Maintenance of Clinical Response With Continued Risankizumab Treatment for Moderate-to-Severe Psoriasis Through 304 Weeks: Interim Analysis of the LIMMitless Open-Label Extension Study

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OBJECTIVE

To evaluate the long-term maintenance of efficacy and safety of risankizumab through 304 weeks of continuous treatment among patients who received risankizumab 150 mg in the phase 3 UltIMMa-1 or UltIMMa-2 studies and continued into the LIMMitless open-label extension study

CONCLUSIONS

Most patients treated with continuous risankizumab maintained Psoriasis Area and Severity Index (PASI) 90 or PASI 100 responses from entry into the open-label extension study through 304 additional weeks in the LIMMitless study

Mean PASI improvement rates remained durable through 304 weeks of treatment

The safety profile of continuous risankizumab treatment in patients with moderate-to-severe plaque psoriasis was consistent with previously reported findings from the LIMMitless study[1]

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BACKGROUND

- Interleukin (IL)-23 plays a key role in the development and maintenance of psoriatic lesions[2]
- Risankizumab is a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits IL-23 by binding to its p19 subunit and is approved for the treatment of moderate-to-severe plaque psoriasis[3]
- Through its clinical trial program, risankizumab demonstrated superior efficacy vs placebo at week 16 and other psoriasis treatments at weeks 16–52[1]; however, additional data on the maintenance of response with long-term risankizumab treatment are needed
- This interim analysis of LIMMitless,[1] an ongoing phase 3, open-label extension (OLE) study, evaluated the long-term maintenance of clinical response with risankizumab through 304 weeks of treatment

METHODS

Study Design and Treatment

- LIMMitless (open-**L**abel extension study to assess the safety and efficacy of r**I**sankizu**M**ab for **M**a**I**n**T**enance in moderate-to-severe p**L**aqu**E** type p**S**oria**S**is; NCT03047395) is an ongoing, phase 3, single-arm, multicenter, international, OLE study[1]
- This 304-week interim analysis included patients who were randomized to receive risankizumab 150 mg at weeks 0 and 4 and every 12 weeks thereafter in the double blind, phase 3, 52-week UltIMMa-1 or UltIMMa-2 studies, completed the UltIMMa-1 or UltIMMa-2 studies, and enrolled into the LIMMitless study in which patients receive risankizumab 150 mg every 12 weeks[1]

Assessments

- Efficacy was assessed through week 304 by:
  - Mean percent improvement from baseline in Psoriasis Area and Severity Index (PASI)
  - Proportion of patients achieving ≥90% or 100% improvement in PASI (PASI 90/100)
- Safety was assessed by monitoring adverse events through the data cutoff date (May 22, 2023)

Statistical Analysis

- Missing efficacy data were imputed using modified nonresponder imputation (mNRI), last observation carried forward (LOCF), or observed cases (OC) methodology
  - For 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

RESULTS

Patients

- Among 598 patients who initially received risankizumab treatment for 52 weeks in the UltIMMa-1 or UltIMMa-2 studies, 525 continued open-label risankizumab treatment in the LIMMitless OLE study

Table 1. Patient Demographics and Baseline Characteristics[a]

Characteristic	Continuous RZB N = 525
Male, n (%)	364 (69.3)
Age, years, mean (SD)	47.7 (13.3)
Race, n (%)	
White	393 (74.9)
Asian	106 (20.2)
Black	16 (3.0)
Other[b]	10 (1.9)
Weight, kg, mean (SD)	89.9 (22.1)
BMI, kg/m^2, mean (SD)	30.4 (6.8)
PASI, mean (SD)	20.4 (7.6)
sPGA of severe (score of 4), n (%)	101 (19.2)
BSA, mean (SD), involvement, %	25.8 (15.4)
Psoriatic arthritis,[c] n (%)	143 (27.2)
Prior biologic therapy, n (%)	196 (37.3)

BMI, body mass index; BSA, body surface area; PASI, Psoriasis Area and Severity Index; RZB, risankizumab; sPGA, static Physician's Global Assessment.
[a]Baseline assessment at the start of the UltIMMa-1 or UltIMMa-2 studies.
[b]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and multirace.
[c]Includes both diagnosed and suspected.

- Baseline demographics and disease characteristics at entry into the UltIMMa-1 or UltIMMa-2 studies were consistent with the population of patients with moderate-to-severe plaque psoriasis **(Table 1)**

Efficacy

- At OLE study entry, most patients (451, 85.9%) achieved PASI 90 and 320 patients (61.0%) achieved PASI 100 by mNRI; PASI 90/100 responses were maintained through week 304 **(Table 2)**

Table 2. Maintenance of PASI Response With Continuous Risankizumab Among Week-52 Responders

Patients, n/N (%)	OLE Study Entry (Week 52)[a]	Week 304[b]		
		mNRI	LOCF	OC
PASI 90	451/525 (85.9)	422/451 (93.6)	418/451 (92.7)	302/322 (93.8)
PASI 100[c]	320/525 (61.0)	209/320 (65.3)	258/320 (80.6)	183/229 (79.9)

LOCF, last observation carried forward; mNRI, modified nonresponder imputation; OC, observed cases; OLE, open-label extension; PASI, Psoriasis Area and Severity Index; PASI 90/100, ≥90%/100% improvement in PASI.
[a]By mNRI.
[b]Total duration of risankizumab therapy (52 weeks during the UltIMMa-1 and UltIMMa-2 studies and 252 weeks of the LIMMitless OLE study).
[c]Differences in the response rates for mNRI vs LOCF/OC for PASI 100 may be due to the mixed-effect model imputation of most patients with missing data as nonresponders.

- Mean PASI improvement from baseline was generally consistent from OLE study entry (95.6% for both LOCF and OC) through week 304 (LOCF, 95.9%; OC, 96.3%; **Figure 1**)
- At week 304, 86.7%–88.8% of patients achieved PASI 90 **(Figure 2)** and 58.9%–66.8% of patients achieved PASI 100 **(Figure 3)**

Safety

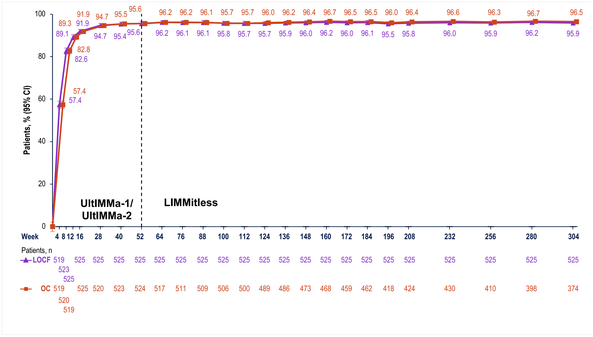
- Risankizumab was well tolerated through the data cutoff date (up to 324 weeks of treatment) with a safety profile consistent with that observed during the 52-week UltIMMa-1 and UltIMMa-2 studies **(Table 3)**

Table 3. Safety Overview for Patients Continuing Risankizumab Treatment in the LIMMitless OLE Study

TEAE, events/100 PY	UltIMMa-1/2 Studies RZB (n = 598) (PY = 618.0)[4]	LIMMitless Study RZB→RZB (n = 525) (PY = 2920.0)
Any AE	1409 (228.0)	3840 (131.5)
Serious AE	58 (9.4)	191 (6.5)
Severe AE	47 (7.6)	158 (5.4)
AEs leading to study drug discontinuation	5 (0.8)	59 (2.0)
Serious infections	11 (1.8)	30 (1.0)
Active tuberculosis	0	0
Adjudicated MACE	2 (0.3)	11 (0.4)[a]
Malignant tumors	3 (0.5)	34 (1.2)
Excluding NMSC	0	19 (0.7)[b]
Serious hypersensitivity	0	3 (0.1)[c]
AEs leading to death	2 (0.3)	7 (0.2)[d]

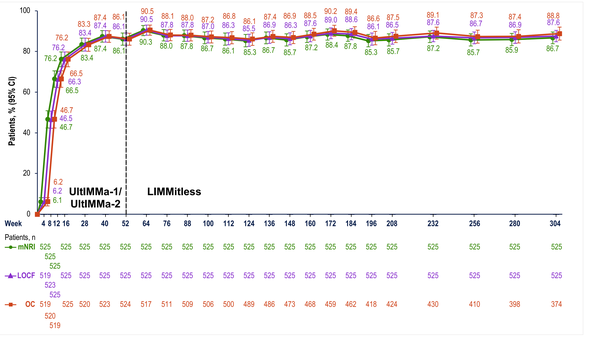
AE, adverse event; MACE, major adverse cardiac event; NMSC, nonmelanoma skin cancer; OLE, open-label extension; PY, patient-years; TEAE, treatment-emergent AE.
[a]MACE rate in the LIMMitless study is consistent with the incidence rate of MACE in the Psoriasis Longitudinal Assessment and Registry (PSOLAR; 0.57 E/100PY; 95% CI, 0.51–0.64).[5]
[b]Malignancy types excluding NMSC were skin (n = 5), colorectal (n = 4), breast (n = 3), prostate (n = 3), urothelial (n = 2), and uterine (n = 2).
[c]Serious hypersensitivity reactions (all considered unrelated to study drug) 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 Bactrim).
[d]Due to accident (n = 1), cardiovascular event (n = 1), cardiac arrest (n = 1), sudden cardiac death (n = 1), cause unknown (n = 2), and COVID-19 infection (n = 1); none related to risankizumab.

Figure 1. Mean Percent Improvement in PASI Over Time



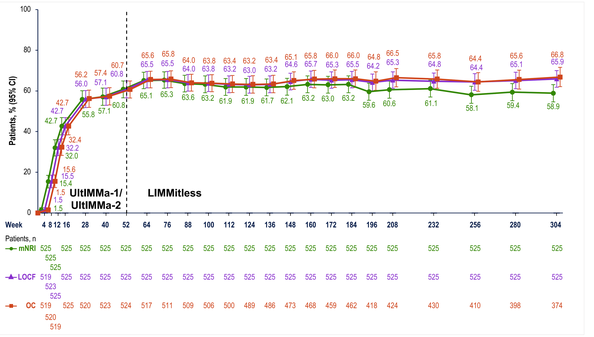
LOCF, last observation carried forward; OC, observed cases; PASI, Psoriasis Area and Severity Index.
Error bars represent the 95% CI. If they are not visible, they are smaller than the symbol.

Figure 2. Achievement of PASI 90 Over Time



LOCF, last observation carried forward; mNRI, modified nonresponder imputation; OC, observed cases; PASI 90, ≥90% improvement in Psoriasis Area and Severity Index.
Error bars represent the 95% CI. If they are not visible, they are smaller than the symbol.

Figure 3. Achievement of PASI 100 Over Time



LOCF, last observation carried forward; mNRI, modified nonresponder imputation; OC, observed cases; PASI 100, 100% improvement in Psoriasis Area and Severity Index.
Error bars represent the 95% CI. If they are not visible, they are smaller than the symbol.