Bimekizumab Safety in Patients with Moderate to Severe Psoriasis: Analysis of Pooled Data from Phase 2 and 3 Clinical Trials

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Objective

To report short- and longer-term safety data in bimekizumab-treated patients with moderate to severe plaque psoriasis pooled from eight phase 2/3 trials.

Background

- Bimekizumab is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.[1,2]
- Given that psoriasis is a chronic disease requiring long-term management, it is important to understand the long-term safety profiles of therapies such as bimekizumab.
- We report short- and longer-term safety data in bimekizumab-treated patients with moderate to severe plaque psoriasis, and short-term data from adalimumab, ustekinumab, and placebo phase 3 comparator arms.

Methods

- Patients were included from four phase 3 trials – BE SURE, BE VIVID, BE READY, and the BE BRIGHT open-label extension (interim cut: November 1, 2019) – and four phase 2 studies – BE ABLE 1, BE ABLE 2, PS0016, and PS0018. Patients received bimekizumab 320 mg every 4 or 8 weeks (Q4W/Q8W; additional doses used in phase 2), adalimumab, ustekinumab, or placebo.
- Short-term safety from the initial treatment periods (Weeks 0–16) of three of the phase 3 trials (BE SURE, BE VIVID, and BE READY) was evaluated for patients who received ≥1 dose of bimekizumab, adalimumab, ustekinumab, or placebo.
- Longer-term safety was also evaluated for patients who received ≥1 dose of bimekizumab in BE SURE, BE VIVID, BE READY, BE BRIGHT, and the four phase 2 trials.
- We report treatment emergent adverse events (TEAEs; n [%]) for the initial treatment period for patients receiving bimekizumab 320 mg Q4W, adalimumab, ustekinumab, and placebo, as well as longer-term TEAEs for patients receiving bimekizumab 320 mg Q4W and all other doses of bimekizumab.
  - Exposure-adjusted incidence rates (EAIRs) are the incidence of new cases per 100 patient-years (PY) in patients receiving bimekizumab 320 mg Q4W (short-term) and all patients receiving any dose of bimekizumab (longer-term).
  - TEAEs were coded using MedDRA v19.0.

Results

Patient Population

- Over 16 weeks, 989 patients with psoriasis received ≥1 bimekizumab dose, 159 patients received adalimumab, 163 patients received ustekinumab, and 169 patients received placebo.
- Patient demographics and baseline disease characteristics are reported in **Table 1**.

Short-Term Safety Outcomes

- 593 (60.0%) bimekizumab-treated patients experienced ≥1 TEAE, versus 96 (60.4%) adalimumab-treated patients, 83 (50.9%) ustekinumab-treated patients, and 74 (43.8%) placebo-treated patients **(Table 2)**.
- Serious TEAEs occurred in <4% of patients in each treatment group, ranging from 1.5% for bimekizumab to 3.1% for ustekinumab.
- Discontinuations due to TEAEs occurred in <5% of patients in each group, ranging from 1.7% for bimekizumab to 4.1% for placebo **(Table 2)**.

Longer-Term Safety Outcomes

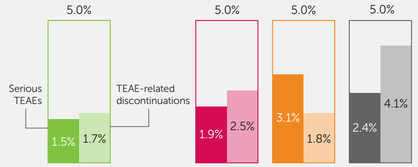
- Over the longer term, TEAEs in bimekizumab-treated patients occurred at a rate of 238.0/100 PY, serious TEAEs at 6.6/100 PY, and discontinuations due to TEAEs at 4.9/100 PY **(Table 2)**.
- Serious infections occurred at a rate of 1.4/100 PY in bimekizumab-treated patients; rates of malignancies and adjudicated major adverse cardiac events were lower, occurring at 0.8/100 PY and 0.7/100 PY, respectively **(Table 3)**.
- There was one active suicidal ideation in a bimekizumab-treated patient with pre-existing psychological conditions and one case of inflammatory bowel disease in a bimekizumab-treated patient **(Table 3)**.
- 17.0% of bimekizumab-treated patients experienced mucocutaneous candida infection TEAEs, out of which 15.1% were oral candidiasis **(Table 4)**.
  - 1 serious case (<0.1%) and 6 candidiasis-related discontinuations (0.3%) occurred.

Synopsis

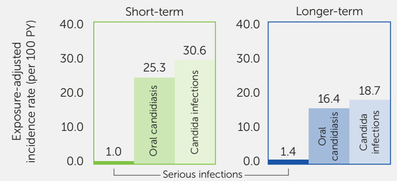
Short-term safety was evaluated for patients receiving bimekizumab 320 mg Q4W compared with adalimumab, ustekinumab, and placebo in three phase 3 trials. Longer-term safety was evaluated for patients receiving any dose of bimekizumab across eight phase 2/3 trials.

	Population exposure	Dosing	Trials administered
Short-term (BE SURE, BE VIVID, and BE READY) Week 0–16			
BKZ	n=989 306.4 PY	320 mg Q4W	3 double-blinded trials
ADA	n=159 48.8 PY	80 mg loading dose, followed by 40 mg Q2W from Week 1	1 double-blinded trial
UST	n=163 50.1 PY	45/90 mg (by weight) Q12W, after Q4W to Week 4	1 double-blinded trial
PBO	n=169 51.6 PY	Placebo	2 double-blinded trials
Longer term (phase 2/3) Data cut-off: November 1, 2019			
BKZ all doses	n=1789 1830.4 PY (Range: 1–670 days)	320 mg Q4W, 320 mg Q8W, 64 mg Q4W (phase 2), 160 mg Q4W (phase 2), 480 mg Q4W (phase 2)	6 double-blinded trials 2 open-label extension studies

Short-Term Safety Outcomes



Short- and Longer-Term Safety for Bimekizumab



Bimekizumab was well-tolerated; the majority of TEAEs were mild to moderate in severity and discontinuations were low. Oral candidiasis was the most frequent candida infection; the vast majority of oral candidiasis TEAEs were mild to moderate and did not lead to discontinuation.

Table 1 Patient demographics and baseline disease characteristics

	Initial treatment period (Week 0–16)				Longer-term
	BKZ 320 mg Q4W[a] (n=989)	ADA[b] (n=159)	UST[c] (n=163)	PBO[d] (n=169)	All BKZ[e] (n=1789)
Age (years), mean ± SD	44.8 ± 13.4	45.5 ± 14.3	46.0 ± 13.6	46.6 ± 13.7	45.2 ± 13.5
Male, n (%)	698 (70.6)	114 (71.7)	117 (71.8)	118 (69.8)	1252 (70.0)
Caucasian, n (%)	841 (85.0)	141 (88.7)	120 (73.6)	142 (84.0)	1468 (82.1)
Weight (kg), mean ± SD	89.6 ± 22.2	90.5 ± 22.1	87.2 ± 21.1	90.4 ± 24.3	89.0 ± 22.0
Duration of plaque psoriasis (years), mean ± SD	18.2 ± 12.5	16.2 ± 11.9	17.8 ± 11.6	19.4 ± 13.2	17.7 ± 12.3
PASI, mean ± SD	20.9 ± 7.6	19.1 ± 5.9	21.3 ± 8.3	20.1 ± 7.2	20.6 ± 7.8
BSA (%), mean ± SD	26.4 ± 15.6	25.0 ± 14.4	27.3 ± 16.7	25.7 ± 16.2	26.7 ± 16.3
IGA, n (%)[f]					
3: moderate	656 (66.3)	114 (71.7)	96 (58.9)	116 (68.6)	1217 (68.0)
4: severe	332 (33.6)	45 (28.3)	66 (40.5)	52 (30.8)	567 (31.7)
DLQI total, mean ± SD	10.4 ± 6.3	10.5 ± 7.4	11.0 ± 6.9	10.7 ± 6.8	10.3 ± 6.6
Prior biologic therapy, n (%)	380 (38.4)	53 (33.3)	63 (38.7)	70 (41.4)	636 (35.6)
anti-TNF	132 (13.3)	14 (8.8)	24 (14.7)	26 (15.4)	234 (13.1)
anti-IL-17	231 (23.4)	35 (22.0)	38 (23.3)	36 (21.3)	341 (19.1)

[a]BKZ initial treatment period (Weeks 0–16) data are included from three pivotal phase 3 studies, BE SURE (NCT03412747), BE VIVID (NCT03370133), and BE READY (NCT03410992); [b]ADA initial treatment period data are from one pivotal phase 3 study, BE SURE; [c]UST initial treatment period data are from one pivotal phase 3 study, BE VIVID; [d]PBO initial treatment period data are from two pivotal phase 3 studies, BE VIVID and BE READY; [e]BKZ longer-term data are pooled from four phase 3 trials (BE SURE, BE VIVID, BE READY, BE BRIGHT [NCT03598790]) and four phase 2 trials (BE ABLE 1, BE ABLE 2, PS0016, and PS0018). [f]In the BKZ, UST, and PBO short-term groups, one patient with mild IGA score was mistakenly enrolled.

Table 2 Occurrence of short- and longer-term TEAEs

	Initial treatment period (Week 0–16)				Short-term	Longer-term
	n (%)				EAIR/100 PY (95% CI)	
	BKZ 320 mg Q4W (n=989)	ADA (n=159)	UST (n=163)	PBO (n=169)	BKZ 320 mg Q4W (n=989)	All BKZ (n=1789)
Any TEAE	593 (60.0)	96 (60.4)	83 (50.9)	74 (43.8)	315.7 (290.8, 342.1)	238.0 (226.0, 250.5)
Serious TEAEs	15 (1.5)	3 (1.9)	5 (3.1)	4 (2.4)	4.9 (2.8, 8.1)	6.6 (5.5, 7.9)
Discontinuation due to TEAEs	17 (1.7)	4 (2.5)	3 (1.8)	7 (4.1)	5.6 (3.3, 8.9)	4.9 (4.0, 6.1)
Drug-related TEAEs	212 (21.4)	32 (20.1)	19 (11.7)	15 (8.9)	79.5 (69.2, 90.9)	47.3 (43.7, 51.1)
Severe TEAEs	12 (1.2)	4 (2.5)	3 (1.8)	4 (2.4)	3.9 (2.0, 6.9)	6.4 (5.2, 7.6)
Deaths	1 (0.1)	1 (0.6)	1 (0.6)	1 (0.6)	0.3 (0.0, 1.8)	0.3 (0.1, 0.6)

Table 3 Occurrence of short- and longer-term TEAEs of interest

	Initial treatment period (Week 0–16)				Short-term	Longer-term
	n (%)				EAIR/100 PY (95% CI)	
	BKZ 320 mg Q4W (n=989)	ADA (n=159)	UST (n=163)	PBO (n=169)	BKZ 320 mg Q4W (n=989)	All BKZ (n=1789)
Serious infections	3 (0.3)	0	2 (1.2)	0	1.0 (0.2, 2.9)	1.4 (0.9, 2.0)
Inflammatory bowel disease	1 (0.1)	0	0	0	0.3 (0.0, 1.8)	0.1 (0.0, 0.3)
Candida infections	90 (9.1)	0	0	0	30.6 (24.6, 37.6)	18.7 (16.7, 21.0)
Oral candidiasis	75 (7.6)	0	0	0	25.3 (19.9, 31.8)	16.4 (14.5, 18.5)
Adjudicated MACE	1 (0.1)	0	0	0	0.3 (0.0, 1.8)	0.7 (0.3, 1.1)
Malignancies (inc. NMSC)	4 (0.4)	1 (0.6)	0	1 (0.6)	1.3 (0.4, 3.4)	0.8 (0.5, 1.4)
Adjudicated SIB	0	0	0	0	0	0.1 (0.0, 0.3)[a]
Serious hypersensitivity reactions	0	0	0	0	0	0.2 (0.0, 0.5)[b]
Injection site reactions	27 (2.7)	3 (1.9)	2 (1.2)	2 (1.2)	9.0 (5.9, 13.1)	3.1 (2.4, 4.1)
Hepatic events	19 (1.9)	9 (5.7)	0	2 (1.2)	6.3 (3.8, 9.8)	5.6 (4.6, 6.8)
Liver function analyses	18 (1.8)	9 (5.7)	0	2 (1.2)	5.9 (3.5, 9.4)	4.8 (3.8, 5.9)

[a]Includes one event adjudicated by the external Neuropsychiatric Committee (active suicidal ideation with some intent to act) in a patient with pre-existing psychiatric conditions; [b]Includes one fatal event of circulatory failure (adjudicated MACE), one event of atopic dermatitis-like disseminated eczema, and one case of anaphylactic shock due to insect sting, all considered unrelated to study treatment.

Table 4 Longer-term candida infections in BKZ-treated patients

	Longer-term all BKZ (n=1789)			
	EAIR per 100 PY (95% CI)	n (%)	Serious | n (%)	Severe | n (%)
Candida infections	18.7 (16.7, 21.0)	304 (17.0)	1 (<0.1)	4 (0.2)
Oral candidiasis	16.4 (14.5, 18.5)	271 (15.1)	0	3 (0.2)
Oropharyngeal candidiasis	1.2 (0.7, 1.8)	21 (1.2)	0	0
Skin candidiasis	0.6 (0.3, 1.1)	11 (0.6)	0	0
Vulvovaginal candidiasis	0.8 (0.5, 1.4)	15 (0.8)	0	0
Esophageal candidiasis	0.3 (0.1, 0.6)	5 (0.3)	1 (<0.1)	1 (<0.1)
Leading to discontinuation	0.3 (0.1, 0.7)	6 (0.3)	1 (<0.1)	1 (<0.1)

Conclusions

Bimekizumab was well-tolerated across the plaque psoriasis clinical program; most TEAEs were mild to moderate and discontinuations were low.

All candida infections were mucocutaneous in origin, with oral candidiasis being most frequent; oral candidiasis TEAEs were predominantly mild to moderate and the vast majority did not lead to discontinuation.

ADA: adalimumab; BKZ: bimekizumab; BSA: body surface area; CI: confidence interval; DLQI: Dermatology Life Quality Index; EAIR: exposure-adjusted incidence rate; IGA: Investigator's Global Assessment; IL: interleukin; MACE: major adverse cardiovascular event; NMSC: non-melanoma skin cancers; PASI: Psoriasis Area and Severity Index; PBO: placebo; PY: patient-years; Q2/4/8/12W: every 2/4/8/12 weeks; SD: standard deviation; SIB: suicidal ideation and behavior; TEAE: treatment emergent adverse event; TNF: tumor necrosis factor; UST: ustekinumab.

Institutions: [1]Center for Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf and *Skinflammation*® Center, Hamburg, Germany; [2]Oregon Medical Research Center, Portland, Oregon, USA; [3]Icahn School of Medicine at Mount Sinai, New York, New York, USA; [4]Probity Medical Research and K Papp Clinical Research, Waterloo, Ontario, Canada; [5]Oregon Dermatology and Research Center, Portland, Oregon, USA; [6]Yale University, New Haven, Connecticut, USA; [7]Central Connecticut Dermatology Research, Cromwell, Connecticut, USA; [8]UCB Pharma, Brussels, Belgium; [9]UCB Pharma, Raleigh, North Carolina, USA; [10]Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester NIHR Biomedical Research Centre, The University of Manchester, Manchester, UK

References: [1]Glatt S, Br J Clin Pharmacol 2017;83:991–1001; [2]Papp KA. J Am Acad Dermatol 2018;79:277–86 e10. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **KR, AB,ML, KAP, PR, BS, DDC, CM, LP, VV, RBW**; drafting of the publication, or revising it critically for important intellectual content: **KR, AB,ML, KAP, PR, BS, DDC, CM, LP, VV, RBW**; final approval of the publication: **KR, AB,ML, KAP, PR, BS, DDC, CM, LP, VV, RBW**. **Author Disclosures: KR:** Served as advisor and/or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Affibody, Almirall, Amgen, Avillion, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Centocor, Covagen, Dermira, Eli Lilly, Forward Pharma, Fresenius Medical Care, Galapagos, GSK, Janssen, Kyowa Kirin, LEO Pharma, Medac, MSD, Miltenyi Biotec, Novartis, Ocean Pharma, Pfizer, Regeneron, Samsung Bioepis, Sanofi, Sun Pharma, Takeda, UCB Pharma, Valeant/Bausch Health, and Xenoport; **AB:** Served as a scientific adviser and/or clinical study investigator for AbbVie, Allergan, Almirall, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Forte, Galderma, Incyte, Janssen, LEO Pharma, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma; paid speaker for AbbVie; **ML:** Employee of Mount Sinai which receives research funds from AbbVie, Amgen, Arcutis, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen, LEO Pharma, Ortho Dermatologics, Pfizer, and UCB Pharma; consultant for Aditum Bio, Allergan, Almirall, Arcutis, Avotres, BirchBioMed, BMD Skincare, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant, Evelo, Facilitate International Dermatologic Education, Foundation for Research and Education in Dermatology, Inozyme Pharma, LEO Pharma, Meiji Seika Pharma, Menlo, Mitsubishi Pharma, Neuroderm, Pfizer, Promius/Dr. Reddy's Laboratories, Serono, Theravance, and Verrica; **KAP:** Honoraria and/or grants from AbbVie, Akros, Amgen, Arcutis, Astellas, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Canfite, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Forward Pharma, Galderma, Genentech, Gilead, GSK, Janssen, Kyowa Kirin, LEO Pharma, MedImmune, Merck (MSD), Merck-Serono, Mitsubishi Pharma, Moberg Pharma, Novartis, Pfizer, PRCI, Research, Regeneron, Roche, Sanofi Genzyme, Sun Pharma, Takeda, UCB Pharma, and Valeant/Bausch Health; consultant (no compensation) for AstraZeneca and Meiji Seika Pharma; **PR:** Research grants due to being principal investigator from AbbVie, Arcutis, Bristol Myers Squibb, Centocor, Dermavant, Eli Lilly, Kadmon, Merck, Novartis, Pfizer, Sun Pharma, and UCB Pharma; **BS:** Consultant (honoraria) from AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly, Equilliurn, 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 Corrona Psoriasis Registry; investigator for AbbVie, Cara Therapeutics, Corrona Psoriasis Registry, Dermavant, Dermira, and Novartis; Editor-in-Chief (honorarium) for Journal of Psoriasis and Psoriatic Arthritis; **DDC, LP, VV:** employees of UCB Pharma; **CM:** employee and shareholder of UCB Pharma; **RBW:** Consulting fees from AbbVie, Almirall, Amgen, Arena, Avillion, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; research grants from AbbVie, Almirall, Amgen, Celgene, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, and UCB Pharma. **Acknowledgements:** This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Mylene Serna, PharmD, UCB Pharma, Smyrna, GA, USA and Susanne Wiegratz, MSc, UCB Pharma, Monheim am Rhein, Germany for publication coordination; Eva Cullen, PhD, UCB Pharma, Brussels, Belgium for critical review; Daniel Smith, BA, Costello Medical, Cambridge, UK for medical writing and editorial assistance; and the Costello Medical Design Team for design support. All costs associated with development of this poster were funded by UCB Pharma.

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