Bimekizumab safety in patients with moderate to severe plaque psoriasis: Analysis of pooled data from up to three years of treatment in phase 2 and 3 clinical trials

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Objectives

To report long-term safety data, pooled to include three years of treatment, in patients with moderate to severe plaque psoriasis treated with bimekizumab (BKZ) across four phase 2 and four phase 3 clinical trials.

Introduction

- BKZ is a monoclonal immunoglobulin G1 antibody which selectively inhibits interleukin (IL)-17F in addition to IL-17A,[1,2] and is used in the treatment of psoriasis.
- Given the chronic nature of psoriasis, it is important to consider long-term safety of treatments.[3]
- Data pooled over two years have indicated that BKZ is generally well-tolerated.[4]
- Here, the first three-year safety data for BKZ in patients with moderate to severe plaque psoriasis are reported, pooled from phase 2 and 3 clinical trials.

Materials and Methods

- Long-term safety data were evaluated for all patients who received ≥1 dose of BKZ in four phase 3 trials (BE SURE, BE VIVID, BE READY, and their ongoing open-label extension BE BRIGHT [data cut-off: 23 Oct 2021]) and four phase 2 trials (BE ABLE 1, BE ABLE 2, PS0016, and PS0018).[5]
- Safety data were also evaluated separately for patients receiving BKZ dosed 320 mg every 4 weeks (Q4W) or every 8 weeks (Q8W); Q8W dosing was only used in maintenance treatment in phase 3 trials, however, most patients were receiving BKZ Q8W by Year 3.
- Treatment-emergent adverse events (TEAEs) were coded using MedDRA v19.0. Data are presented cumulatively as exposure-adjusted incidence rates (EAIRs), defined as the incidence of new cases per 100 patient-years (PY).

Results

- Baseline demographics were similar between BKZ dose groups (**Table 1**).
- Safety data observed over three years of BKZ treatment were consistent with those observed over two years;[4] EAIRs did not increase with longer BKZ exposure, and were generally lower in Q8W- vs Q4W-treated patients (**Figure 1**, **Table 2**).
- The three most common TEAEs in the phase 2/3 trials with BKZ were nasopharyngitis, oral candidiasis, and upper respiratory tract infection, consistent with previous reports (**Table 2**).[4]
- Eighteen deaths occurred; all were deemed unrelated to BKZ except one (relationship unknown) at the time of the data cut-off.
- The rates of inflammatory bowel disease, adjudicated major adverse cardiac events, malignancies, adjudicated suicidal ideation and behavior, and neutropenia remained low, and were comparable to two-year data (**Table 2**).[4] There were no cases of active tuberculosis.
- Rates of oral candidiasis decreased with longer duration of bimekizumab exposure (**Figure 1C**; **Table 2**). No serious oral candidiasis events occurred; the vast majority were mild or moderate (99.4%). Over three years of BKZ treatment, 79.9% of patients experienced no oral candidiasis events. Of those who did experience such events, most had either one (9.8%) or two (5.1%) occurrences.

Summary

		Phase 2 and 3[a]	Phase 3[b]		
		BKZ Total	BKZ Q4W	BKZ Q8W	BKZ Total
	Population	N=1,789	N=1,456	N=1,289	N=1,495
	Exposure	4,245.3 PY	1,965.6 PY	1,914.5 PY	3,876.4 PY
	Dosing	320 mg Q4W 320 mg Q8W 64 mg Q4W (phase 2) 160 mg Q4W (phase 2) 480 mg Q4W (phase 2)	320 mg Q4W	320 mg Q8W	320 mg Q4W 320 mg Q8W
	Trials administered	6 double-blinded trials and 2 OLEs	3 double-blinded trials and 1 OLE	2 double-blinded trials and 1 OLE	3 double-blinded trials and 1 OLE

BKZ was well-tolerated over three years of treatment. Safety data were consistent with those observed over two years of BKZ treatment; no safety signals were identified.

The majority of patients were receiving BKZ Q8W by Year 3. [a]Phase 2 and phase 3 data are pooled from the initial and maintenance treatment periods of the BE SURE, BE VIVID, and BE READY phase 3 trials, their open-label extension BE BRIGHT, and four phase 2 trials (BE ABLE 1, BE ABLE 2, PS0016, PS0018); [b]Phase 3 data are pooled from the initial and maintenance treatment periods of the BE SURE, BE VIVID, and BE READY phase 3 trials, and their open-label extension BE BRIGHT.

Table 1 Baseline characteristics

	Phase 2 and 3	Phase 3		
	BKZ Total[a] (N=1,789)	BKZ 320 mg Q4W (N=1,456)	BKZ 320 mg Q8W (N=1,289)	BKZ Total[a] (N=1,495)
Age (years), mean ± SD	45.2 ± 13.5	45.4 ± 13.5	45.5 ± 13.3	45.4 ± 13.4
Male, n (%)	1,252 (70.0)	1,042 (71.6)	934 (72.5)	1,067 (71.4)
Caucasian, n (%)	1,468 (82.1)	1,173 (80.6)	1,057 (82.0)	1,208 (80.8)
Region, n (%)				
North America	635 (35.5)	534 (36.7)	432 (33.5)	542 (36.3)
Central/Eastern Europe	728 (40.7)	535 (36.7)	528 (41.0)	558 (37.3)
Western Europe	168 (9.4)	164 (11.3)	144 (11.2)	168 (11.2)
Asia/Australia	258 (14.4)	223 (15.3)	185 (14.4)	227 (15.2)
Weight (kg), mean ± SD	89.0 ± 22.0	89.1 ± 22.3	89.0 ± 21.7	89.1 ± 22.3
Disease duration (years), mean ± SD	17.7 ± 12.3	17.8 ± 12.3	18.3 ± 12.4	17.9 ± 12.3
Prior biologic therapy, n (%)	636 (35.6)	559 (38.4)	508 (39.4)	576 (38.5)
Anti-TNF	240 (13.4)	200 (13.7)	180 (14.0)	207 (13.8)
Anti-IL-17	343 (19.2)	331 (22.7)	312 (24.2)	343 (22.9)
Prior systemic therapy, n (%)	1,360 (76.0)	1,135 (78.0)	1,019 (79.1)	1,166 (78.0)

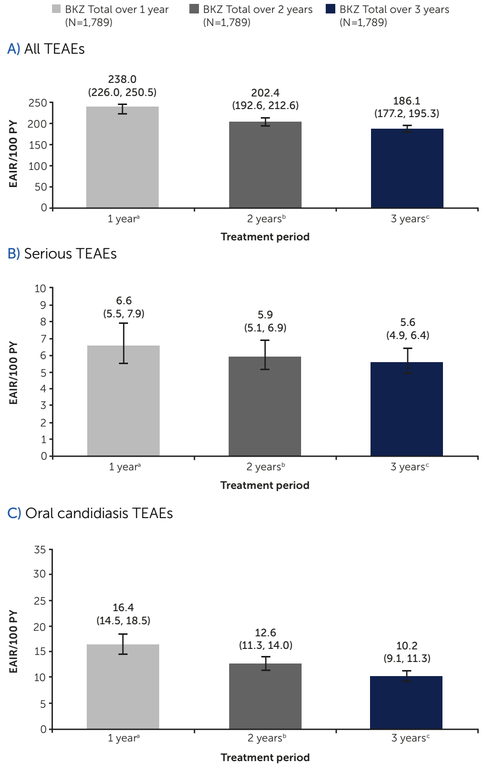
[a]Patients who received both BKZ 320 mg Q4W and Q8W are included in the population count of both treatment groups, but only once in each BKZ Total group.

Table 2 Summary of treatment exposure, summary of TEAEs, most common TEAEs, and TEAEs of interest in BKZ-treated patients in the phase 2 and 3 trials

	TEAEs over two years[d]	TEAEs over three years			
	Phase 2 and 3	Phase 2 and 3	Phase 3		
	BKZ Total[a] (N=1,789)	BKZ Total[a] (N=1,789)	BKZ 320 mg Q4W (N=1,456)	BKZ 320 mg Q8W (N=1,289)	BKZ Total[a] (N=1,495)
Summary of treatment exposure					
Total exposure, PY	3,109.7	4,245.3	1,965.6	1,914.5	3,876.4
Mean exposure ± SD, days	608.5 ± 232.6	837.0 ± 365.7	476.2 ± 284.4	536.5 ± 290.8	932.4 ± 317.7
Median exposure (range), days	673.0 (1–1,037)	995.0 (1–1,326)	504.0 (23–1,093)	448.0 (1–1,214)	1,058.0 (23–1,326)
Summary of TEAEs, EAIR/100 PY (95% CI)					
Any TEAE	202.4 (192.6, 212.6)	186.1 (177.2, 195.3)	217.9 (205.8, 230.5)	115.6 (108.2, 123.3)	175.5 (166.4, 185.0)
Severe TEAEs	5.4 (4.6, 6.3)	4.9 (4.3, 5.6)	5.3 (4.3, 6.4)	4.2 (3.3, 5.2)	4.5 (3.9, 5.3)
TEAEs leading to discontinuation	3.8 (3.1, 4.6)	3.5 (3.0, 4.1)	3.8 (2.9, 4.7)	2.5 (1.9, 3.3)	3.2 (2.6, 3.8)
Treatment-related TEAEs	35.4 (32.9, 38.0)	29.4 (27.4, 31.5)	42.3 (38.8, 45.9)	21.1 (18.8, 23.5)	28.9 (26.8, 31.1)
Serious TEAEs	5.9 (5.1, 6.9)	5.6 (4.9, 6.4)	6.2 (5.1, 7.4)	5.4 (4.4, 6.5)	5.5 (4.8, 6.4)
TEAEs leading to death	0.4 (0.2, 0.6)	0.4 (0.3, 0.7)	0.4 (0.2, 0.8)	0.4 (0.2, 0.8)	0.4 (0.2, 0.7)
Three most common TEAEs, EAIR/100 PY (95% CI)					
Nasopharyngitis	19.1 (17.4, 20.9)	15.3 (13.9, 16.7)	21.1 (18.9, 23.5)	10.0 (8.5, 11.6)	15.0 (13.6, 16.5)
Oral candidiasis	12.6 (11.3, 14.0)	10.2 (9.1, 11.3)	15.9 (14.1, 17.9)	7.1 (5.9, 8.5)	10.1 (9.1, 11.3)
Upper respiratory tract infection	8.9 (7.8, 10.1)	7.1 (6.2, 8.0)	8.9 (7.6, 10.4)	4.9 (3.9, 6.1)	6.5 (5.7, 7.4)
TEAEs of interest, EAIR/100 PY (95% CI)					
Serious infections	1.0 (0.7, 1.4)	1.2 (0.9, 1.5)	1.4 (0.9, 2.0)	1.1 (0.7, 1.7)	1.2 (0.9, 1.6)
Active tuberculosis	0.0	0.0	0.0	0.0	0.0
Fungal infections	20.1 (18.4, 22.0)	16.6 (15.3, 18.1)	25.0 (22.6, 27.6)	12.6 (10.9, 14.4)	16.7 (15.3, 18.3)
Oral candidiasis	12.6 (11.3, 14.0)	10.2 (9.1, 11.3)	15.9 (14.1, 17.9)	7.1 (5.9, 8.5)	10.1 (9.1, 11.3)
Inflammatory bowel disease	0.1 (0.0, 0.3)	0.1 (0.0, 0.3)	0.2 (0.0, 0.4)	0.1 (0.0, 0.4)	0.1 (0.0, 0.3)
Adjudicated MACE	0.5 (0.3, 0.8)	0.6 (0.4, 0.8)	0.7 (0.4, 1.1)	0.5 (0.2, 0.9)	0.6 (0.4, 0.9)
Malignancies	0.8 (0.5, 1.2)	0.9 (0.6, 1.2)	0.6 (0.3, 1.1)	1.2 (0.7, 1.8)	0.9 (0.6, 1.2)
NMSC	0.3 (0.2, 0.6)	0.3 (0.2, 0.6)	0.3 (0.1, 0.7)	0.3 (0.1, 0.7)	0.3 (0.2, 0.5)
Adjudicated SIB	0.0 (0.0, 0.2)	0.1 (0.0, 0.2)	0.1 (0.0, 0.4)	0.1 (0.0, 0.3)	0.1 (0.0, 0.2)
Neutropenia events	0.8 (0.6, 1.2)	0.6 (0.4, 0.9)	0.8 (0.4, 1.3)	0.2 (0.0, 0.5)	0.4 (0.3, 0.7)
Hepatic events	4.3 (3.6, 5.2)	4.0 (3.4, 4.7)	3.7 (2.9, 4.7)	3.2 (2.5, 4.1)	3.2 (2.7, 3.8)
AST or ALT elevations[b]					
>3x ULN	2.4 (1.9, 3.0)	2.2 (1.7, 2.7)	2.8 (2.1, 3.6)	1.9 (1.3, 2.6)	2.1 (1.7, 2.6)
>5x ULN[c]	0.8 (0.5, 1.2)	0.6 (0.4, 0.9)	0.7 (0.4, 1.2)	0.5 (0.2, 0.9)	0.6 (0.4, 0.9)
Serious hypersensitivity reactions[d]	0.2 (0.1, 0.4)	0.1 (0.0, 0.3)	0.2 (0.0, 0.4)	0.1 (0.0, 0.3)	0.1 (0.0, 0.3)
Injection site reactions	2.3 (1.8, 2.9)	1.9 (1.5, 2.3)	2.7 (2.0, 3.5)	1.2 (0.8, 1.8)	1.8 (1.4, 2.3)

Data are shown as of the data cut-off (two years: 9 Nov 2020; three years: 23 Oct 2021). [a]Patients are included in the relevant BKZ dose group based on the dose most recently received prior to the date of the adverse event or assessment. Patients who received both BKZ 320 mg Q4W and Q8W are included in the population count of both treatment groups, but only once in each BKZ Total group; [b]Not all hepatic laboratory parameter elevations were reported as adverse events; [c]>3x and >5x elevations are evaluated independently, hence patients with >5x elevations are also included in the >3x data; [d]No anaphylactic reactions associated with BKZ were reported.

Figure 1 Cumulative EAIRs for TEAEs over three years in the phase 2 and 3 trials



Error bars represent 95% CIs. Data are pooled from four phase 2 and four phase 3 trials. Phase 2 data were not collected beyond 2 years. Data are reported as of the relevant data cut-offs: [a]1 Nov 2019; [b]9 Nov 2020; [c]23 Oct 2021.

ALT: alanine aminotransferase; **AST:** aspartate aminotransferase; **BKZ:** bimekizumab; **CI:** confidence interval; **EAIR:** exposure-adjusted incidence rate; **IL-17:** interleukin-17; **MACE:** major adverse cardiac event; **NMSC:** non-melanoma skin cancer; **OLE:** open-label extension; **PY:** patient-years; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SD:** standard deviation; **SIB:** suicidal ideation and behavior; **TEAE:** treatment-emergent adverse event; **TNF:** tumour necrosis factor; **ULN:** upper limit of normal.

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References: [1]Glatt S *et al.* Ann Rheum Dis 2018;77:523–32; [2]Adamu R *et al.* Front Immunol 2020;11:1894; [3]Warren RB *et al.* J Invest Dermatol 2015;135:2632–40; [4]Gordon KB *et al.* JAMA Dermatol 2022;158(7):755–744; [5]BE SURE (NCT03412747); BE VIVID (NCT03370133); BE READY (NCT03410992); BE BRIGHT (NCT03598790); BE ABLE 1 (NCT02905006); BE ABLE 2 (NCT03010527); PS0016 (NCT03025542); PS0018 (NCT03230292). **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **KBG, RGL, RBW, YO, DR, ML, LP, CM, DdC, NNG, DT**; Drafting of the publication, or revising it critically for important intellectual content: **KBG, RGL, RBW, YO, DR, ML, LP, CM, DdC, NNG, DT**; Final approval of the publication: **KBG, RGL, RBW, YO, DR, ML, LP, CM, DdC, NNG, DT**. **Author Disclosures: KBG:** Received consulting fees from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma; research support from AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and UCB Pharma. **RGL:** Principal investigator for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer, UCB Pharma; served on scientific advisory boards for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer, UCB Pharma; provided lectures for AbbVie, Amgen, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, and Pfizer. **RBW:** Received consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; received research grants to institution from AbbVie, Almirall, Janssen, LEO Pharma, Novartis, and UCB Pharma; honoraria from Astellas, DiCE, GSK, and Union. **YO:** Received research grants from Eisai, Maruho, Shiseido, Torii; current consulting/advisory board agreements from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Janssen, Sun Pharma; speakers bureau from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eisai, Eli Lilly, Janssen, Jimro, Kyowa Kirin, LEO Pharma, Maruho, Novartis, Pfizer, Sanofi, Sun Pharma, Taiho, Tanabe-Mitsubishi, Torii, UCB Pharma; clinical trials sponsored by AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, LEO Pharma, Maruho, Pfizer, Sun Pharma, and UCB Pharma. **DR:** Received honoraria as a consultant for AbbVie, Abcuro, AltruBio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Concert, Dermavant, Dermira, Eli Lilly, Incyte, Janssen, Kyowa Kirin, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, UCB Pharma, VielaBio; has received research support from AbbVie, Amgen, Bristol Myers Squibb, Cara Therapeutics, Celgene, Dermira, Eli Lilly, Galderma, Incyte, Janssen, Merck, Novartis, Pfizer, and Regeneron; served as a paid speaker for AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Regeneron, and Sanofi. **ML:** Employee of Mount Sinai; receives research funds from AbbVie, Amgen, Arcutis, Avotres Therapeutics, Boehringer Ingelheim, Cara Therapeutics for YO, Dermavant, Eli Lilly, Incyte, Janssen, Ortho Dermatologics, Regeneron, and UCB Pharma; consultant for Aditum Bio, Almirall, AltruBio, AnaptysBio, Arcutis, Aristea Therapeutics, Arrive Technologies, Avotres Therapeutics, BiomX, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, CorEvitas (formerly Corrona), Dermavant, Dr. Reddy's Laboratories, Evelo Biosciences, Evommune, Facilitation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Helsinn Therapeutics, Hexima, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Samsung, Seanergy, and Verrica. **LP, CM, DdC:** Employees and shareholders of UCB Pharma. **NNG:** Former employee and shareholder of UCB Pharma. **DT:** Honoraria for participation on advisory boards, as a speaker and for consultancy from AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly, Galapagos, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma and UCB Pharma; received research grants received from LEO Pharma and Novartis. **Acknowledgements:** This study was funded by UCB Pharma. 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Conclusions

BKZ was well-tolerated over three years of treatment; no safety signals were identified. EAIRs of TEAEs did not increase compared with data from two years of treatment.[4]