Long-term safety and efficacy of risankizumab for the treatment of moderate-to-severe plaque psoriasis: Interim analysis of the LIMMitless open-label extension trial up to 5 years of follow-up

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Background: Psoriasis is a chronic, inflammatory skin disease often requiring long-term therapy.

Objective: To evaluate the long-term safety and efficacy of risankizumab in patients with psoriasis.

Methods: LIMMitless is an ongoing phase 3, open-label extension study evaluating the long-term safety and efficacy of continuous risankizumab 150 mg every 12 weeks for adults with moderate-to-severe plaque psoriasis following multiple phase 2/3 base studies. This interim analysis assessed safety (ie, monitored treatment-emergent adverse events [TEAEs]) through 304 weeks. Efficacy assessments included determining the proportion of patients who achieved ≥90% or 100% improvement in Psoriasis Area and Severity Index (PASI 90/100), static Physician's Global Assessment of clear/almost clear (sPGA 0/1), and Dermatology Life Quality Index of no effect on patient's life (DLQI 0/1) through 256 weeks.

Results: Among 897 patients randomized to risankizumab in the base studies, 706 were still ongoing at data cutoff. Rates of TEAEs, TEAEs leading to discontinuation, and TEAEs of safety interest were low. At week 256, 85.1%/52.3% of patients achieved PASI 90/100, respectively, 85.8% achieved sPGA 0/1, and 76.4% achieved DLQI 0/1.

Limitations: Open-label study with no placebo or active-comparator group.

Conclusions: Long-term continuous risankizumab treatment for up to 5 years was well tolerated and demonstrated high and durable efficacy. (J Am Acad Dermatol 2023;89:1149-58.)

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INTRODUCTION

Psoriasis is a chronic, immune-mediated, inflammatory skin condition characterized by red, scaly plaques and varies in severity from small, localized areas to complete body coverage.[1] Given the chronicity and severity of the disease, psoriasis can negatively influence patients' psychologic well-being, which may substantially affect their overall quality of life.[2] Biologic therapies have demonstrated effectiveness for the initial treatment of psoriasis, but these therapies may show diminished response over time.[3] The durability and sustainability of long-term biologic therapy are of interest to many health care providers.

CAPSULE SUMMARY

- Risankizumab—an anti-interleukin-23 monoclonal antibody—is approved to treat moderate-to-severe plaque psoriasis in adults. Long-term safety and efficacy data regarding interleukin-23 inhibitors are limited.
- Risankizumab's safety profile remained favorable and consistent with profiles reported in short-term studies, with sustained high rates of efficacy through almost 5 years of continuous therapy.

Interleukin (IL)-23 plays an important role in the pathogenesis and maintenance of psoriatic lesions.[4] Risankizumab is a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits IL-23 by binding to its p19 subunit, and it is approved for the treatment of moderate-to-severe plaque psoriasis.[5] In multiple phase 2/3 clinical trials, risankizumab demonstrated superior efficacy vs placebo at week 16[6-8] and other psoriasis treatments at weeks 16 to 52, including ustekinumab,[6] fumaric acid esters,[9] adalimumab,[10] secukinumab,[11] and methotrexate.[12]

LIMMitless (NCT03047395; 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) is an ongoing, phase 3, open-label extension study. In a previous interim analysis of the LIMMitless study, risankizumab was well tolerated and demonstrated durable long-term efficacy beyond 3 years of continuous use.[13] Herein, we report the latest interim update on the LIMMitless study through almost 5 years of continuous use.

METHODS

Study design and treatment

Detailed descriptions of the LIMMitless study design, patients, assessments, and statistical analyses were reported in a previous study.[13] Briefly, LIMMitless is an ongoing, phase 3, single-arm, multicenter, open-label extension study following multiple phase 2/3 base studies (UltIMMa-1/NCT02684370, UltIMMa-2/NCT02684357, SustaIMM/NCT03000075, NCT03255382, IMMvent/NCT02694523, or IMMhance/NCT02672852).[6-10] Patients who were initially randomized to receive subcutaneous risankizumab 150 mg and completed a double-blind, placebo-controlled, phase 2/3 base study were eligible to continue receiving open-label risankizumab 150 mg every 12 weeks for an additional 252 weeks. Efficacy and safety assessments were performed every 12 weeks until week 156 and every 24 weeks thereafter. This interim analysis assessed safety until the data cutoff date (November 1, 2021; up to 304 weeks of treatment) and efficacy until 256 weeks of continuous risankizumab treatment.

The study protocol, informed consent forms, and recruitment materials were approved by central (Advarra IRB Services) and local independent ethics committees and/or institutional review boards at each study site before patient enrollment. The studies were conducted in accordance with the International Conference for Harmonisation guidelines, applicable regulations, and the Declaration of Helsinki. All patients provided written informed consent before screening.

Patients

Eligible patients were adults with a history of moderate-to-severe chronic plaque psoriasis who had completed a preceding study. Detailed descriptions of the inclusion and exclusion criteria have been reported.[13]

Assessments

Safety assessments throughout the study included monitoring of reported adverse events (AEs). Treatment-emergent AEs (TEAEs), defined as AEs with onset or worsening after the first dose of risankizumab and up to 140 days after the last dose, were summarized using numbers and percentages of patients, tabulated using Medical Dictionary for Regulatory Activities system organ class and preferred terms (version 24.0), and calculated as exposure-adjusted event rates (events/100 patient-years [E/100 PY]).

Abbreviations used:

AEs:	adverse events
ADA:	antidrug antibodies
DLQI 0/1:	Dermatology Life Quality Index of no effect on patient's life
E/100 PY:	events/100 patient-years
IL:	interleukin
LOCF:	last observation carried forward
mNRI:	modified nonresponder imputation
NAb:	neutralizing antibodies
NMSC:	nonmelanoma skin cancer
OC:	observed cases
TEAE:	treatment-emergent adverse event
PASI:	Psoriasis Area and Severity Index
PSOLAR:	Psoriasis Longitudinal Assessment Registry
PY:	patient-years
sPGA 0/1:	static Physician's Global Assessment of clear or almost clear

Efficacy assessments included determining the proportion of patients achieving a ≥90%/100% improvement from baseline in the Psoriasis Area and Severity Index (PASI 90/PASI 100), the proportion of patients achieving an absolute PASI <3 and mean improvement in PASI from baseline, and the proportion of patients who achieved static Physician's Global Assessment of clear or almost clear (sPGA 0/1), Dermatology Life Quality Index of no effect on patient's life (DLQI 0/1), ≥4-point improvement in DLQI from baseline, and both PASI 90 and DLQI 0/1.

Risankizumab plasma concentrations were measured using samples collected before dosing on visits at weeks 48, 96, 156, and 204; antidrug antibodies (ADAs), including neutralizing antibodies (NAb), were evaluated using a validated electrochemiluminescence assay, as previously described.[14] The impact of immunogenicity on risankizumab plasma concentration, safety (incidence of hypersensitivity and injection-site reactions), and efficacy (proportion of patients achieving PASI 90 or sPGA 0/1) was assessed.

Statistical analysis

Safety and efficacy were assessed in all patients who received ≥1 dose of risankizumab in the LIMMitless study. Data were presented using summary statistics and analyzed using the SAS software (SAS Institute Inc.). Efficacy was summarized using 3 statistical methods (as previously described[13]) as follows: (1) modified nonresponder imputation (mNRI), (2) last observation carried forward (LOCF), and (3) observed cases (OC). In the mNRI method, nonresponse was only imputed for patients with treatment failures (defined as patients who discontinued the treatment because of worsening of psoriasis), and a mixed-effect model was used to impute missing data from patients without treatment failures.

RESULTS

Patients

Of 955 patients randomized to receive risankizumab 150 mg in the base studies, 897 continued into the LIMMitless study and 706 (78.7%) were still ongoing at the time of data cutoff (Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g). Median exposure of risankizumab treatment was 5.3 years. In the LIMMitless study, the most frequent reasons for study discontinuation were withdrawal by the patient (5.8%) and TEAEs (5.7%); no specific pattern was noted regarding the reasons for withdrawal or type of TEAEs. Baseline demographics and disease characteristics (as previously reported[13]) were representative of the psoriasis population (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g). The mean (SD) patient age was 46.9 (13.5) years, and 70.6% of patients were males. At baseline, patients had a mean PASI of 20.5 and a mean DLQI score of 13.9; 80.6% and 18.6% of patients had a moderate or severe sPGA score, respectively. At baseline, 37.8% of patients had received prior biologic treatment.

Safety

A broader population consisting of all patients who received ≥1 dose of risankizumab in the LIMMitless study, regardless of treatment group in the base study, included 2170 patients with 10,071.9 patient years (PYs) of risankizumab exposure. Herein, we report results from 897 patients who received continuous risankizumab 150 mg from baseline of the base study and included patients with at least 3 years of continuous risankizumab treatment with the standard labeled dosing regimen. When comparing with safety for the primary psoriasis safety pool (16 weeks, 402.2 PY) with long-term results (up to 304 weeks; 4297.7 PY), the cumulative rates of TEAEs (318.0 and 155.3 E/100 PY, respectively), serious AEs (9.9 and 6.9 E/100 PY, respectively), and TEAEs leading to discontinuation (2.7 and 1.7 E/100 PY, respectively) were similar or declined over time (Table I). An enhanced content video summarizing the safety results is presented in Supplementary Video 1 (available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g). The most frequently reported TEAEs were nasopharyngitis (13.7 E/100 PY), upper respiratory tract infection (8.0 E/100 PY), and arthralgia (4.3 E/100 PY; Supplementary Table II, available via Mendeley

Table I. Summary of treatment-emergent adverse events

	Primary psoriasis safety pool 16 wk*		LIMMitless study ≤304 wk
	RZB 150 mg *N* = 1306 PY = 402.2	Placebo *N* = 300 PY = 92.0	Continuous RZB 150 mg *N* = 897 PY = 4297.7
Parameter	**E (E/100 PY)**		
Any TEAE	1279 (318.0)	261 (283.7)	6673 (155.3)
Serious AE	40 (9.9)	16 (17.4)	296 (6.9)
AE leading to discontinuation of study medication	11 (2.7)	9 (9.8)	74 (1.7)
Deaths	2 (0.5)	0	8 (0.2)†
TEAEs of safety interest			
Adjudicated MACE	1 (0.2)	1 (1.1)	17 (0.4)‡
CVA	0	1 (1.1)	7 (0.2)§
Serious infections	7 (1.7)	1 (1.1)	49 (1.1)
Active TB	0	1 (1.1)	0
Malignant tumors (including NMSC)	6 (1.5)	1 (1.1)	37 (0.9)¶
NMSC	3 (0.7)	1 (1.1)	18 (0.4)
Excluding NMSC	3 (0.7)	0	19 (0.4)
Serious hypersensitivity reactions	0	0	3 (<0.1)‖
Candida infection	2 (0.5)	0	25 (0.6)**
Systemic Candidiasis	0	0	0
Opportunistic infections excluding herpes zoster and TB	0	0	7 (0.2)
Inflammatory bowel disease	0	0	1 (<0.1)
Crohn disease	0	0	0
Ulcerative colitis	0	0	1 (<0.1)
Psychiatric disorders	13 (3.2)	8 (8.7)	115 (2.7)
Suicidal ideation	0	1 (1.1)	0
Suicide attempt	1 (0.2)	0	1 (<0.1)

AE, adverse event; *CVA*, cerebrovascular accident; *E,* events; *MACE,* major adverse cardiac event; *NMSC,* nonmelanoma skin cancer; *PY,* patient-years; *RZB,* risankizumab; *TB,* tuberculosis; *TEAE,* treatment-emergent adverse event.

*Primary psoriasis safety pool includes data from UltIMMa-1,[6] UltIMMa-2,[6] IMMhance,[8] IMMvent,[10] and NCT0205448120 studies.[27]

†Due to natural causes (*n* = 1), accident (*n* = 1), cardiovascular event (*n* = 1), cardiac arrest (*n* = 1), sudden cardiac death (*n* = 1), unknown cause (*n* = 2), and COVID-19 infection (*n* = 1); no deaths were related to study drug.

‡MACE rate in the LIMMitless study is consistent with the incidence rate of MACE reported in the Psoriasis Longitudinal Assessment and Registry (PSOLAR, 0.57 E/100 PY; 95% CI, 0.50-0.65).[15]

§CVA rate in the LIMMitless study is consistent with the incidence rate of CVA reported in the Psoriasis Longitudinal Assessment and Registry (PSOLAR, 0.20 E/100 PY; 95% CI, 0.16-0.25).[15]

¶Malignancies were adenocarcinoma of colon (*n* = 1), basal cell carcinoma (*n* = 10), bladder cancer (*n* = 1), Bowen disease (*n* = 1), breast cancer (*n* = 3), colon cancer (*n* = 1), colorectal adenocarcinoma (*n* = 2), endometrial cancer (*n* = 1), gastric cancer (*n* = 1), invasive breast carcinoma (*n* = 1), lentigo maligna (*n* = 1), malignant melanoma in situ (*n* = 2), metastatic colon cancer (*n* = 1), metastatic squamous cell carcinoma (*n* = 1), transitional cell carcinoma (*n* = 1), prostate cancer (*n* = 2), rectal cancer (*n* = 1), squamous cell carcinoma (*n* = 3), and squamous cell carcinoma of the skin (*n* = 3).

‖Serious hypersensitivity reactions (all considered unrelated to the 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), Stevens-Johnson syndrome (*n* = 1; severe, attributed to addition of chlorpromazine).

**Twenty-five *Candida*-related events were reported in 21 patients. More than half occurred in patients with known risk factors such as diabetes, steroid use, and prior *Candida* episodes. None were serious or led to discontinuation of study drug.

at https://data.mendeley.com/datasets/jtz2cnyp4g). The most frequently reported serious AE was osteoarthritis (0.2 E/100 PY). Among the TEAEs leading to study drug discontinuation, 29.2% were considered possibly related to the study drug (Supplementary Table III, available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g).

Regarding the areas of safety interest, incidence of TEAEs remained stable and numerically low in the 16-week primary psoriasis safety pool and 304-week long-term data sets (major adverse cardiovascular events [0.2 and 0.4 E/100 PY, respectively], malignancies [1.5 and 0.9 E/100 PY, respectively], and serious infectious [1.7 and 1.1 E/100 PY, respectively]). Rates of adjudicated major adverse cardiovascular events (including cerebrovascular accident, myocardial infarction, and cardiovascular death) and cerebrovascular accident were consistent with reference rates for moderate-to-severe plaque psoriasis in the Psoriasis Longitudinal Assessment Registry

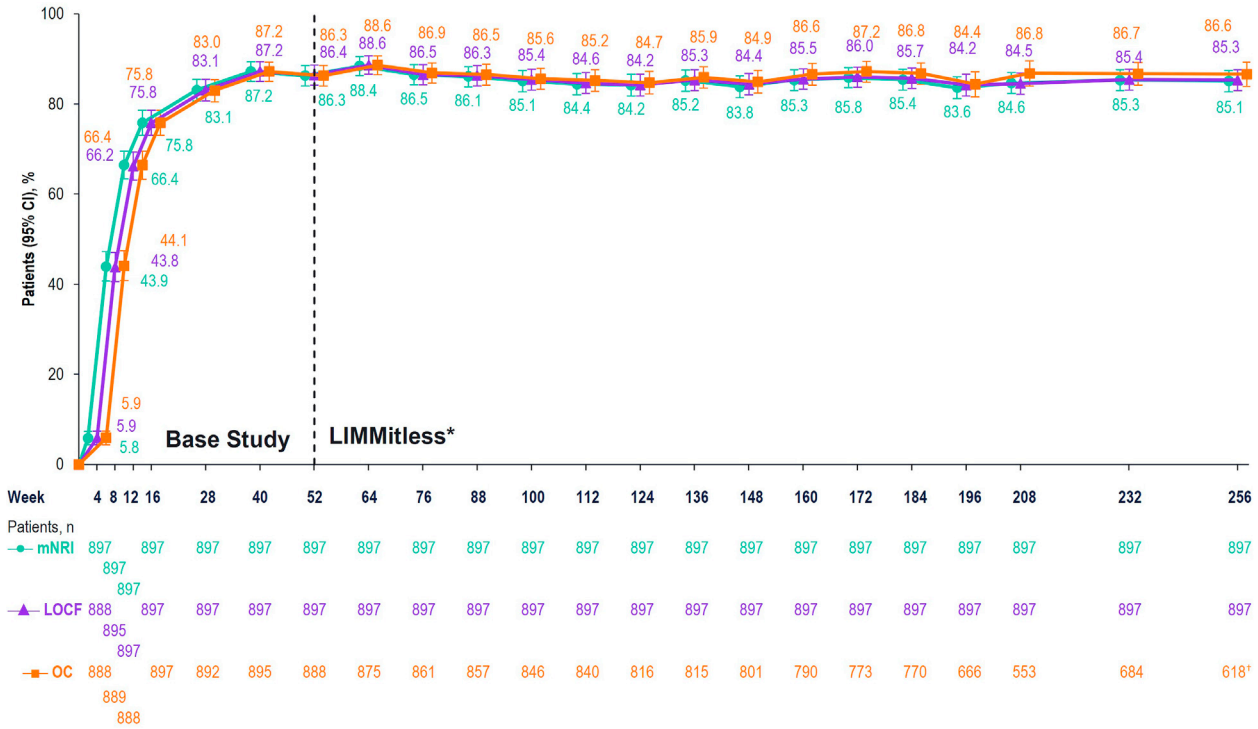

Fig 1. Proportion of patients achieving PASI 90 response. *Because of the differences in base study lengths, some patients were enrolled in the LIMMitless study before 52 weeks. †Of the 706 ongoing patients, 618 completed the assessment visit at week 256; 41 ongoing patients have reached the assessment window but not yet completed the assessment visit at week 256. *LOCF,* last observation carried forward; *mNRI,* modified nonresponder imputation; *OC,* observed cases; *PASI 90,* ≥90% improvement in Psoriasis Area and Severity Index from baseline.

(PSOLAR; 0.57 E/100 PY [95% CI: 0.50-0.65] and 0.20 E/100 PY [95% CI: 0.16-0.25], respectively).[15]

Almost half of the malignancies were nonmelanoma skin cancer (NMSC), and the ratio of squamous cell carcinoma to basal cell carcinoma was ~1:2. Most malignancies, excluding NMSC, observed in the LIMMitless study (0.4 E/100 PY) were those that were commonly observed in the general population (colon, breast, melanoma, and prostate; all <0.1 E/100 PY).[16] Rates of malignancies, excluding NMSC, were consistent with the reference rates for moderate-to-severe plaque psoriasis in PSOLAR (0.48-0.84 E/100 PY[17]) and lower than those reported in the MarketScan database cohort study for psoriasis (1.4 E/100 PY).[18]

Through up to 304 weeks, the most frequently reported treatment-emergent serious infection was diverticulitis (<0.1 E/100 PY; Supplementary Table IV, available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g). Most serious infections did not lead to study drug discontinuation. Rates of serious infections were consistent with those reported for moderate-to-severe plaque psoriasis in PSOLAR (0.93-2.91 E/100 PY).[17] There were no reports of active tuberculosis. All opportunistic infections were *Candida* infections, none of which were serious or led to treatment discontinuation. The incidence of fungal infections was 3.0 E/100 PY; none were serious and most were tinea infections. No systemic *Candida* infection was reported. *Candida* infections were reported at a rate of 0.6 E/100 PY; the most frequently reported locations were oral (0.2 E/100 PY), esophageal (0.1 E/100 PY), and vulvovaginal (0.1 E/100 PY). Incidence of herpes zoster was low (0.4 E/100 PY); 2 events were serious and considered related to risankizumab, but neither event led to study drug discontinuation. None of the 3 serious hypersensitivity reactions were considered related to risankizumab and there were no reports of adjudicated anaphylaxis. The standardized mortality ratio for treatment-emergent deaths at the time of data cutoff was 0.31 (95% CI: 0.13-0.61).

Efficacy

The efficacy of risankizumab was maintained throughout 256 weeks of continuous treatment. Consistent results were observed using all 3 statistical

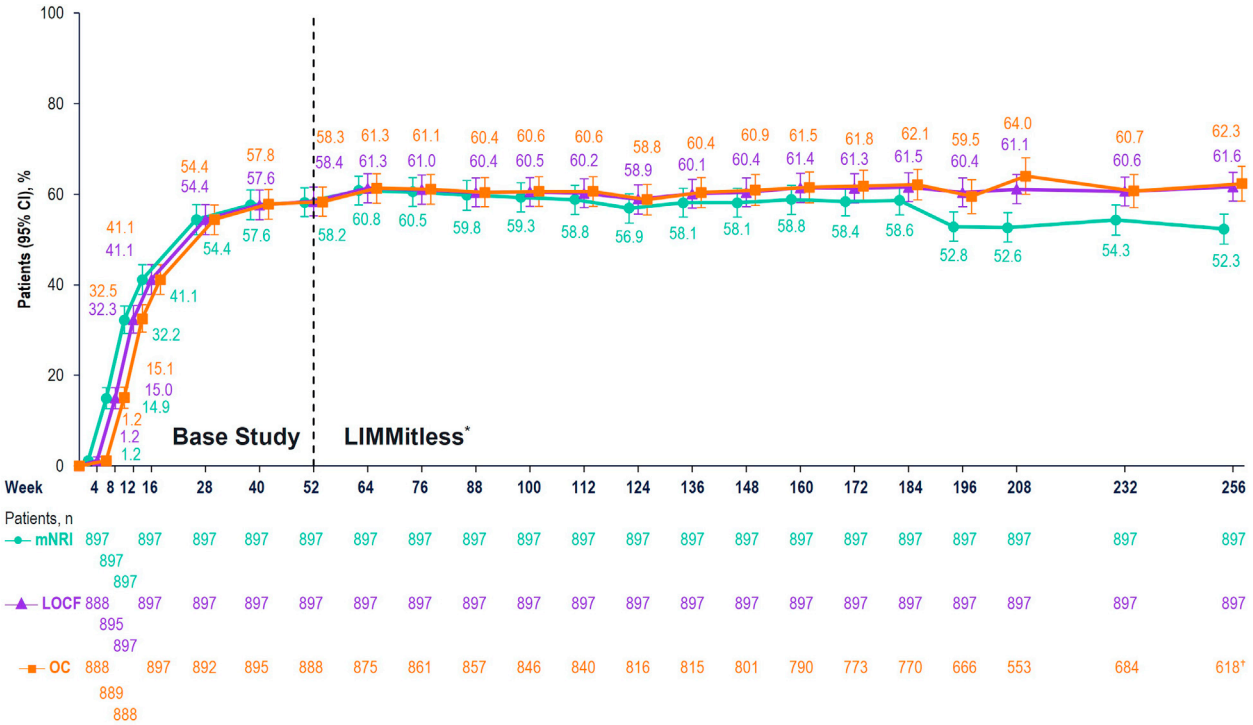

Fig 2. Proportion of patients achieving PASI 100 response. *Because of the differences in base study lengths, some patients were enrolled in the LIMMitless study before 52 weeks.[†]Of the 706 ongoing patients, 618 completed the assessment visit at week 256; 41 ongoing patients have reached the assessment window but not yet completed the assessment visit at week 256. *LOCF,* last observation carried forward; *mNRI,* modified nonresponder imputation; *OC,* observed cases; *PASI 100,* 100% improvement in Psoriasis Area and Severity Index from baseline.

analyses (mNRI, LOCF, and OC). As previously reported,[13] >86% and >58% of patients had achieved PASI 90 and PASI 100 on completion of the base studies (week 52; Figs 1 and 2). At week 256, >85% and >52% of patients achieved PASI 90 and PASI 100, respectively. At week 256, >90% of patients achieved absolute PASI <3 (Supplementary Fig 2, available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g). Furthermore, mean change from baseline in PASI remained ≥95% from weeks 28 to 256 (Supplementary Fig 3, available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g). Response rates were also consistently high for sPGA 0/1; >82% of patients achieved sPGA 0/1 at week 12 of the base studies, and efficacy was maintained through 256 weeks (Fig 3). An enhanced content video summarizing the efficacy results is presented in Supplementary Video 2 (available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g).

Pharmacokinetics and immunogenicity

Geometric mean risankizumab trough plasma concentrations were maintained throughout the study (range, 1.34-1.58 μg/mL from weeks 48 to 204). Approximately 14.4% (123/855) and 5.0% (43/855) of evaluable patients developed treatment-emergent ADAs and NAbs, respectively. Mean risankizumab plasma trough concentrations in ADA- or NAb-positive patients were generally similar or slightly lower than those in patients who did not develop ADA or NAb during the study. Incidence of hypersensitivity and injection-site reactions through week 304 were lower in both ADA- or NAb-positive patients compared with ADA- or NAb-negative patients (Supplementary Table V, available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g). Similar proportions of ADA-positive and -negative patients achieved PASI 90 or sPGA 0/1 at week 256, whereas the proportion of patients achieving PASI 90 or sPGA 0/1 was lower in NAb-positive patients than in NAb-negative patients (Supplementary Table VI, available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g).

Health-related quality of life

Consistent improvements in patient-reported outcomes measuring health-related quality of life were observed with long-term risankizumab treatment. By week 16 of treatment, >66% of patients achieved

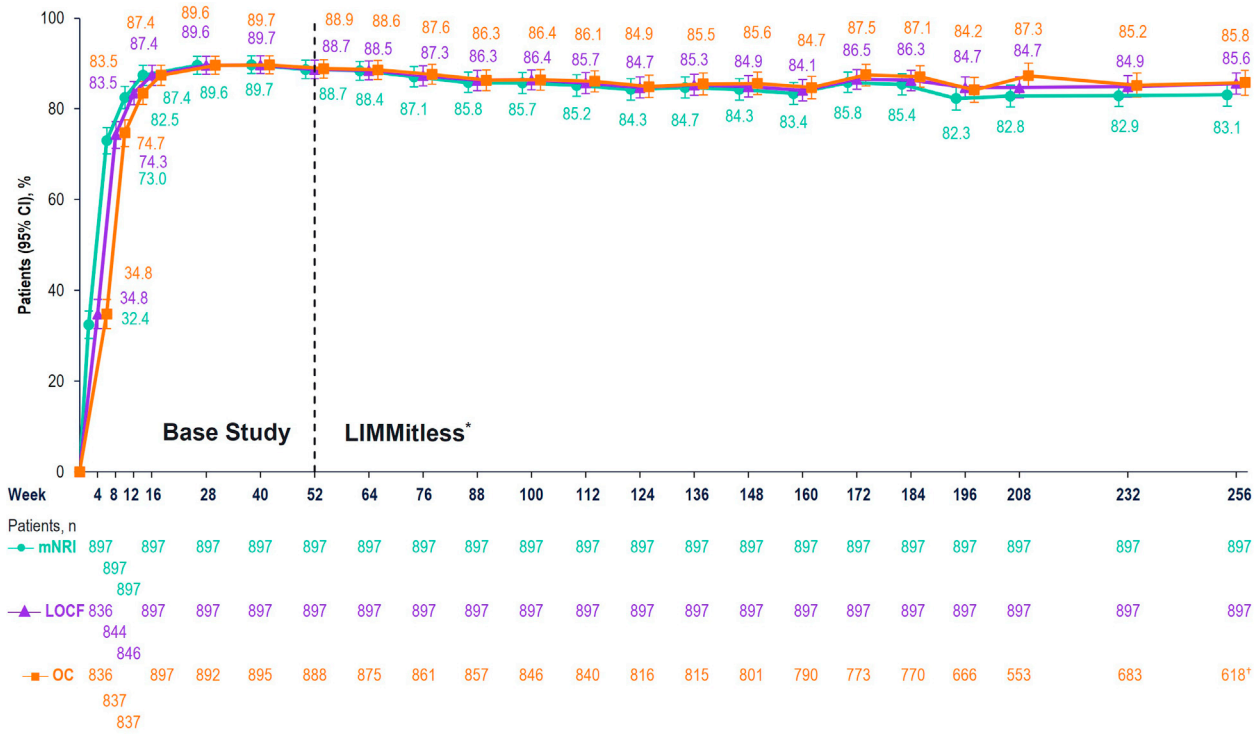

Fig 3. Proportion of patients achieving sPGA 0/1. *Because of the differences in base study lengths, some patients were enrolled in the LIMMitless study before 52 weeks.†Of the 706 ongoing patients, 618 completed the assessment visit at week 256; 41 ongoing patients have reached the assessment window but not yet completed the assessment visit at week 256. *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).

DLQI 0/1, and these proportions further increased and were maintained in >76% of patients through week 256 (Fig 4). At week 256, >96% of patients receiving continuous risankizumab achieved the minimal clinically important difference threshold value for DLQI (≥4-point improvement; Supplementary Fig 4, available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g).[19] Furthermore, >70% of patients achieved both PASI 90 and DLQI 0/1 by week 256 (Supplementary Fig 5, available via Mendeley at https://data.mendeley.com/datasets/jtz2cnyp4g).

DISCUSSION

Through 5 years of continuous treatment with risankizumab, long-term safety profiles remained similar to those observed in previous psoriasis studies, with no additional or unexpected safety signals. Additionally, rates of TEAEs through week 304 of continuous treatment did not increase. Exposure-adjusted rates of TEAEs, including those of TEAEs of safety interest or TEAEs leading to discontinuation, were low and consistent with those observed in the primary psoriasis safety pool.

Patients experienced long-term, clinically relevant improvements in disease severity and skin clearance. High clinical responses (PASI 90, PASI 100, and sPGA 0/1) were sustained over 256 weeks of treatment, regardless of the analysis method used. Of note, a disparate decline over time is expected to impact the most stringent outcome (PASI 100) when using mNRI analysis relative to OC or LOCF. As long-term extension studies progress, increasing missed visits and patient attrition have a disproportional influence on the mNRI imputation method compared with OC and LOCF, thus affecting PASI 100 achievement per mNRI disproportionately. Clinical improvements in skin clearance are associated with improvements in patients' quality of life.[20] More than three-quarters of patients reported no impact of psoriasis on daily life, as measured by DLQI 0/1 throughout the LIMMitless study. Overall, these findings demonstrate the consistent and robust long-term efficacy of risankizumab in a large study population.

Biologic therapies have the potential to induce undesirable immune responses resulting in the formation of ADAs and NAbs, which can alter

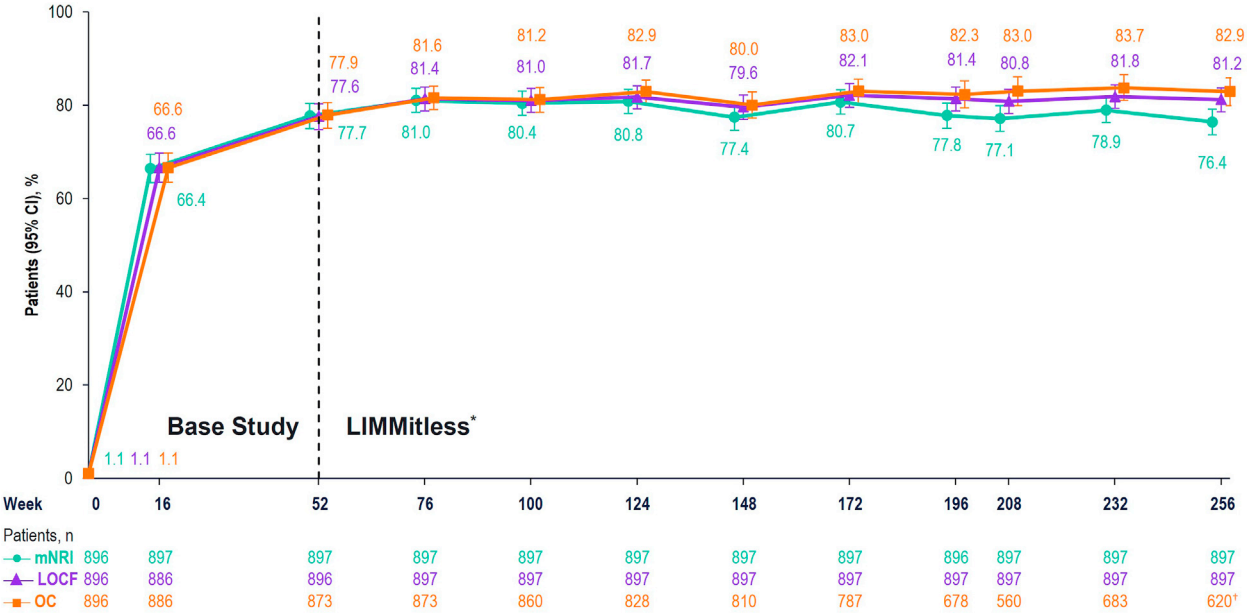

Fig 4. Proportion of patients achieving DLQI 0/1. *Because of the differences in base study lengths, some patients were enrolled in the LIMMitless study before 52 weeks.†Of the 706 ongoing patients, 620 completed the assessment visit at week 256; 39 ongoing patients have reached the assessment window but not yet completed the assessment visit at week 256. *DLQI 0/1,* Dermatology Life Quality Index of no effect on quality of life; *LOCF,* last observation carried forward; *mNRI,* modified nonresponder imputation; *OC,* observed cases.

pharmacologic and/or pharmacokinetic properties of the drug and impact overall drug safety and efficacy.[21] In this study, although NAb presence in a small number of patients appeared to have a mild impact on risankizumab plasma concentration and efficacy, PASI 90 and sPGA0/1 rates were consistent, regardless of ADA status at week 256. Neither ADA nor NAb presence increased AEs of hypersensitivity or injection-site reactions, indicating no impact of immunogenicity on safety.

In this study, the rates of sustained response observed with risankizumab were comparable or greater than those observed for other IL-23 inhibitors for the treatment of plaque psoriasis after 4 to 5 years of continuous therapy. In the phase 3 reSURFACE 1 and 2 studies evaluating tildrakizumab, 65.9% to 69.5% of patients achieved PASI 90 after 244 weeks of treatment.[22] In the phase 3 VOYAGE 1 and 2 studies evaluating guselkumab, 82.0% to 84.1% of patients achieved PASI 90 at week 252.[23] In the phase 3 PHOENIX 2 study of the IL-12/23 inhibitor ustekinumab, 50.0% to 55.0% of patients achieved PASI 90 at week 244.[24] We found that over 85.0% of patients in the current study achieved PASI 90 with risankizumab at week 256. Efficacy comparisons with other psoriasis treatments have been previously reported in several meta-analyses; however, comparisons are limited because of differences in study designs and the lack of active-controlled comparator groups.[25,26]

Strengths of this study include long-term evaluation of a large population of patients for up to 5 years of continuous risankizumab treatment with low rates of discontinuation. Results were generally consistent using 3 different statistical analysis methods to handle missing data. Limitations of this study include the absence of a control group and the open-label nature of the study, which may introduce reporting bias for patients and attribution bias for investigators. Nonetheless, a high proportion of patients who continued risankizumab treatment from the base studies maintained clinical response for up to 5 years of therapy.

Overall, these comprehensive results demonstrate a consistent long-term safety profile and high and durable clinical response with continuous risankizumab treatment for up to 5 years. In addition, the benefits of continuous risankizumab treatment may have long-term positive effects on overall health-related quality of life in patients with psoriasis. The LIMMitless study is still ongoing; however, the findings from this interim analysis highlight that the long-term use of risankizumab is a viable option for the safe and effective management of moderate-to-severe plaque psoriasis.

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Conflicts of interest

Dr Papp has received research funds from or is a consultant and/or speaker for AbbVie, Amgen, Arcutis, Astellas, Bausch Health, Baxalta, Baxter, BI, Bristol Myers Squibb, Celgene, Coherus, Dermavant, Dermira, EMD Serono, Evelo, 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. He is a committee member for PSOLAR and PURE registries. Dr Blauvelt has served as a speaker (received honoraria) for AbbVie, Bristol Myers Squibb, Lilly, Pfizer, Regeneron, and Sanofi, served as a scientific adviser (received honoraria) for AbbVie, Abcentra, Aclaris, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Dermavant, EcoR1, Escient, Evelo, Evommune, Forte, Galderma, HighlightII Pharma, Incyte, InnoventBio, Janssen, Landos, Leo, Lilly, Merck, Novartis, Pfizer, Rani, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, TLL Pharmaceutical, TrialSpark, UCB, Union, Vibliome, and Xencor, and has acted as a clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Concert, Dermavant, Evelo, Evommune, Galderma, Incyte, Janssen, LEO, Lilly, Merck, Novartis, Pfizer, Regeneron, Sun Pharma, and UCB. Dr Puig has received consultancy/speaker's honoraria from and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Baxalta, Biogen, BI, Celgene, EMD Serono, Gebro, Janssen, LEO, Lilly, Merck, Mylan, Novartis, Pfizer, Regeneron, Roche, Samsung, Sandoz, Sanofi, and UCB. Dr Ohtsuki has received honoraria or fees for serving on advisory boards or speakers' bureaus, fees for consulting, and grants for investigator activities from AbbVie, Amgen, BI, Bristol Myers Squibb, Celgene, Eisai, Janssen, Kyowa Kirin, LEO, Lilly, Maruho, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Sun Pharma, Taiho, Torii, and UCB. Dr Beissert has received honoraria as an advisory board member and/or speaker for AbbVie, Actelion, Almirall, Amgen, Bristol Myers Squibb, Celgene, Galderma, GSK, Janssen, LEO, Lilly, Menlo Therapeutics, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, and UCB. Dr Gooderham is or has been an investigator, adviser, and/or speaker for AbbVie, Akros, Amgen, AnaptysBio, Arcutis, Aristea, Bausch, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus BioSciences, Dermira, Dermavant, Galderma, GlaxoSmithKline, Janssen, Kyowa Kirin, LEO, Lilly, Medimmune, Merck, Meiji, Moonlake, Nimbus, Novartis, Pfizer, Regeneron, Reistone, Roche, Sanofi Genzyme, Sun Pharma, UCB, and Ventyx. Dr Amin is a consultant and speaker for AbbVie, Amgen, Janssen, Lilly, Pfizer, Sanofi Genzyme, and UCB. Ms Liu, Dr Wu, Dr Azam, Dr Stakias, Dr Espaillat, Dr Sinvhal, Dr Soliman, Dr Pang, and Dr Chen are full-time employees of AbbVie Inc., and may hold AbbVie stock, stock options, and/or patents. Dr Lebwohl is an employee of Mount Sinai and receives research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Dermavant Sciences, Eli Lilly, Incyte, Janssen Research & Development LLC, Ortho Dermatologics, Regeneron, and UCB Inc., and is a consultant for Aditum Bio, Almirall, AltruBio Inc., AnaptysBio, Arcutis Inc., Aristea Therapeutics, Avotres Therapeutics, Brickell Biotech, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Celltrion, Corevitas, Dermavant Sciences, Dr. Reddy, EPI, Evommune Inc., Facilitation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Helsinn, Hexima Ltd., Incyte, LEO, Meiji Seika Pharma, Mindera, Pfizer, Seanergy, Strata, Trevi, and Verrica.

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