Bimekizumab safety and tolerability in moderate to severe plaque psoriasis: Pooled analysis from up to 4 years of treatment in 5 phase 3/3b clinical trials

Kenneth B. Gordon,[1] Diamant Thaçi,[2] Melinda Gooderham,[3] Yukari Okubo,[4] Bruce Strober,[5] Luke Peterson,[6] Delphine Deherder,[7] José M. López Pinto,[8] Paolo Gisondi[9]

Objective

To evaluate bimekizumab (BKZ) safety data up to 4 years in patients with moderate to severe plaque psoriasis, using the largest pool of phase 3/3b safety data at the time of this study.

To assess whether rates of treatment-emergent adverse events (TEAEs) changed with each year of BKZ treatment.

Background

- BKZ is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A.[1]
- Psoriasis is a chronic condition requiring long-term management, thus evaluating long-term safety of treatments is essential to informing decision-making for clinicians, while managing risk for patients.[2]
- We report the first 4-year safety data for BKZ in patients with moderate to severe psoriasis.

Methods

- Data were pooled from the BE SURE, BE VIVID, and BE READY phase 3 trials, their open-label extension (OLE) BE BRIGHT, the BE RADIANT phase 3b trial, and the BE RADIANT OLE.[3–7] The BE RADIANT trial ran for 3 years; therefore, the overall total pooled exposure only included BE RADIANT data to Year 3, in addition to BE BRIGHT data to Year 4. Data were pooled for all patients who received ≥1 BKZ dose in the included studies (**Figure 1**).
- Included patients received BKZ 320 mg every 4 weeks (Q4W) or every 8 weeks (Q8W); all received Q8W from Week 64 (BE RADIANT)/OLE Week 48 (BE BRIGHT) or the next scheduled clinic visit. Patients who switched from adalimumab, ustekinumab, or secukinumab to BKZ in BE SURE, BE VIVID, and BE RADIANT, respectively, were also included following the switch to BKZ.
- TEAEs were reported over 4 years using exposure-adjusted incidence rates (EAIRs) per 100 patient-years (PY).
- TEAEs were evaluated separately for Years 1, 2, 3, and 4 (Weeks 0–52, 52–104, 104–156, and 156–208) of BKZ treatment.

Results

- Total BKZ exposure was 6,324.3 PY (N=2,186; Year 1, Year 2, Year 3, Year 4: 2,053.3 PY [n=2,186], 1,904.3 PY [n=2,013], 1,521.1 PY [n=1,803], 819.5 PY [n=1,309]; **Table 1**).
- TEAEs occurred at an EAIR of 170.5/100 PY (Year 1, Year 2, Year 3, Year 4: 230.9/100 PY, 137.7/100 PY, 107.1/100 PY, 99.9/100 PY), serious TEAEs at 5.5/100 PY (6.5/100 PY, 5.9/100 PY, 5.8/100 PY, 5.6/100 PY), and TEAEs leading to discontinuation at 2.9/100 PY (4.6/100 PY, 2.3/100 PY, 2.3/100 PY, 1.1/100 PY). Overall, the EAIR of TEAEs decreased with longer BKZ exposure over 4 years (**Figure 2**).
- The most common TEAEs were nasopharyngitis at 12.7/100 PY (Year 1, Year 2, Year 3, Year 4: 25.8/100 PY, 13.2/100 PY, 5.4/100 PY, 5.9/100 PY), oral candidiasis at 8.9/100 PY (18.9/100 PY, 10.7/100 PY, 6.8/100 PY, 5.4/100 PY), and upper respiratory tract infection at 5.7/100 PY (10.4/100 PY, 5.7/100 PY, 3.7/100 PY, 3.9/100 PY; **Table 2**).
- Fewer TEAEs over 4 years occurred with BKZ Q8W versus (vs.) Q4W (115.4/100 PY vs. 224.4/100 PY), including for oral candidiasis (6.5/100 PY vs. 16.7/100 PY).

Conclusions

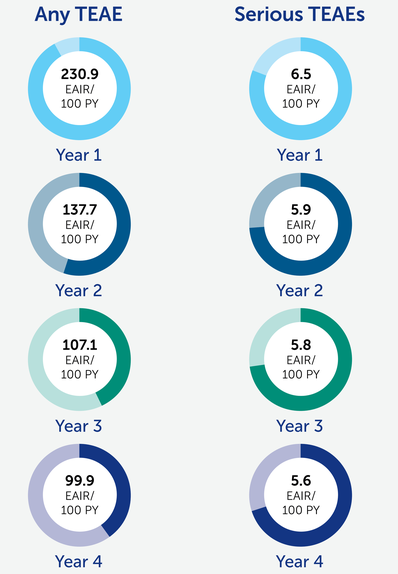
Bimekizumab demonstrated good tolerability and a comparable safety profile over 4 years in patients with moderate to severe plaque psoriasis.

EAIRs of TEAEs remained consistent or decreased with longer Bimekizumab exposure over 4 years, with no new safety signals observed.

Summary

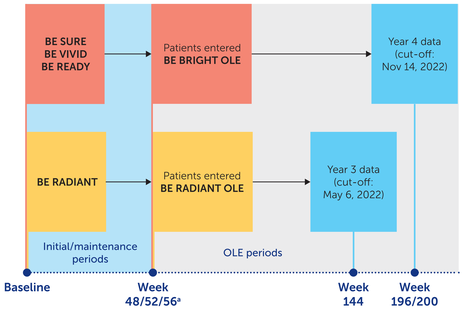
Safety data up to 4 years for BKZ in patients with moderate to severe psoriasis were pooled from 5 phase 3/3b trials

Patients included in this analysis received ≥1 dose of BKZ 320 mg Q4W or Q8W



EAIR of TEAEs remained consistent or decreased with longer BKZ exposure over 4 years

Figure 1 Included studies



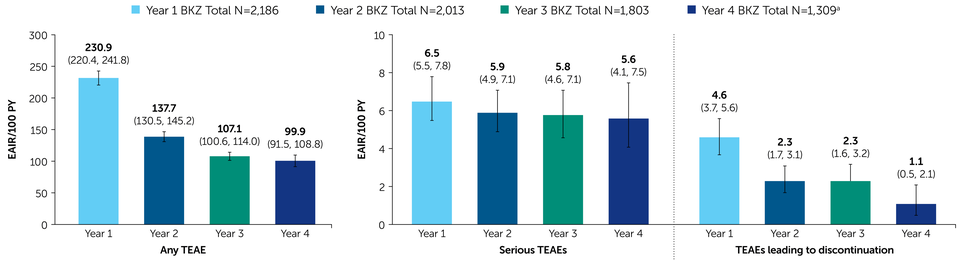
Data and any adjudication are shown as of the data cut-offs (BE RADIANT: May 6, 2022; BE BRIGHT: November 14, 2022). [a]Patients entered the BE BRIGHT OLE at Week 52 if they were enrolled in BE VIVID and Week 56 if they were enrolled in BE SURE or BE READY; patients in BE RADIANT entered the BE RADIANT OLE period at Week 48.

Table 1 Summary of exposure and TEAEs

	KZ Total				
	Year 1 N=2,186	Year 2 N=2,013	Year 3 N=1,803	Year 4 N=1,309	Overall N=2,186
Weeks	0–52	52–104[a]	104–156[a]	156–208	All[b]
Total exposure, PY	2,053.3	1,904.3	1,521.1	819.5	6,324.3[c]
Mean exposure ± SD, days	345.7 ± 63.4	340.9 ± 62.2	328.5 ± 58.8	237.0 ± 94.0	988.4 ± 388.5
Median exposure (range), days	364 (23–364)	364 (1–364)	364 (7–364)	281 (1–364)	1,013 (23–1,569)
TEAE summary, EAIR/100 PY (95% CI)					
Any TEAE	230.9 (220.4, 241.8)	137.7 (130.5, 145.2)	107.1 (100.6, 114.0)	99.9 (91.5, 108.8)	170.5[d] (163.2, 178.1)
Serious TEAEs	6.5 (5.0, 7.8)	5.9 (4.9, 7.1)	5.8 (4.6, 7.1)	5.6 (4.1, 7.5)	5.5[e] (4.9, 6.2)
TEAEs leading to discontinuation	4.6 (3.7, 5.6)	2.3 (1.7, 3.1)	2.3 (1.6, 3.2)	1.1 (0.5, 2.1)	2.9 (2.5, 3.3)
Severe TEAEs	6.0 (5.5, 7.2)	5.0 (4.1, 6.2)	4.8 (3.7, 6.0)	5.1 (3.7, 6.9)	4.8 (4.3, 5.4)
TEAEs leading to death	0.3 (0.1, 0.6)	0.3 (0.1, 0.7)	0.5 (0.2, 0.9)	0.2 (0.0, 0.9)	0.3 (0.2, 0.5)

Data were pooled for all patients who received ≥1 BKZ dose in each of the periods examined (BKZ Total). [a]All patients were switched to BKZ 320 mg Q8W at the next scheduled clinic visit on or after the Week 64/Week 104 visit (BE RADIANT/BE BRIGHT) following protocol amendment; [b]Entire pooled study period; [c]Total BKZ exposure over 4 years is greater than the sum of BKZ exposure in individual years, as data beyond Week 208 were included due to the use of a cut-off date; [d]The EAIR of TEAEs over 4 years was numerically lower in patients receiving BKZ Q8W vs. Q4W (115.4/100 PY vs. 224.4/100 PY); [e]The rate of serious TEAEs over 4 years is lower than the rate in any individual year due to time not accounted for in the individual year summaries.

Figure 2 Incidence rates of TEAEs: Any, serious, and discontinuations over time (BKZ Total)



Data are reported as EAIRs; error bars represent 95% CI. Data are presented for the BKZ Total for the full pooled trial period, and separately for Years 1 (Weeks 0–52), 2 (Weeks 52–104), 3 (Weeks 104–156), and 4 (Weeks 156–208). Data were pooled for all patients who received ≥1 BKZ dose in each of the periods examined (BKZ Total). [a]BE RADIANT patients were not included after Year 3.

Table 2 Most common TEAEs and TEAEs of interest (BKZ Total)

	Year 1 N=2,186	Year 2 N=2,013	Year 3 N=1,803[a]	Year 4 N=1,309[a]	Overall N=2,186
Most common TEAEs, EAIR/100 PY (95% CI)					
Nasopharyngitis	25.8 (23.5, 28.3)	13.2 (11.6, 15.0)	5.4 (4.3, 6.7)	5.9 (4.4, 7.9)	12.7 (11.7, 13.8)
Oral candidiasis	18.9 (16.9, 21.0)	10.7 (9.2, 12.3)	6.8 (5.6, 8.3)	5.4 (3.9, 7.3)	8.9 (8.1, 9.7)[b]
Upper respiratory tract infection	10.4 (9.0, 12.0)	5.7 (4.7, 6.9)	3.7 (2.8, 4.9)	3.9 (2.6, 5.5)	5.7 (5.1, 6.4)
TEAEs of interest, EAIR/100 PY (95% CI)					
Serious infections	1.7 (1.2, 2.3)	0.8 (0.5, 1.4)	1.4 (0.9, 2.1)	1.1 (0.5, 2.1)	1.3 (1.0, 1.6)
Active tuberculosis	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
Fungal infections	30.6 (28.0, 33.3)	18.8 (16.8, 21.0)	11.9 (10.2, 13.8)	8.6 (6.6, 10.9)	15.7 (14.6, 16.9)
Candida infections	22.2 (20.1, 24.4)	12.8 (11.2, 14.6)	7.8 (6.5, 9.4)	5.7 (4.1, 7.6)	10.4 (9.5, 11.3)
Oral candidiasis	18.9 (16.9, 21.0)	10.7 (9.2, 12.3)	6.8 (5.6, 8.3)	5.4 (3.9, 7.3)	8.9 (8.1, 9.7)[b]
Adjudicated inflammatory bowel disease[c]	0.3 (0.1, 0.7)	0.2 (0.0, 0.5)	0.1 (0.0, 0.4)	0.1 (0.0, 0.7)	0.2 (0.1, 0.3)
Adjudicated major adverse cardiac event	0.5 (0.3, 1.0)	0.3 (0.1, 0.7)	0.6 (0.3, 1.1)	1.1 (0.5, 2.1)	0.6 (0.4, 0.8)
Malignancies	0.9 (0.6, 1.5)	1.1 (0.7, 1.7)	0.9 (0.5, 1.5)	1.0 (0.4, 1.9)	0.9 (0.6, 1.1)
Excluding non-melanoma skin cancer	0.4 (0.2, 0.8)	0.6 (0.3, 1.1)	0.7 (0.4, 1.3)	0.9 (0.3, 1.8)	0.6 (0.4, 0.8)
Adjudicated suicidal ideation and behavior	0.1 (0.0, 0.4)	0.2 (0.0, 0.5)	0.1 (0.0, 0.5)	0.0 (0.0, 0.0)	0.1 (0.1, 0.2)
Neutropenia events	0.8 (0.5, 1.3)	0.5 (0.3, 1.0)	0.1 (0.0, 0.5)	0.2 (0.0, 0.9)	0.5 (0.3, 0.7)
ALT or AST elevations					
>3× ULN	2.6 (1.9, 3.4)	2.4 (1.7, 3.2)	1.9 (1.3, 2.8)	1.8 (1.0, 3.0)	1.9 (1.6, 2.3)
>5× ULN[d]	0.8 (0.5, 1.3)	0.3 (0.1, 0.7)	0.5 (0.2, 1.0)	0.6 (0.2, 1.4)	0.5 (0.4, 0.7)
Serious hypersensitivity reactions[e]	0.1 (0.0, 0.4)	0.1 (0.0, 0.4)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.1 (0.0, 0.2)
Injection site reactions	3.3 (2.5, 4.2)	1.1 (0.6, 1.6)	1.2 (0.7, 1.9)	0.4 (0.1, 1.1)	1.7 (1.4, 2.0)

Data were pooled from the BE SURE, BE VIVID, and BE READY feeder trials, their OLE BE BRIGHT, BE RADIANT, and the BE RADIANT OLE. Data are presented for BKZ Total for the full pooled trial period, and separately for Years 1 (Weeks 0–52), 2 (Weeks 52–104), 3 (Weeks 104–156), and 4 (Weeks 156–208). Data were pooled for all patients who received ≥1 BKZ dose in each of the periods examined (BKZ Total). [a]Confounding factors linked to the COVID-19 pandemic, including social isolation, mask-wearing, and lockdowns, may have impacted Year 3 and Year 4 data, particularly respiratory infection TEAEs such as nasopharyngitis; [b]The EAIR for oral candidiasis over 4 years was numerically lower in patients receiving BKZ Q8W vs. Q4W (6.5/100 PY vs. 16.7/100 PY); [c]Includes any TEAE adjudicated as definite or probable inflammatory bowel disease; [d]Patients with elevations >5× ULN were a subset of patients with elevations >3× ULN; [e]No anaphylactic reactions associated with BKZ were reported.

ALT: alanine aminotransferase; **AST:** aspartate aminotransferase; **BKZ:** bimekizumab; **CI:** confidence interval; **COVID-19:** Coronavirus disease 2019; **EAIR:** exposure-adjusted incidence rate; **OLE:** open-label extension; **PY:** patient-years; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SD:** standard deviation; **TEAE:** treatment-emergent adverse event; **ULN:** upper limit of normal; **vs.:** versus.

Institutions: [1]Department of Dermatology, Medical College of Wisconsin, Milwaukee, WI, USA; [2]Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany; [3]SKIN Centre for Dermatology, Probity Medical Research, Peterborough and Queen's University, Kingston, Ontario, Canada; [4]Department of Dermatology, Tokyo Medical University, Tokyo, Japan; [5]Department of Dermatology, Yale University, New Haven, CT, USA; Central Connecticut Dermatology Research, Cromwell, CT, USA; [6]UCB Pharma, Morrisville, NC, USA; [7]UCB Pharma, Braine-l'Alleud, Belgium; [8]UCB Pharma, Madrid, Spain; [9]Dermatology and Venereology, Department of Medicine, Università di Verona, Verona, Italy.

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