Long-Term Efficacy and Safety of Risankizumab (RZB) for the Treatment of Moderate-to-Severe Plaque Psoriasis: Interim Analysis of Results from the LIMMitless Open-Label Extension Trial Beyond 4.5 Years of Follow-Up

Kim A. Papp[1], Mark G. Lebwohl[2], Lluís Puig[3], Mamitaro Ohtsuki[4], Stefan Beissert[5], Jiewei Zeng[6], Jie Liu[6], Simone Rubant[6], Ranjeeta Sinvhal[6], Ahmed M. Soliman[6], Stefan Beeck[6]

[1]K Papp Clinical Research and Probity Medical Research, Waterloo, ON, Canada; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [4]Jichi Medical University, Tochigi, Japan; [5]Department of Dermatology, University Hospital Carl Gustav Carus, TU Dresden, Dresden, Germany; [6]AbbVie Inc., North Chicago, IL, USA

OBJECTIVE

To assess the long-term efficacy and safety of continuous RZB treatment beyond 4.5 years in adults with moderate-to-severe plaque psoriasis

CONCLUSIONS

Long-term treatment up to 256 weeks with RZB once every 12 weeks provides high durable efficacy response and sustained improvements in health-related quality of life for patients with moderate-to-severe psoriasis

Overall, long-term continuous RZB treatment is well tolerated, with no new safety signals noted through more than 5.5 years of continuous exposure

For additional information or 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 2022 DRS scientific presentations:

https://abbvie1.outsystemsenterprise.com/CMAEventPublications/Assets.aspx?Conferenceid=364

QR code expiration: March 8, 2023

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

AbbVie Inc. participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving of this e-poster. All authors had access to the data, participated in the development and review of the document, and agreed in the decision to present this poster at the 2022 American Academy of Dermatology Annual Meeting (AAD 2022). AbbVie and the authors thank all the study investigators for their contributions and the patients who participated in these studies. AbbVie funded the research for this study and provided writing support for this e-poster. Medical writing assistance, funded by AbbVie, was provided by Marion France, PhD, and Callie A.S. Corsa, PhD, of JB Ashtin. No honoraria or payments were made for authorship.

KAP has received research funds from, is a consultant, and/or speaker for AbbVie, Amgen, Arcutis, Astellas, Bausch Health, Baxalta, Baxter, BI, BMS, Celgene, Cohesia, Dermasent, Dermira, EMD Serono, Forward Pharma, Galderma, Genentech, Gilead, Incyte, Janssen, LEO, Lilly, Meiji Seika Pharma, Merck, Mitsubishi Tanabe Pharma, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sandoz, Sanofi-Genzyme, Stiefel, Sun Pharma, Takeda, and UCB, and is a committee member for PSOLAR and PURE registries. MGL is an employee of; receives research funds from, and/or consultant for AbbVie, Adlium Bio, Almirall, Altrubio, Amgen, AnaptysBio, Arcutis, Aristea, Arrive, Avotres, BI, BioniX, BMS, Cara, Castle, Corrona, Dermavant, Dr Reddy's, Evelo, Evommune, Facilitation of International Dermatology Education, Forte, Foundation for Research and Education in Dermatology, Helsinn, Hexima, Incyte, Janssen, LEO, Lilly, Meiji Seika Pharma, Mindera, Mount Sinai, Ortho Dermatologics, Pfizer, Regeneron, Seanergy, Vertica, and UCB. LP has received consultancy/speaker's honoraria from and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Biasatta, Biogen, BI, Celgene, EMD Serono, Gebro, Janssen, LEO, Lilly, Merck, Mylan, Novartis, Pfizer, Regeneron, Roche, Samsung, Sandoz, Sanofi, and UCB. MO has received honoraria or fees for serving on advisory boards, speakers' bureaus, or consulting; and grants for investigator activities from AbbVie, Amgen, BI, BMS, Celgene, Eisai, Janssen, Kyowa Kirin, LEO, Lilly, Maruho, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Sun Pharma, Taiho, Torii, and UCB. S Beissert has received honoraria as an advisory board member and/or speaker for AbbVie, Actelion, Almirall, Amgen, BMS, Celgene, Galderma, GSK, Janssen, LEO, Lilly, Merck Serono, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, and UCB. JZ, JL, SR, RS, AMS, and S Beeck are full-time employees of AbbVie Inc., and may hold AbbVie stock, stock options, and/or patents.

References

1. Puig L. *Expert Rev Clin Immunol*. 2017;13:525–34.
2. Gordon KB, et al. *Lancet*. 2018;392:650–61.
3. Ohtsuki M, et al. *J Dermatol*. 2019;46:599–94.
4. Thaçi D, et al. *J Eur Acad Dermatol Venereol*. 2021;35:1686–91.
5. Reich K, et al. *Lancet*. 2019;394:576–86.
6. Warren RB, et al. *Br J Dermatol*. 2021;184:50–9.
7. Papp KA, et al. *N Engl J Med*. 2017;376:1551–60.
8. Blauvelt A, et al. *JAMA Dermatol*. 2020;156:649–58.
9. Papp KA, et al. *J Drugs Dermatol*. 2020;19:571–2.

Presented at the 2022 Dermatology Refresher Symposium (DRS), April 8–10, 2022, San Antonio, TX, USA

INTRODUCTION

- The interleukin (IL) 23/IL-17 immune axis plays a key role in the development and maintenance of psoriatic lesions[1]
- Risankizumab (RZB) is a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits IL-23 by binding to its p19 subunit
- RZB demonstrated superior efficacy compared with placebo (UltIMMa-1, UltIMMa-2, and SustaIMM trials),[2,3] and multiple systemic therapies including ustekinumab (UltIMMa-1 and UltIMMa-2 trials),[2] fumaric acid esters (NCT03255382),[4] adalimumab (IMMvent trial),[5] and secukinumab (IMMerge trial)[6]
- LIMMitless is an ongoing open-label extension study designed to evaluate long-term efficacy and safety of RZB treatment in adults with moderate-to-severe plaque psoriasis who completed 1 of the aforementioned phase 2/3 trials

METHODS

Study Design

- LIMMitless (open-Label extension study to assess the safety and efficacy of rIsankizuMab for Maintenance in moderate-to-severe plaque type psoriasis; NCT03047395) is the ongoing, phase 3, international, multicenter, open-label extension study in which adults receive open-label RZB 150 mg every 12 weeks for up to 5 years of continuous RZB treatment
- This interim analysis assessed efficacy and safety through 256 weeks of continuous RZB treatment
- In the ongoing LIMMitless open-label extension study, patients initially randomized to receive RZB 150 mg in 5 double-blind, placebo-controlled phase 2/3 studies (UltIMMa-1, UltIMMa-2, SustaIMM, IMMvent, and NCT03255382)[2–5] were eligible to continue open-label RZB 150 mg every 12 weeks

Analysis

- Missing efficacy data were imputed using the following methods:
  - Modified nonresponder imputation (mNRI)—nonresponse was imputed only for treatment failures, defined as patients who had worsening of psoriasis, then a mixed-effect model was used on the imputed dataset; used for dichotomous analyses only
  - Last observation carried forward (LOCF)—used completed evaluation from the most recent visit to impute missing data
  - Observed cases (OC)—no imputation of missing data; patients missing data at a visit were excluded from the observed analysis for that visit

Assessments

Efficacy was assessed every 12 weeks by:
- ≥90% improvement in Psoriasis Area and Severity Index (PASI 90)
- 100% improvement in PASI (PASI 100)
- Static Physician's Global Assessment of clear or almost clear (sPGA 0/1)
- Mean PASI percent improvement

Health-related quality of life was assessed every 24 weeks by:
- Dermatology Life Quality Index reflecting no effect on the patient's quality of life (DLQI 0/1)

Safety was assessed via:
- Adverse event (AE) monitoring through the cutoff date for this analysis (November 23, 2021)

Patients

Key Inclusion Criteria
- Adults (aged ≥18 years)
- History of chronic moderate-to-severe plaque psoriasis
- Completed the UltIMMa-1,[2] UltIMMa-2,[2] SustaIMM,[3] NCT03255382,[4] or IMMvent[5] studies
- A candidate for prolonged open-label risankizumab treatment, according to investigator judgment

Key Exclusion Criteria

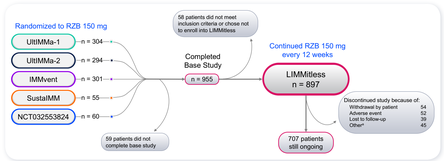
If during UltIMMa-1, UltIMMa-2, SustaIMM, NCT03255382, or IMMvent the patient:
- Prematurely discontinued for any reason
- Developed guttate, erythrodermic, pustular, or drug-induced psoriasis
- Used prohibited medication
- Developed active or suspected malignancy, except appropriately treated basal cell carcinoma, squamous cell carcinoma of the skin, or in situ carcinoma of the uterine cervix
- Had known or laboratory evidence of HIV, hepatitis B, hepatitis C, or active tuberculosis infection
- Had >8 weeks' time elapse since completion visit of the base study

RESULTS

Patients

- Of 955 patients who completed a base study, 897 entered the LIMMitless study and continued to receive RZB **(Figure 1)**

Figure 1. Patient Disposition



RZB, risankizumab.
*Includes 5 patients who discontinued due to COVID-19 logistical restrictions; no patients discontinued due to COVID-19 infection.

Table 1. Demographics and Baseline Disease Characteristics[a]

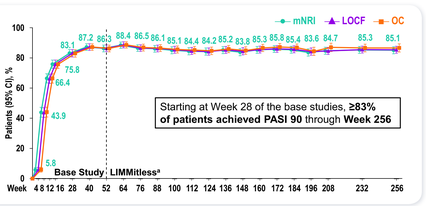
Parameter	Continuous RZB N = 897
Male, n (%)	633 (70.6)
Age, years	
Mean (SD)	46.9 (13.5)
Median (Q1, Q3)	47.0 (37.0, 57.0)
Weight, kg	
Mean (SD)	88.5 (22.4)
Median (Q1, Q3)	85.2 (72.7, 102.0)
Psoriatic arthritis,[b,c] n (%)	195 (23.3)
Prior treatment, n (%)	
Naive to systemic therapy[c]	259 (30.9)
Prior biologic therapy[c]	317 (37.8)
Prior TNF antagonist therapy	163 (19.5)
BSA involvement, %	
Mean (SD)	26.7 (16.5)
Median (Q1, Q3)	21.0 (15.0, 33.0)
PASI	
Mean (SD)	20.5 (8.0)
Median (Q1, Q3)	18.0 (14.7, 23.7)
sPGA, n (%)	
Moderate (score of 3)	723 (80.6)
Severe (score of 4)	167 (18.6)
DLQI, mean (SD)	13.9 (7.2)

BSA, body surface area; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; Q1/Q3, quartile 1/3; sPGA, static Physician's Global Assessment; TNF, tumor necrosis factor.
[a]Baseline at the start of base study.
[b]Diagnosed or suspected.
[c]Based on N = 838; not collected in NCT03525382.

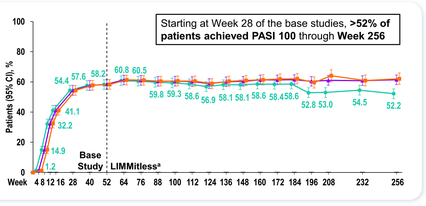
Efficacy

Figure 2. Patients Achieving PASI Response Over Time

PASI 90

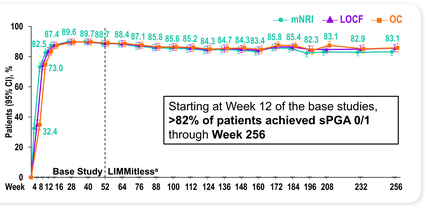


PASI 100



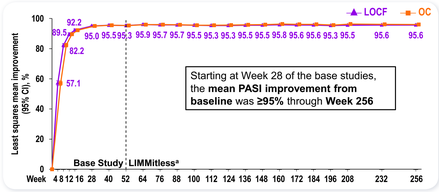
LOCF, last observation carried forward; mNRI, modified nonresponder imputation; OC, observed cases; PASI 90/100, ≥90%/100% improvement in Psoriasis Area and Severity Index.
N = 897 from Week 0 to Week 256 (mNRI and LOCF). In the OC analysis, N = 897 at Week 0; 618 of the 707 ongoing patients completed the assessment visit at Week 256; 53 ongoing patients have reached the assessment window but have not yet completed the assessment visit at Week 256.
[a]Because of differences in base study lengths, some patients enrolled in the LIMMitless study earlier than 52 weeks.

Figure 3. Patients Achieving sPGA 0/1 Over Time



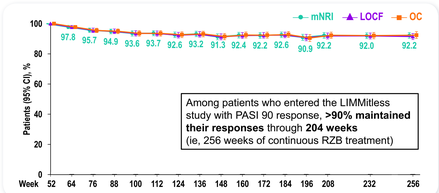
LOCF, last observation carried forward; mNRI, modified nonresponder imputation; OC, observed cases; sPGA 0/1, static Physician's Global assessment of clear (0) or almost clear (1).
N = 836–897 from Week 0 to Week 256 (mNRI and LOCF). In the OC analysis, N = 897 at Week 0; 618 of the 707 ongoing patients completed the assessment visit at Week 256; 53 ongoing patients have reached the assessment window but have not yet completed the assessment visit at Week 256.
[a]Because of differences in base study lengths, some patients enrolled in the LIMMitless study earlier than 52 weeks.

Figure 4. Mean PASI Percent Improvement Over Time



LOCF, last observation carried forward; OC, observed cases; PASI, Psoriasis Area and Severity Index.
N = 888–897 from Week 0 to Week 256 (LOCF). In the OC analysis, N = 897 at Week 0; 618 of the 707 ongoing patients completed the assessment visit at Week 256; 53 ongoing patients have reached the assessment window but have not yet completed the assessment visit at Week 256.
[a]Because of differences in base study lengths, some patients enrolled in the LIMMitless study earlier than 52 weeks.

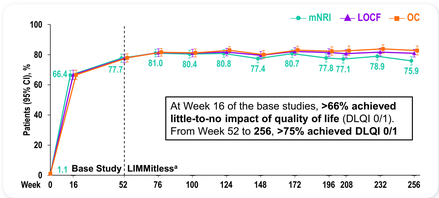
Figure 5. Patients Maintaining PASI 90 Response in the LIMMitless Study Over Time



N = 749–761 from Week 52 to Week 256 (mNRI and LOCF). In the OC analysis, N = 761 at Week 52 and N = 528 at Week 256. Because of differences in base study lengths, some patients enrolled in the LIMMitless study earlier than 52 weeks.
LOCF, last observation carried forward; mNRI, modified nonresponder imputation; OC, observed cases; PASI 90, ≥90% improvement in Psoriasis Area and Severity Index.

Quality of Life

Figure 6. Patients Achieving DLQI 0/1 Over Time



DLQI 0/1, Dermatology Life Quality Index of no (0) or little (1) effect on quality of life; LOCF, last observation carried forward; mNRI, modified nonresponder imputation; OC, observed cases.
N = 896–897 from Week 0 to Week 256 (mNRI and LOCF). In the OC analysis, N = 897 at Week 0; 620 of the 707 ongoing patients completed the assessment visit at Week 256; 51 ongoing patients have reached the assessment window but have not yet completed the assessment visit at Week 256.
[a]Because of differences in base study lengths, some patients enrolled in the LIMMitless study earlier than 52 weeks.

Safety

- With 4453.0 patient-years exposure, rates of AEs remained stable up to 304 weeks of follow-up compared with the rates observed in the primary psoriasis safety pool **(Table 2)**
- Rates of serious AEs, AEs leading to discontinuation, and AEs of safety interest were low in the LIMMitless study and remained comparable with the rates observed in the primary psoriasis safety pool **(Table 2)**
- There were no cases of systemic Candida infection, inflammatory bowel disease, or active tuberculosis

Table 2. Treatment-Emergent Adverse Event Summary

	Primary Psoriasis Safety Pool 16 Weeks[a]		LIMMitless Study ≤304 Weeks
	RZB 150 mg N = 1306	Placebo N = 300	Continuous RZB 150 mg N = 897
Events (events/100 PYs)	PYs = 402.2	PYs = 92.0	PYs = 4453.0
Any TEAE	1279 (318.0)	261 (283.7)	6372 (143.1)
Serious AE	40 (9.9)	16 (17.4)	294 (6.6)
AE leading to discontinuation of study medication	11 (2.7)	9 (9.8)	72 (1.6)
Deaths	2 (0.5)	0	8 (0.2)[b]
TEAEs of safety interest			
Adjudicated MACE	1 (0.2)	1 (1.1)	16 (0.4)[c]
Serious infections	7 (1.7)	1 (1.1)	48 (1.1)
Malignant tumors			
Including NMSC	6 (1.5)	1 (1.1)	37 (0.8)
Excluding NMSC	3 (0.7)	0	19 (0.4)
Serious hypersensitivity reactions	0	0	3 (<0.1)[d]

AE, adverse event; MACE, major adverse cardiac event; NMSC, nonmelanoma skin cancer; PYs, patient-years; RZB, risankizumab; TEAE, treatment-emergent AE.
[a]Primary psoriasis safety pool includes NCT02054481,[7] UltIMMa-1,[2] UltIMMa-2,[2] IMMhance (NCT02728532),[8] and IMMvent trials.[5]
[b]Due to natural causes (n = 1), car accident (n = 1), cardiopulmonary arrest (n = 1), sudden cardiac death (n = 1), secondary to cardiac issues/pacemaker (n = 1), cause unknown (n = 2), COVID-19 (n = 1); no deaths were determined by the investigator to be related to RZB.
[c]MACE rate in the LIMMitless study is consistent with the incidence rate of MACE in the Psoriasis Longitudinal Assessment and Registry (PSOLAR; 0.57 E/100PY; 95% CI, 0.50–0.65).[9]
[d]Serious hypersensitivity reactions (none of which were determined by the investigator to be related to RZB) were paraphenylenediamine allergy (n = 1; mild, attributed to hair dye application), generalized microbial eczema (n = 1; moderate, attributed to prolonged duration of generalized eczema and lack of response to treatment with hydrocortisone), and Stevens-Johnson syndrome (n = 1; severe, attributed to addition of chlorpromazine).