Efficacy and Safety of Risankizumab Compared with Apremilast in Patients with Moderate Plaque Psoriasis: Mean PASI and BSA Results from the Phase 4 IMMpulse Trial

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OBJECTIVE

To evaluate the improvement in Psoriasis Area and Severity Index (PASI) and Body Surface Area (BSA) in patients with moderate psoriasis (PsO) treated with risankizumab (RZB)

CONCLUSIONS

Treatment with RZB was associated with greater clinical response compared to apremilast (APR) in systemic-eligible adult patients with moderate plaque PsO

In APR-treated patients not achieving PASI 75 at week 16, switching to RZB resulted in greater improvements in both PASI and BSA compared to continued treatment with APR through to week 52

RZB treatment was found to be safe; no additional safety concerns were identified in patients who switched from APR to RZB without washout

These results support the opportunity to elevate treatment outcomes with RZB in systemic-eligible patients with moderate plaque PsO

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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 Susan Olalekan, PhD 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: Linda F Stein Gold: grants and personal fees from AbbVie, Pfizer, Incyte, Arcutis, and Dermavant; grants from Lilly; and personal fees from Regeneron and Sanofi during the conduct of the study. Jerry Bagel: research funds from Amgen, Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, CorEvitas' (Corrona) Psoriasis Registry, Dermavant, Dermira/UCB, Eli Lilly, Glenmark, Janssen Biotech, Kadmon, Leo Pharma, Lycera, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sun Pharma, Taro, and Valeant; has served as a consultant for AbbVie, Amgen, Celgene, Eli Lilly, Janssen Biotech, Novartis, Sun Pharma, and Valeant; and has served as a speaker for AbbVie, Celgene, Eli Lilly, Janssen Biotech, and Novartis. Stephen Keith Tyring: Investigator on an AbbVie funded trial. H. Chih-ho Hong: investigator and/or speaker and/or consultant for AbbVie, Amgen, Arcutis, Bausch Health, Boehringer-Ingelheim, Bristol Meyers Squibb, Celgene, Cutanea, Dermira, Dermavant, DS Biopharma, Eli Lilly, Galderma, GSK, Incyte, Janssen, Leo Pharma, Medimmune, Merck, Mirimar, Novartis, Pfizer, Regeneron, Sanofi-Genzyme, Regeneron, Roche, UCB. Lev Pavlovsky: investigator for AbbVie, Coherus, Novartis, Janssen Biotech, and Eli Lilly, and as an advisor, consultant, and/or invited lecturer for AbbVie, Janssen Biotech, Novartis Pharmaceuticals Corporation, Pfizer Inc., Dexcel Pharma, and Eli Lilly. Andreas Pinter: investigator and/or speaker and/or advisor for the following pharmaceutical companies: AbbVie, Almirall-Hermal, Amgen, Biogen Idec, Boehringer-Ingelheim, Celgene, GSK, Eli-Lilly, Galderma, Hexal, Janssen, LEO-Pharma, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Tigercat Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi-Genzyme, Schering-Plough und UCB Pharma. Adam Reich: consultant or speaker for AbbVie, Bioderma, Celgene, Chema Elektromet, Eli Lilly, Galderma, Janssen, Leo Pharma, Medac, Menlo Therapeutics, Novartis, Pierre-Fabre, Sandoz, and Trevi and principal investigator or sub-investigator in clinical trials sponsored by AbbVie, Drug Delivery Solutions Ltd., Galderma, Genentech, Janssen, Kymab Limited, Leo Pharma, Menlo Therapeutics, MetrioPharm, MSD, Novartis, Pfizer, and Trevi. Leonidas Drogaris, Tianshuang Wu, Huzefa Photowala, Vassilis Stakias, and Sven Richter: Employees of AbbVie and may own stock/options. Kim Papp: Speakers bureau for AbbVie, Amgen, Astellas, Celgene, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Leo Pharma, Merck Sharp & Dohme, Novartis, Pfizer, and Valeant; has received grant/research support from AbbVie, Akros, Allergan, Amgen, Anacor, Arcutis, AstraZeneca, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, Leo Pharma, MedImmune, Meiji Seika Pharma, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Takeda, UCB, and Valeant; has served as a consultant for AbbVie, Akros, Amgen, Arcutis, Astellas, AstraZeneca, Baxalta, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, CanFite, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Forward Pharma, Galderma, Genentech, Janssen, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, Merck Serono, Merck Sharp & Dohme, Mitsubishi Pharma, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Takeda, UCB, and Valeant; has received honoraria from AbbVie, Akros, Amgen, Baxter, Boehringer Ingelheim, Celgene, Coherus, Eli Lilly, Forward Pharma, Galderma, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, Merck Serono, Merck Sharp & Dohme, Novartis, Pfizer, Takeda, UCB, and Valeant; and has served as a scientific officer, on a steering committee, and on an advisory board for AbbVie, Akros, Amgen, Anacor, Astellas, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dow Pharma, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Merck Serono, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and Valeant

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1. Stein Gold et al. *Br J Dermatol.* 2023

Presented at the Fall Clinical Dermatology Conference (Fall CDC), October 19, 2023, Las Vegas, Nevada, United States

INTRODUCTION

RZB demonstrated improved efficacy compared to APR in patients with moderate PsO[1]

- Psoriasis is an immune-mediated disease characterized by inflammation that manifests as thick, scaly plaques
- Apremilast is a phosphodiesterase inhibitor approved for the treatment of psoriasis
- Risankizumab is an approved, IL-23 inhibitor targeting the p19 subunit with high affinity and specificity for the treatment of moderate-to-severe psoriasis, psoriatic arthritis and Crohn's disease
- In the phase 4 IMMpulse trial, RZB demonstrated superior efficacy compared to APR in systemic-eligible patients with moderate psoriasis
  - At week 16, PASI 90 was achieved by 55.9% and 5.1% of patients treated with RZB and APR respectively ($p < 0.001$)[1]
  - At week 16, sPGA 0/1 was achieved by 75.4% and 18.4% of patients treated with RZB and APR respectively ($p < 0.001$)[1]
- Here, we present the mean PASI and BSA results from the phase IMMpulse trial

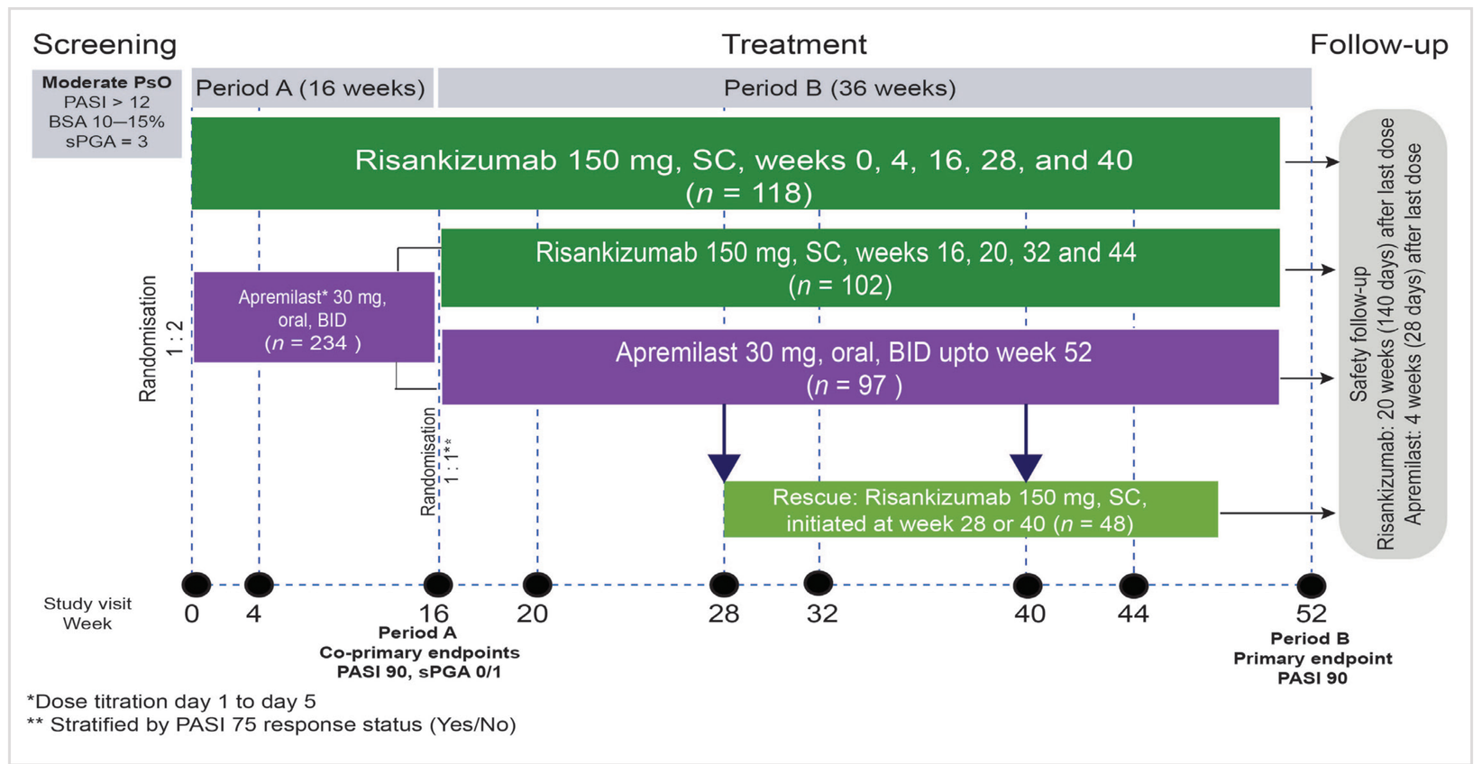
RZB, risankizumab; APR, apremilast; PsO, psoriasis; PASI 90, ≥ 90% improvement in Psoriasis Area and Severity Index; sPGA, static Physician's Global Assessment

METHODS

IMMpulse (NCT04908475) is a phase 4, multi-center, randomized, open-label assessor-blinded, active comparator study

- Systemic-eligible patients with moderate PsO (sPGA = 3, BSA 10-15% and PASI ≥ 12) were enrolled in this study
- In Period A, patients were randomized 1:2 to receive subcutaneous RZB 150 mg or oral APR30 mg twice daily (BID) for 16 weeks
- In Period B, patients treated with APR in period A who were PASI 75 non-responders were re-randomized 1:1 to RZB or APR
- All patients treated with RZB in period A continued till week 52
- Pre-specified additional efficacy endpoints included change in PASI and BSA from baseline
- Nominal p-values are presented for efficacy endpoints not adjusted for multiplicity
- For continuous endpoints, a mixed model repeat measures (MMRM) analysis was used; treatment, visit and treatment x visit interaction was used in the model for variance estimation
- For mean PASI, A last observation carried forward (LOCF) sensitivity analysis is also presented

Overall Study Design


Screening
Treatment
Follow-up
Period A (16 weeks)
Period B (36 weeks)
Risankizumab 150 mg, SC, weeks 0, 4, 16, 28, and 40 (n = 118)
Risankizumab 150 mg, SC, weeks 16, 20, 32 and 44 (n = 102)
Apremilast 30 mg, oral, BID upto week 52 (n = 97)
Randomization
Study visit Week
0
4
16
20
28
32
40
44
52
*Dose titration day 1 to day 5
** Stratified by PASI 75 response status (Yes/No)

RZB, risankizumab; APR, apremilast; PsO, psoriasis; PASI, Psoriasis Area and Severity Index; PASI 75, ≥ 75% improvement in Psoriasis Area and Severity Index sPGA, static Physician's Global Assessment; BSA, Body Surface Area

RESULTS

Demographics and Baseline Clinical Characteristics of Patients Enrolled in the IMMpulse Trial

	RZB N = 118	APR N = 234
Age years, mean (SD)	45.5 (13.6)	46.2 (14.3)
Sex, n (%)		
Female	42 (35.6)	79 (33.8)
Male	76 (64.4)	155 (66.2)
Weight[†] (kg) - n (%)		
≤ 100	87 (73.7)	169 (72.2)
> 100	31 (26.3)	65 (27.8)
Psoriasis Area Severity Index, mean (SD)	14.5 (2.5)	14.6 (2.6)
Body Surface Area, mean (SD)	13.0 (1.7)	13.1 (1.7)
Static Physician's Global Assessment categories, n(%)		
≤ 2	0	1 (0.4)
3	118 (100)	232 (99.1)
4	0	1 (0.4)
Psoriasis Symptom Scale, mean (SD)	8.8 (3.4)	9.0 (3.4)
Dermatology Life Quality Index, mean (SD)	12.6 (6.9)	12.7 (7.1)
Prior systemic and/or biologic treatment ≥ 1[†], n (%)	37 (31.4)	76 (32.5)
Duration of plaque psoriasis (years), mean (SD)	18.5 (11.8)	17.8 (13.6)

RZB, risankizumab; APR, apremilast; n, number; kg, kilogram; SD, standard deviation; [†]Stratification factors for randomization

Overview of Treatment-Emergent Adverse Events in the IMMpulse Trial

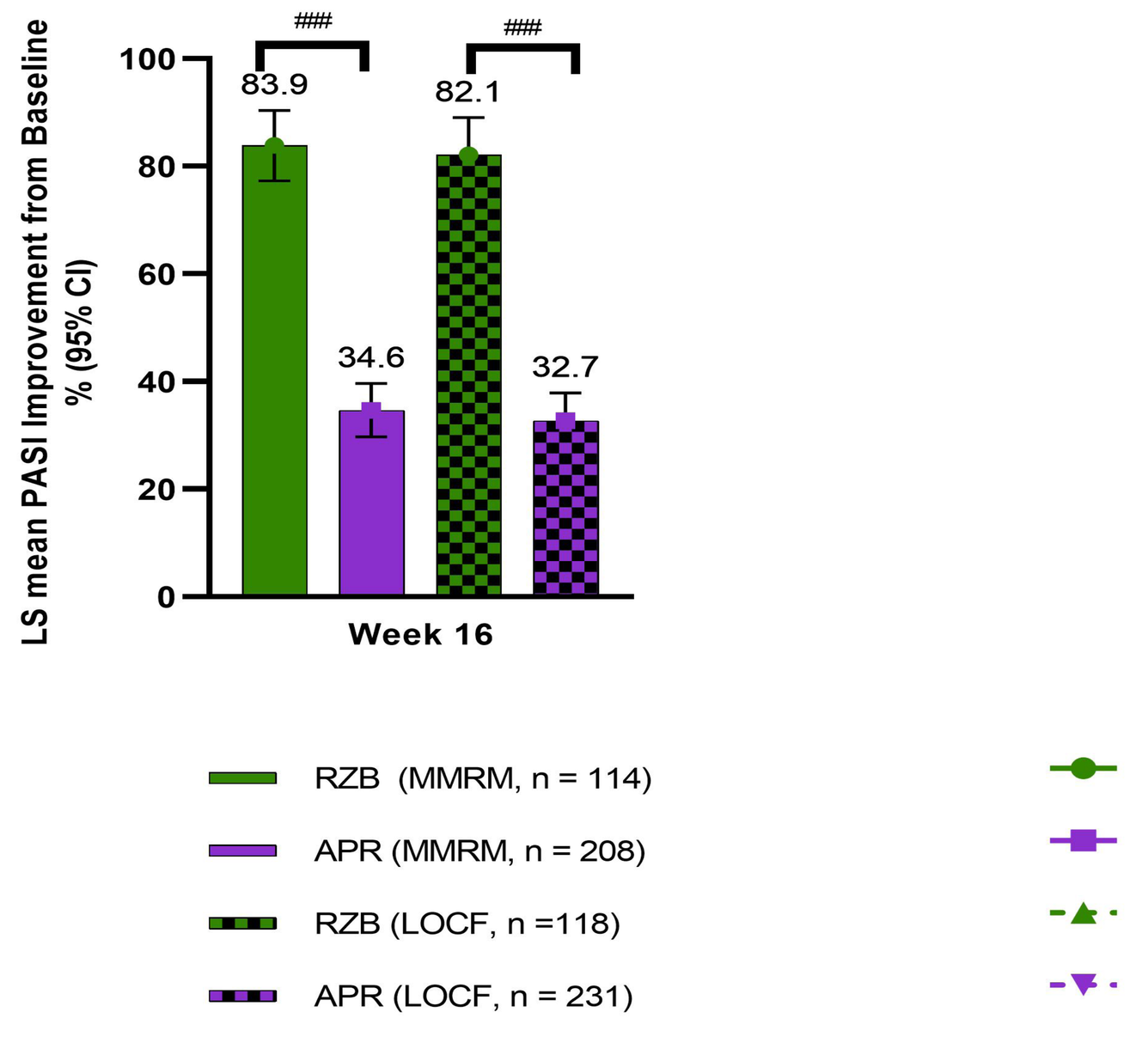
TEAEs	Period A, baseline to week 16			
	RZB 150 mg N = 118 n (%)	**RZB 150 mg N = 118 E (E/100 PY) PY = 35.8**	**APR 30 mg N = 234 n (%)**	**APR 30 mg N = 234 E (E/100 PY) PY = 67.3**
Adverse event (AE)	49 (41.5)	81 (226.3)	143 (61.1)	308 (457.7)
AE with reasonable possibility of being related to study treatment	6 (5.1)	9 (25.1)	98 (41.9)	169 (251.1)
Serious AEs	1 (0.8)	1 (2.8)	4 (1.7)	4 (5.9)
AE leading to discontinuation of study drug	0	0	16 (6.8)	34 (50.5)
AE leading to death	0	0	0	0
TEAEs reported in ≥ 5% of patients				
Diarrhoea	1 (0.8)	1 (2.8)	47 (20.1)	50 (74.3)
Nausea	0	0	41 (17.5)	45 (66.9)
Headache	3 (2.5)	3 (8.4)	27 (11.5)	28 (41.6)
COVID-19	13 (11.0)	13 (36.3)	16 (6.8)	16 (23.8)
TEAEs	**Period B, all patients randomized to APR at baseline**			
	APR/RZB N = 102 n (%)	**APR/RZB N = 102 E (E/100 PY) PY = 86.9**	**APR/APR N = 97 n (%)**	**APR/APR N = 97 E (E/100 PY) PY = 40.2**
Adverse event (AE)	57 (55.9)	123 (141.5)	45 (46.4)	91 (226.4)
AE with reasonable possibility of being related to study treatment	11 (10.8)	13 (15.0)	14 (14.4)	19 (47.3)
Serious AEs	3 (2.9)	6 (6.9)	2 (2.1)	2 (5.0)
AE leading to discontinuation of study drug	0	0	5 (5.2)	5 (12.4)
AE leading to death	0	0	0	0
TEAEs reported in ≥ 5% of patients				
COVID-19	12 (11.8)	12 (13.8)	14 (14.4)	14 (34.8)
Nasopharyngitis	10 (9.8)	11 (12.7)	8 (8.2)	10 (24.9)
Upper respiratory tract infection	6 (5.9)	8 (9.2)	3 (3.1)	3 (7.5)
Headache	5 (4.9)	6 (6.9)	4 (4.1)	4 (10.0)

RZB, risankizumab; APR, apremilast; APR/RZB, patients who switched from apremilast to risankizumab at week 16; APR/APR, patients who continued to receive APR treatment; AE, adverse event; TEAE, treatment-emergent adverse event; E, event; PY, patient years

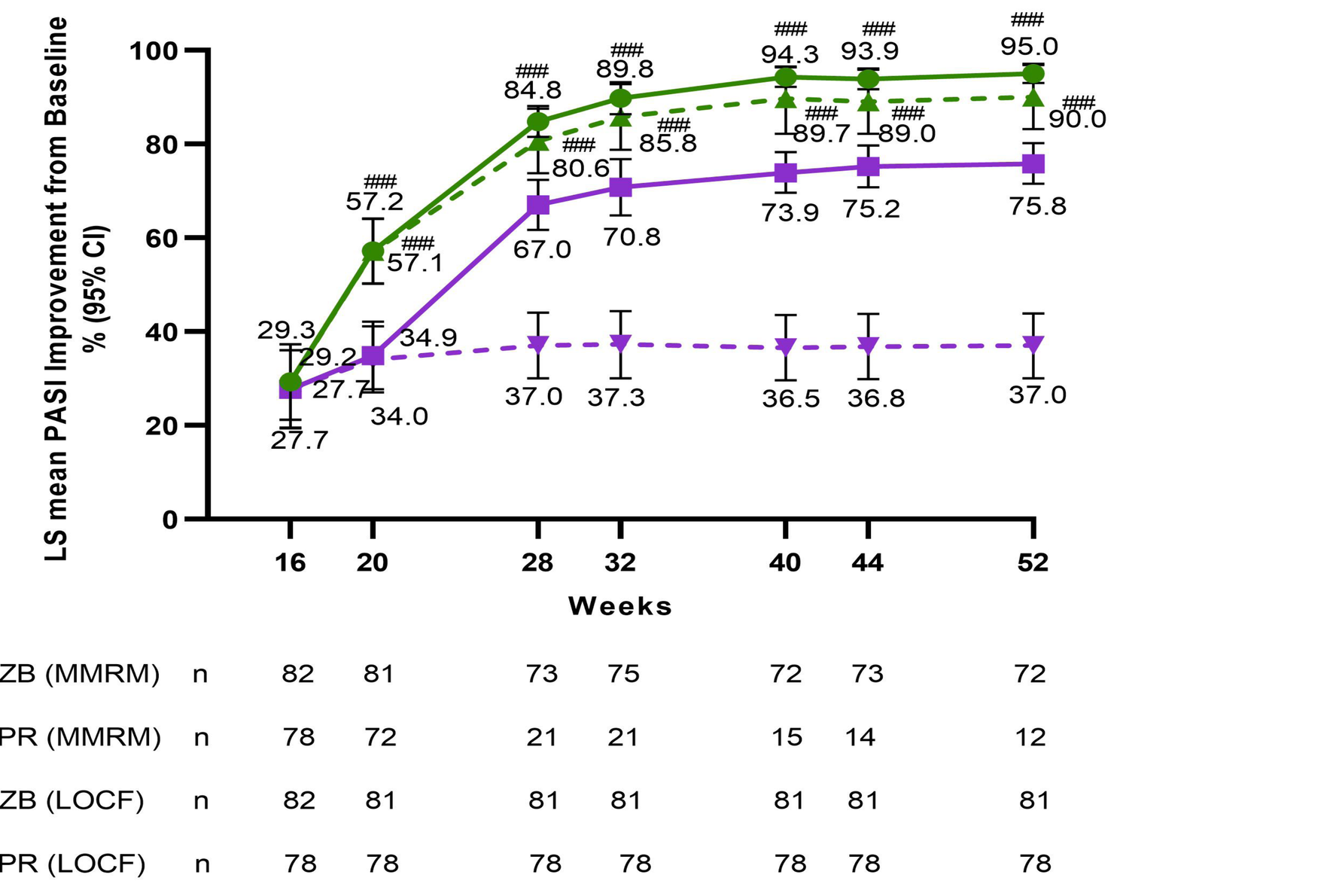
- TEAEs and AEs leading to study drug discontinuation were more frequently observed with APR
- Discontinuation remained low and stable with RZB
- No additional safety concerns were identified in patients who switched from APR to RZB without washout

Patients Treated with RZB Demonstrated Increased PASI Improvement Compared to Patients Treated with APR

Mean PASI Improvement from Baseline: Period A



Mean PASI Improvement from Baseline: Period B*

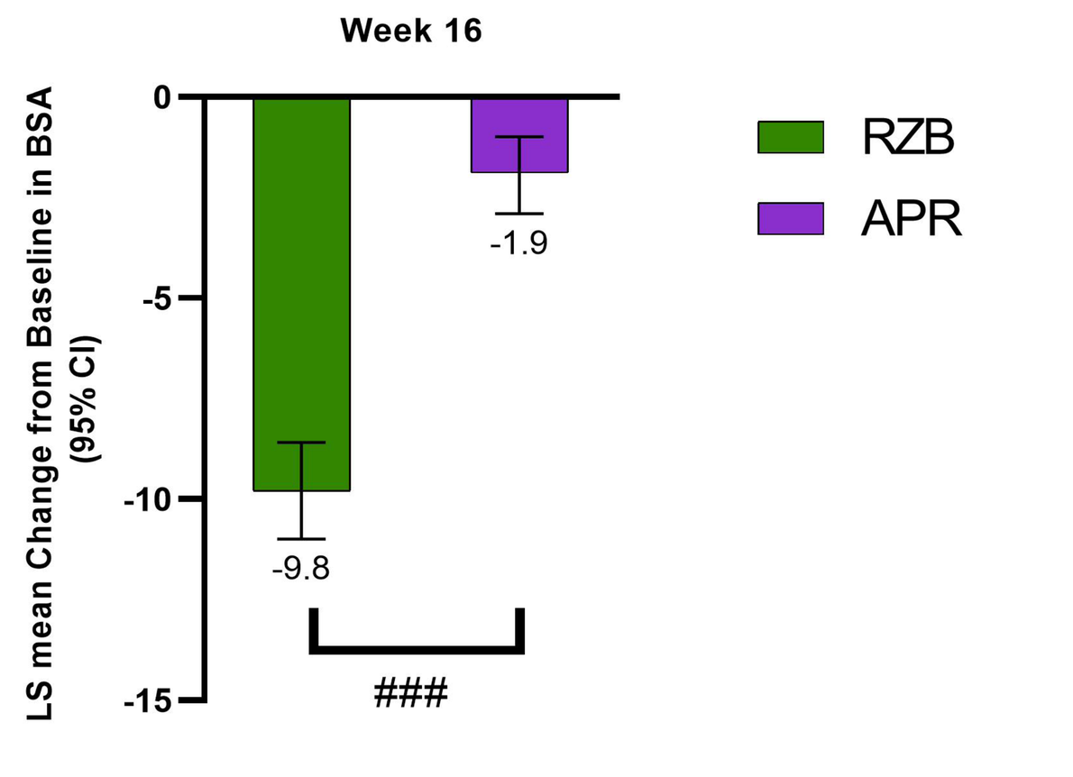


Period B*, in patients not achieving PASI 75 with APR at week 16; RZB, risankizumab; APR, apremilast; APR/RZB, patients not achieving PASI 75 at week 16 who switched from apremilast to risankizumab at week 16; APR/APR, patients who continued to receive APR treatment; PASI, Psoriasis Area and Severity Index LS, least square; MMRM, mixed models for repeated measures; LOCF, last observation carried forward; ### nominal p-value <0.001 (not controlled for multiplicity) indicating differences between RZB or APR-treated patients within MMRM or LOCF analysis; In period B (APR/APR), n dropped from 72 to 21 at week 28 because many patients had to be rescued and therefore not counted in the analysis

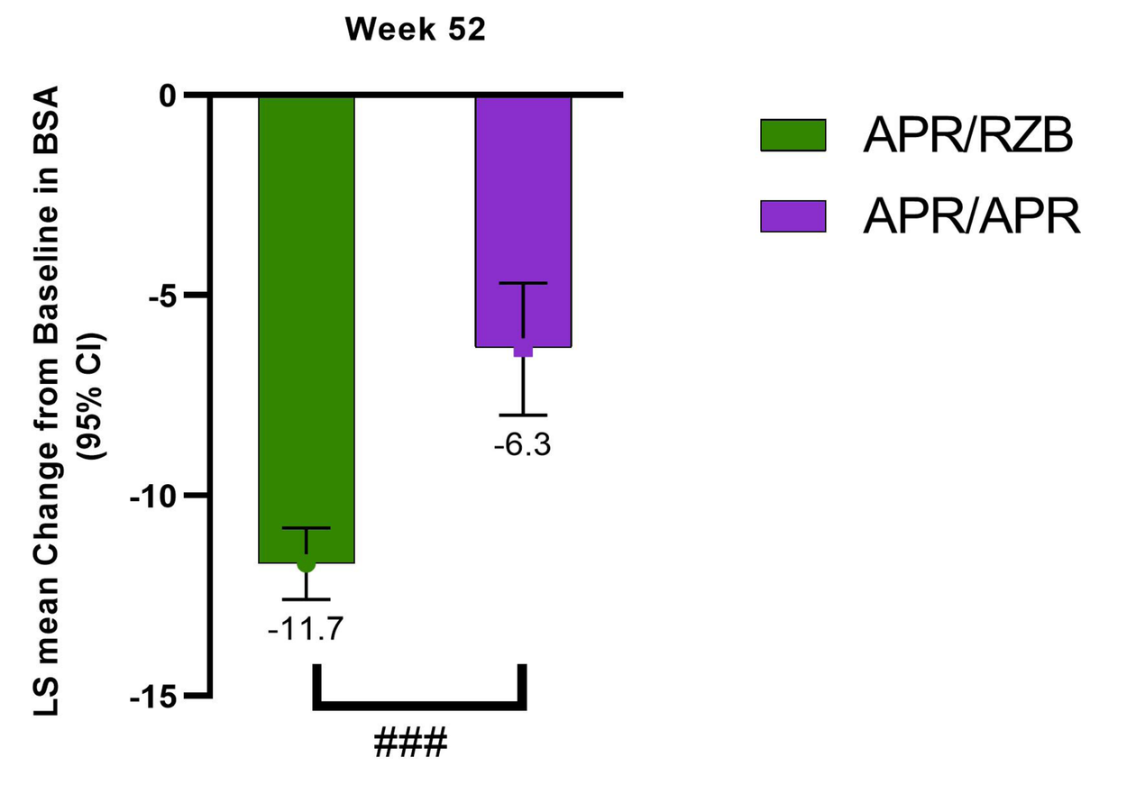
- At week 16, mean PASI improvement from baseline (95% CI) was 82.1% (75.2, 89.0) for RZB-treated patients and 32.7% (27.6, 37.9) for APR-treated patients (LOCF analysis)
- Absolute mean PASI in Period A (week 16) was
  - MMRM: RZB 1.7 (n = 114) and APR 8.8 (n = 208)
  - LOCF: RZB 2.0 (n = 118) and APR 9.2 (n = 231)
- At week 52, in patients who switched from APR to RZB, the mean PASI improvement was 90.0% (83.2, 96.9) compared to patients who continued APR 37.0% (30.0, 43.9) (LOCF analysis)
- Absolute mean PASI in Period B (week 52) was
  - MMRM: APR/RZB 0.7 (n = 72) and APR/APR 3.1 (n = 12)
  - LOCF: APR/RZB 1.4 (n = 81) and APR/APR 9.1 (n = 78)

Patients Who Switched from APR to RZB Displayed an Improved Change in BSA

Change from Baseline in BSA: Period A (MMRM)



Change from Baseline in BSA: Period B* (MMRM)



MMRM, mixed model repeat analysis; Period B*, in patients not achieving PASI 75 with APR at week 16; RZB, risankizumab; APR, apremilast; APR/RZB, patients not achieving PASI 75 at week 16 who switched from apremilast to risankizumab at week 16; APR/APR, patients who continued to receive APR treatment; PASI, Psoriasis Area and Severity Index LS, least square ###, nominal p-value <0.001 (not controlled for multiplicity)

- At week 16, BSA improvement from baseline (95% CI) was -9.8 (-5.6, -11.0) for RZB-treated patients and -1.9 (-1.0, -2.9) for APR-treated patients
- In patients who switched from APR to RZB the improvement in BSA was -11.7 (-10.8, -12.6)
- In patients who continued APR, the improvement in BSA was -6.3 (-4.7, -8.0)