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Bimekizumab safety in patients with moderate to severe plaque psoriasis: Safety topics of interest over time using pooled data from up to three years of treatment in five phase 3/3b clinical trials

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Objective

To evaluate treatment-emergent adverse events (TEAEs) of interest over up to 3 years for patients with moderate to severe plaque psoriasis receiving bimekizumab (BKZ), using pooled safety data from five phase 3/3b trials.

Background

- Psoriasis is a chronic, inflammatory, systemic disease which requires long-term management;[1] therefore, it is important to consider the long-term safety of psoriasis treatments.[2]
- BKZ is a monoclonal IgG1 antibody which selectively inhibits interleukin (IL)-17F in addition to IL-17A,[3] that has demonstrated efficacy and safety in the treatment of psoriasis.[4–8]

Methods

- Rates of TEAEs of interest were evaluated for all patients who received ≥1 BKZ dose at any point in BE SURE, BE VIVID or BE READY, their open-label extension (OLE) BE BRIGHT (3-year data) or the BE RADIANT phase 3b trial (2-year data) (**Figure 1**).[4–8]
- Patients could receive BKZ 320 mg every 4 weeks (Q4W) or every 8 weeks (Q8W) during the double-blinded periods of the trials; all received BKZ Q4W or Q8W upon OLE entry, depending on double-blinded treatment, dosing and Psoriasis Area and Severity Index (PASI) response.
- All patients received BKZ Q8W dosing from Week 64 (OLE Week 16, BE RADIANT) or Week 100/104 (OLE Week 48, BE BRIGHT), or the next scheduled clinic visit.
- TEAEs were coded using MedDRA v19.0 and reported using exposure-adjusted incidence rates (EAIRs), defined as incidence of new cases reported per 100 patient-years (PY), with 95% confidence intervals (CIs).

Results

- Total BKZ exposure was 4,932.1 PY among the 2,186 patients included in the BKZ Total group (see **Summary**).
- Rates of serious infections were low over 3 years (**Table 1**) and did not increase from Year 1 to Year 3 (**Figure 2**). Rates of fungal infections, including oral candidiasis, decreased with longer exposure (**Figure 3**).
  - The global COVID-19 pandemic was concurrent with the BE RADIANT and BE BRIGHT OLEs. Serious infections including and related to coronavirus infection likely contributed to numerically increased incidence rates in Year 3 compared with Year 2.
- There were no cases of active tuberculosis reported.
- No deaths were reported as treatment-related by the investigators.
- The incidence rates of other TEAEs of interest, including malignancies, inflammatory bowel disease (IBD) and suicidal ideation and behaviour (SIB), were low across 3 years of BKZ treatment (**Table 1**; **Figure 2**).
- Hepatic TEAEs occurred at rates of 4.3, 3.5 and 3.4/100 PY in Year 1, Year 2 and Year 3, respectively.
  - Most were cases of elevated liver enzymes, at 3.7, 2.6 and 3.1/100 PY in Year 1, Year 2 and Year 3. EAIRs of laboratory liver serum transaminases >3x and >5x the upper limit of normal (ULN) did not increase from Year 1 to Year 3 (**Figure 4**).

Conclusions

BKZ was well-tolerated throughout 3 years of treatment across phase 3/3b trials, with no unexpected safety findings identified.

EAIRs of TEAEs of interest did not increase with longer BKZ treatment duration.

Summary

Data pool

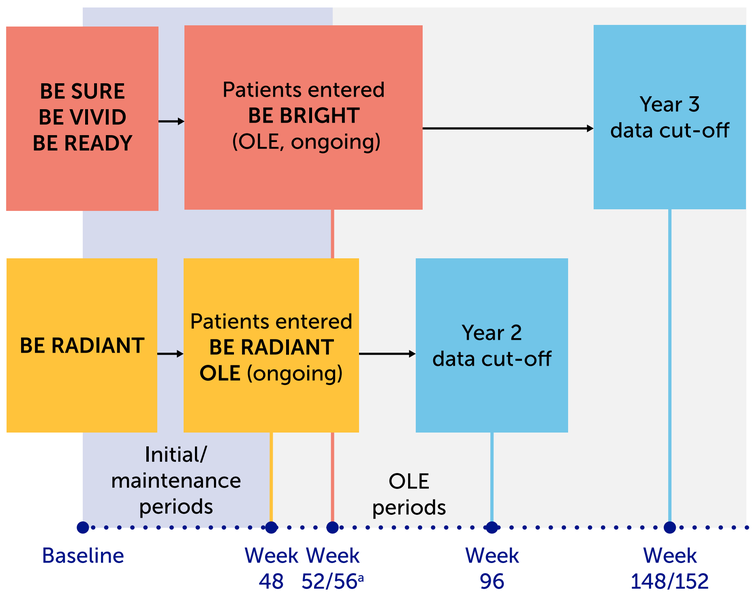
	By time period			Over 3 years
	BKZ Total			BKZ Total
	Year 1	Year 2	Year 3	
Weeks	0–52	>52–104	>104–156	0–data cut-off
Number of patients	n=2,186	n=1,907	n=1,444[a]	N=2,186
Total exposure, PY	2,044.7	1,657.3	1,081.5	4,932.1[b]
Mean exposure (SD), days	344.3 (63.5)	319.7 (98.2)	265.5 (122.4)	811.1 (339.4)
Median exposure (range), days	364.0 (23–364)	364.0 (1–364)	337.0 (1–364)	874.5 (23–1,326)

Data were pooled for all patients who received ≥1 BKZ dose in BE SURE, BE VIVID, BE READY, their OLE BE BRIGHT (data cut-off: 23 Oct 2021) or BE RADIANT (data cut-off: 20 Apr 2021).[4–8] Data are presented for the full pooled trial period, and separately for Years 1 (Week 0–52), 2 (Week >52–104) and 3 (Week >104–156). [a]Patient numbers decrease in Year 3 as BE RADIANT data are only through 2 years; [b]Total BKZ exposure over 3 years is greater than the sum of BKZ exposure in individual years, as data beyond Week 156 are included in the BKZ Total group due to the use of cut-off dates (some patients had proceeded past Week 156 by the cut-off date).

BKZ was well-tolerated throughout 3 years of treatment across phase 3/3b trials, with no unexpected safety findings identified with longer-term exposure.

Rates of TEAEs of interest were generally low and did not increase with longer duration of BKZ exposure.

Figure 1 Included patients



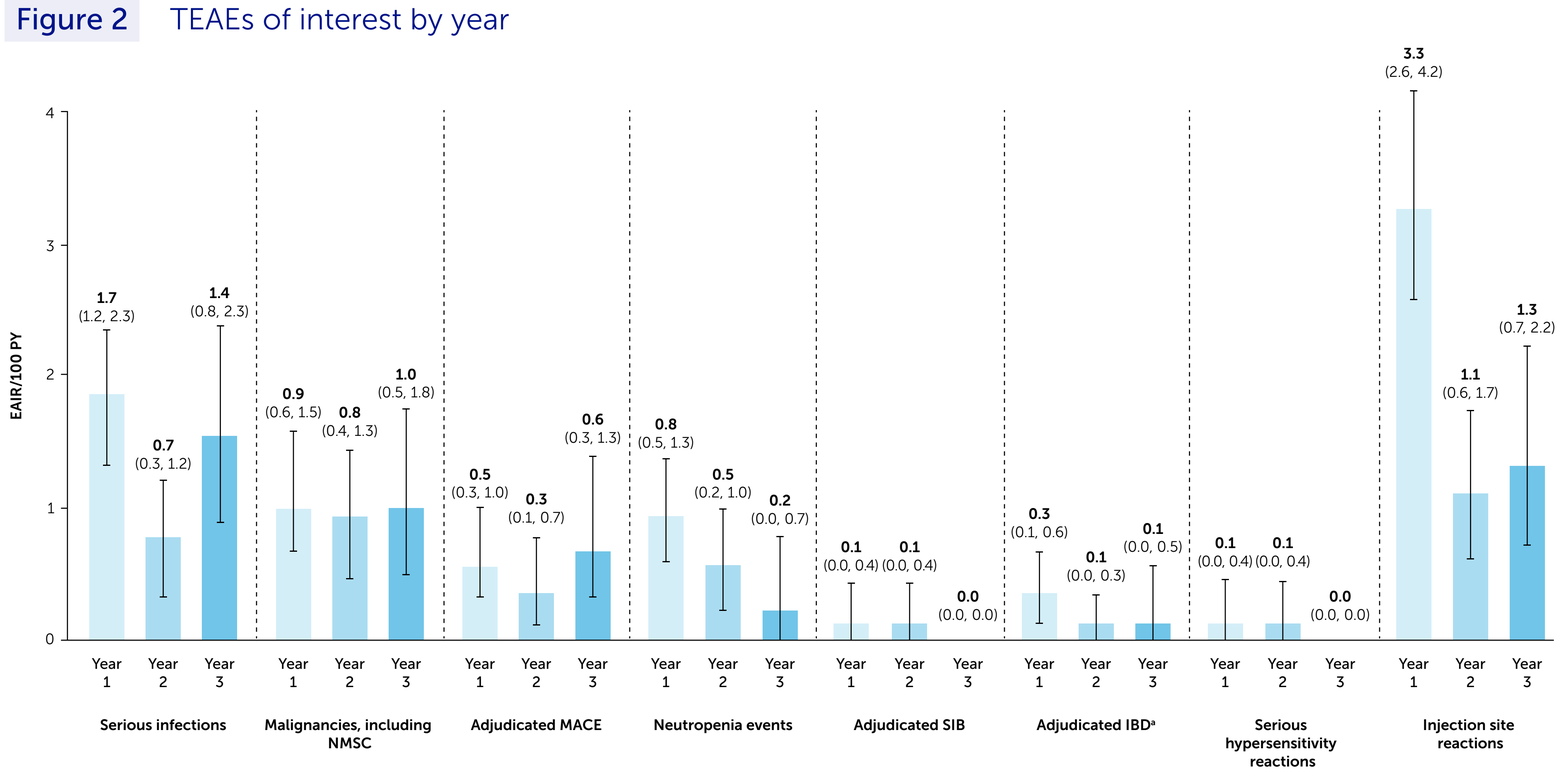
Data were pooled for all patients who received ≥1 BKZ dose in the included trials (BKZ Total). Patients that received BKZ 320 mg in BE SURE, BE READY and BE RADIANT could receive Q4W or Q8W dosing; in BE VIVID, patients could only receive BKZ Q4W. Data cut-offs were the dates on which the last enrolled patient completed Week 96 in BE RADIANT (20 April 2021) and Week 148/152 in BE BRIGHT (23 October 2021). Both studies are ongoing. [a]Patients entered the BE BRIGHT OLE at Week 52 if they were enrolled in BE VIVID and Week 56 if they were enrolled in BE SURE or BE READY.

Table 1 TEAEs of interest over 3 years

	Over 3 years
	BKZ Total[a] N=2,186 (4,932.1 PY) EAIR/100 PY (95% CI)
Serious infections	1.3 (1.0, 1.7)
Fungal infections	18.5 (17.2, 20.0)
Malignancies	0.8 (0.6, 1.1)
Excluding NMSC	0.5 (0.3, 0.7)
Adjudicated MACE	0.5 (0.3, 0.8)
Neutropenia events	0.5 (0.3, 0.8)
Adjudicated SIB	0.1 (0.0, 0.2)
Adjudicated IBD[b]	0.2 (0.1, 0.3)
Serious hypersensitivity reactions[c]	0.1 (0.0, 0.2)
Injection site reactions	2.0 (1.6, 2.5)
Hepatic events	3.4 (2.9, 4.0)
Elevated liver enzymes	2.9 (2.4, 3.4)
AST or ALT elevations[d]	
>3x ULN	2.1 (1.8, 2.6)
>5x ULN	0.6 (0.4, 0.8)

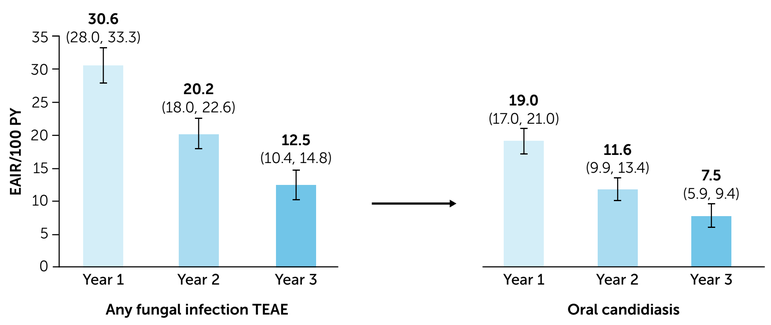
[a]Data were pooled for all patients who received ≥1 BKZ dose in the included studies (BKZ Total); [b]Includes any TEAE adjudicated as definite or probable IBD. The EAIR of unadjudicated IBD identified using the MedDRA high-level term 'Colitis (excl infective)' was 0.1/100 PY; [c]No anaphylactic reactions associated with BKZ were reported; [d]Not all hepatic laboratory parameter elevations were reported as adverse events.

Figure 2 TEAEs of interest by year



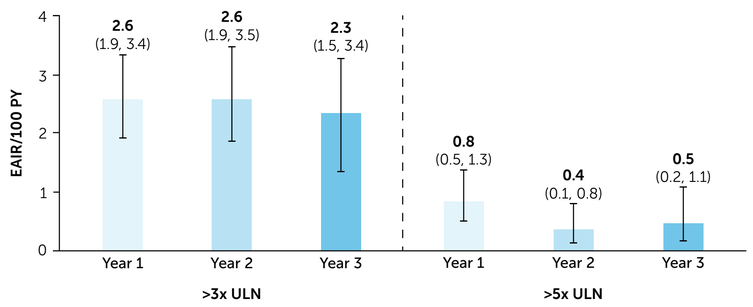
Error bars represent 95% CIs. Year 1, n=2,186; Year 2, n=1,907; Year 3, n=1,444. [a]Includes any TEAE adjudicated as definite or probable IBD. The EAIR of unadjudicated IBD identified using the MedDRA high-level term 'Colitis (excl infective)' was 0.1/100 PY in Year 1, 0.1/100 PY in Year 2 and 0.2/100 PY in Year 3.

Figure 3 Fungal infections by year



Error bars represent 95% CIs. Year 1, n=2,186; Year 2, n=1,907; Year 3, n=1,444. All EAIRs were calculated from the overall BKZ Total patient group for each year.

Figure 4 Laboratory elevations of liver transaminases by year



Error bars represent 95% CIs. Year 1, n=2,186; Year 2, n=1,907; Year 3, n=1,444. Not all hepatic laboratory parameter elevations were reported as adverse events. Patients with elevations >5x ULN were a subset of patients with elevations >3x ULN. All EAIRs were calculated from the overall BKZ Total patient group for each year.

ALT: alanine aminotransferase; **AST:** aspartate aminotransferase; **BKZ:** bimekizumab; **CI:** confidence interval; **EAIR:** exposure-adjusted incidence rate; **IBD:** inflammatory bowel disease; **IL:** interleukin; **MACE:** major adverse cardiac event; **MedDRA:** Medical Dictionary for Regulatory Activities; **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 behaviour; **TEAE:** treatment-emergent adverse event; **ULN:** upper limit of normal.

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References: [1]Gisondi P *et al.* Int J Mol Sci 2017;18:2427; [2]Al-Janabi A & Yiu ZZN. Psoriasis (Auckl) 2022;12:1–14; [3]Adams R *et al.* Front Immunol 2020;11:1894; [4]Warren RB *et al.* N Engl J Med 2021;385:130–41, NCT03412747; [5]Reich K *et al.* Lancet 2021;397:487–98, NCT03370133; [6]Gordon KB *et al.* Lancet 2021;397:475–86, NCT03410992; [7]BE BRIGHT: clinicaltrials.gov/ct2/show/NCT03598790; [8]Reich K *et al.* N Engl J Med 2021;385:142–52, NCT03536884. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **DT, SI, MG, BS, LP, CM, BSz, DD, KBG;** Drafting of the publication, or revising it critically for important intellectual content: **DT, SI, MG, BS, LP, CM, BSz, DD, KBG;** Final approval of the publication: **DT, SI, MG, BS, LP, CM, BSz, DD, KBG**. **Author Disclosures: DT:** Served as an investigator and/or consultant/advisor for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly, Galapagos, Galderma, Janssen, Kyowa Kirin, LEO Pharma, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi Genzyme, Target-Solution and UCB Pharma; research grants received from AbbVie, LEO Pharma and Novartis. **SI:** Received grants from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Kyowa Kirin, LEO Pharma, Pfizer and UCB Pharma; speaker fees from AbbVie, Daiichi Sankyo, Eisai, Eli Lilly, GSK, Janssen, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi-Tanabe, Novartis, Sun Pharma and Taiho Pharma. MG: Investigator, speaker, consultant or advisory board member for AbbVie, Akros, Amgen, AnaptysBio, Arcutis, Aslan, Aristea, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, GSK, Incyte, Janssen, Kyowa Kirin, MedImmune, Meiji, Merck, Moonlake, Nimbus, Novartis, Pfizer, Regeneron, Reistone, Sanofi Genzyme, Sun Pharma and UCB Pharma. **BS:** Consultant (honoraria) for AbbVie, Almirall, Alumis, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Bristol Myers Squibb, Connect Biopharma, Dermavant, Eli Lilly, Evelo Biosciences, Immunic Therapeutics, Janssen, LEO Pharma, Maruho, Meiji Seika Pharma, Mindera Health, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, Regeneron, UCB Pharma, Union Therapeutics, Ventyxbio and vTv Therapeutics; stock options for Connect Biopharma and Mindera Health; speaker for AbbVie, Arcutis, Dermavant, Eli Lilly, Incyte, Janssen, Regeneron and Sanofi Genzyme; Scientific Co-Director (consulting fee) for CorEvitas (formerly Corrona) Psoriasis Registry; investigator for AbbVie, Cara, CorEvitas Psoriasis Registry, Dermavant, Dermira and Novartis; Editor-in-Chief (honorarium) for the Journal of Psoriasis and Psoriatic Arthritis. **LP, CM, BSz, DD:** Employees and shareholders of UCB Pharma. **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. **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 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 Creative team, Costello Medical, UK for graphic design assistance. All costs associated with development of this poster were funded by UCB Pharma.

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