Long-Term Efficacy and Safety of Risankizumab for csDMARD-IR Patients With Active Psoriatic Arthritis: 196-Week Results From the KEEPsAKE 1 Trial

Frank Behrens,[1] Mauro Keiserman,[2] Kim Papp,[3] Douglas White,[4] Angela Crowley,[5] Tshepiso Madihlaba,[6] Thomas Iyile,[6] Kyle Carter,[6] Ahmed M Soliman,[6] Doug Ashley,[6] Lila Glotfelty[6]

[1]Rheumatology, Immunology, Inflammation Medicine University Hospital & Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Goethe University, Frankfurt, Germany; [2]Rheumatology Section, Pontifical Catholic University, School of Medicine, Porto Alegre, Brazil; [3]Probity Medical Research – Alliance Clinical Trials, Waterloo, Ontario, Canada & Division of Dermatology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada; [4]Rheumatology Department, Waikato Hospital, Hamilton, New Zealand & Waikato Clinical School; University of Auckland, Auckland, New Zealand [5]Illinois Bone and Joint Institute LLC, Hinsdale, Illinois, United States; [6]AbbVie Inc., North Chicago, IL, USA

OBJECTIVE

To report the long term efficacy and safety of risankizumab through 196 weeks in adult PsA patients with an inadequate response to csDMARDs

CONCLUSIONS

Long term treatment with risankizumab through 196 weeks provides a durable efficacy response in treating the different clinical manifestations and improving health-related quality of life for adult patients with active PsA and an inadequate response to csDMARD(s)

Risankizumab is generally well tolerated with no new safety signals

INTRODUCTION

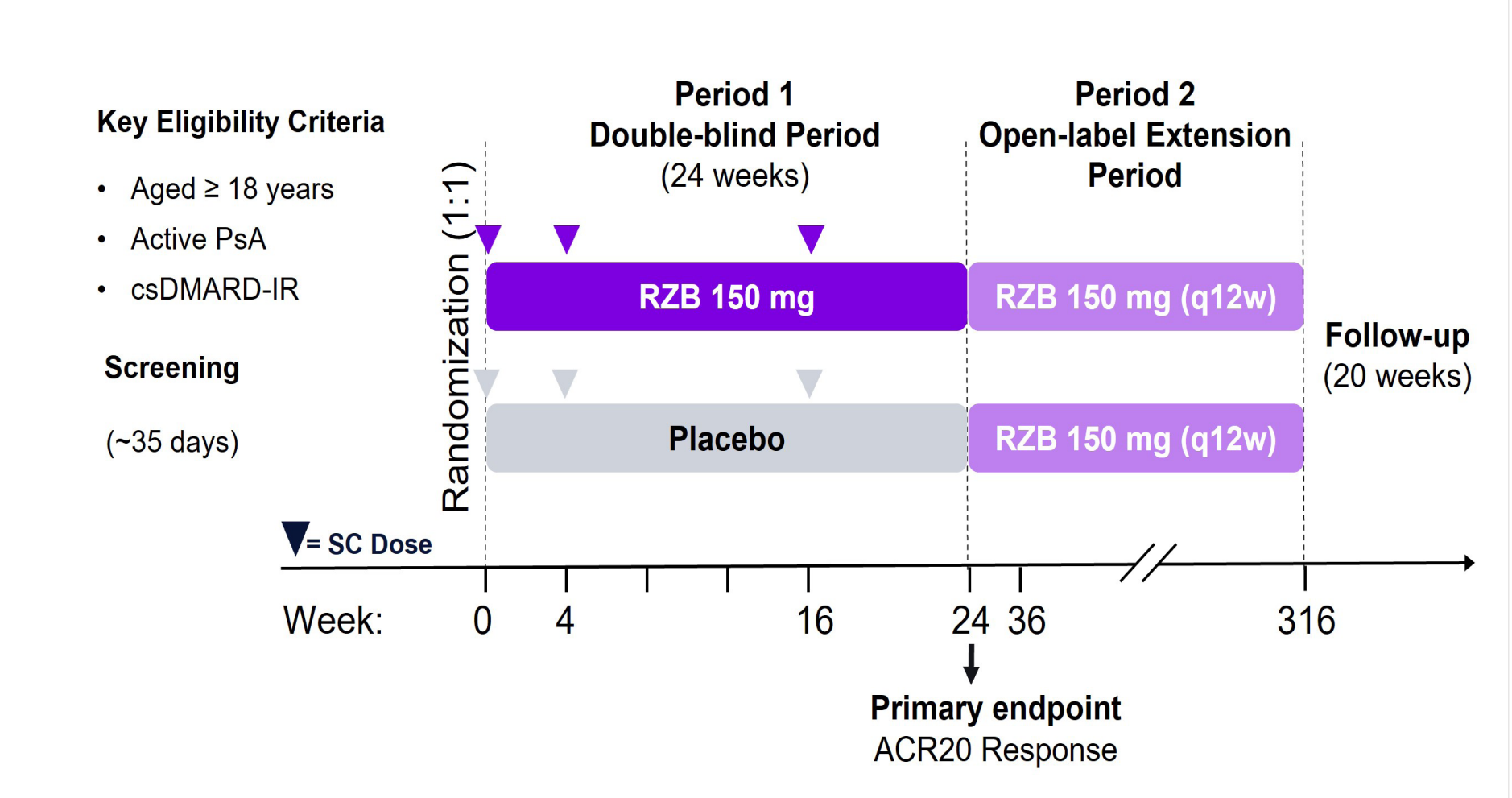
- Risankizumab (RZB), a humanized immunoglobulin G1 monoclonal antibody that inhibits interleukin-23 by targeting its p19 subunit with high affinity and specificity, is approved for the treatment of adult patients with PsA
- KEEPsAKE 1 (NCT03675308) is an ongoing, global, phase 3, multicenter clinical trial to evaluate the efficacy and safety of RZB versus placebo (PBO) in adults with active PsA who have a history of inadequate response or intolerance to ≥1 conventional synthetic disease modifying anti-rheumatic drug (csDMARD-IR) therapy
- More patients randomized to RZB compared to PBO in the KEEPsAKE 1 trial achieved the primary endpoint of ACR20 at week 24, and the trial has demonstrated efficacy of treatment with continuous RZB 150 mg across several disease domains[1]
- Here, we report the long-term efficacy, safety, and tolerability of RZB through week 196

METHODS

Study Design

- Following a 24-week double-blind, placebo-controlled, parallel-group treatment period (period 1), patients continued into an open-label extension treatment period from week 24 through week 316 (period 2)
- In period 1, patients were randomized 1:1 to receive subcutaneous RZB 150 mg or placebo at weeks 0, 4 and 16
- Starting at week 28, all patients received open-label RZB 150 mg every 12 weeks until week 316
- Data are reported as observed (AO); missing data for categorical endpoints were imputed using non-responder imputation (NRI), with exception for data missing due to COVID-19 or geo-political conflict in Ukraine and Russia, which are imputed by multiple imputations; results for continuous endpoints were reported by mixed-effect model repeated measurement (MMRM)

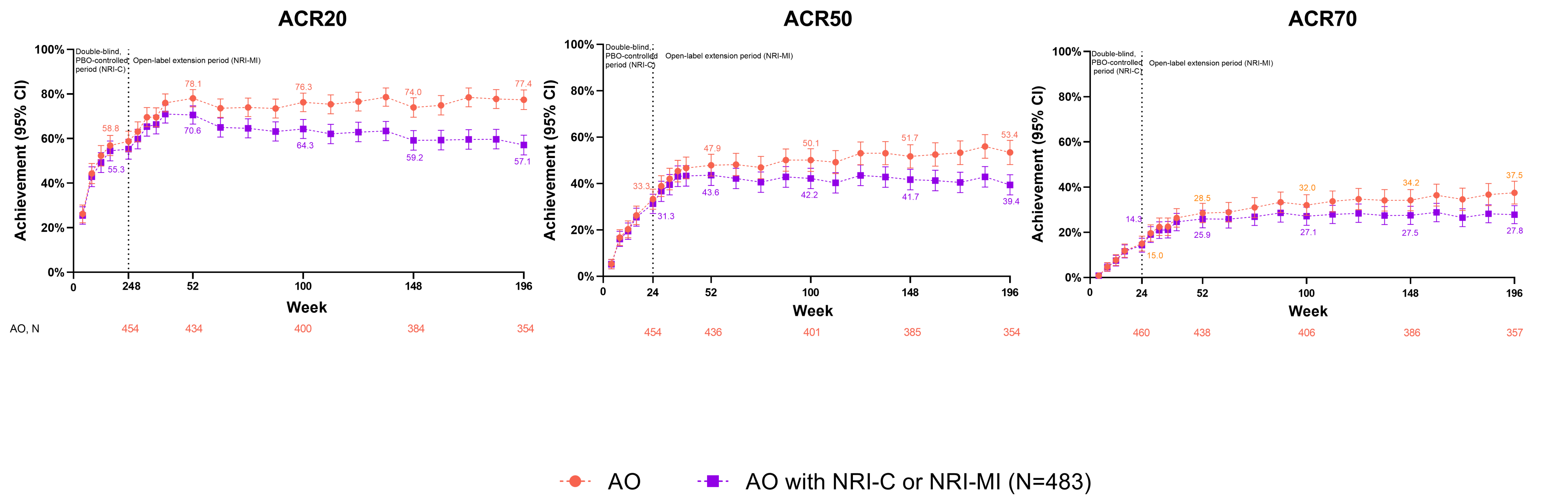
Figure 1. Study Design



RESULTS

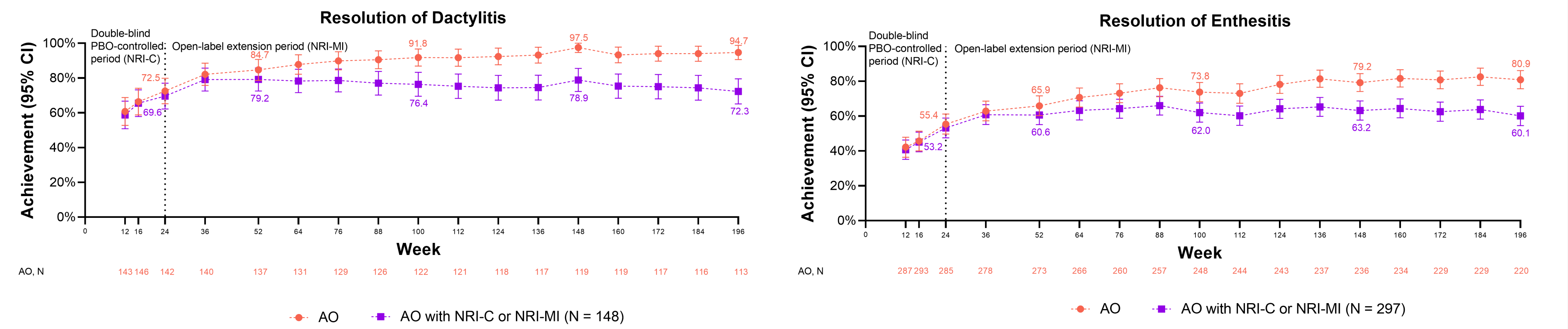
- Patients treated with RZB demonstrated durable, long-term improvement in key signs and symptoms of PsA including achievement of ACR20, ACR50, ACR70, PASI90, MDA, resolution of enthesitis and dactylitis through 196 weeks
- The overall rates of treatment-emergent adverse events (TEAEs; 121.4 E/100PY), serious TEAEs (7.7 E/100PY) and AEs leading to discontinuation of study drug (1.8 E/100PY) have remained stable and comparable to those reported in period 1
- RZB is generally well tolerated with no new safety signals

Figure 2. Achievement of ACR Responses in Patients Originally Randomized to RZB



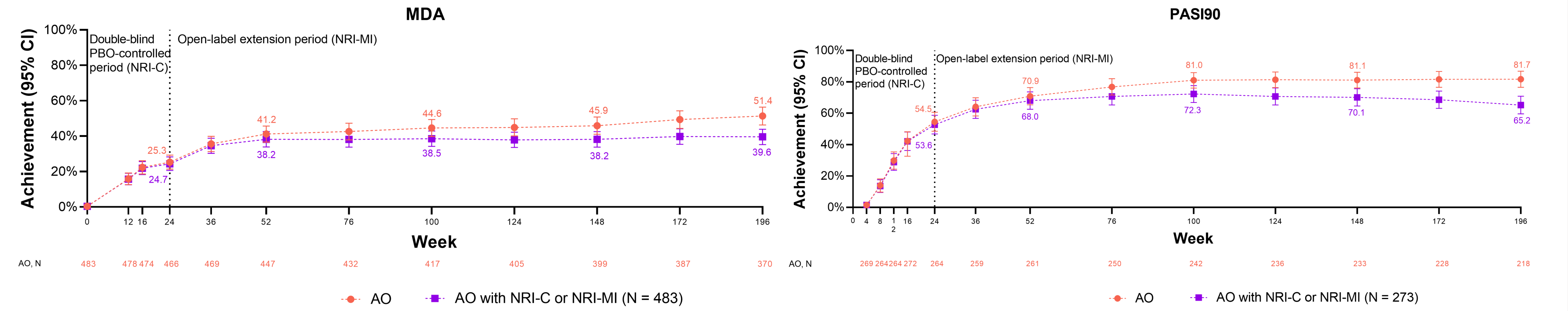
ACR20/50/70, ≥ 20/50/70% improvement in American College of Rheumatology score; AO with NRI-MI, as observed (AO) with missing data imputed as non-responders, except those missing due to COVID-19 or geo-political conflict in Ukraine and Russia, which are imputed by multiple imputations; NRI-C, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; PBO, placebo; RZB, risankizumab.

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



Enthesitis defined as Leeds Enthesitis Index (LEI) = 0 and reported among patients with LEI > 0 at baseline (RZB, n = 297; PBO/RZB, n = 290).
Dactylitis defined as Leeds Dactylitis Index (LDI) = 0 and reported among patients with LDI > 0 at baseline (RZB, n = 148; PBO/RZB, n = 147).
AO with NRI-MI, as observed (AO) with missing data imputed as non-responders except those missing due to COVID-19 or geo-political conflict in Ukraine and Russia, which are imputed by multiple imputations; NRI-C, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; PBO, placebo; RZB, risankizumab.

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



AO with NRI-MI, as observed (AO) with missing data imputed as non-responders except those missing due to COVID-19 or geo-political conflict in Ukraine and Russia, which are imputed by multiple imputations; MDA, minimal disease activity; NRI-C, non-responder imputation 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.

Table 1. Safety Profile Through Week 196

Parameter, E (Events/100PY)	RZB Week 24^a (N = 483) PY = 224.1	PBO Week 24^a (N = 481) PY = 223.5	All RZB Week 196 (N = 946) PYs = 3083.9
TEAE	398 (177.6)	387 (173.2)	3744 (121.4)
Serious TEAE	15 (6.7)	22 (9.8)	236 (7.7)
TEAE leading to discontinuation of study drug	6 (2.7)	4 (1.8)	57 (1.8)
COVID-19 related TEAE	1 (0.4)	2 (0.9)	247 (8.0)
Adjudicated MACE	0	0	10 (0.3)
Cardiovascular death–sudden cardiac death	0	0	2 (< 0.1)
Non-fatal myocardial infarction	0	0	1 (< 0.1)
Non-fatal stroke	0	0	4 (0.1)
Serious infection	6 (2.7)	8 (3.6)	54 (1.8)
Opportunistic infections excluding TB and herpes zoster	0	0	1 (< 0.1)
Active TB	0	0	0
Herpes zoster	2 (0.9)	1 (0.4)	7 (0.2)
Malignant tumors	0	2 (0.9)	22 (0.7)
NMSC	0	0	3 (< 0.1)
Excluding NMSC	0	2 (0.9)	19 (0.6)
Adjudicated anaphylactic reaction	0	0	0
Serious hypersensitivity	0	0	2 (< 0.1)
All Deaths (including non-treatment-emergent)	1 (0.4)	0	10 (0.3)^b

Treatment-emergent adverse events (TEAE) were defined as any AE with an onset date that was on or after the first dose of risankizumab and up to 140 days after the last dose of risankizumab if the patient discontinued the study drug prematurely.
[a] 24 week data from KEEPsAKE 1 was previously published in Kristensen, et. al. Ann Rheum Dis. 2022;81(2):225-231.
[b] There were 9 trearment-emergent deaths. 2 deaths were related to COVID 19; 1 was due to complications related to acute leukemia; 1 was due to dyspnoea; 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 urosepsis 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; 2 patients died of unknown causes (one had a 40 year history of smoking and died after COPD exacerbation). Additionally, 1 patient died on day 363 (166 days after last dose; non treatment emergent) from cardiorespiratory arrest. MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PBO, placebo; PYs, patient-years; RZB, risankizumab; TB, tuberculosis; TEAE, treatment-emergent adverse events.

Table 2. Additional Efficacy Endpoints Through Week 196

	Week 52		Week 148		Week 196	
	RZB	PBO to RZB	RZB	PBO to RZB	RZB	PBO to RZB
ACR20, % (n)	70.0 (338)	63.0 (303)	58.3 (281)	60.7 (292)	57.1 (276)	56.5 (272)
ACR50, % (n)	43.3 (209)	37.4 (180)	41.1 (199)	41.5 (200)	39.4 (191)	38.1 (183)
ACR70, % (n)	25.9 (125)	20.0 (96)	27.4 (132)	26.1 (126)	27.8 (134)	25.5 (123)
MDA, % (n)	37.9 (183)	27.4 (132)	38.1 (184)	35.5 (171)	39.6 (191)	35.2 (169)
Change from baseline in TJC*	-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)	-16.6 [N = 480] (-17.1, -16.1)	-16.5 [N = 478] (-17.0, -16.0)
Change from baseline in SJC*	-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)	-10.7 [N = 480] (-11.0, -10.5)	-10.6 [N = 478] (-10.9, -10.4)
Change from baseline in patient's assessment of pain (VAS)*	-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)	-27.9 [N = 479] (-30.3, -25.6)	-24.6 [N = 476] (-26.9, -22.3)
Change in mNAPSI, mean (95% CI)#	-12.86 [N = 306] (-13.85, -11.87)	-11.26 [N = 334] (-12.21, -10.30)	-15.01 [N = 253] (-15.81, -14.21)	-13.99 [N = 280] (-14.75, -13.22)	-14.99 [N = 306] (-15.68, -14.29)	-14.73 [N = 334] (-15.39, -14.07)
Change in PGA-F, mean (95% CI)#	-1.2 [N = 292] (-1.3, -1.1)	-1.1 [N = 311] (-1.2, -1.0)	-1.5 [N = 253] (-1.6, -1.4)	-1.4 [N = 280] (-1.5, -1.3)	-1.5 [N = 306] (-1.6, -1.4)	-1.5 [N = 334] (-1.6, -1.4)
Resolution of enthesitis, % (n/N)+	60.6 (180/297)	60.0 (174/290)	62.6 (186/297)	62.4 (181/290)	60.1 (178/297)	63.4 (184/290)
Resolution of dactylitis, % (n/N)~	78.4 (116/148)	73.5 (108/147)	77.5 (115/148)	74.8 (110/147)	72.3 (107/148)	77.6 (114/147)
Change in HAQ-DI, mean (95% CI)	-0.41 [N = 479] (-0.46, -0.36)	-0.32 [N = 476] (-0.37, -0.27)	-0.41 [N = 479] (-0.46, -0.36)	-0.35 [N = 476] (-0.40, -0.29)	-0.40 [N = 479] (-0.45, -0.35)	-0.33 [N = 476] (-0.38, -0.27)
PASI90, % (n/N)^	67.8 (185/273)	59.9 (163/272)	69.3 (189/273)	67.1 (183/272)	65.2 (178/273)	62.9 (171/272)
PASI100, % (n/N)^	50.2 (137/273)	41.5 (113/272)	52.9 (144/273)	51.7 (141/272)	53.1 (145/273)	50.0 (136/272)
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)	8.98 [N = 476] (8.14, 9.82)	7.21 [N = 473] (6.37, 8.05)
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)	7.7 [N = 476] (6.7, 8.6)	5.6 [N = 473] (4.6, 6.5)

All changes are least square mean changes from baseline.For binary endpoints, missing data due to COVID-19 or geo-political conflict in Ukraine, Russia, or Israel are imputed by multiple imputation; all other missing data are imputed as non-responders. Results for continuous endpoints are reported by mixed-effect model repeated measurement (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. RZB, N = 483; PBO/RZB, N = 481.
^Reported for patients with ≥ 3% of body surface area (BSA) affected by psoriasis at baseline (RZB, n = 273; PBO/RZB, n = 272), as AO with imputation at week 52 and AO with NRI-MI at week 148 and week 196.
#Reported for patients with nail psoriasis at baseline (RZB, n = 309; PBO/RZB, n = 338).
*Reported as AO for week 52, and as MMRM/AO with NRI-MI for week 148 and week 196.
+Defined as Leeds Enthesitis Index (LEI) = 0 and reported among patients with LEI > 0 at baseline (RZB, n = 297; PBO/RZB, n = 290).
~Defined as Leeds Dactylitis Index (LDI) = 0 and reported among patients with LDI > 0 at baseline (RZB, n = 148; PBO/RZB, n = 147).
FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue Questionnaire; HAQ-DI, Health Assessment Questionnaire-Disability Index; PASI 90 and PASI100, 90% and 100% reduction in Psoriasis Area and Severity Index, respectively; PBO, placebo; PGA-F, Physician Global Assessment of Fingernail Psoriasis; RZB, risankizumab; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary.

To obtain a PDF of this poster

Scan QR code or use the following link to download an electronic version of this presentation and other AbbVie FallCDC 2024 scientific presentations

https://abbvie1.outsystemsenterprise.com/CongressPublications/CongressHome?CongressId=1237

QR code expiration: September 1, 2025

To submit a medical question, please visit www.abbviemedinfo.com

AbbVie 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 Amrita Balachandran, Ph.D. 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: **F Behrens** has received research grants, honoraria or fees for serving as a consultant or speaker from AbbVie, Acelyrin, Affibody, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Galapagos, Genzyme, Gilead, GlaxoSmithKline, Janssen, Lilly, Merck, Moonlake, Novartis, Pfizer, Roche, Sandoz and Sanofi, UCB. **M Keiserman** has received honoraria or fees for serving on advisory boards, as a speaker or as a consultant, and has received grants as a principal investigator from AbbVie, Amgen, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Novartis, Pfizer, Roche and UCB. **K Papp** has received honoraria and/or grants from AbbVie, Acelyrin, Akros, Alumis, Amgen, Arcutis, Bausch Health/Valeant, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite Biopharma, Celltrion, Concert Pharmaceuticals, Dermavant, Dermira, DiCE Pharmaceuticals, DiCE Therapeutics, Eli Lilly and Company, Evelo Biosciences, Forbion, Galderma, Horizon Therapeutics, Incyte, Janssen, Kymab, Kyowa Hakko Kirin, LEO Pharma, Meiji Seika Pharma, Mitsubishi Pharma, Nimbus Therapeutics, Novartis, Pfizer, Reistone, Sanofi-Aventis/Genzyme, Sandoz, Sun Pharma, Takeda, Tarsus Pharmaceuticals, UCB Pharma, and Zai Lab. **D White** has received honoraria or fees for serving on advisory boards or as a speaker or consultant from AbbVie and Novartis. **A Crowley** has received research funds, honoraria or fees for serving as a consultant or speaker from AbbVie, Acelyrin, Amgen, AstraZeneca, GSK, Kiowa-Kirin, Janssen, Lilly, Novartis, SetPoint Medical, and UCB. **T Madihlaba**, **T Iyile**, **K Carter**, **D Ashley**, **L Glotfelty** are full-time employees of AbbVie and may hold AbbVie stock or stock options. **AM Soliman** is a full-time employee of AbbVie, may hold AbbVie stock or stock options and is a co-inventor on AbbVie patents.

References

1. Kristensen, et. al. *Ann Rheum Dis.* 2022;81(2):225-231

Presented at the 44th Anniversary Fall Clinical Dermatology Conference (FallCDC), October 24-27, 2024, Las Vegas, NV (Ref DV-013225)