Bimekizumab response maintenance through two years of treatment in patients with moderate to severe plaque psoriasis who responded after 16 weeks: Interim results from the BE BRIGHT open-label extension trial

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Presented at the Fall Clinical Dermatology Conference 2021 | October 21–24 | Las Vegas, NV

Objective

Evaluate maintenance of response rates among patients with moderate to severe plaque psoriasis receiving BKZ who had an initial response (IGA 0/1, BSA ≤1%, PASI 100) at Week 16 of the three phase 3 feeder studies and received continuous Q4W or Q8W BKZ maintenance dosing over two years.

Introduction

- Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively binds to and inhibits both interleukin (IL)-17A and IL-17F.[1]
- In phase 3 clinical trials, BKZ led to substantial clinical improvements in patients with moderate to severe plaque psoriasis, with no unexpected safety findings.[2–5]
- Given that psoriasis is a chronic disease, it is important to understand long-term treatment efficacy.

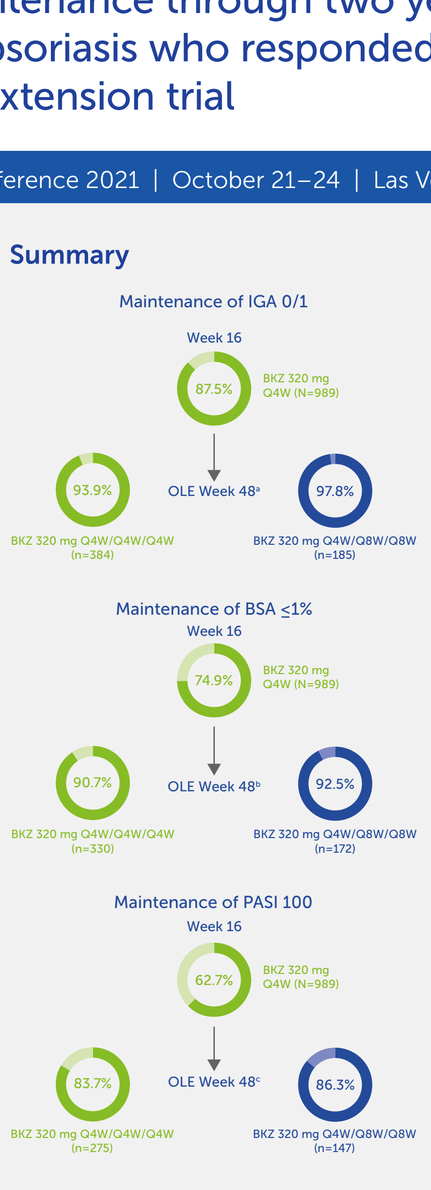
Methods

- Patients who completed one of three phase 3 studies (BE VIVID: NCT03370133; BE SURE: NCT03412747; BE READY: NCT03410992) could enroll in the BE BRIGHT (NCT03598790) two-year open-label extension (OLE).[1–3] These analyses include patients randomized to BKZ 320 mg every 4 weeks (Q4W) who responded at Week 16 of the feeder study, received BKZ 320 mg Q4W or every 8 weeks (Q8W) maintenance dosing from Week 16, and enrolled in BE BRIGHT **(Figure 1)**.
- We report maintenance of Investigator's Global Assessment (IGA) 0/1, psoriasis body surface area (BSA) ≤1%, and 100% improvement in the Psoriasis Area and Severity Index (PASI 100, complete skin clearance) through two years of treatment (OLE Week 48) among Week 16 responders who received continuous BKZ maintenance dosing in the OLE (Q4W/Q4W/Q4W or Q4W/Q8W/Q8W).
- Missing data were imputed using modified non-responder imputation (mNRI), non-responder imputation (NRI), and observed case (OC).
  - mNRI: Multiple imputation was used for missing data, except for patients with missing data following treatment discontinuation due to lack of efficacy where they were considered non-responders.
- Safety over two years was evaluated for all patients who received ≥1 dose of BKZ in the phase 3 feeder studies or the OLE.
  - Treatment-emergent adverse events (TEAEs) were coded using MedDRA v19.0. Exposure-adjusted incidence rates (EAIRs) are the incidence of new cases per 100 patient-years (PY).

Results

- Patient demographics and baseline characteristics for Week 16 responders are reported in **Table 1**.
- 989 patients were initially randomized to BKZ 320 mg Q4W; at Week 16, 87.5% achieved IGA 0/1, 74.9% achieved BSA ≤1%, and 62.7% achieved PASI 100 (NRI).
- Among Week 16 IGA 0/1, BSA ≤1%, and PASI 100 responders, respectively, response rates were maintained to OLE Week 48 with both Q4W and Q8W maintenance dosing regimens **(Figure 2)**.
- The most common TEAEs (incidence >5%) were nasopharyngitis, oral candidiasis, and upper respiratory tract infection. No new safety signals were identified in the phase 3 feeder studies or the BE BRIGHT OLE **(Table 2)**.

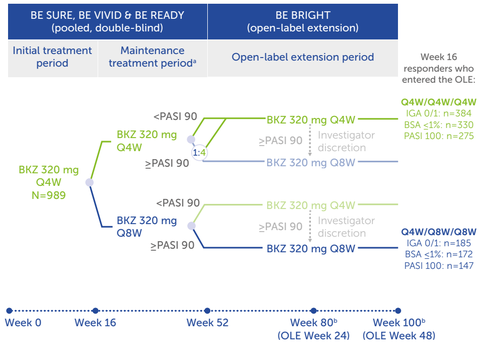
Summary



Among all BKZ-treated patients over two years, the most frequent adverse events were nasopharyngitis, oral candidiasis, and upper respiratory tract infection, consistent with results through one year.

[a]Among Week 16 IGA 0/1 responders; [b]Among Week 16 BSA ≤1% responders; [c]Among Week 16 PASI 100 responders.

Figure 1 BE BRIGHT study design: Included patients



All patients in the Q4W/Q8W/Q8W arm achieved PASI 90 on entering the OLE. [a]BE VIVID: All BKZ-randomized patients continued Q4W treatment at Week 16;[1] BE SURE: Patients allocated to BKZ treatment were randomized 1:1 at baseline to either continue Q4W or switch to Q8W at Week 16;[2] BE READY: BKZ-randomized Week 16 PASI 90 responders were re-randomized 1:1:1 to BKZ Q4W, Q8W, or placebo (PASI 90 non-responders entered an escape arm);[3] BE SURE and BE READY had a Week 56 visit that was not included in the BE BRIGHT pooled analysis.

Table 1 Baseline demographics and disease characteristics

	Week 16 responders[a]		
	IGA 0/1 responders (n=685)	BSA ≤1% responders (n=597)	PASI 100 responders (n=503)
Age (years), mean ± SD	44.9 ± 13.4	44.9 ± 13.3	44.8 ± 13.2
Male, n (%)	488 (71.2)	420 (70.4)	352 (70.0)
Caucasian, n (%)	591 (86.3)	513 (85.9)	441 (87.7)
Weight (kg), mean ± SD	89.2 ± 20.8	88.4 ± 20.3	87.8 ± 19.3
Duration of psoriasis (years), mean ± SD	18.4 ± 12.4	18.3 ± 12.6	18.0 ± 12.3
PASI, mean ± SD	21.4 ± 7.6	21.1 ± 7.4	21.2 ± 7.2
BSA (%), mean ± SD	27.4 ± 15.6	26.7 ± 15.2	26.7 ± 14.9
IGA, n (%)			
3: moderate	451 (65.8)	400 (67.0)	331 (65.8)
4: severe	233 (34.0)	196 (32.8)	171 (34.0)
DLQI total, mean ± SD	10.5 ± 6.3	10.7 ± 6.3	10.9 ± 6.4
Any prior systemic therapy, n (%)	547 (79.9)	486 (81.4)	415 (82.5)
Prior biologic therapy,[b] n (%)	275 (40.1)	245 (41.0)	210 (41.7)
anti-TNF	96 (14.0)	86 (14.4)	74 (14.7)
anti-IL-17	171 (25.0)	150 (25.1)	126 (25.0)
anti-IL-23	34 (5.0)	33 (5.5)	29 (5.8)
anti-IL-12/23	37 (5.4)	32 (5.4)	28 (5.6)

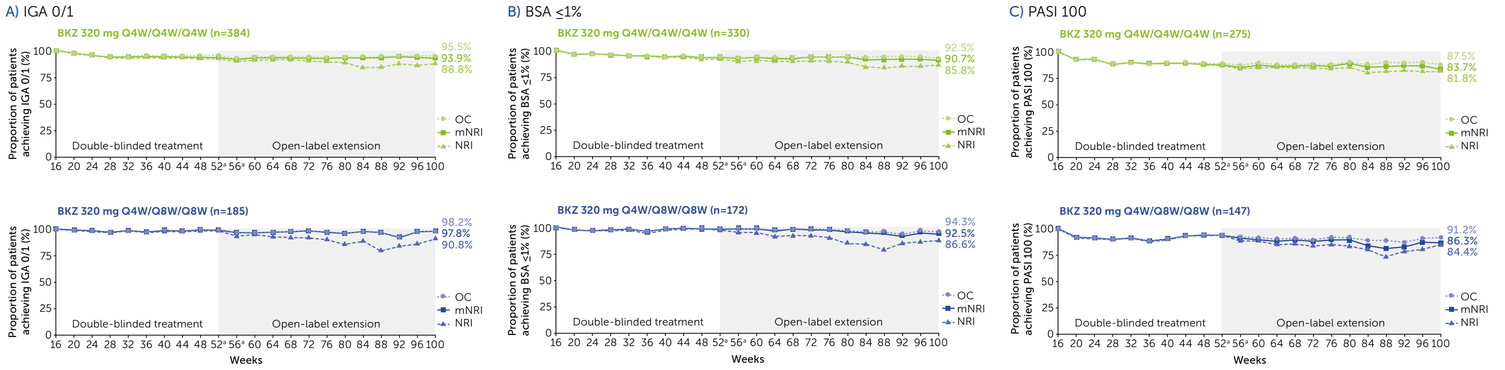
[a]Data are reported for all patients with a response at Week 16 who enrolled in BE BRIGHT; [b]Includes patients with multiple prior biologic use.

Table 2 Two-year pooled safety

	BKZ 320 mg Q4W (n=1456) EAIR/100 PY (95% CI)	BKZ 320 mg Q8W (n=930) EAIR/100 PY (95% CI)	BKZ Total (N=1495) EAIR/100 PY (95% CI)
Any TEAE	219.6 (207.3, 232.3)	141.4 (129.6,153.9)	192.7 (182.5, 203.3)
Serious TEAEs	6.2 (5.1, 7.4)	5.3 (3.8, 7.0)	5.9 (5.0, 6.9)
TEAEs leading to discontinuation	3.6 (2.8, 4.5)	2.7 (1.8, 4.1)	3.3 (2.7, 4.1)
Treatment-related TEAEs	43.4 (39.8, 47.1)	28.9 (25.0, 33.2)	35.5 (32.8, 38.3)
Severe TEAEs	5.3 (4.3, 6.5)	4.8 (3.4, 6.5)	5.0 (4.2, 5.9)
TEAEs leading to death	0.3 (0.1, 0.7)	0.3 (0.1, 1.0)	0.3 (0.2, 0.6)
Most common TEAEs[a]			
Nasopharyngitis	21.7 (19.4, 24.2)	17.2 (14.3, 20.4)	19.3 (17.5, 21.2)
Oral candidiasis	16.4 (14.5, 18.5)	9.6 (7.6, 12.0)	12.9 (11.5, 14.4)
Upper respiratory tract infection	9.1 (7.8, 10.7)	8.3 (6.5, 10.5)	8.4 (7.3, 9.6)

The data cut-off for the ongoing BE BRIGHT trial was November 9, 2020. TEAEs were assigned to the dose most recently received prior to the date of onset of the TEAE. Patients who received both BKZ 320 mg Q4W and Q8W at different times in the trials are included in the population count of both treatment groups, but only once in each BKZ total group. [a]TEAEs occurring in >5% patients in the BKZ total group.

Figure 2 Maintenance of response through two years (pooled; mNRI, NRI, OC)



[a]The BE READY and BE SURE feeder studies ran for 56 weeks, while BE VIVID ran for 52 weeks; to pool the data across all 3 studies, Week 56 data from the feeder studies were not included.

BKZ: bimekizumab; BSA: body surface area; CI: confidence interval; DLQI: Dermatology Life Quality Index; EAIR: exposure-adjusted incidence rate; IGA 0/1: score of 0 (clear) or 1 (almost clear) with ≥2-category improvement relative to baseline in Investigator's Global Assessment; IL: interleukin; mNRI: modified non-responder imputation; NRI: non-responder imputation; OC: observed case; OLE: open-label extension; PASI 90: ≥90% improvement from baseline in Psoriasis Area and Severity Index; PASI 100: 100% improvement from baseline in Psoriasis Area and Severity Index; PY: patient-years; Q4W: every 4 weeks; Q8W: every 8 weeks; SD: standard deviation; TEAE: treatment-emergent adverse event; TNF: tumor necrosis factor.

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Author Contributions: Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **BS**, **AA**, **UM**, **ML**, **PF**, **RGL**, **JB**, **CC**, **NC**, **MW**, **CP**; Drafting of the publication, or revising it critically for important intellectual content: **BS**, **AA**, **UM**, **ML**, **PF**, **RGL**, **JB**, **CC**, **NC**, **MW**, **CP**; Final approval of the publication: **BS**, **AA**, **UM**, **ML**, **PF**, **RGL**, **JB**, **CC**, **NC**, **MW**, **CP**.

Author Disclosures: BS: Consultant (honoraria) from AbbVie, Amirall, Amgen, Arcutis, Arena, Aristea, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly, Equillium, GSK, Janssen, LEO Pharma, Meiji Seika Pharma, Mindera, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma; speaker for AbbVie, Amgen, Eli Lilly, Janssen, and Ortho Dermatologics; Scientific Director (consulting fee) for CorEvitas Psoriasis Registry; investigator for AbbVie, Cara Therapeutics, CorEvitas Psoriasis Registry, Dermavant, Dermira and Novartis; Editor-in-Chief (honorarium) for Journal of Psoriasis and Psoriatic Arthritis. **AA**: Honoraria and/or research grants from AbbVie, Celgene, Eisai, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi Pharma, Sun Pharma, Taiho Pharma, Torii Pharmaceutical, and UCB Pharma. **UM**: Served as advisor and/or clinical study investigator for, and/or received honoraria and/or grants from AbbVie, Almirall, Aristea, Boehringer Ingelheim, Celgene, Dr. Reddy's Laboratories, Eli Lilly, Foamix, Formycon, Forward Pharma, Janssen, LEO Pharma, Medac, Novartis, Phi-Stone, Pierre Fabre, Sanofi, and UCB Pharma. **ML**: Employee of Mount Sinai and receives research funds from Abbvie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen Research & Development, LLC, Ortho Dermatologics, Regeneron, and UCB Pharma; consultant for Aditum Bio, AnaptysBio, Almirall, Arcutis, Aristea, Arrive technology, Avotres Therapeutics, BioMx, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Dr. Reddy, Evelo, Evommune, Facilitate International Dermatologic Education, Forte, Foundation for Research and Education in Dermatology, Helsinn, LEO Pharma, Meiji, Mindera, Pfizer, Seanergy, and Verrica. **PF**: Grant support from AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Sanofi, and Sun Pharma; served as an investigator for AbbVie, Akaal, Amgen, Arcutis, Aslan, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Botanix, Celgene, Celtaxsys, CSL, Cutanea, Dermira, Eli Lilly, Galderma, Genseq, Genentech, GSK, Hexima, Janssen, LEO Pharma, Medimmune, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals Inc, Reistone, Roche, Sanofi, Sun Pharma, UCB Pharma, and Valeant; served on advisory boards for AbbVie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, Mayne Pharma, Merck, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma, and Valeant; served as a consultant for Bristol Myers Squibb, Eli Lilly, Galderma, Janssen, LEO Pharma, Mayne Pharma, MedImmune, Novartis, Pfizer, Roche, UCB Pharma, and Wintermute; received travel grants from AbbVie, Eli Lilly, Galderma, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Roche, Sun Pharma, and Sanofi; served as a speaker for or received honoraria from AbbVie, Amgen, Celgene, Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Roche, Sanofi, Sun Pharma, and Valeant. **RGL**: Principal investigator for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer, and UCB Pharma; served on scientific advisory boards for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Leo Pharma, Merck, Novartis, Pfizer, and UCB Pharma; provided lectures for AbbVie, Amgen, Celgene, LEO Pharma, Merck, Novartis, and Pfizer. **JB**: Attended advisory boards and/or received consultancy fees and/or spoken at sponsored symposia and/or received grant funding from AbbVie, Almirall, Amgen, Anaptys-Bio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Samsung, Sienna, Sun Pharma, and UCB Pharma. **CC, NC, MW**: Employees and shareholders of 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. **Acknowledgments:** This study was funded by UCB Pharma. We would like to thank the patients and their caregivers in addition to all of the investigators and their teams who contributed to this study. The authors acknowledge Susanne Wiegratz, MSc, UCB Pharma, Monheim, Germany, for publication coordination, Natalie Nunez Gomez, MD, UCB Pharma, Brussels, Belgium, for critical review, and Evelyn Turner, BSc, and Claire Hews, PhD, Costello Medical, Cambridge, UK, for medical writing and editorial assistance. All costs associated with development of this presentation were funded by UCB Pharma.

Previously presented at AAD FiRST 2021

Conclusions

Among Week 16 responders, response rates were maintained through to two years of BKZ treatment.

IGA 0/1, BSA ≤1%, and PASI 100 response rates were maintained with BKZ with both Q4W and Q8W maintenance dosing regimens.

Among all BKZ-treated patients over two years, the most frequent adverse events were nasopharyngitis, oral candidiasis, and upper respiratory tract infection, consistent with results through one year.[2–4]