Bimekizumab efficacy and safety in patients with moderate to severe plaque psoriasis: Two-year interim results from the open-label extension of the randomized BE RADIANT phase 3b trial

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Background: Bimekizumab is a monoclonal IgG1 antibody that inhibits interleukin-17A/F. Bimekizumab is more efficacious than secukinumab over 1 year in the treatment of psoriasis.

Objective: Evaluate the safety and efficacy of bimekizumab through 2 years in patients with moderate to severe plaque psoriasis.

Methods: The BE RADIANT phase 3b randomized controlled trial consisted of a 48-week double-blinded period, where patients received bimekizumab (320 mg every 4 or 8 weeks) or secukinumab (300 mg weekly to Week 4, then every 4 weeks), and an open-label extension (OLE). From Week 48, all patients received bimekizumab in the OLE.

Results: At Week 48, more patients achieved complete skin clearance (PASI 100; modified non-responder imputation) with bimekizumab than secukinumab (74.8% vs 52.8%). PASI 100 responses were maintained to Week 96 in continuous bimekizumab patients (70.8%); patients who switched from secukinumab to bimekizumab had increased rates at Week 96 (76.6%). The most common adverse events were: nasopharyngitis, oral candidiasis, and urinary tract infection. Safety data were consistent with the known safety profile of bimekizumab.

Limitations: Limited racial diversity; overlap with the COVID-19 pandemic.

Conclusions: High PASI 100 responses achieved with bimekizumab over 48 weeks were sustained through Week 96; secukinumab patients who switched to bimekizumab achieved similar responses by Week 96. (J Am Acad Dermatol 2023;89:486-95.)

Key words: bimekizumab; clinical trial; efficacy; open-label; plaque psoriasis; psoriasis; safety; secukinumab.

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INTRODUCTION

The interleukin (IL)-17 cytokine family, comprising isoforms IL-17A–F, mediates an intercellular signaling network regulating local tissue homeostasis.[1] Overexpression of IL-17s is a pathologic driver for many inflammatory diseases, including psoriasis.[2] IL-17A and IL-17F have been implicated in psoriasis;[3] although IL-17A is more potent, IL-17F expression is higher in psoriatic skin.[4]

IL-17A inhibitors, such as secukinumab and ixekizumab, are used to treat psoriasis.[5] IL-17A and IL-17F are homodimeric cytokines, which can also form IL-17A/F heterodimers.[6] Dual neutralization of IL-17F and IL-17A could be more efficacious than neutralization of IL-17A alone.[7,8] Bimekizumab is a monoclonal IgG1 antibody that selectively inhibits IL-17A and IL-17F, which was efficacious and safe in the treatment of moderate to severe plaque psoriasis in phase 3 trials.[7,9-11]

BE RADIANT (NCT03536884) was the first phase 3 trial comparing dual IL-17A and IL-17F inhibition via bimekizumab with IL-17A inhibition alone via secukinumab.[12] Per results from Year 1 of BE RADIANT, bimekizumab was more effective than secukinumab over 48 weeks, including in complete skin clearance (100% improvement in Psoriasis Area and Severity Index [PASI] from baseline; PASI 100). Bimekizumab was well-tolerated, with nasopharyngitis, oral candidiasis, and upper respiratory tract infection as the most commonly reported adverse events (AEs).[12]

Given the chronic nature of psoriasis and the potential loss of clinical response over time with biologics, considering the long-term safety and efficacy of bimekizumab is important.[13] As IL-17 inhibitors are a relatively new antipsoriatic treatment, within-class switching data are sparse, with existing studies limited by small cohort sizes and short durations.[14-18] Therefore, establishing the safety and efficacy of bimekizumab following prior IL-17A inhibition via secukinumab is also important. Here, we report bimekizumab efficacy and safety through 2 years in BE RADIANT.

CAPSULE SUMMARY

- Long-term treatment with, or switching between, biologics may result in loss of response in patients with psoriasis.
- The interleukin-17A/F inhibitor bimekizumab showed high rates of response over 96 weeks. Switching from secukinumab (interleukin-17A inhibitor) to bimekizumab was successful. The most common adverse events were nasopharyngitis, urinary tract infection, and *Candida* infections.

METHODS

Patients

Patients who completed the 48-week double-blinded period of BE RADIANT were eligible to continue in the open-label extension (OLE). Full baseline eligibility criteria have been published.[12] Patients entering the OLE signed new consent forms, providing written informed consent documented in accordance with local regulations, the International Conference on Harmonization-Good Clinical Practice requirements, and the ethical principles originating from the Declaration of Helsinki.

Study design

BE RADIANT is a phase 3b, multicenter trial, with a 16-week double-blinded initial treatment period, 32-week double-blinded maintenance period, and ongoing OLE (Fig 1).

Patients were initially randomized 1:1 to bimekizumab 320 mg every 4 weeks (Q4W) or secukinumab 300 mg weekly to Week 4, then Q4W (label dosing at time of study design).[19] At Week 16, patients receiving bimekizumab were re-randomized 1:2 to bimekizumab 320 mg Q4W or every 8 weeks (Q8W) to Week 48. Secukinumab-randomized patients continued on secukinumab Q4W until Week 48, at which point they switched to open-label bimekizumab. Full double-blinded study details have been reported.[12] The OLE began at Week 48 and is ongoing at the time of writing, lasting until Week 144 with final doses at Week 136 (following protocol amendment, the OLE will be optionally extended by 48 weeks for US/Canadian sites). We report the results of a Week 96 interim analysis.

On OLE entry, all patients received open-label bimekizumab. Dose frequency (320 mg Q4W or Q8W) was dependent on Week 48 PASI 90 (≥90% improvement from baseline in PASI) response and double-blinded period treatment (Fig 1); patients and study sites remained blinded to double-blinded period treatments.

All patients who did not achieve PASI 90 at Week 48 received bimekizumab Q4W upon OLE entry. Patients who received bimekizumab Q8W in the maintenance period and achieved PASI 90 at Week 48 continued on Q8W. Patients who received bimekizumab Q4W or secukinumab in the maintenance period and achieved PASI 90 at Week 48 were randomized 1:1 to bimekizumab Q4W or Q8W.

Following protocol amendment, resulting from phase 3 data on the similar efficacy of bimekizumab Q8W and Q4W maintenance treatment, all patients

Abbreviations used:

AE:	adverse event
BSA:	body surface area
DLQI:	Dermatology Life Quality Index
EAIR:	exposure-adjusted incidence rate
IGA:	Investigator's Global Assessment
IL:	interleukin
mNRI:	modified non-responder imputation
NRI:	non-responder imputation
OC:	observed case
OLE:	open-label extension
PASI:	Psoriasis Area and Severity Index
PASI 90/100:	≥90%/100% improvement from baseline in PASI
PY:	patient-years
Q4W:	every 4 weeks
Q8W:	every 8 weeks
SAE:	serious adverse event
TEAE:	treatment-emergent adverse event

receiving bimekizumab Q4W were switched to bimekizumab Q8W at the next scheduled visit at or after Week 64.

Efficacy

Efficacy outcomes are reported for patients who entered the OLE, grouped by baseline randomization to bimekizumab (continuous bimekizumab patients) or secukinumab (secukinumab/bimekizumab patients).

We report percentages of patients achieving PASI 100, Investigator's Global Assessment (IGA) 0/1 (clear or almost clear) with ≥2-category improvement from baseline, body surface area (BSA) <1%, and absolute PASI ≤2 (key treat-to-target outcomes),[20,21] PASI 90, and Dermatology Life Quality Index (DLQI) of 0/1 (no effect of skin disease on patient's quality of life)[22] from Weeks 0–96. Outcomes are also reported among patients who received bimekizumab Q4W to Week 16, Q8W through Week 48, and continued receiving Q8W in the OLE (Q4W/Q8W); this dosing regimen is approved for plaque psoriasis for the vast majority of patients with plaque psoriasis, dependent on weight, by several regulatory agencies, including the European Medicines Agency.[23,24]

Safety

Treatment-emergent AEs (TEAEs), serious AEs (SAEs), and TEAEs leading to discontinuation, each adjusted according to patient exposure duration, were pre-specified outcomes. TEAEs were AEs with start dates on or following the first dose of study treatment through the final dose of study treatment, plus 140 days. If determining whether AEs were treatment-emergent was not possible due to partial dates, they were assumed to be treatment-emergent. TEAEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA) v19.0. SAEs were AEs leading to ≥1 of death, life-threatening event, significant or persistent disability/incapacity, congenital anomaly/birth defect, important medical event, or initial/prolonged hospitalization.

Safety topics of interest were infections (serious, opportunistic, fungal, and tuberculosis), inflammatory bowel disease, suicidal ideation and behavior, malignancies, hypersensitivity, neutropenia, major adverse cardiovascular events, and liver enzyme elevations (adjudication details provided in the Supplementary Materials, available via Mendeley at https://data.mendeley.com/datasets/tk3ds9x7gc/1).

Safety data, presented as exposure-adjusted incidence rates (EAIRs) of new cases per 100 patient-years (PY), are reported in Year 2 for continuous bimekizumab and secukinumab/bimekizumab patients. Year 2 safety data are reported from Week 48 to data cut-off (April 20, 2021; the date on which the last ongoing patient completed Week 96). On this date, the furthest time point reached by any patient was Week 132. Year 1 (Week 0–48) safety data have been reported previously and are presented here as EAIRs for comparison.[12]

Statistical analysis

Data are reported for patients who entered the OLE; efficacy outcomes are reported through Week 96, and safety outcomes up to the data cut-off (20 April 2021). At the data cut-off, some patients had completed Week 96; safety data beyond Week 96 are included for these patients. Missing data were accounted for using modified non-responder imputation (mNRI), NRI, and observed case (OC). For mNRI, patients who discontinued due to lack of efficacy or AEs deemed treatment-related by investigators were considered non-responders; multiple imputation was used for all other missing data. Efficacy data reported in the text use mNRI. An alternative mNRI analysis, in which only patients who discontinued due to lack of efficacy were considered nonresponders, with multiple imputation used for all other missing data, is presented in Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/tk3ds9x7gc/1.

RESULTS

Patients

At baseline, 743 patients were randomized to bimekizumab (*N* = 373) or secukinumab (*N* = 370; Fig 1). Of these, 336 of 373 (90.1%) and 318 of 370 (85.9%) entered the OLE, respectively; demographics and baseline characteristics were consistent across randomization groups and Q4W/Q8W patients (*N* = 177; Supplementary Table I, available via

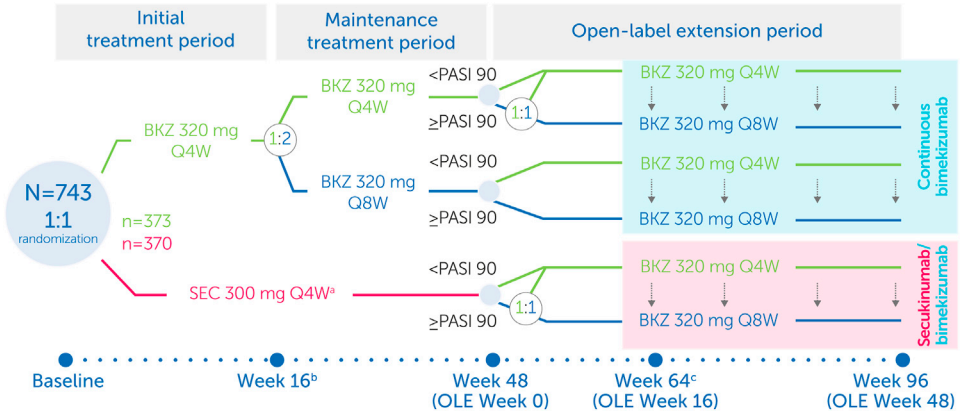

Fig 1. BE RADIANT study design up to Week 96. In this analysis, BKZ Q4W and Q8W treatment arms are pooled. **A,** SEC 300 mg was administered at baseline, Weeks 1, 2, 3, and 4, then Q4W for the remainder of the double-blinded treatment period; **B,** Re-randomization at Week 16 was due to a protocol amendment, hence some patients had already passed Week 16 at the time of protocol amendment implementation; **C,** Following a protocol amendment, all patients receiving BKZ 320 mg Q4W in the OLE period were switched to BKZ 320 mg Q8W at the next scheduled clinic visit on or after the Week 64 visit. *BKZ*, Bimekizumab; *OLE*, open-label extension; *PASI 90*, ≥90% improvement from baseline in Psoriasis Area and Severity Index; *Q4W*, every 4 weeks; *Q8W*, every 8 weeks; *SEC*, secukinumab.

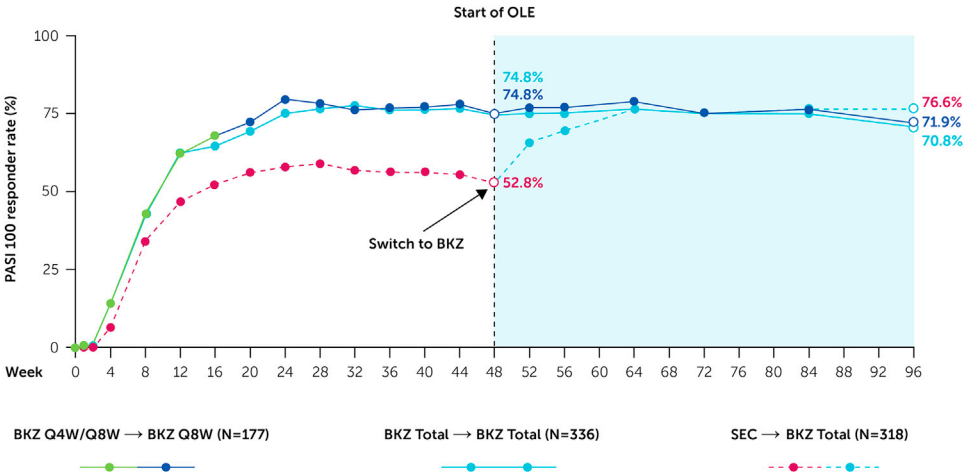

Fig 2. PASI 100 responses through Weeks 0–96 by initial randomization group (modified non-responder imputation). Data presented are for patients who entered the OLE only. Patients who discontinued due to lack of efficacy or an adverse event deemed to be treatment-related were counted as non-responders, multiple imputation was used for all other missing data. Q4W/Q8W patients are the subgroup of continuous BKZ patients who received BKZ Q4W to Week 16, followed by BKZ Q8W through to Week 96. *BKZ*, Bimekizumab; *OLE*, open-label extension; *PASI 100*, 100% improvement in Psoriasis Area and Severity Index from baseline; *Q4W*, every 4 weeks; *Q8W*, every 8 weeks; *SEC*, secukinumab.

Mendeley at https://data.mendeley.com/datasets/tk3ds9x7gc/1). Patient disposition is shown in Supplementary Figure 1, available via Mendeley at https://data.mendeley.com/datasets/tk3ds9x7gc/1.

Efficacy

The proportion of continuous bimekizumab patients achieving PASI 100 was maintained with a slight numerical decrease from Week 48–96: 74.8% achieved PASI 100 at Week 48, and 70.8% at Week 96; results were consistent for Q4W/Q8W patients (mNRI; Fig 2). For patients switching from secukinumab to bimekizumab at Week 48, PASI 100 rates increased from Week 48 (52.8%) to Week 96 (76.6%).

Proportions of continuous bimekizumab patients achieving IGA 0/1 were 94.0% at Week 48 and 90.9%

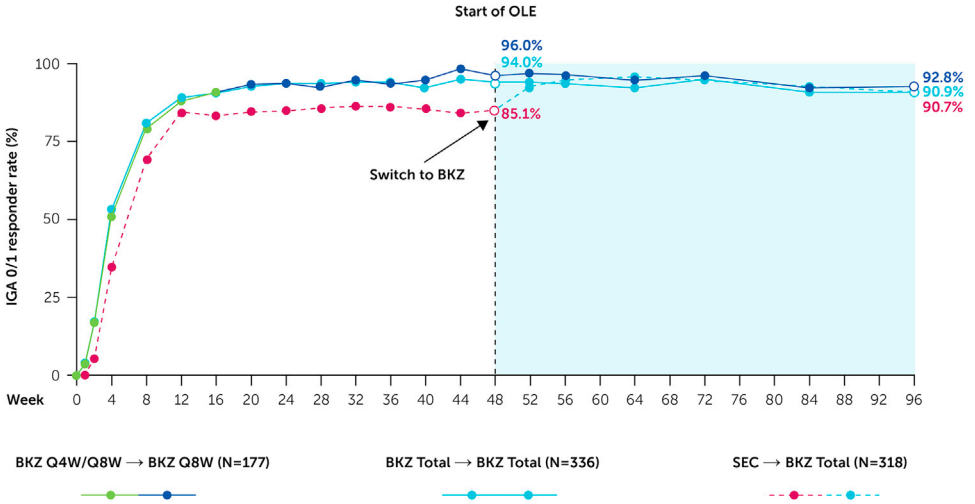

Fig 3. IGA 0/1 responses through Weeks 0–96 by initial randomization group (modified non-responder imputation). Data presented are for patients who entered the OLE only. Patients who discontinued due to lack of efficacy or an adverse event deemed to be treatment-related were counted as non-responders, multiple imputation was used for all other missing data. Q4W/Q8W patients are the subgroup of continuous BKZ patients who received BKZ Q4W to Week 16, followed by BKZ Q8W through to Week 96. *BKZ*, Bimekizumab; *IGA 0/1*, clear or almost clear with improvement of ≥2 categories from baseline in the Investigator's Global Assessment; *OLE*, open-label extension; *Q4W*, every 4 weeks; *Q8W*, every 8 weeks; *SEC*, secukinumab.

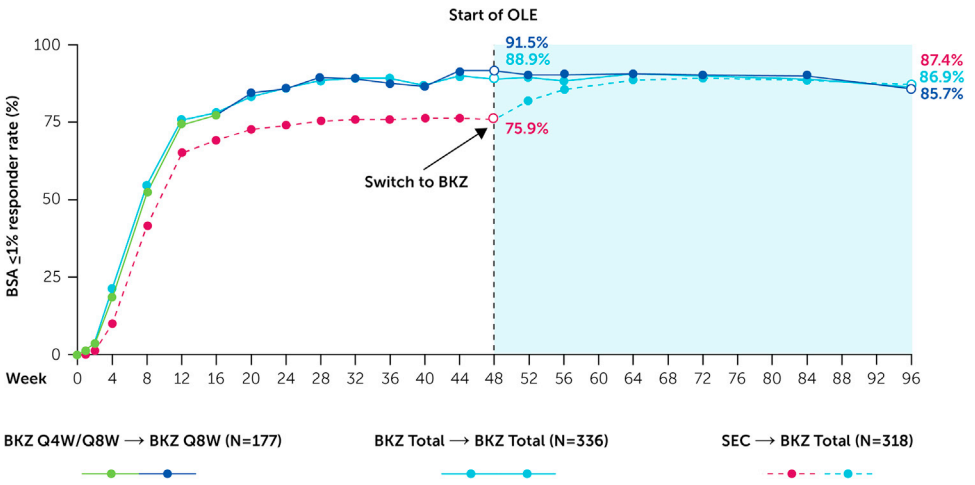

Fig 4. BSA ≤1% responses through Weeks 0–96 by initial randomization group (modified non-responder imputation). Data presented are for patients who entered the OLE only. Patients who discontinued due to lack of efficacy or an adverse event deemed to be treatment-related were counted as non-responders, multiple imputation was used for all other missing data. Q4W/Q8W patients are the subgroup of continuous BKZ patients who received BKZ Q4W to Week 16, followed by BKZ Q8W through to Week 96. *BKZ*, Bimekizumab; *BSA ≤1%*, ≤1% body surface area affected; *OLE*, open-label extension; *Q4W*, every 4 weeks; *Q8W*, every 8 weeks; *SEC*, secukinumab.

at Week 96. Consistent trends were seen in Q4W/Q8W patients (Fig 3). IGA 0/1 rates were sustained among secukinumab/bimekizumab patients following the switch to bimekizumab (Week 48: 85.1%; Week 96: 90.7%).

The proportion of continuous bimekizumab patients achieving BSA ≤1% at Week 96 was 86.9%, maintained from 88.9% at Week 48; trends were similar for Q4W/Q8W patients (Fig 4). Secukinumab/bimekizumab patients had increased

Table I. Exposure-adjusted incidence rates of TEAEs through Year 1 and Year 2 by initial randomization group

Event	Year 1, EAIR per 100 PY [95% CI]		Year 2, EAIR per 100 PY [95% CI]	
	Bimekizumab *N* = 373	Secukinumab *N* = 370	Continuous Bimekizumab *N* = 336	Secukinumab/ Bimekizumab *N* = 318
Any TEAE	282.5 [252.4, 315.1]	229.8 [204.5, 257.2]	131.6 [115.5, 149.2]	158.7 [139.4, 180.0]
Serious TEAEs	6.6 [4.2, 10.0]	6.5 [4.0, 9.9]	5.0 [3.0, 7.9]	5.3 [3.2, 8.4]
Discontinuation due to TEAEs	3.9 [2.1, 6.6]	3.0 [1.5, 5.6]	2.2 [0.9, 4.3]	2.9 [1.4, 5.3]
Severe TEAEs	7.9 [5.2, 11.6]	4.6 [2.6, 7.5]	5.6 [3.4, 8.6]	5.0 [2.9, 8.0]
Death	0.3 [0.0, 1.6]	0.3 [0.0, 1.7]	0	0.3 [0.0, 1.6]*
Most Common TEAEs				
Nasopharyngitis	30.0 [24.1, 37.0]	36.9 [30.1, 44.8]	11.8 [8.5, 16.1]	12.1 [8.6, 16.6]
Oral candidiasis	24.2 [18.9, 30.4]	3.4 [1.7, 6.0]	7.8 [5.1, 11.3]	12.2 [8.6, 16.6]
Urinary tract infection	7.6 [4.9, 11.2]	6.8 [4.3, 10.3]	4.5 [2.6, 7.3]	5.7 [3.4, 8.9]
Coronavirus infection	0	0	3.8 [2.1, 6.4]	3.8 [2.0, 6.5]
Upper respiratory tract infection	13.1 [9.5, 17.7]	11.5 [8.0, 15.9]	3.9 [2.1, 6.5]	3.6 [1.8, 6.2]
TEAEs of Interest				
Serious infections	2.4 [1.0, 4.7]	2.4 [1.0, 4.8]	0.8 [0.2, 2.4]	1.5 [0.5, 3.4]
Opportunistic infections	1.2 [0.3, 3.0]	0.3 [0.0, 1.7]	0.8 [0.2, 2.4]	1.2 [0.3, 3.0]
Fungal infections	38.7 [31.7, 46.7]	11.1 [7.7, 15.5]	20.0 [15.4, 25.6]	22.4 [17.4, 28.5]
Candida infections	26.9 [21.3, 33.6]	5.2 [3.1, 8.4]	11.2 [7.9, 15.4]	15.6 [11.5, 20.6]
Oral candidiasis	24.2 [18.9, 30.4]	3.4 [1.7, 6.0]	7.8 [5.1, 11.3]	12.2 [8.6, 16.6]
Genital candidiasis	0	0.3 [0.0, 1.7]	0.3 [0.0, 1.5]	0
Oropharyngeal candidiasis	0.6 [0.1, 2.1]	0.3 [0.0, 1.7]	0	0.3 [0.0, 1.6]
Skin *Candida*	1.2 [0.3, 3.0]	0.6 [0.1, 2.2]	1.1 [0.3, 2.8]	1.5 [0.5, 3.4]
GI candidiasis†	0	0	0.8 [0.2, 2.4]	0.9 [0.2, 2.6]
Vulvovaginal candidiasis	0.9 [0.2, 2.6]	0.9 [0.2, 2.7]	1.1 [0.3, 2.8]	1.8 [0.6, 3.8]
Active tuberculosis	0	0	0	0
IBD	0.3 [0.0, 1.6]	0.3 [0.0, 1.7]	0	0
Adjudicated SIB	0.3 [0.0, 1.6]	0	0	0
Malignancies	1.5 [0.5, 3.5]	0.9 [0.2, 2.7]	0.8 [0.2, 2.4]	0.3 [0.0, 1.6]
NMSC	0.9 [0.2, 2.6]	0.9 [0.2, 2.7]	0.3 [0.0, 1.5]	0.3 [0.0, 1.6]
Serious hypersensitivity reactions	0	0	0	0.3 [0.0, 1.6]‡
Neutropenia	1.2 [0.3, 3.0]	0.9 [0.2, 2.7]	1.4 [0.4, 3.2]	0
Adjudicated MACE	0	0.6 [0.1, 2.2]	0.5 [0.1, 2.0]	0.3 [0.0, 1.6]
Hepatic events	6.7 [4.2, 10.1]	6.5 [4.0, 9.9]	3.6 [1.9, 6.1]	3.2 [1.6, 5.8]
Elevated liver enzymes TEAE	6.4 [4.0, 9.8]	5.9 [3.5, 9.2]	3.3 [1.7, 5.8]	2.0 [0.8, 4.2]
>3x ULN elevation of AST or ALT§	3.0 [1.4, 5.5]	4.6 [2.6, 7.6]	1.9 [0.8, 3.9]	2.0 [0.8, 4.2]
>5x ULN elevation of AST or ALT§	0.6 [0.1, 2.1]	0.9 [0.2, 2.6]	0.3 [0.0, 1.5]	0.3 [0.0, 1.6]
Administration and injection site reactions	5.3 [3.1, 8.5]	3.5 [1.7, 6.2]	1.6 [0.6, 3.6]	2.4 [1.0, 4.7]

ALT, Alanine aminotransferase; *AST*, aspartate aminotransferase; *CI*, confidence interval; *EAIR*, exposure-adjusted incidence rate; *GI*, gastrointestinal; *IBD*, inflammatory bowel disease; *MACE*, major adverse cardiac event; *NMSC*, non-melanoma skin cancer; *PY*, patient-years; *SIB*, suicidal ideation and behavior; *TEAE*, treatment-emergent adverse event; *ULN*, upper limit of normal.

*One death occurred which was not considered treatment-related, the patient had not consented for further clinical record details to be shared.

†These cases were all reported by the same study site, were mild to moderate in severity, and were not confirmed by biopsy or other procedures.

‡One serious hypersensitivity reaction of eczema occurred; no anaphylactic reactions occurred.

§Not all hepatic laboratory parameter elevations were reported as adverse events.

BSA ≤1% responses following the switch to bimekizumab (Week 48: 75.9%; Week 96: 87.4%).

PASI ≤2 and PASI 90 trends were similar (Supplementary Figures 1 and 2, Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/tk3ds9x7gc/1).

DLQI 0/1 response rates were maintained through Weeks 48–96 for continuous bimekizumab (Week 48:

87.4%; Week 96: 86.3%) and secukinumab/bimekizumab patients (Week 48: 80.7%; Week 96: 81.5%); trends were consistent for Q4W/Q8W patients. mNRI, NRI, and OC data for all outcomes are summarized in Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/tk3ds9x7gc/1.

Safety

Safety data from Year 2 are presented in Table I, alongside Year 1 data.[12] In Year 2, EAIRs of any TEAEs were 131.6/100 PY in continuous bimekizumab patients and 158.7/100 PY in secukinumab/bimekizumab patients, and were generally lower than EAIRs in either treatment arm through Year 1 (Table I). SAE EAIRs were 5.0 and 5.3/100 PY in continuous bimekizumab and secukinumab/bimekizumab patients and did not increase with a longer duration of bimekizumab exposure. One death occurred during Year 2 in a secukinumab/bimekizumab patient, which was not considered treatment-related. The patient had not consented to further clinical record details to be shared. The most common TEAEs were nasopharyngitis (continuous bimekizumab: 11.8/100 PY; secukinumab/bimekizumab: 12.1/100 PY), oral candidiasis (7.8/100 PY; 12.2/100 PY), and urinary tract infection (4.5/100 PY; 5.7/100 PY).

Nasopharyngitis EAIRs in both treatment groups were lower than those observed with bimekizumab and secukinumab through Year 1 (Table I; see discussion). As observed previously, most fungal infections were *Candida* infections; EAIRs of *Candida* infections and oral candidiasis in Year 2 were 11.2 and 7.8/100 PY for continuous bimekizumab patients, and 15.6 and 12.2/100 PY for secukinumab/bimekizumab patients. Most oral candidiasis events were mild or moderate; 2 led to discontinuation in secukinumab/bimekizumab patients. Gastrointestinal, genital, and oropharyngeal candidiasis rates were low (Table I). Coronavirus infection EAIRs were 3.8/100 PY for continuous bimekizumab and secukinumab/bimekizumab patients. There was 1 serious case of confirmed COVID-19 in a secukinumab/bimekizumab patient.

Serious infection rates were low (Table I); there was 1 SAE of systemic candidiasis in a secukinumab/bimekizumab patient with insulin-dependent diabetes mellitus, severe obesity, and a history of recurrent urinary tract infections. The events occurred in a setting of fungal urinary tract infection with obstruction and recent urinary tract instrumentation with bladder biopsies. This was resolved with antifungal therapy, nephrostomy, and intravenous antibiotic therapy; the patient discontinued. No cases of active tuberculosis occurred in either group.

No serious hypersensitivity reactions occurred in continuous bimekizumab patients; rates were low in secukinumab/bimekizumab patients (0.3/100 PY, corresponding to 1 serious case of eczema). No anaphylactic reactions occurred. Rates of other safety topics of interest were low (Table I). Overall, EAIRs were generally lower in Year 2 versus Year 1 for safety topics of interest.

DISCUSSION

The high levels of clinical response seen through the first 48 weeks of bimekizumab treatment were generally sustained through 96 weeks, demonstrating that the rapid responses reported previously were durable.[12] Results for physician-assessed endpoints show patients who switched from secukinumab (IL-17A inhibitor) to bimekizumab (IL-17A and F inhibitor) at Week 48 without washout or induction experienced well-tolerated and sustained improvements in clinical responses. These Week 96 responses were comparable to those in patients receiving bimekizumab continuously.

Psoriasis can significantly impact patients' quality of life and mental well-being;[25-27] when assessing efficacy, considering both patient-reported and clinical outcomes is important.[28] High DLQI 0/1 rates accompanying skin clearance reported here indicate notable and sustained improvements in quality of life with bimekizumab treatment. Rates for both continuous bimekizumab and secukinumab/bimekizumab patients increased to Week 48 and were maintained to Week 96.

In continuous bimekizumab patients, AE rates in the OLE generally decreased or stayed consistent relative to 1-year data.[12] AEs in patients who switched from secukinumab to bimekizumab were generally comparable to those seen with bimekizumab through Year 1, suggesting no additional safety risk when switching within the IL-17 inhibitor class. However, Year 2 safety data include a greater proportion of patients receiving Q8W dosing than Year 1, which has previously been associated with lower rates versus Q4W for some TEAEs; this may have contributed to the lower TEAE rates reported through Year 2.[12]

The IL-17 pathway plays a major role in host defense against fungal infections at mucosal surfaces.[29] The more complete blockage of IL-17-mediated immune pathways via dual IL-17A/F inhibition with bimekizumab has previously resulted in increased oral candidiasis rates.[12] Consistent with the safety profile of bimekizumab, oral candidiasis EAIRs increased in secukinumab/bimekizumab patients over Year 2 after switching to bimekizumab. The majority of oral candidiasis cases reported here were mild or moderate and rarely led to bimekizumab

discontinuation. Notably, continuous bimekizumab patients reported decreased *Candida* infection rates in Year 2 versus Year 1. In this analysis, 1 complex, serious case of systemic candidiasis occurred in a patient with significant risk factors. Although bimekizumab treatment is associated with a higher rate of *Candida* infections compared with other IL-17 inhibitors,[30-33] serious events are rare; a previous analysis of phase 2 and phase 3 studies pooled to include 3,110 PY of bimekizumab exposure reported only 1 serious *Candida* infection (esophageal candidiasis).[30]

Psoriasis is associated with several comorbidities, including obesity, diabetes, and hyperuricemia,[34] which can impact hepatic function. Higher-than-average alcohol consumption is common in psoriasis patients,[35] who have up to 60% greater risk of death from alcohol-related causes versus age- and sex-matched individuals in the general population.[36] EAIRs of most TEAEs of interest, including hepatic events, were low and did not increase with increased bimekizumab exposure.

Strengths of this study include its duration and large sample, enabling comprehensive analysis. Furthermore, data for a regulatory agency-approved dosing regimen (for the vast majority of patients, weight-dependent; Q4W/Q8W) are highlighted;[23,24] efficacy in this group was consistent with the overall mixed-dose group. High response rates were observed using all imputation methods considered, suggesting results were robust as a result of low discontinuation rates and minimal missing data.

While baseline characteristics were consistent across randomization groups, racial diversity was limited, potentially restricting generalizability of our findings among non-white individuals. Furthermore, this analysis includes only patients who entered the OLE; any patients who discontinued in Year 1 due to lack of efficacy or AEs are not accounted for as non-responders in the mNRI analysis here. However, the number of patients who discontinued in Year 1 was low (Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/tk3ds9x7gc/1).[12]

Data may have been impacted by the COVID-19 pandemic, overlapping with Weeks 48—96 for some patients (June 2019—March 2021). The introduction of confounding factors, including mask-wearing, social isolation, and national lockdowns, may have altered AE rates, particularly respiratory infections such as nasopharyngitis. Drawing definitive conclusions on the pandemic's effects is challenging, as each country introduced different infection control measures at varying time points.

In conclusion, the high levels of clinical responses seen through the first 48 weeks of bimekizumab treatment were sustained to Week 96. Additionally, patients switching from secukinumab to bimekizumab saw improved clinical responses at Week 96 after switching, similar to those who received 96 weeks of continuous bimekizumab. Bimekizumab was well-tolerated with longer-term exposure and in patients who switched from secukinumab without washout or induction. Overall, safety data were consistent with the known safety profile. These data indicate that longer-term bimekizumab treatment and switching from another anti-IL-17 biologic to bimekizumab are generally well-tolerated and efficacious treatment options for patients with moderate to severe plaque psoriasis.

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Data sharing statement

Underlying data from this manuscript may be requested by qualified researchers six months after product approval in the US and/or Europe, or global development is discontinued, and 18 months after trial completion. Investigators may request access to anonymized individual patient-level data and redacted trial documents, which may include: analysis-ready datasets, study protocol, annotated case report form, statistical analysis plan, dataset specifications, and clinical study report. Prior to use of the data, proposals need to be approved by an independent review panel at www.Vivli.org and a signed data sharing agreement will need to be executed. All documents are available in English only, for a pre-specified time, typically 12 months, on a password protected portal.

Conflicts of interest

Dr Strober is a consultant (honoraria) for AbbVie, Alumis, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Bristol-Myers-Squibb, Connect Biopharma, Dermavant, Eli Lilly, EPI Health, Evelo Biosciences, Immunic Therapeutics, Janssen, LEO Pharma Maruho, Meiji Seika Pharma, Mindera Health, Novartis, Ono, Pfizer, Regeneron, Sanofi-Genzyme, Sun Pharma, UCB Pharma, Union Therapeutics, Ventyxbio, vTv Therapeutics; has stock options from Connect Biopharma and Mindera Health; is a speaker for AbbVie, Eli Lilly, Incyte, Janssen, Regeneron, Sanofi-Genzyme; is a scientific codirector (consulting fee) for CorEvitas (formerly Corrona) Psoriasis Registry; is an investigator for AbbVie, Cara, CorEvitas Psoriasis Registry, Dermavant, Dermira, and Novartis; and serves as editor-in-chief (honorarium) of *Journal of Psoriasis and Psoriatic Arthritis*. Dr Paul receives consulting fees and/or grants from AbbVie, Almirall, Amgen, Aslan, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Galderma, GSK, Janssen, LEO Pharma,

Eli Lilly, Mylan, Novartis, Pierre Fabre, Pfizer, Sanofi Regeneron, and UCB Pharma. Dr Blauvelt has served as a speaker (received honoraria) for AbbVie, Arcutis, Bristol Myers Squibb, Eli Lilly, Pfizer, Regeneron, Sanofi, and UCB Pharma; served as a scientific adviser (received honoraria) for AbbVie, Abcentra, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Dermavant, EcoR1, Eli Lilly, Escient, Evelo, Evommune, Forte, Galderma, HighlightII Pharma, Incyte, InnoventBio, Janssen, Landos, LEO Pharma, Merck, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, TLL Pharmaceutical, TrialSpark, UCB Pharma, Vibliome, and Xencor; and has served as a clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Almirall, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Concert, Dermavant, Eli Lilly, Evelo, Evommune, Galderma, Incyte, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, Sun Pharma, and UCB Pharma. Dr Thaçi receives honoraria for participation on advisory boards; as a speaker and for consultancy from AbbVie, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Janssen, LEO Pharma, Morphosis, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi Genzyme, and UCB Pharma; and has research grants received from LEO Pharma and Novartis. Dr Puig received consultancy/speaker's honoraria from and/or participated in trials sponsored by AbbVie, Almirall, Amgen, Baxalta, Biogen, Boehringer Ingelheim, Celgene, Eli Lilly, Gebro, Janssen, JS BIOCAD, LEO Pharma, Merck-Serono, MSD, Mylan, Novartis, Pfizer, Regeneron, Roche, Samsung-Bioepis, Sandoz, Sanofi Genzyme, and UCB Pharma. Dr Lebwohl is an employee of Mount Sinai; receives research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen, LLC, Ortho Dermatologics, Regeneron, and UCB Pharma; and is a consultant for Aditum Bio, Almirall, AltruBio Inc, AnaptysBio, Arcutis, Inc, Aristea Therapeutics, Arrive Technologies, Avotres Therapeutics, BiomX, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant, Dr. Reddy's Laboratories, Evelo Biosciences, Evommune, Inc, Facilitation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Helsinn Therapeutics, Hexima Ltd, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Seanergy, and Verrica. Ms White, Ms Vanvoorden, and Ms Deherder are employees and shareholders of UCB Pharma. Dr Gomez is a former employee and shareholder of UCB Pharma. Dr Eyerich is a speaker and/or advisor for AbbVie, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Janssen, LEO Pharma, Pfizer, Novartis, Sanofi and UCB Pharma.

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