Bimekizumab safety in patients with moderate to severe plaque psoriasis: Infection rates using pooled data from up to three years of treatment in five phase 3/3b clinical trials

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Objective

To evaluate infection rates 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, including infection rates.[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 infection treatment-emergent adverse events (TEAEs) 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

- Over the pooled trial period (over 3 years), total BKZ exposure was 4,932.1 PY (N=2,186; see **Summary**).
- The three most common infections were nasopharyngitis, oral candidiasis and upper respiratory tract infections (**Table 1**).
  - The global COVID-19 pandemic was concurrent with the BE RADIANT and BE BRIGHT OLEs. Potential confounding factors, such as social isolation, mask-wearing and lockdowns may have affected rates of TEAEs, particularly respiratory infections such as nasopharyngitis.
- The EAIR of infection TEAEs decreased with longer BKZ exposure (**Figure 2**).
- In total, 35 patients discontinued due to infections (0.7/100 PY).
  - Of these, three were deaths reported due to coronavirus infection in non-fully vaccinated participants.
- No cases of active tuberculosis were reported.

Serious infections

- Rates of serious infections were low over 3 years (**Table 1**) and did not increase from Year 1 to Year 3 (**Figure 3**).
- Coronavirus infection was the most common serious infection.

Fungal infections

- Overall, fungal infections occurred at 18.5/100 PY over 3 years (**Table 1**) and decreased from Year 1 to Year 3 (**Figure 4**).
- The majority were *Candida* infections (12.4/100 PY) (**Table 1**), most of which were oral candidiasis (**Table 1**; **Figure 4**).
- The EAIR of oral candidiasis decreased with longer BKZ exposure (**Figure 4**); the vast majority of events were mild or moderate (99.1%) and did not lead to discontinuation (EAIR: 0.1/100 PY).
  - Increasing proportions of patients switching to the approved maintenance dose of BKZ Q8W over time may have contributed to the decrease in oral candidiasis incidence over time.
- Over 3 years, approximately 80% of patients experienced no oral candidiasis events. In patients who did experience oral candidiasis, most had either one or two events (**Figure 5**).

Opportunistic infections

- Opportunistic infection rates were low (**Table 1**); most were localised mucocutaneous fungal infections pre-defined as opportunistic by company convention.
- Exceptions include one serious case each of ophthalmic herpes zoster (resolved with treatment; did not lead to discontinuation) and systemic candidiasis (resolved; patient discontinued following the event and associated pyelonephritis and obstructive nephropathy).

Conclusions

Over 3 years of BKZ treatment, the most common infections were nasopharyngitis, oral candidiasis and upper respiratory tract infections. Rates of serious infections and discontinuations due to infections were low. Infection EAIRs decreased 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)

The most common infections were nasopharyngitis, oral candidiasis and upper respiratory tract infections.

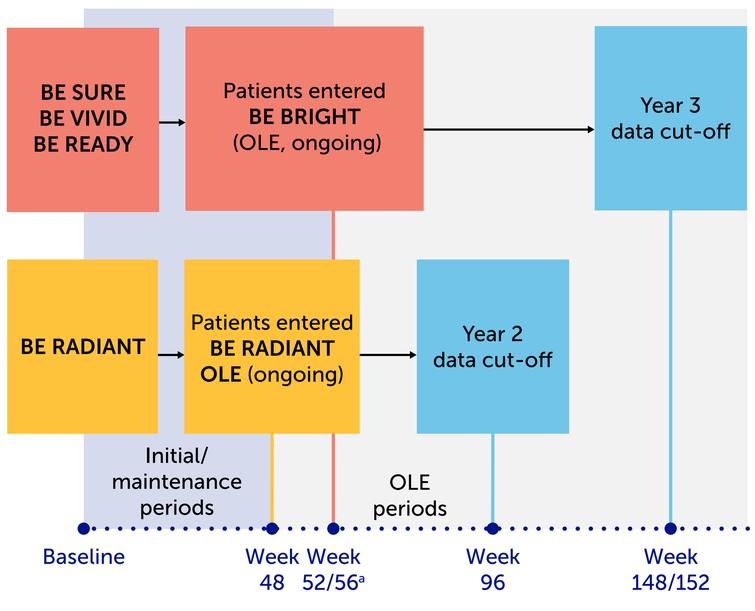
Infection rates decreased with longer BKZ treatment duration.

99.1% of all oral candidiasis events were mild or moderate and the vast majority did not lead to discontinuation.

Rates of serious infections were low and did not increase with longer duration of BKZ exposure; discontinuations due to infections were low.

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).

Figure 1 Included patients



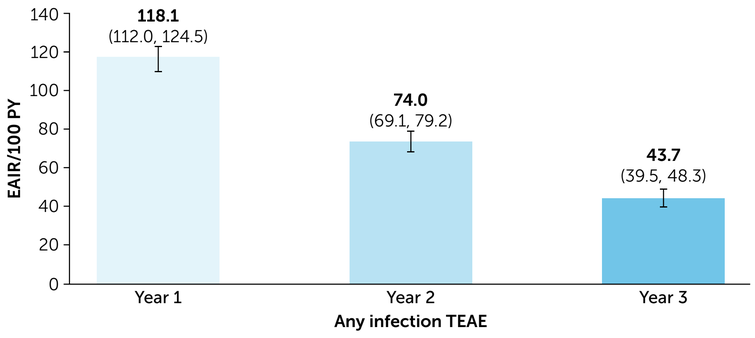
Data were pooled for all patients who received ≥1 BKZ dose in the included trials (BKZ Total). Patients that received BKZ 320 mg in BE SURE, BE READY and BE RADIANT could receive Q4W or Q8W dosing; in BE VIVID, patients could only receive BKZ Q4W. Data cut-offs were the dates on which the last enrolled 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 Infections over 3 years

	Over 3 years
	BKZ Total[a] N=2,186 (4,932.1 PY) EAIR/100 PY (95% CI)
Summary of infections	
Infections	84.1 (80.0, 88.3)
Staphylococcal infections	1.0 (0.7, 1.3)
Streptococcal infections	0.8 (0.6, 1.1)
Active tuberculosis	0.0
Discontinuations due to infections	0.7 (0.5, 1.0)
Serious infections	1.3 (1.0, 1.7)
Coronavirus infection	0.2 (0.1, 0.4)
Most common infections	
Nasopharyngitis	15.3 (14.1, 16.6)
Oral candidiasis	10.8 (9.9, 11.9)
Upper respiratory tract infections	6.5 (5.8, 7.3)
Summary of opportunistic and fungal infections	
Opportunistic infections	0.9 (0.7, 1.3)
Fungal infections	18.5 (17.2, 20.0)
Candida infections	12.4 (11.4, 13.6)
Oral candidiasis	10.8 (9.9, 11.9)
Skin candidiasis	0.7 (0.5, 1.0)
Vulvovaginal candidiasis	0.6 (0.4, 0.8)
Oropharyngeal candidiasis	0.6 (0.4, 0.8)
Gastrointestinal candidiasis	0.2 (0.1, 0.3)
Oesophageal candidiasis	0.1 (0.0, 0.3)
Tinea infections	2.6 (2.1, 3.1)
Fungal infections NEC	3.1 (2.6, 3.7)

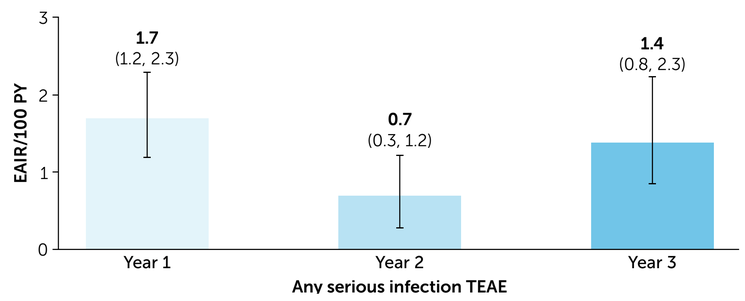
[a]Data were pooled for all patients who received ≥1 BKZ dose in the included studies (BKZ Total).

Figure 2 Infections by year



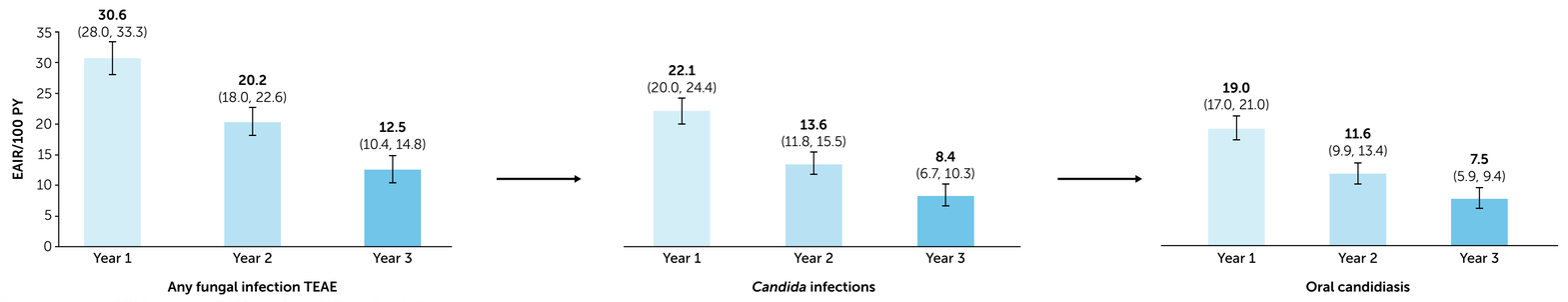
Error bars represent 95% CIs. Year 1, n=2,186; Year 2, n=1,907; Year 3, n=1,444.

Figure 3 Serious infections by year



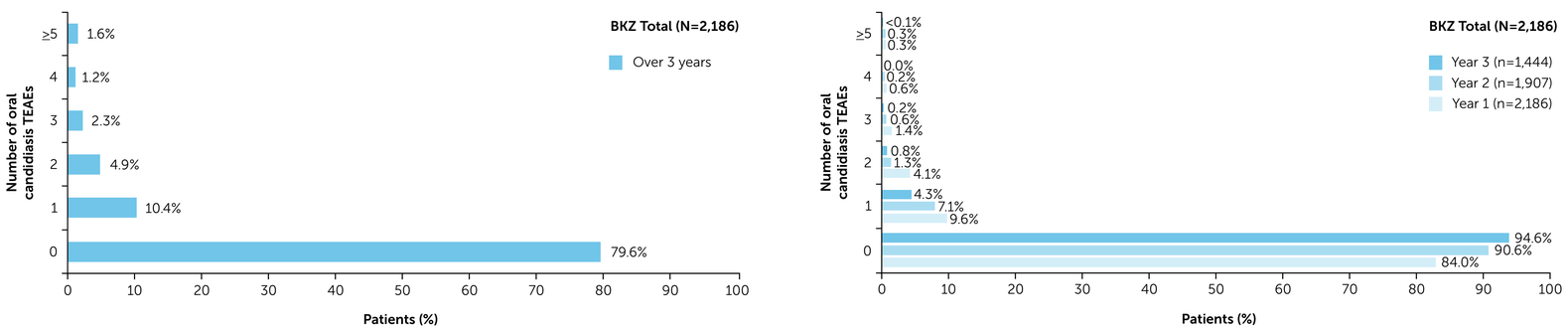
Error bars represent 95% CIs. Year 1, n=2,186; Year 2, n=1,907; Year 3, n=1,444.

Figure 4 Fungal infections by year



Error bars represent 95% CIs. Year 1, n=2,186; Year 2, n=1,907; Year 3, n=1,444.

Figure 5 Proportions of patients with 0, 1 or ≥2 oral candidiasis TEAEs



BKZ: bimekizumab; **CI:** confidence interval; **EAIR:** exposure-adjusted incidence rate; **IL:** interleukin; **MedDRA:** Medical Dictionary for Regulatory Activities; **NEC:** not elsewhere classified; **OLE:** open-label extension; **PASI:** Psoriasis Area and Severity Index; **PY:** patient-years; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SD:** standard deviation; **TEAE:** treatment-emergent adverse event.

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