA and PASI90 in Patients Originally Randomized to RZB**



AO, as observed; MDA, minimal disease activity; NRI-C, nonresponder imputation incorporating multiple imputation to handle missing data due to COVID-19; NRI-MI, missing data imputed as nonresponders except those missing due to COVID-19 or geopolitical conflict in Ukraine, Russia, or Israel, which are imputed by multiple imputations; PASI 90,  $\geq 90\%$  reduction in Psoriasis Area and Severity Index; RZB, risankizumab.

**Table 1. Safety Profile Through Week 244**

Parameter, Events (E/100 PY)	RZB Week 24 <sup>a</sup> N = 483, PY = 224.1	PBO Week 24 <sup>a</sup> N = 481, PY = 223.5	All RZB <sup>b</sup> Week 244 N = 946, PY = 3820.6
TEAE	398 (177.6)	387 (173.2)	4546 (119.0)
Serious TEAE	15 (6.7)	22 (9.8)	289 (7.6)
TEAE leading to discontinuation of study drug	6 (2.7)	4 (1.8)	69 (1.8)
COVID-19-related TEAE	1 (0.4)	2 (0.9)	260 (6.8)
Adjudicated MACE <sup>c,d</sup>	0	0	13 (0.3)
Serious infection	6 (2.7)	8 (3.6)	57 (1.5)
Opportunistic infections (excluding TB and herpes zoster)	0	0	1 (< 0.1)
Active TB	0	0	0
Herpes zoster <sup>e</sup>	2 (0.9)	1 (0.4)	11 (0.3)
Malignant tumors	0	2 (0.9)	26 (0.7)
NMSC <sup>f</sup>	0	0	5 (0.1)
Excluding NMSC <sup>g</sup>	0	2 (0.9)	21 (0.5)
Adjudicated anaphylactic reaction	0	0	0
Serious hypersensitivity	0	0	2 (< 0.1)
All deaths (including non-treatment-emergent) <sup>h</sup>	1 (0.4)	0	12 (0.3)

AE, adverse event; MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PBO, placebo; PsA, psoriatic arthritis; PY, patient-years; RZB, risankizumab; TB, tuberculosis; TEAE, treatment-emergent adverse events. TEAEs were defined as any adverse event with an onset date that was on or after the first dose of RZB and up to 140 days after the last dose of RZB if the patient discontinued the study drug prematurely.

<sup>a</sup>24-week data from KEEPSAKE 1.<sup>1</sup>

<sup>b</sup>Reported for all randomized patients who received at least one dosage of RZB through week 244.

<sup>c</sup>There were 13 adjudicated MACE occurrences, 3 (< 0.1 E/100 PY) cardiovascular deaths, 6 (0.2 E/100 PY) nonfatal myocardial infarctions, and 4 (0.1 E/100 PY) nonfatal strokes.

<sup>d</sup>The incidence rate of MACE for patients with PsA is 0.46 E/100 PY, as derived from population-based epidemiological studies.<sup>2</sup>

<sup>e</sup>The incidence rate of herpes zoster for patients with PsA is about 1.0 E/100 PY, as derived from population-based epidemiological studies.<sup>3</sup>

<sup>f</sup>The incidence rate of NMSC for patients with PsA is 0.61 E/100 PY, as derived from population-based epidemiological studies.<sup>4</sup>

<sup>g</sup>The incidence rate of malignant tumors (excluding NMSC) for patients with PsA is 0.48 E/100 PY, as derived from population-based epidemiological studies.<sup>4</sup>

<sup>h</sup>There were 11 treatment-emergent deaths. Two deaths were related to COVID-19; 1 was due to complications related to acute leukemia; 1 was due to dyspnea; 1 patient with anemia from diverticulosis died due to multiorgan failure from septicemia as a complication from anastomosis surgery (left hemicolectomy surgery); 1 patient, who was 81 years old with dementia, was hospitalized for pneumonia, developed urepsis, and died from related complications; 1 patient was hospitalized for anxiety and depression, developed septicemia, nausea, vomiting, fever, and loss of appetite a week after discharge, and died from unknown causes a week later; 3 patients died of unknown causes (one had a 40-year history of smoking and died after Chronic Obstructive Pulmonary Disease exacerbation); 1 patient with history of hypertension, obesity, and dyslipidemia died due to cardiomyopathy. Additionally, 1 nontreatment-emergent death occurred 166 days after the last dose of RZB.

## RESULTS (CONTINUED)

Table 2. Additional Efficacy Endpoints Through Week 244

Endpoint	Week 52		Week 148		Week 244	
	RZB	PBO to RZB	RZB	PBO to RZB	RZB	PBO to RZB
Change from baseline in TJC, mean (95% CI) <sup>a</sup>	-16.1 [N = 443] (-17.2, -14.9)	-14.8 [N = 439] (-15.9, -13.8)	-16.4 [N = 480] (-17.0, -15.9)	-16.4 [N = 478] (-17.0, -15.9)	-16.7 [N = 480] (-17.5, -16.0)	-16.9 [N = 478] (-17.6, -16.1)
Change from baseline in SJC, mean (95% CI) <sup>a</sup>	-10.5 [N = 443] (-11.1, -9.8)	-10.5 [N = 439] (-11.2, -9.8)	-10.6 [N = 480] (-10.9, -10.3)	-10.8 [N = 478] (-11.0, -10.5)	-10.8 [N = 480] (-11.2, -10.3)	-10.8 [N = 478] (-11.3, -10.4)
Change from baseline in mTSS, mean (95% CI) <sup>a</sup>	0.38 [N = 430] (0.16, 0.60)	0.43 [N = 431] (0.21, 0.65)	0.55 [N = 365] (0.12, 0.97)	0.94 [N = 367] (0.52, 1.37)	0.93 [N = 337] (0.17, 1.68)	2.07 [N = 342] (1.32, 2.81)
No radiographic progression (change from baseline mTSS ≤ 0.5), % (n/N) <sup>b</sup>	93.5 (402/430)	90.3 (389/431)	91.2 (332/364)	86.6 (316/365)	90.5 (305/337)	83.6 (286/342)
Change from baseline in patient's assessment of pain (VAS), mean (95% CI) <sup>a</sup>	-27.5 [N = 440] (-30.1, -24.9)	-23.1 [N = 435] (-25.8, -20.5)	-27.3 [N = 479] (-29.5, -25.0)	-24.5 [N = 476] (-26.7, -22.2)	-26.1 [N = 479] (-28.3, -23.8)	-24.4 [N = 476] (-26.6, -22.2)
Change in mNAPSI, mean (95% CI) <sup>c</sup>	-12.86 [N = 306] (-13.85, -11.87)	-11.26 [N = 334] (-12.21, -10.30)	-15.01 [N = 306] (-15.81, -14.21)	-13.99 [N = 334] (-14.75, -13.22)	-14.70 [N = 306] (-15.44, -13.96)	-14.71 [N = 334] (-15.42, -14.00)
Change in PGA-F, mean (95% CI) <sup>c</sup>	-1.2 [N = 306] (-1.3, -1.1)	-1.1 [N = 334] (-1.2, -1.0)	-1.5 [N = 306] (-1.6, -1.4)	-1.4 [N = 334] (-1.5, -1.3)	-1.6 [N = 306] (-1.7, -1.5)	-1.5 [N = 334] (-1.6, -1.4)
BASDAI 50, % (n/N) <sup>e</sup>	35.7 (30/84)	43.7 (38/87)	31.5 (30/94)	35.8 (34/95)	19.1 (18/94)	29.5 (28/95)
Change from baseline in BASDAI, mean (95% CI) <sup>d</sup>	-2.26 [N = 84] (-2.73, -1.78)	-2.77 [N = 87] (-3.23, -2.32)	-2.62 [N = 91] (-3.10, -2.13)	-2.80 [N = 93] (-3.27, -2.33)	-2.21 [N = 91] (-2.71, -1.70)	-2.56 [N = 93] (-3.05, -2.08)
Change from baseline in ASDAS, mean (95% CI) <sup>d</sup>	-1.14 [N = 84] (-1.37, -0.90)	-1.35 [N = 86] (-1.57, -1.13)	-1.25 [N = 91] (-1.48, -1.01)	-1.40 [N = 93] (-1.62, -1.17)	-1.06 [N = 91] (-1.31, -0.81)	-1.34 [N = 93] (-1.57, -1.10)
ASDAS Clinically Important Improvement, % (n/N) <sup>e</sup>	51.2 (43/84)	53.5 (46/86)	37.7 (35/94)	45.5 (43/95)	24.1 (23/94)	34.9 (33/95)
PASI100, % (n/N) <sup>f</sup>	52.5 (137/261)	45.7 (113/247)	52.9 (144/273)	51.7 (141/272)	48.4 (132/273)	48.9 (133/272)
Change in HAQ-DI, mean (95% CI)	-0.41 [N = 479] (-0.45, -0.37)	-0.32 [N = 476] (-0.36, -0.27)	-0.41 [N = 479] (-0.46, -0.36)	-0.35 [N = 476] (-0.40, -0.29)	-0.38 [N = 479] (-0.42, -0.33)	-0.34 [N = 476] (-0.39, -0.29)
Change in SF-36 PCS score, mean (95% CI)	8.43 [N = 476] (7.79, 9.08)	7.32 [N = 473] (6.67, 7.97)	8.61 [N = 476] (7.83, 9.39)	7.78 [N = 473] (7.00, 8.57)	7.68 [N = 476] (6.68, 8.69)	7.90 [N = 473] (6.90, 8.90)
Change in FACIT-Fatigue score, mean (95% CI)	7.9 [N = 476] (7.2, 8.7)	6.5 [N = 473] (5.7, 7.3)	7.4 [N = 476] (6.5, 8.2)	6.4 [N = 473] (5.5, 7.2)	7.2 [N = 476] (6.3, 8.1)	6.0 [N = 473] (5.1, 6.9)

AO, as observed; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASDAI 50, 50% reduction in Bath Ankylosing Spondylitis Disease Activity Index; BSA, Body Surface Area; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue Questionnaire; HAQ-DI, Health Assessment Questionnaire-Disability Index; MMRM, Mixed-Effect Model Repeated Measurement; mNAPSI, modified Nail Psoriasis Severity Index; mTSS, modified Total Sharp Score; NRI-MI, nonresponder imputation incorporating multiple imputation to handle data missing due to COVID-19 or geopolitical conflict in Ukraine, Russia, or Israel, all other missing data imputed as nonresponders; PASI100, 100% reduction in Psoriasis Area and Severity Index; PBO, placebo; PGA-F, Physician Global Assessment of Fingernail Psoriasis; RZB, risankizumab; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary; SJC, Swollen Joint Count; TJC, Tender Joint Count; VAS, Visual Analog Scale.

All changes are least-square mean changes from baseline. Results for continuous endpoints are reported by MMRM. Number of unique patients contributing to MMRM model estimates: patients with at least one available change from baseline value and no missing data for the factors and covariates in the model. The MMRM N is not visit-specific and is displayed for model estimates for all visits.

<sup>a</sup>Reported AO at week 52 and with MMRM for week 148 and week 244.

<sup>b</sup>Reported AO at week 52, 148, and 244.

<sup>c</sup>Reported for patients with nail psoriasis at baseline (RZB, n = 309; PBO/RZB, n = 338).

<sup>d</sup>Reported for patients with axial spondylitis at baseline, AO at week 52, and with MMRM at week 148 and 244.

<sup>e</sup>Reported for patients with axial spondylitis at baseline, AO at week 52, and with NRI-MI at week 148 and 244.

<sup>f</sup>Reported for patients with ≥ 3% of body surface area affected by psoriasis at baseline (RZB, n = 273; PBO/RZB, n = 272), AO at week 52 and with NRI-MI at week 148 and week 244.

## CONCLUSIONS

- Long-term treatment with risankizumab demonstrates durable efficacy through 244 weeks in treating clinical manifestations of PsA and improving quality of life, with low rates of radiographic progression, in adult patients with an inadequate response or intolerance to csDMARD(s)
- The safety profile of risankizumab remains consistent with previous studies, with no new safety risks identified

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## DISCLOSURES & ACKNOWLEDGMENTS

AbbVie Inc. and the authors thank the participants, study sites, and investigators who participated in this clinical trial.

AbbVie funded this trial and participated in the trial design, research, analysis, data collection, interpretation of data, and the review and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. Medical writing support was provided by Wendy Geslewitz, PhD, MPH, of AbbVie. Editorial support was provided by Catherine Barone, PhD, and Michael Austin of AbbVie.

Financial arrangements of the authors with companies whose products may be related to the present report are listed as declared by the authors: M Keiserman has received research funds from AbbVie, Biogen, Bristol Myers Squibb, Eli Lilly, MSD, Janssen, Horizon Therapeutics Ireland DAC, Novartis, Pfizer, Roche, Merck, MoonLake, Novartis, Sandoz, Sanofi, and UCB. K Papp has research funds and honoraria or fees for serving as a consultant or speaker for AbbVie, Accelely, Amgen, Arcutis, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Forward Pharma, Galderma, Incyte, Janssen, LEO Pharma, Eli Lilly, Meiji Seika Pharma, Mitsubishi Tanabe Pharma, Novartis, Ortho Dermatologics, Pfizer, Sanofi Genzyme, Sun Pharma, Takeda, and UCB. D White has received honoraria or fees for serving on advisory boards or as a speaker and consultant for AbbVie. A Crowley has received research funds and honoraria or fees for serving as a consultant or speaker for AbbVie/Abbott, Amgen, Aqtaul, Astra Zeneca, Eli Lilly, Exagen, GSK, Horizon, Janssen, Kiowa Kirin, Novartis, Scipher Medicine, SetPoint Medical, Sun Pharma, and UCB. JF Merola has received fees for serving as a consultant or private investigator for AbbVie, Amgen, Biogen, Bristol Myers Squibb, Dermavent, Janssen, LEO Pharma, Eli Lilly, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB. H Barnard, A Biljan, T Ilye, L Luo, D Ashley, AR Setty, and H Yamazaki are full-time employees of AbbVie and may hold AbbVie stock or stock options. F Behrens has received research funds and honoraria or fees for serving as a consultant or speaker from AbbVie, Amgen, Affibody, Acelyrin, Bristol Myers Squibb, Boehringer Ingelheim, Chugai, Celltrion, Galapagos, Genzyme, Gilead, GSK, Janssen, Eli Lilly, Merck, MoonLake, Novartis, Pfizer, Roche, Sandoz, and Sanofi.