Efficacy of Switching to Risankizumab Compared With Continued Adalimumab Treatment in Patients With Moderate-to-Severe Plaque Psoriasis

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Presented at the American Academy of Dermatology Annual Meeting • Washington, DC • March 1 – 5, 2019

BACKGROUND

- Psoriasis is a chronic, debilitating immune-mediated disease characterized by marked inflammation that is driven by expression of proinflammatory cytokines, including interleukin 23 (IL-23), IL-17, and tumor necrosis factor-alpha (TNF-α)[1,2]
- Risankizumab (RZB) is a fully humanized IgG1 monoclonal antibody that selectively inhibits IL-23, a cytokine that plays a key role in the development and maintenance of psoriatic lesions by binding to its p19 subunit[3-6]
- The superior efficacy of RZB compared with adalimumab (ADA) at 16 weeks has been demonstrated in IMMvent, a phase 3 trial in moderate-to-severe plaque psoriasis

OBJECTIVE

- To evaluate the efficacy of switching to RZB compared with continued ADA therapy in patients who had a 50% to < 90% improvement of their baseline Psoriasis Area Severity Index (PASI 50 to < 90) after an initial 16 weeks of treatment

METHODS

STUDY DESIGN AND TREATMENT

- IMMvent (NCT02694523) was a multinational, phase 3, randomized, double-blind, double-dummy, active-controlled trial
  - Part A, patients were randomized 1:1 to receive via subcutaneous injection RZB 150 mg at weeks 0 and 4 or ADA 80 mg at week 0 and 40 mg every 2 weeks from week 1 to week 15 (**Figure 1**)
  - Part B (weeks 16-44), patients initially randomized to receive ADA who achieved PASI 50 to <90 at week 16 were re-randomized 1:1 to receive RZB 150 mg at weeks 16, 20, and 32 or ADA 40 mg every 2 weeks up to week 41

PATIENTS

- Main inclusion criteria:
  - Male or female patients (women of childbearing potential using birth control)
  - Age ≥18 years at screening
  - Stable chronic plaque psoriasis (with or without psoriatic arthritis) for ≥6 months before the administration of study drug
    - Involved body surface area (BSA) ≥10%
    - Psoriasis Area Severity Index (PASI) ≥12
    - Static Physician's Global Assessment (sPGA) score ≥3
- Main exclusion criteria:
  - Patients with:
    - Non-plaque forms of psoriasis
    - Current drug-induced psoriasis
    - Active ongoing inflammatory diseases other than psoriasis and psoriatic arthritis

ASSESSMENTS

- Clinical outcomes assessed included:
  - Part A (0–16 weeks)
    - Proportion of patients who achieved 90% and 100% improvement in PASI (PASI 90 and PASI 100)
  - Part B (16–44 weeks)
    - Proportion of patients who achieved PASI 90 among the re-randomized groups: ADA/RZB vs ADA/ADA
    - Mean PASI improvement from baseline among the overall re-randomized groups, and subgroups of patients based on PASI response (50 to <75 vs 75 to <90)
    - Proportion of patients who achieved Dermatology Life Quality Index score of no effect or a little effect on quality of life (DLQI 0 or 1) among the overall re-randomized groups
- Safety was assessed throughout the study
  - Please refer to poster 10218 for safety analyses of the IMMvent trial, and posters 9891, 9793, and 9876 for the RZB psoriasis Clinical Development Program

STATISTICAL ANALYSIS

- All comparisons were done with 2-sided tests, with a type 1 error of .05
- The difference between the 2 treatment groups was analyzed using the Cochran-Mantel-Haenszel risk difference estimate stratified by the randomization factors of weight (≤100 kg vs >100 kg) and prior exposure to TNF antagonists (0 vs ≥1)
- Patients with missing efficacy data for categorical variables were processed with non-responder imputation and for continuous variables with last observation carried forward

RESULTS

PATIENT CHARACTERISTICS AND DISPOSITION

- A total of 301 patients were randomized to receive RZB and 304 patients were randomized to receive ADA at baseline
- At week 16, among patients receiving ADA, 109 patients achieved PASI 50 to <90; 53 patients were re-randomized to receive RZB and 56 were re-randomized to continue ADA therapy
- Baseline demographics and disease characteristics were similar between the 2 original treatment arms in part A and the re-randomized treatment arms in part B (**Table 1**)

EFFICACY ASSESSMENTS

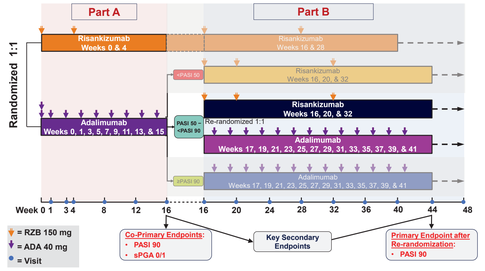
Part A

- Through 16 weeks of treatment, significantly more patients treated with RZB achieved PASI 90 and PASI 100 compared with patients receiving ADA ($P < .001$; **Figures 2A** and **2B**)
  - At week 16, 72.4% of RZB-treated patients achieved PASI 90 vs 47.4% of ADA-treated patients ($P < .001$)
  - At week 16, 39.9% of RZB-treated patients achieved PASI 100 vs 23.0% of ADA-treated patients ($P < .001$)

Part B: Re-randomized Patients

- Among those who achieved PASI 50 to <90 at week 16 with ADA treatment, significantly more patients who switched to RZB achieved PASI 90 through 44 weeks of treatment compared with patients continuing with ADA treatment ($P < .001$; **Figure 3**)
  - Significant differences in PASI 90 were first observed 4 weeks after re-randomization and at each subsequent time point throughout the study; at week 44, 66.0% of patients who switched to RZB achieved PASI 90 vs 21.4% of patients continuing ADA therapy ($P < .001$)
- Mean PASI improvement from baseline was significantly greater in patients switched to RZB compared with patients continuing with ADA treatment through 44 weeks of treatment ($P < .001$; **Figure 4A**)
  - At week 44, mean PASI improvement from baseline was 92.9% in patients switched to RZB vs 71.9% in patients continuing ADA therapy ($P < .001$)
- Switching to RZB also correlated with significantly greater improvement in quality of life as measured by the proportion of patients switched to RZB achieving DLQI 0/1 at week 44 vs patients continuing ADA therapy (66.0% vs 28.6%; $P < .001$; **Figure 4B**)
- Greater mean PASI improvements from baseline were also observed through week 44 in patients switched to RZB compared with patients continuing ADA in both PASI subgroups: (PASI 50 to <75 and PASI 75 to <90; **Figures 5** and **6**)
  - In the PASI 50 to <75 subgroup, the mean PASI improvement from baseline was 87.3% in patients switched to RZB vs 71.2% in patients continuing ADA therapy ($P = .083$) at week 44
  - In the PASI 75 to <90 subgroup, the mean PASI improvement from baseline was 94.8% in patients switched to RZB vs 71.0% in patients continuing ADA therapy ($P < .001$) at week 44

Figure 1. IMMvent Study Design



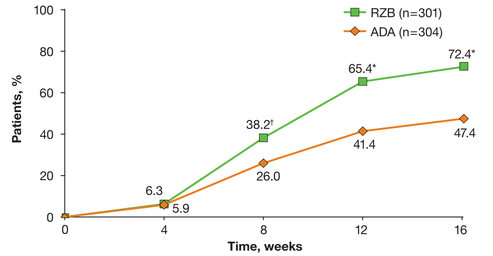
ADA = adalimumab; PASI = Psoriasis Area and Severity Index; RZB = risankizumab; sPGA = static Physician's Global Assessment.

Table 1. Baseline Demographics and Disease Characteristics

	Part A		Part B	
	RZB n=301	ADA n=304	ADA → RZB n=53	ADA → ADA n=56
Age, years, mean (SD)	45.3 (13.8)	47.0 (13.1)	49.5 (14.8)	45.8 (11.3)
Female, n (%)	91 (30.2)	92 (30.3)	18 (34.0)	16 (28.6)
Race, White, n (%)	245 (81.4)	263 (86.5)	42 (79.2)	44 (78.6)
Weight, kg, mean (SD)	88.8 (23.1)	91.4 (24.6)	89.4 (25.9)	92.6 (25.0)
Weight >100 kg, n (%)	82 (27.2)	87 (28.6)	13 (24.5)	16 (28.6)
BMI, kg/m^2, mean (SD)	30.2 (7.9)	30.8 (7.4)	30.1 (7.6)	31.1 (7.2)
PASI, mean (SD)	20.0 (7.5)	20.0 (7.5)	20.4 (8.3)	19.3 (7.6)
sPGA of severe, n (%)	58 (19.3)	58 (19.1)	6 (11.3)	13 (23.2)
BSA, %, mean (SD)	26.5 (16.5)	25.5 (16.8)	27.6 (19.9)	24.3 (16.4)
Any prior biologic therapy, n (%)	118 (39.2)	111 (36.5)	20 (37.7)	24 (42.9)
Prior TNFi	44 (14.6)	45 (14.8)	9 (17.0)	12 (21.4)
Prior non-TNFi	95 (31.6)	83 (27.3)	16 (30.2)	14 (25.0)

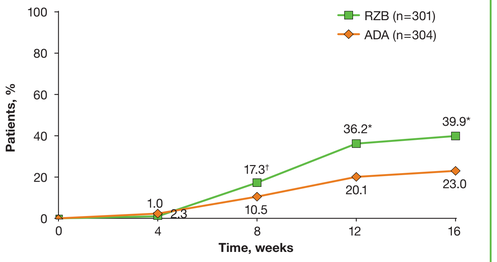
ADA = adalimumab; BMI = body mass index; BSA = body surface area; PASI = Psoriasis Area and Severity Index; RZB = risankizumab; SD = standard deviation; sPGA = static Physician's Global Assessment; TNFi = tumor necrosis factor inhibitor.

Figure 2A. PASI 90 Responses Through Week 16 in Part A (NRI)



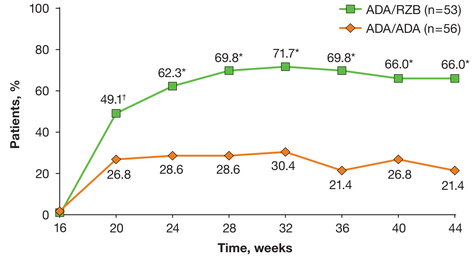
*P < .001; †P = .001; ADA = adalimumab; NRI = non-responder imputation; PASI = Psoriasis Area and Severity Index; RZB = risankizumab.

Figure 2B. PASI 100 Responses Through Week 16 in Part A (NRI)



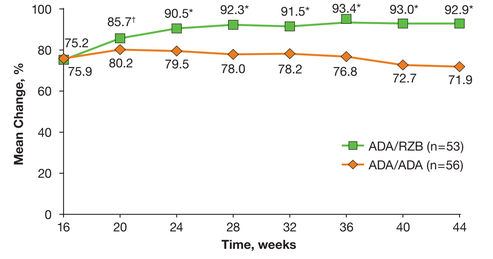
*P < .001; †P < .05; ADA = adalimumab; NRI = non-responder imputation; PASI = Psoriasis Area and Severity Index; RZB = risankizumab.

Figure 3. PASI 90 Responses Through Week 44 in Part B Among PASI 50 to <90 Responders (NRI)



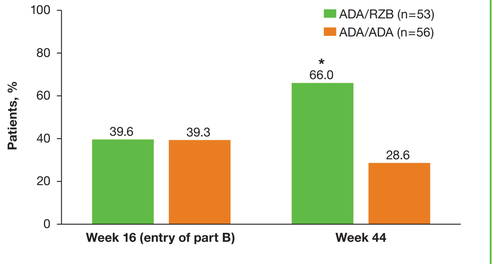
*P < .001; †P < .05; ADA = adalimumab; NRI = non-responder imputation; PASI = Psoriasis Area and Severity Index; RZB = risankizumab.

Figure 4A. Mean PASI Improvement (%) from Baseline Among PASI 50 to <90 Responders in Part B (LOCF)



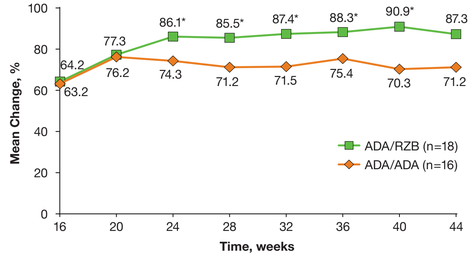
*P < .001; †P < .05; ADA = adalimumab; LOCF = last observation carried forward; PASI = Psoriasis Area and Severity Index; RZB = risankizumab.

Figure 4B. Proportion of Patients with DLQI 0/1 at Week 44 Among PASI 50 to <90 Responders (NRI)



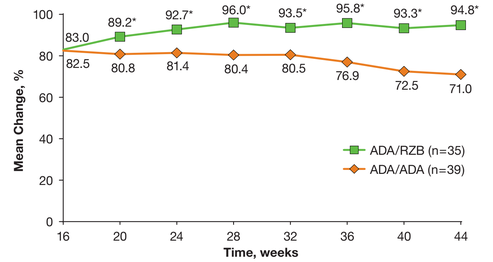
*P < .001; ADA = adalimumab; DLQI = Dermatology Life Quality Index; NRI = non-responder imputation; PASI = Psoriasis Area and Severity Index; RZB = risankizumab.

Figure 5. Mean PASI Improvement (%) from Baseline Among PASI 50 to <75 Responders in Part B (LOCF)



*P < .05; ADA = adalimumab; LOCF = last observation carried forward; PASI = Psoriasis Area and Severity Index; RZB = risankizumab.

Figure 6. Mean PASI Improvement (%) from Baseline Among PASI 75 to <90 Responders in Part B (LOCF)



*P < .001; ADA = adalimumab; LOCF = last observation carried forward; PASI = Psoriasis Area and Severity Index; RZB = risankizumab.

CONCLUSIONS

- In patients initially achieving PASI 50 to <90 responses with ADA at week 16, switching to RZB resulted in significantly higher PASI 90 response rates at week 44 compared with patients who continued ADA therapy
- Mean improvements in PASI scores were also greater at week 44 among patients switched to RZB compared with patients continuing ADA, regardless of their initial PASI response at week 16

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DISCLOSURES & ACKNOWLEDGEMENTS

This study was funded by AbbVie Inc. AbbVie participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this poster for presentation. **CR** has participated in speakers' bureaus for AbbVie, Eli Lilly, Janssen, Leo, and Novartis; and has served as a consultant for AbbVie, Boehinger Ingelheim, Dermira, Dr Reddys, Janssen, Leo, Eli Lilly, Regeneron-Sanofi, and UCB. **JC** has received grant/research support from AbbVie, Amgen, Celgene, Janssen, Novartis, Merck, Lilly, Pfizer, UCB, MC2 Therapeutics, Verrica, Sandoz, and Regeneron; has participated in speakers' bureaus for AbbVie, Lilly, Novartis, Janssen, Sanofi-Genzyme and Regeneron; and has served as a consultant for AbbVie, Lilly, Novartis, Janssen, Sanofi-Genzyme, Regeneron, UCB, and Amgen. **KR** has served as advisor and/or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Affibody, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene, Centocor, Covagen, Forward Pharma, Fresenius Medical Care, GlaxoSmithKline, Janssen-Cilag, Kyowa Kirin, Leo, Lilly, Medac, Merck Sharp & Dohme, Novartis, Miltenyi Biotec, Ocean Pharma, Pfizer, Regeneron, Samsung Bioepis, Sanofi, Takeda, UCB, Valeant, and Xenoport. **WCV** and **TW** are full-time employees of AbbVie Inc. and may hold stock or stock options. Medical writing assistance, funded by AbbVie, was provided by Bhawana Bariar, MS, PhD, and Lamara D. Shrode, PhD, CMPP™, of JB Ashtin. AbbVie and the authors thank the patients who participated in this trial and all study investigators for their contributions.

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