Bimekizumab Efficacy and Safety Through 4 Years in Moderate to Severe Plaque Psoriasis: Long-term Results from a Phase 3 Study and Open-Label Extension

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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 its long-term safety in patients with moderate to severe plaque psoriasis through 4 years of treatment.

Background

- BKZ is a monoclonal IgG1 antibody which selectively inhibits interleukin (IL)-17F in addition to IL-17A.[1]
- Clinical improvements over 3 years, with no unexpected safety findings, were previously reported with BKZ in the BE SURE (NCT03412747) phase 3 trial and BE BRIGHT open-label extension (OLE; NCT03598790).[2,3]

Methods

- Patients who completed the 56-week BE SURE phase 3 trial could enroll in the BE BRIGHT OLE (**Figure 1**).
- Efficacy data, in terms of PASI 90 (≥90% improvement from baseline in PASI) and PASI 100 response rates, are reported through to Week 200 by initial randomization treatment groups. Patients who discontinued due to lack of efficacy or treatment-related adverse events were considered non-responders; multiple imputation was used for other missing data (modified non-responder imputation; mNRI).
- Treatment-emergent adverse events (TEAEs) occurring whilst receiving BKZ (incidence/100 patient-years [PY]) are reported through Weeks 0–200 for patients receiving ≥1 dose of BKZ (BKZ Total) and the subset receiving BKZ Q4W/Q8W/Q8W (dose approved for most patients).

Results

- In BE SURE, a total of 478 patients were randomized to BKZ Q4W/Q8W (N=161), BKZ Q4W/Q4W (N=158), and adalimumab (ADA)/BKZ (N=159) (**Figure 1**). Baseline characteristics have been reported previously and were similar between the groups examined.[2]
- At Week 200, PASI 90 was achieved by 83.2% of BKZ Q4W/Q8W-randomized patients, 82.4% of BKZ Q4W/Q4W-randomized patients, and 87.6% of ADA/BKZ-randomized patients (mNRI; **Figure 2A**). PASI 100 was achieved by 58.5%, 61.9%, and 69.5%, respectively (mNRI; **Figure 2B**).
- Through Weeks 0–200, the rate of serious TEAEs with BKZ was low (4.9/100 PY; **Table 1**). The most common TEAEs were nasopharyngitis (12.3/100 PY), oral candidiasis (8.3/100 PY), and upper respiratory tract infection (6.0/100 PY).
- Most oral candidiasis events (99.2%) were mild or moderate, and no cases of oral candidiasis led to discontinuation. There were 5 deaths, none were related to treatment.
- Rates of TEAEs of interest are reported in **Table 2**.

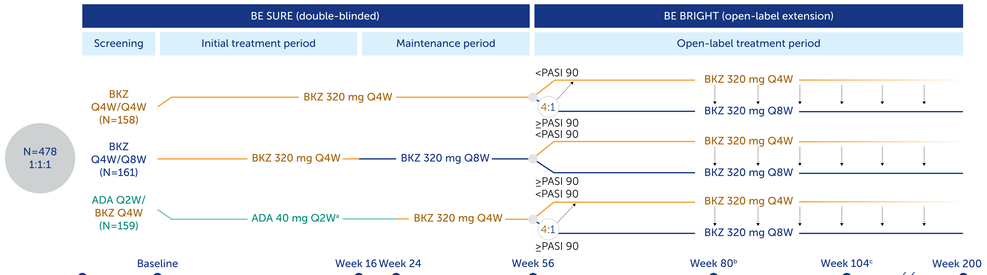
Conclusions

Clinical improvements achieved after one year of bimekizumab treatment were maintained through 4 years.

Efficacy outcomes improved in adalimumab-treated patients who switched to bimekizumab at Week 24 and high responses were durable to Week 200.

Bimekizumab was well-tolerated through Week 200 and no new safety signals were identified with longer exposure, including in the subset of patients who received the bimekizumab dosing regimen approved for most patients (Q4W/Q8W/Q8W).

Figure 1 BE SURE and BE BRIGHT study design



[a] ADA was dosed 80 mg at Week 0 and 40 mg at Week 1, then Q2W until Week 24, at which point patients were switched to BKZ 320 mg Q4W; **[b]** At Week 80 (OLE Week 24), patients achieving ≥PASI 90 could switch to Q8W at the investigator's discretion; **[c]** All patients were switched to BKZ 320 mg Q8W at the next scheduled clinic visit on or after the Week 104 visit (OLE Week 48) following protocol amendment.

Table 1 Overview of TEAEs through Week 200

EAIR/100 PY (95% CI)	BKZ Total (N=468) 1,509 PY	BKZ 320 mg Q4W/Q8W/Q8W (N=106) 392 PY
TEAE Summary		
Any TEAE	139.1 (126.4, 152.6)	149.7 (122.1, 181.8)
Serious TEAEs	4.9 (3.8, 6.2)	4.1 (2.3, 6.7)
Discontinuation due to TEAEs	3.0 (2.2, 4.0)	2.0 (0.9, 4.0)
Drug-related TEAEs	22.9 (20.0, 26.1)	25.8 (19.6, 33.4)
Severe TEAEs	4.6 (3.5, 5.8)	3.7 (2.0, 6.3)
TEAEs leading to death	0.3 (0.1, 0.8)	0.3 (0.0, 1.4)
Most Common TEAEs		
Nasopharyngitis	12.3 (10.3, 14.5)	11.1 (7.6, 15.6)
Oral candidiasis	8.3 (6.8, 10.1)	9.6 (6.4, 13.7)
Upper respiratory tract infection	6.0 (4.8, 7.5)	5.9 (3.6, 9.1)

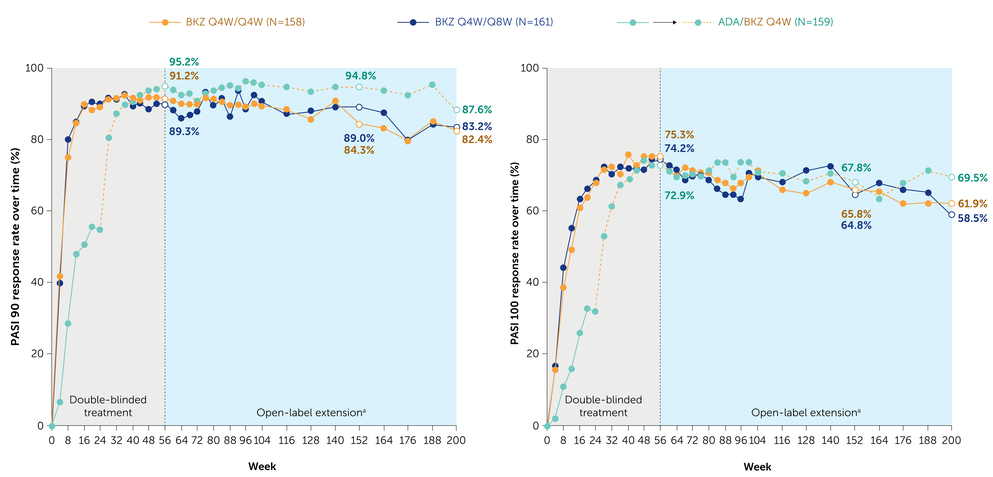
Data cut-off: November 14, 2022. Data were pooled for all patients who received ≥1 dose of BKZ throughout the study (BKZ Total). Data are also presented for the subset of these patients who received BKZ Q4W during the initial treatment period, BKZ Q8W during the maintenance treatment period and BKZ Q8W during the OLE period (BKZ Q4W/Q8W/Q8W).

Table 2 TEAEs of interest through Week 200

EAIR/100 PY (95% CI)	BKZ Total (N=468) 1,509 PY	BKZ 320 mg Q4W/Q8W/Q8W (N=106) 392 PY
Infections and infestations	71.9 (64.8, 79.5)	81.6 (65.8, 100.1)
Serious infections	1.2 (0.7, 1.9)	0.8 (0.2, 2.3)
Active tuberculosis	0	0
Fungal infections	14.2 (12.1, 16.6)	13.6 (9.6, 18.6)
Candida infections	9.3 (7.7, 11.2)	10.4 (7.0, 14.7)
Oral candidiasis	8.3 (6.8, 10.1)	9.6 (6.4, 13.7)
Definite or probable adjudicated IBD	0.2 (0.0, 0.6)	0.3 (0.0, 1.4)
Adjudicated suicidal ideation and behavior	0	0
Adjudicated major adverse cardiac event	0.5 (0.2, 1.0)	0.5 (0.1, 1.8)
Malignancies	1.0 (0.6, 1.7)	1.9 (0.7, 3.8)
Any malignancies (excluding NMSC)	0.7 (0.4, 1.3)	1.0 (0.3, 2.6)
Serious hypersensitivity reactions	0.1 (0.0, 0.4)	0
Injection site reactions	1.5 (0.9, 2.3)	2.4 (1.1, 4.6)
Hepatic events	3.4 (2.5, 4.5)	1.6 (0.6, 3.4)
ALT or AST >3x ULN	2.2 (1.5, 3.1)	0.8 (0.2, 2.3)
ALT or AST >5x ULN[a]	0.6 (0.3, 1.1)	0.3 (0.0, 1.4)

Data cut-off: November 14, 2022. Data were pooled for all patients who received ≥1 dose of BKZ throughout the study (BKZ Total). Data are also presented for the subset of these patients who received BKZ Q4W during the initial treatment period, BKZ Q8W during the maintenance treatment period and BKZ Q8W during the OLE period (BKZ Q4W/Q8W/Q8W). **[a]** Patients with elevations >5x ULN were a subset of patients with elevations >3x ULN.

Figure 2 PASI 90 and PASI 100 response rates through Week 200



Week	Year 1	Year 2	Year 3	Year 4
	56	104	152	200
BKZ Q4W/Q4W (OC), n/N (%)	134/140 (95.7)	121/129 (93.8)	113/123 (91.9)	107/117 (91.5)
BKZ Q4W/Q8W (OC), n/N (%)	133/143 (93.0)	119/126 (94.4)	111/116 (95.7)	98/109 (89.9)
ADA/BKZ Q4W (OC), n/N (%)	130/133 (97.7)	121/123 (98.4)	113/115 (98.3)	98/104 (94.2)

Week	Year 1	Year 2	Year 3	Year 4
	56	104	152	200
BKZ Q4W/Q4W (OC), n/N (%)	114/140 (81.4)	102/129 (79.1)	95/123 (77.2)	84/117 (71.8)
BKZ Q4W/Q8W (OC), n/N (%)	113/143 (79.0)	101/126 (80.2)	90/116 (77.6)	78/109 (71.6)
ADA/BKZ Q4W (OC), n/N (%)	106/133 (79.7)	98/123 (79.7)	92/115 (80.0)	84/104 (80.8)

Data are presented for all patients initially randomized to receive treatment, by initial randomization group. **[a]** All patients were switched to BKZ 320 mg Q8W at the next scheduled clinic visit on or after the Week 104 visit (OLE Week 48) following protocol amendment.

ADA: adalimumab; **ALT:** alanine aminotransferase; **AST:** aspartate aminotransferase; **BKZ:** bimekizumab; **CI:** confidence interval; **EAIR:** exposure-adjusted incidence rate; **IBD:** inflammatory bowel disease; **IL:** interleukin; **mNRI:** modified non-responder imputation; **NMSC:** non-melanoma skin cancer; **OC:** observed case; **OLE:** open-label extension; **PASI:** Psoriasis Area and Severity Index; **PY:** patient-years; **Q2W:** every 2 weeks; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **TEAE:** treatment-emergent adverse event; **ULN:** upper limit of normal.

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References: [1]Adams R. Front Immunol 2020;11:1894; [2]Thaçi D. Br J Dermatol 2023;188:22–31; [3]Thaçi D. Presented at EADV 2022, P1572. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **DT**, **LP**, **JFM**, **DJ**, **AC**, **MW**, **DD**, **JMLP**, **ML**; Drafting of the publication, or reviewing it critically for important intellectual content: **DT**, **LP**, **JFM**, **DJ**, **AC**, **MW**, **DD**, **JMLP**, **ML**; Final approval of the publication: **DT**, **LP**, **JFM**, **DJ**, **AC**, **MW**, **DD**, **JMLP**, **ML**. **Author Disclosures: DT:** Served as an investigator and/or consultant/advisor for AbbVie, Almirall, Amgen, Boehringer Ingelheim, BMS, Celltrion, Eli Lilly and Company, Galderma, Janssen-Cilag, Kyowa Kirin, LEO Pharma, L'Oreal, New Bridge, Novartis, Pfizer, Regeneron, Samsung, Sanofi, Target-RWE, and UCB, received grants from AbbVie, LEO Pharma, and Novartis. **LP:** Received consultancy/speaker's honoraria from and/or participated in trials sponsored by AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, BMS, Eli Lilly and Company, Fresenius Kabi, Horizon, Janssen, LEO Pharma, Novartis, Pfizer, Sandoz, STADA, and UCB. **JFM:** Consultant and/or investigator for AbbVie, Amgen, AstraZeneca, Biogen, BMS, Boehringer Ingelheim, Dermavant, Eli Lilly and Company, Incyte, Janssen, LEO Pharma, MoonLake Immunotherapeutics, Novartis, Pfizer, Sanofi-Regeneron, Sun Pharma, and UCB. **DJ:** Served as a board member and/or consultant for AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, BMS, Celgene, Eli Lilly and Company, Fresenius Kabi, Janssen, LEO Pharma, MEDAC, MSD, Novartis, Pfizer, Sanofi, and UCB; received payment for development of educational presentations including service on speakers' bureaus from AbbVie, Celgene, Eli Lilly and Company, Janssen, LEO Pharma, MEDAC, Novartis, Pfizer, and travel/accommodations expenses covered or reimbursed by AbbVie, Amgen, Biogen, Celgene, Eli Lilly and Company, Fresenius Kabi, Janssen, LEO Pharma, MEDAC, MSD, Novartis, Pfizer, Sanofi, and UCB. **AC:** Investigator and/or speaker and/or advisor for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Sandoz, Sanofi, and UCB. **MW, DD, JMLP:** Employees and shareholders of UCB. **ML:** Employee of Mount Sinai and receives research funds from Abbvie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Dermavant, Eli Lilly and Company, Incyte, Inozyme, Janssen, LLC, Ortho Dermatologics, Sanofi-Regeneron, and UCB; consultant for Almirall, AltruBio Inc., AnaptysBio, Apogee, Arcutis, AstraZeneca, Atomwise, Avotres, Boehringer Ingelheim, Brickell Biotech, BMS, Castle Biosciences, Celltrion, CorEvitas, Dermavant, EPI, Evommune, Inc., Facilitation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Galderma, Genentech, Incyte, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Sanofi-Regeneron, Seanergy, Strata, Trevi, and Verrica. **Acknowledgments:** These studies were funded by UCB. We would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to these studies. The authors acknowledge Susanne Wiegratz, MSc, UCB, Monheim, Germany, and Joe Dixon, PhD, UCB, Slough, UK, for publication coordination, Sana Yaar, PhD, Costello Medical, Manchester, UK, for medical writing support and editorial assistance, and the Costello Medical Creative team for graphic design assistance. All costs associated with development of this presentation were funded by UCB.

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