Bimekizumab Maintenance of Response and Safety in Patients with Moderate to Severe Plaque Psoriasis: Results from the Open-label Extension Period (Weeks 48–144) of the BE RADIANT Phase 3b Trial

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Objective

To evaluate the efficacy of bimekizumab (BKZ), as measured by complete or near-complete skin clearance using the Psoriasis Area and Severity Index (PASI), and long-term safety of BKZ in patients with moderate to severe plaque psoriasis over Weeks 48–144 of the BE RADIANT phase 3b trial.

Background

- Patients who completed the 48-week double-blind period in the BE RADIANT (NCT03536884) phase 3b trial could enter the open-label extension (OLE).[1]
- Clinical improvements in BKZ-treated patients, including patients who switched to BKZ from secukinumab (SEC), have been reported previously through Week 96 of BE RADIANT, with no unexpected safety findings.[1–3]

Methods

- This analysis included patients who were randomized to BKZ or SEC at baseline and who were enrolled in the OLE (Weeks 48–144) of the BE RADIANT phase 3b trial.
- All patients received BKZ 320 mg every 4 weeks (Q4W) or 8 weeks (Q8W) in the OLE; all switched to Q8W from Week 64 onwards (**Figure 1**).

Efficacy

- PASI response rates were evaluated for patients who were treated with BKZ or SEC until Week 48 and entered the OLE.
- Efficacy data are reported using observed case (OC), modified non-responder imputation (mNRI), and non-responder imputation (NRI).
  - For mNRI, patients discontinuing due to lack of efficacy or treatment-related adverse events were considered non-responders; multiple imputation was used for other missing data.

Safety

- Safety data, evaluated as incidence of new cases per 100 patient-years (PY), were grouped for all patients who received ≥1 BKZ dose in the OLE.
  - Data were pooled for all patients who received ≥1 BKZ dose at Week 48 or later (BKZ Total), up to the data cut-off of May 31, 2022, the date on which the last enrolled patient reached Week 144.
- Treatment-emergent adverse events (TEAEs) were coded according to MedDRA v19.0.

Results

- Baseline characteristics have been reported previously and were similar between the groups examined.[2]
- PASI responses were maintained or improved throughout the OLE period to Week 144; 89.8% of patients in the Continuous BKZ group, and 87.0% of patients who switched to BKZ from SEC, achieved PASI ≤2 at Week 144. Similarly, 68.8% of patients in the Continuous BKZ group, and 69.1% of patients in the SEC/BKZ group, achieved PASI 100 at Week 144 (**Figure 2**).
- Incidence rates of serious TEAEs and discontinuations were low (**Table 1**).
- Four deaths occurred; two from coronavirus infection in high-risk (obesity and diabetes mellitus) unvaccinated patients. None of the deaths were assessed as treatment-related.
- The most frequent fungal infection was oral candidiasis. Most oral candidiasis cases were mild or moderate (98.3%); none were serious, and three led to discontinuation.

Conclusions

Clinical improvements achieved after one year of bimekizumab treatment were maintained for up to two further years, throughout the OLE (Weeks 48–144), among patients who entered this period.

Outcomes improved and were durable to Week 144 in secukinumab-treated patients who switched to bimekizumab upon entering the OLE.

Adverse events reported over the second and third year of treatment were consistent with the safety profile of bimekizumab-treated groups reported previously over one and two years of treatment.[1,2,4]

Summary

Patients included in this analysis:

Initial Treatment Period
Randomized to BKZ Q4W or SEC Q4W

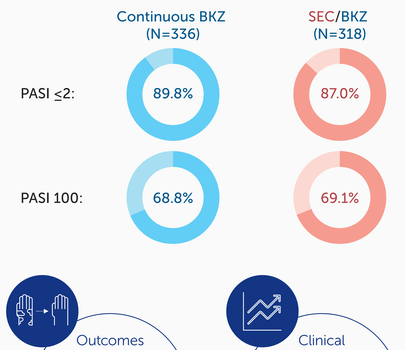
↓

Maintenance Treatment Period
Randomized to BKZ Q4W, BKZ Q8W or SEC Q4W

↓

Open-Label Extension Period
Continuous BKZ (N=336); SEC/BKZ (N=318)

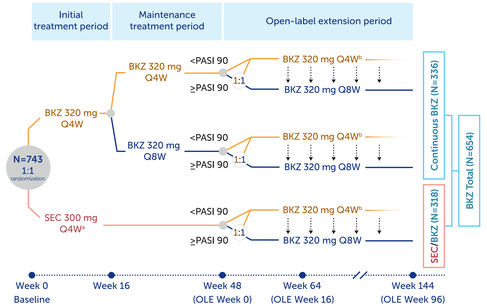
Week 144 PASI responses:



Outcomes improved and were durable to Week 144 in SEC-treated patients who switched to BKZ

Clinical improvements after one year of BKZ treatment were maintained for up to two additional years

Figure 1 BE RADIANT study design



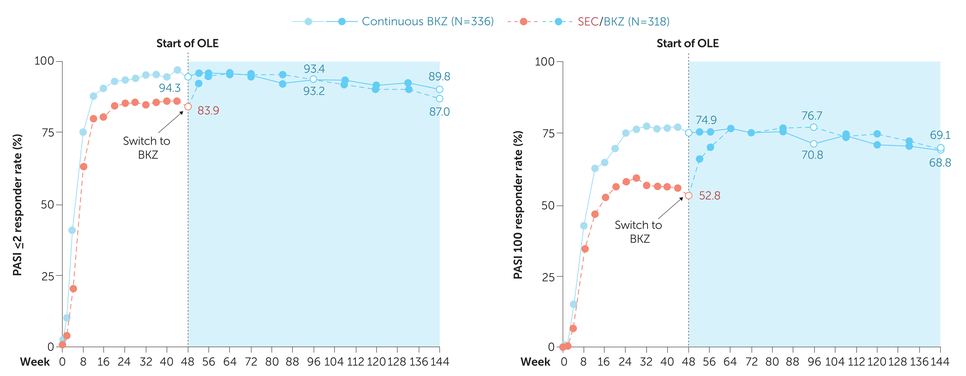
In the analysis presented, efficacy analyses include Continuous BKZ and SEC/BKZ groups, safety analyses include both groups pooled (BKZ Total). [a] SEC 300 mg was administered at baseline, weekly to Week 4, then Q4W for the remainder of the double-blind treatment period; [b] At Week 64, or the next scheduled clinic visit, after the implementation of a protocol amendment, patients switched from BKZ 320 mg Q4W to Q8W.

Table 1 Incidence rates of TEAEs through Weeks 48–144

	BKZ Total N=654 Total Exposure: 1,244 PY EAIR per 100 PY (95% CI)
Any TEAE	126.5 (116.2, 137.5)
Serious TEAEs	5.4 (4.1, 6.9)
Discontinuation due to TEAEs	2.7 (1.8, 3.8)
Severe TEAEs	5.1 (3.9, 6.5)
Deaths	0.3 (0.1, 0.8)
Most Common TEAEs	
Nasopharyngitis	8.4 (6.8, 10.3)
Oral candidiasis	7.1 (5.6, 8.8)
Coronavirus infection	5.1 (3.9, 6.5)
TEAEs of Interest	
Serious infections[a]	1.4 (0.8, 2.2)
Fungal infections[b]	16.0 (13.6, 18.6)
Definite or probable adjudicated inflammatory bowel disease	0.2 (0.0, 0.6)
Adjudicated suicidal ideation and behavior	0.2 (0.0, 0.6)
Malignancies including non-melanoma skin cancer	0.9 (0.4, 1.6)
Serious hypersensitivity reactions	0.1 (0.0, 0.5)
Adjudicated major adverse cardiac event	0.5 (0.2, 1.1)
Hepatic events	3.7 (2.7, 4.9)
AST or ALT elevations >3x upper limit of normal	1.5 (0.9, 2.3)
AST or ALT elevations >5x upper limit of normal	0.2 (0.1, 0.7)
Administration and injection site reactions	1.4 (0.8, 2.2)

Two-year safety data have been reported previously (Weeks 0–96).[1,2] [a] Includes one event of systemic candidiasis in a patient with non-dependent diabetes mellitus, severe obesity, and a history of recurrent urinary tract infections. Events occurred in a setting of fungal urinary tract infection with obstruction and recent urinary tract instrumentation with bladder biopsies. This was resolved with nephrostomy, intravenous antibiotic therapy, and antifungal therapy; the patient discontinued. [b] Includes the HLTs *Candida* infections, fungal infections NEC, and *Tinea* infections.

Figure 2 PASI responses through Week 144 in patients who entered the OLE after receiving BKZ or SEC in the double-blind period (mNRI[a])



Week		48	96	144
OC; % (n/N)	Continuous BKZ	94.2 (310/329)	95.5 (294/308)	93.3 (264/283)
	SEC/BKZ	84.1 (264/314)	96.2 (275/286)	91.4 (245/268)
mNRI;[a] %	Continuous BKZ	94.3	93.2	89.8
	SEC/BKZ	83.9	93.4	87.0
NRI; %	Continuous BKZ	92.3	87.5	78.6
	SEC/BKZ	83.0	86.5	77.0

Week		48	96	144
OC; % (n/N)	Continuous BKZ	75.4 (248/329)	74.4 (229/308)	76.0 (215/283)
	SEC/BKZ	53.2 (167/314)	81.8 (234/286)	76.1 (204/268)
mNRI;[a] %	Continuous BKZ	74.9	70.8	68.8
	SEC/BKZ	52.8	76.7	69.1
NRI; %	Continuous BKZ	73.8	68.2	64.0
	SEC/BKZ	52.5	73.6	64.2

Data are presented for patients who entered the OLE only, during which all patients received BKZ. [a] Missing data were imputed using mNRI: patients who discontinued study treatment due to lack of efficacy or adverse events deemed treatment-related by investigators were considered non-responders at subsequent timepoints; multiple imputation was used for all other missing data.

ALT: alanine aminotransferase; **AST:** aspartate aminotransferase; **BKZ:** bimekizumab; **CI:** confidence interval; **COVID-19:** Coronavirus disease 2019; **EAIR:** exposure-adjusted incidence rate; **HLT:** high level term; **MedDRA:** Medical Dictionary for Regulatory Activities; **mNRI:** modified non-responder imputation; **NEC:** not elsewhere classified; **NRI:** non-responder imputation; **OC:** observed case; **OLE:** open-label extension; **PASI:** Psoriasis Area and Severity Index; **PASI 90:** ≥90% improvement from baseline in PASI; **PASI 100:** 100% improvement from baseline in PASI; **PY:** patient-years; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2; **SEC:** secukinumab; **TEAE:** treatment-emergent adverse event.

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References: 1Reich K, N Engl J Med. 2021;385(2):142–52; 2Strober B. Presented at AAD 2022, poster 33812; 3Lebwohl M. Presented at AAD 2022, poster 34321; 4Lebwohl M. Presented at AAD 2022, poster 33817; 5Gordon KB. JAMA Dermatol. 2022;158(7):735–4. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **BS**, **LP**, **AB**, **DT**, **BE**, **MW**, **VV**, **DD**, **FS**, **SW**, **JFM**, **CP**; Drafting of the publication, or reviewing it critically for important intellectual content: **BS**, **LP**, **AB**, **DT**, **BE**, **MW**, **VV**, **DD**, **FS**, **SW**, **JFM**, **CP**; Final approval of the publication: **BS**, **LP**, **AB**, **DT**, **BE**, **MW**, **VV**, **DD**, **FS**, **SW**, **JFM**, **CP**. **Author Disclosures: BS:** Consultancy (honoraria) for AbbVie, Alamar, Almirall, Alumis, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Bristol Myers Squibb, Capital One, Connect Biopharma, CorEvitas (previously Corrona), Dermavant, Eli Lilly, Evelo Biosciences, Immunic Therapeutics, Janssen, Kangpu Pharmaceuticals, LEO Pharma, Maruho, Meiji Seika Pharma, Mindera Health, Monte Carlo, Novartis, Pfizer, Protagonist Therapeutics, Regeneron, Sanofi Genzyme, Sun Pharma, Takeda/Nimbus, UCB Pharma, Union Therapeutics, Ventyxbio, and vTv Therapeutics; stock options from Connect Biopharma and Mindera Health; speaker for AbbVie, Arcutis, Dermavant, Eli Lilly, Incyte, Janssen, Regeneron, and Sanofi Genzyme; scientific co-director (consulting fee) for CorEvitas (formerly Corrona) Psoriasis Registry; investigator for CorEvitas Psoriasis Registry; editor-in-chief (honorarium) for Journal of Psoriasis and Psoriatic Arthritis. **LP:** 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. **AB:** Speaker (received honoraria) for AbbVie, Bristol Myers Squibb, Eli Lilly, Pfizer, Regeneron, and Sanofi; scientific adviser (received honoraria) for AbbVie, Abcentra, Aclaris, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Apogee, Arcutis, Arena, Asian, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Dermavant, Ecoll, Eli Lilly, Escient, Evelo, Evommune, Forte, Galderma, Highlight Pharma, Incyte, InnoventBio, Janssen, Landos, LEO Pharma, Lipidio, Merck, Monte Rosa Therapeutics, Nektar, Novartis, Overtone Therapeutics, Pfizer, Ralx, Ragor, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, Takeda, TLL Pharmaceutical, TrialSpark, UCB Pharma, Union, Ventyx, Viblome, and Xencor; clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Almirall, Alumis, 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. **DT:** Served as an investigator and/or consultant/advisor for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly, Galapagos, Galderma, Janssen-Cilag, Kyowa Kirin, LEO Pharma, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Target-Solution, and UCB Pharma. He has received grants from AbbVie, LEO Pharma, and Novartis. **BE:** Received research support as funding to Case Western Reserve University from AbbVie, Anaptysbio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Incyte, LEO Pharma, Merck, Merck, Novartis, Pfizer, Regeneron, Sun Pharma, Valeant, and Vanda; consultant (honoraria) for Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer, Sun Pharma, UCB Pharma, Valeant, and Verrica. **MW**, **VV**, **DD**, **FS**, **SW:** Employees and shareholders of UCB Pharma. **JFM:** Consultant and/or investigator for AbbVie, Amgen, Biogen, Bristol Myers Squibb, Dermavant, Eli Lilly, Janssen, LEO Pharma, Pfizer, Novartis, Regeneron, Sanofi, Sun Pharma, and UCB Pharma. **CP:** Consulting fees and/or grants from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, GSK, Janssen Cilag, LEO Pharma, Novartis, Pierre Fabre, Pfizer, Sanofi Regeneron, and UCB Pharma. **Acknowledgements:** This study was funded by UCB Pharma. We would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to this study. The authors acknowledge Radhika Bhalsa, PhD, UCB Pharma, Slough, UK, for publication coordination, and Phoebe Kennedy, MSc, Costello Medical, Bristol, UK, for medical writing support and editorial assistance. All costs associated with development of this presentation were funded by UCB Pharma.

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