Bimekizumab efficacy and safety through three years in patients with moderate to severe plaque psoriasis: Long-term results from the BE SURE randomized controlled trial and the BE BRIGHT open-label extension

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Objectives

To evaluate the long-term efficacy and safety of bimekizumab (BKZ) over three years in patients with moderate to severe plaque psoriasis who enrolled in the BE SURE phase 3 trial and entered the BE BRIGHT open-label extension (OLE).

Introduction

- In BE SURE (NCT03412747), BKZ demonstrated superior efficacy compared with adalimumab (ADA) over 24 weeks. After patients switched from ADA to BKZ at Week 24, responses improved and were maintained over two years, with no unexpected safety findings.[1]
- Here, we consider long-term efficacy and safety over three years.

Materials and Methods

- Treatment in BE SURE was as shown in **Figure 1**.
- Upon completion of BE SURE, patients could enrol in the BE BRIGHT OLE (NCT03598790; **Figure 1**).[1–3]
- Dose adjustments (to BKZ 320 mg every 4 weeks [Q4W] or every 8 weeks [Q8W]) could occur at Week 56 and Week 80 (OLE Week 24) based on the achievement of ≥90% improvement from baseline in Psoriasis Area and Severity Index (PASI 90). All patients received BKZ Q8W from Week 104 (OLE Week 48; or next clinic visit).
- Efficacy outcomes are reported for the intention-to-treat (ITT) population through Week 152 by initial randomisation group at BE SURE baseline.
- Data are reported using modified non-responder imputation (mNRI), NRI, and observed case (OC).
  - For mNRI, patients who discontinued treatment due to lack of efficacy were considered non-responders at subsequent timepoints; multiple imputation was used for all other missing data.
- Safety data are reported for Weeks 104–152 (data cut-off: 23 Oct 2021), and include treatment-emergent adverse events (TEAEs) reported using exposure-adjusted incidence rates (EAIRs). Two-year safety data have been reported previously (Weeks 0–104).[1,2]
  - The overview of adverse events and the most common TEAEs is reported both by initial randomization group regardless of BKZ OLE dosing regimen, and for all patients pooled (BKZ Total). BKZ Total was only used for safety topics of interest.

Results

- In BE SURE, 478 patients were randomized 1:1:1 to: BKZ Q4W/Q4W (N=158), BKZ Q4W/Q8W (N=161), and ADA/BKZ Q4W (N=159) (**Figure 1**). Baseline demographics have been reported previously and were aligned across treatment arms.[2]
- BKZ-randomized patients maintained high levels of PASI 90 and PASI 100 responses to three years of treatment (Week 152/OLE Week 96; **Figure 2**; **Table 1**).
- Among ADA-randomized patients, the rapid increases seen in PASI 90 and PASI 100 responses for after the Week 24 ADA to BKZ switch were durable to Week 152, reaching similar levels to BKZ-randomized patients (**Figure 2**; **Table 1**).
- These trends were also reflected in DLQI 0/1 responses over three years (**Figure 2**; **Table 1**).
- The most common TEAEs across BKZ-treated patients were coronavirus infection, oral candidiasis, and nasopharyngitis (**Table 2**). Rates of safety topics of interest were low (**Table 3**).
- Two coronavirus infections were reported as serious; of which only one was confirmed by testing.

Summary

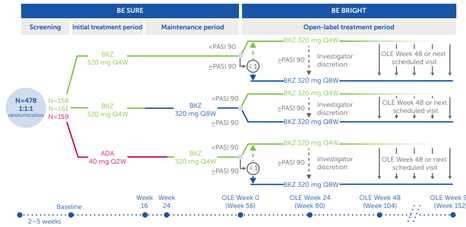
High initial PASI 90 response rates among BKZ-randomized patients were maintained to Week 152. Additionally, PASI 90 response rates in patients switching from ADA to BKZ rapidly increased and were sustained over three years of treatment. There were no unexpected safety findings.

Table 1 Overview of efficacy outcomes (mNRI, NRI, OC)

	BKZ Q4W/Q4W N=158			BKZ Q4W/Q8W N=161			ADA/BKZ Q4W N=159		
	mNRI, %	NRI, n (%)	OC, n/N (%)	mNRI, %	NRI, n (%)	OC, n/N (%)	mNRI, %	NRI, n (%)	OC, n/N (%)
PASI 90									
Week 56	92.6	134 (84.8)	134/140 (95.7)	89.6	133 (82.6)	133/143 (93.0)	94.3	130 (81.8)	130/133 (97.7)
Week 104	90.2	121 (76.6)	121/129 (93.8)	89.0	119 (73.9)	119/126 (94.4)	97.1	121 (76.1)	121/123 (98.4)
Week 152	**85.5**	**113 (71.5)**	**113/123 (91.9)**	**87.3**	**110 (68.3)**	**110/115 (95.7)**	**96.1**	**112 (70.4)**	**112/114 (98.2)**
PASI 100									
Week 56	78.3	114 (72.2)	114/140 (81.4)	75.8	113 (70.2)	113/143 (79.0)	74.0	106 (66.7)	106/133 (79.7)
Week 104	72.0	102 (64.6)	102/129 (79.1)	67.5	101 (62.7)	101/126 (80.2)	71.3	98 (61.6)	98/123 (79.7)
Week 152	**65.8**	**95 (60.1)**	**95/123 (77.2)**	**62.3**	**89 (55.3)**	**89/115 (77.4)**	**69.2**	**92 (57.9)**	**92/114 (80.7)**
DLQI 0/1									
Week 56	78.5	117 (74.1)	117/140 (83.6)	81.9	127 (78.9)	127/142 (89.4)	81.0	116 (73.0)	116/132 (87.9)
Week 104	80.8	112 (70.9)	112/130 (86.2)	82.1	110 (68.3)	110/126 (87.3)	82.0	112 (70.4)	112/124 (90.3)
Week 152	**77.1**	**101 (63.9)**	**101/121 (83.5)**	**81.4**	**103 (64.0)**	**103/115 (89.6)**	**78.0**	**101 (63.5)**	**101/112 (90.2)**

Data to Week 104 have been reported previously.[1] Data are presented for the ITT population by initial randomization group. Week 104 corresponds to OLE Week 48, and Week 152 to OLE Week 96.

Figure 1 Study design



In BE SURE, patients were randomized 1:1:1 to: BKZ 320 mg Q4W for 56 weeks; BKZ 320 mg Q4W for 16 weeks then Q8W through Weeks 16–56; or ADA 40 mg Q2W for 24 weeks followed by BKZ 320 mg Q4W to Week 56. At Week 56, dose adjustments (to BKZ 320 mg Q4W or Q8W) could occur based on whether patients achieved PASI 90. Patients receiving BKZ 320 mg Q4W at Week 56 who achieved PASI 90 were randomized 4:1 to BKZ 320 mg Q4W or Q8W. At Week 24 of BE BRIGHT, for patients receiving BKZ 320 mg Q4W, if PASI 90 was achieved, the investigator could change the patient's dosing interval from 320 mg Q4W to 320 mg Q8W. 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 2 Overview of adverse events during BKZ treatment in patients from BE SURE who entered BE BRIGHT, Weeks 104–152

EAIR/100 PY (95% CI)	BKZ Total N=380	BKZ Q4W/Q4W N=132	BKZ Q4W/Q8W N=124	ADA/BKZ Q4W N=124
Any TEAE	101.7 (88.7, 116.0)	108.0 (85.5, 134.6)	99.4 (77.6, 125.4)	97.6 (76.2, 123.1)
Serious TEAEs	6.2 (3.9, 9.5)	5.1 (1.9, 11.1)	8.2 (3.7, 15.5)	5.5 (2.0, 11.9)
Discontinuation due to TEAEs	2.9 (1.4, 5.4)	2.5 (0.5, 7.4)	3.5 (1.0, 9.1)	2.7 (0.6, 7.9)
Severe TEAEs	5.0 (2.9, 8.0)	3.4 (0.9, 8.7)	8.2 (3.7, 15.5)	3.6 (1.0, 9.2)
Deaths	1.2 (0.3, 3.0)	1.7 (0.2, 6.1)	0.9 (0.0, 4.9)	0.9 (0.0, 5.0)
Most Common TEAEs[a]				
Coronavirus infection	**6.6 (4.1, 10.0)**	**5.2 (1.9, 11.3)**	**8.3 (3.8, 15.8)**	**6.4 (2.6, 13.3)**
Nasopharyngitis	**4.8 (2.7, 7.7)**	**4.3 (1.4, 10.1)**	2.7 (0.6, 7.8)	**7.4 (3.2, 14.6)**
Oral candidiasis	**6.3 (3.9, 9.7)**	**6.1 (2.5, 12.6)**	**7.3 (3.2, 14.4)**	**5.6 (2.0, 12.1)**
Urinary tract infection	3.5 (1.8, 6.2)	3.4 (0.9, 8.8)	**5.4 (2.0, 11.7)**	1.8 (0.2, 6.6)

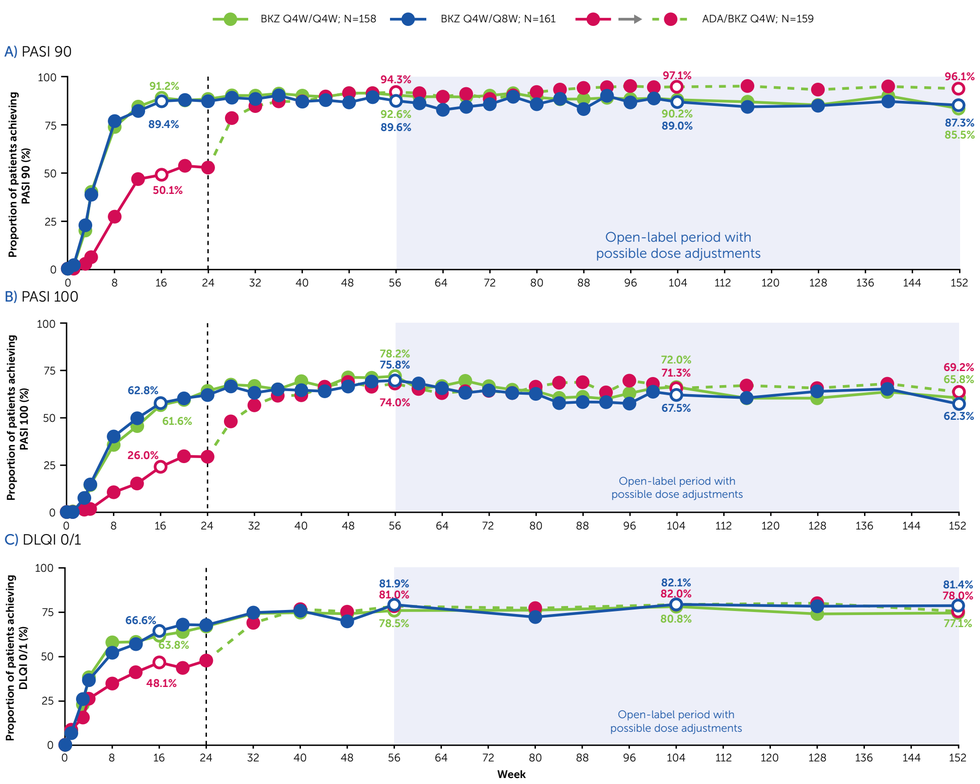
Two-year safety data have been reported previously (Weeks 0–104).[1,2] Data are presented as EAIRs of new cases per 100 patient-years from Weeks 104–152 for all patients who received ≥1 BKZ dose in the Week 104–152 period (data cut-off: 23 Oct 2021), both by initial randomization group regardless of BKZ OLE dosing regimen, and for all patients pooled (BKZ Total). All patients received BKZ Q8W from Week 104 (OLE Week 96; or next visit). [a]Values in bold are the three most common TEAEs for the treatment group.

Table 3 Safety topics of interest (BKZ Total)

EAIR/100 PY (95% CI)	BKZ Total (N=380)
Serious infections	1.8 (0.6, 3.8)
Active tuberculosis	0.0
IBD	0.6 (0.1, 2.1)
Malignancies	0.6 (0.1, 2.1)
NMSC	0.0
Adjudicated SIB	0.0
Serious hypersensitivity reactions	0.0
Adjudicated MACE	0.9 (0.2, 2.6)
Elevated liver enzymes	3.2 (1.6, 5.8)

Two-year safety data have been reported previously (Weeks 0–104).[1,2] Data are presented as EAIRs of new cases per 100 patient-years from Weeks 104–152 for all patients who received ≥1 BKZ dose in the Week 104–152 period (data cut-off: 23 Oct 2021) for all patients pooled (BKZ Total). All patients received BKZ Q8W from Week 104 (OLE Week 96; or next visit).

Figure 2 Efficacy responses by randomized treatment group through Week 152 (mNRI)



Data are presented for the ITT population by initial randomisation group. The vertical line at Week 24 indicates when patients randomized to ADA switched to BKZ Q4W. Week 104 corresponds to OLE Week 48, and Week 152 to OLE Week 96.

ADA: adalimumab; **BKZ:** bimekizumab; **CI:** confidence interval; **DLQI:** Dermatology Life Quality Index; **EAIR:** exposure-adjusted incidence rate; **IBD:** inflammatory bowel disease; **ITT:** intention-to-treat; **MACE:** major adverse cardiac event; **mNRI:** modified non-responder imputation; **NMSC:** non-melanoma skin cancer; **NRI:** non-responder imputation; **OC:** observed case; **OLE:** open-label extension; **PASI 90/100:** ≥90%/100% improvement from BE SURE baseline in Psoriasis Area and Severity Index; **PY:** patient-years; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SIB:** suicidal ideation and behavior; **TEAE:** treatment-emergent adverse event.

Conclusions

Clinical and health-related quality of life responses observed during the first two years of treatment were sustained to three years of treatment, regardless of BKZ maintenance dose frequency prior to the third year.

Additionally, responses were sustained in the third year, regardless of all patients switching to BKZ every 8 weeks.

Increases in responses after the ADA to BKZ switch were also sustained to Week 152.

BKZ was well-tolerated over three years, with no unexpected safety findings.

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References: [1]Thaçi D *et al.* Presented at EADV 2021. P1324.; [2]Warren RB *et al. N Engl J Med* 2021;385:130–41. NCT03412747; [3]BE BRIGHT. clinicaltrials.gov/ct2/show/NCT03598790. **Author Contributions:** Substantial contributions to study conception/design; or acquisition/analysis/interpretation of data: **DT, RV, MdR, CC, JS, BS, MW, NC, DD, NNG, ABG**. Drafting of the publication, or revising it critically for important intellectual content: **DT, RV, MdR, CC, JS, BS, MW, NC, DD, NNG, ABG**. Final approval of the publication: **DT, RV, MdR, CC, JS, BS, MW, NC, DD, NNG, ABG**. **Author Disclosures: DT:** Honoraria for participation on advisory boards, as a speaker and for consultancy from AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Eli Lilly, Galapagos, Janssen, LEO Pharma, Morphosis, Novartis, Pfizer, Regeneron, Samsung, Sanofi Genzyme, Sun Pharma, and UCB Pharma; research grants received from Celgene, LEO Pharma, and Novartis. **RV:** Grants/Research Support: AbbVie, Amgen, Centocor, Dermira, Dermavant, Eli Lilly, Galderma, GSK, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, Takeda, and UCB Pharma; speakers bureau/honoraria: AbbVie, Actelion, Amgen, Bausch Health, Celgene, Cipher, Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, Takeda, and UCB Pharma; consulting fees: AbbVie, Actelion, Amgen, Bausch Health, Celgene, Cipher, Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, Merck, Novartis, Pfizer, and UCB Pharma. **MdR:** Honoraria for participation on advisory boards, as a speaker and for consultancy from AbbVie, Almirall, Artax Biopharma, Biogen, Celgene, Eli Lilly, Janssen-Cilag, Janssen, LEO Pharma, Novartis, and UCB Pharma. **CC:** Consultant and/or principal investigator in clinical trials for: AbbVie, Actelion, Amgen, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galderma, Incyte, Janssen-Cilag, LEO Pharma, MSD, Novartis, Pfizer, Samsung, Sanofi Genzyme, and UCB Pharma. **JS:** Honoraria and/or consulting fees from Amgen, Celgene, Dermavant, National Psoriasis Foundation, Ortho Dermatologics, and Regeneron; grants and consulting fees from Abbvie, Actelion, Boeringher Ingelheim, Dermira, Eli Lilly, Janssen, LEO Pharma, Novartis Pharma, and UCB Pharma; research grants from Cassiopeia, Galderma, and Pfizer. **BS:** Consultant (honoraria): AbbVie, 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, and vTv Therapeutics; Stock Options: Connect Biopharma, Mindera Health. Speaker: AbbVie, Eli Lilly, Janssen, Regeneron, and Sanofi Genzyme. Scientific Co-Director (consulting fee): CorEvitas (formerly Corrona) Psoriasis Registry; Investigator: AbbVie, Cara, CorEvitas Psoriasis Registry, Dermavant, Dermira, and Novartis; Editor-in-Chief (honorarium): Journal of Psoriasis and Psoriatic Arthritis. **MW, NC, DD:** Employees and shareholders of UCB Pharma. **NNG:** Former employee and shareholder of UCB Pharma, current employee of Boehringer Ingelheim. **ABG:** Honoraria as an advisory board member and consultant for: Amgen, AnaptysBio, Avotres Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Incyte, Janssen, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma, and Xbiotech (stock options for an RA project); Research/educational grants from: AnaptysBio, Boehringer Ingelheim, Janssen, Novartis, Ortho Dermatologics, Sun Pharma, and UCB Pharma; All funds go to Mount Sinai Medical School. **Acknowledgements:** These studies were funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to these studies. The authors acknowledge Susanne Wiegratz, MSc, UCB Pharma, Monheim, Germany, for publication coordination, Poppy Wilson, MBiol, Costello Medical, London, UK, for medical writing and editorial assistance and the Design team at Costello Medical for graphic design assistance. All costs associated with development of this poster were funded by UCB Pharma.

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