Bimekizumab infection rates in patients with moderate to severe plaque psoriasis: Analysis of pooled data from 2 years of treatment in phase 3 and 3b clinical trials

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Objective

To report long-term infection rates in patients with moderate to severe plaque psoriasis receiving bimekizumab (BKZ) 320 mg every four weeks (Q4W) or every eight weeks (Q8W), pooled to include 2 years of treatment across five phase 3/3b trials, the largest two-year data pool for BKZ in plaque psoriasis.

Introduction

- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.[1]
- Psoriasis is a chronic disease requiring long-term management; therefore, it is important to assess the long-term safety of treatments, including infection rates.

Materials and Methods

- Rates of infection for treatment-emergent adverse events (TEAEs) over a two-year period were evaluated for all patients who received ≥1 BKZ dose in BE SURE, BE VIVID, BE READY, their open-label extension (OLE) BE BRIGHT (data cut-off: November 9, 2020), or BE RADIANT (data cut-off: April 20, 2021).[2–6]
- Rates of infection TEAEs were also evaluated separately for patients who were receiving BKZ dosed 320 mg Q4W or Q8W at the time of the TEAE.
- TEAEs were coded using MedDRA, Medical Dictionary for Regulatory Activities v19.0.
- Data are reported as exposure-adjusted incidence rates (EAIRs), defined as incidence of new cases reported per 100 patient-years (PY), and are presented with 95% confidence intervals (CIs).

Results

- Overall infection rates decreased over Year 2 relative to Year 1 and were lower in Q8W- versus Q4W-treated patients (**Table 1**).
- The most common infections seen with BKZ were nasopharyngitis, oral candidiasis, and upper respiratory tract infections (**Table 2**).
- No cases of active tuberculosis were reported over the two-year period.

Serious infections

- Rates of serious infections were low across BKZ-treated patients (**Table 3**).
- The most common serious infections were appendicitis and cellulitis; four events of each occurred.

Fungal infections

- The majority of fungal infections were *Candida* infections, most of which were oral candidiasis (**Table 4**).
- Rates of oral candidiasis were lower in Q8W- versus Q4W-treated patients (**Figure 1**; **Table 4**); cumulative two-year rates were lower than rates for Year 1 (**Table 4**).
- Over two years, approximately 80% of patients experienced no oral candidiasis events. In patients who did experience such events, most had either one or two (**Figure 2**).
- The vast majority of oral candidiasis events over two years (98.1%) were mild or moderate.
- Five BKZ Q4W-treated patients discontinued BKZ due to oral candidiasis in Year 1 versus none in Year 2; no Q8W-treated patients discontinued due to oral candidiasis.

Opportunistic infections

- Rates of opportunistic infections were low (**Table 1**); almost all were localized mucocutaneous fungal infections pre-defined as opportunistic by company convention.
- Exceptions to the above included 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).

Summary

	Dosing		
	BKZ Total	**BKZ Q4W**	**BKZ Q8W[a]**
Population	N=2,186	N=2,025	N=1,576
Exposure	3,796 PY	2,329 PY	1,471 PY
Trials administered	4 double-blinded trials and 2 OLEs[b]	4 double-blinded trials and 2 OLEs[b]	3 double-blinded trials and 2 OLEs[b]

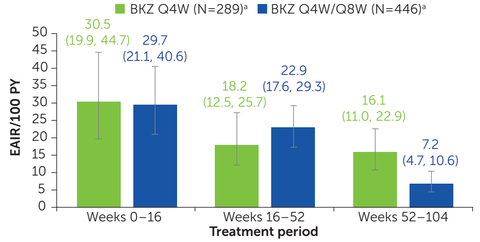
Data were pooled for all patients who received ≥1 BKZ dose in BE SURE, BE VIVID, BE READY, their OLE BE BRIGHT (data cut-off: November 9, 2020), or BE RADIANT (data cut-off: April 20, 2021).[2–6] [a]BE VIVID did not use Q8W dosing; [b]BE RADIANT is comprised of a 48-week double-blinded study period and an ongoing OLE. Data from both study periods were included here; the trial is included in the total numbers of both double-blinded trials and OLEs.

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

98.1% of oral candidiasis events observed over two years were mild or moderate

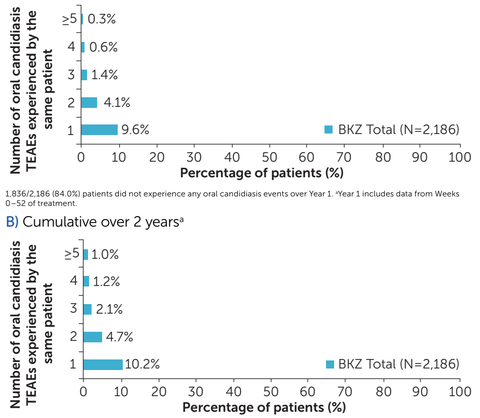
Rates of serious infections were low in all groups and did not increase with longer duration of BKZ exposure

Figure 1 EAIRs of oral candidiasis over two years by treatment period and continuous BKZ dosing



Error bars/values in parentheses represent 95% CIs. Data are reported for all patients who received BKZ at Week 16 and received either BKZ Q4W or Q8W continuously during the maintenance period and in the OLE. All patients received BKZ Q4W through Weeks 0–16. [a]For Weeks 52–104, N=233 for BKZ Q4W only and N=416 for BKZ Q4W/Q8W only.

Figure 2 Patients with oral candidiasis TEAEs



1,836/2,186 (84.0%) patients did not experience any oral candidiasis events over Year 1. [a]Year 1 includes data from Weeks 0–52 of treatment.

1,767/2,186 (80.8%) patients did not experience any oral candidiasis events over two years. [a]Data are reported from Weeks 0–104 of treatment.

Table 1 Overall infection rates

	Year 1[a]	Year 2[b]	Cumulative over two years		
	BKZ Total N=2,186	BKZ Total N=1,710	BKZ 320 mg Q4W N=2,025	BKZ 320 mg Q8W N=1,576	BKZ Total N=2,186
Summary of treatment exposure					
Total exposure, PY	2,049	1,291	2,329	1,471	3,796
Summary of infection TEAEs, EAIR/100 PY (95% CI)					
Any infection TEAE	116.8 (110.6, 123.1)	83.7 (77.8, 90.0)	110.2 (104.2, 116.5)	77.7 (71.9, 83.9)	93.9 (89.3, 98.7)
Opportunistic infections	1.8 (1.3, 2.5)	0.5 (0.2, 1.1)	1.7 (1.2, 2.3)	0.5 (0.2, 1.0)	1.2 (0.9, 1.6)
Staphylococcal infections	1.5 (1.0, 2.1)	0.9 (0.5, 1.6)	1.3 (0.9, 1.9)	0.9 (0.5, 1.5)	1.1 (0.8, 1.5)
Streptococcal infections	1.1 (0.7, 1.7)	1.0 (0.5, 1.7)	1.0 (0.6, 1.4)	1.1 (0.6, 1.8)	1.0 (0.7, 1.4)
Leading to discontinuation	1.1 (0.7, 1.6)	0.3 (0.1, 0.8)	0.9 (0.6, 1.4)	0.3 (0.1, 0.8)	0.7 (0.5, 1.0)
Active tuberculosis	0.0	0.0	0.0	0.0	0.0

[a]Year 1 includes data from Weeks 0–52 of treatment; [b]Year 2 includes data from Weeks 52–104 of treatment.

Table 2 Most common infections

	Year 1[a]	Year 2[b]	Cumulative over two years		
	BKZ Total N=2,186	BKZ Total N=1,710	BKZ 320 mg Q4W N=2,025	BKZ 320 mg Q8W N=1,576	BKZ Total N=2,186
Most common infection TEAEs, EAIR/100 PY (95% CI)					
Nasopharyngitis	25.2 (22.9, 27.7)	17.8 (15.4, 20.3)	22.0 (19.9, 24.2)	15.5 (13.5, 17.9)	18.4 (17.0, 20.0)
Oral candidiasis	18.4 (16.5, 20.5)	13.3 (11.3, 15.5)	17.1 (15.4, 19.0)	10.5 (8.9, 12.4)	13.0 (11.8, 14.3)
Upper respiratory tract infection	10.3 (8.9, 11.8)	7.3 (5.9, 9.0)	8.8 (7.6, 10.2)	7.3 (5.9, 8.8)	7.8 (6.9, 8.8)

[a]Year 1 includes data from Weeks 0–52 of treatment; [b]Year 2 includes data from Weeks 52–104 of treatment.

Table 3 Serious infections

	Year 1[a]	Year 2[b]	Cumulative over two years		
	BKZ Total N=2,186	BKZ Total N=1,710	BKZ 320 mg Q4W N=2,025	BKZ 320 mg Q8W N=1,576	BKZ Total N=2,186
Summary of serious infection TEAEs, EAIR/100 PY (95% CI)					
Serious infections	1.7 (1.2, 2.3)	0.5 (0.2, 1.1)	1.4 (1.0, 2.0)	0.9 (0.5, 1.5)	1.2 (0.9, 1.6)
Most common serious infection TEAEs (four events each over two years), EAIR/100 PY (95% CI)					
Appendicitis	0.1 (0.0, 0.4)	0.1 (0.0, 0.4)	0.0 (0.0, 0.2)	0.2 (0.0, 0.6)	0.1 (0.0, 0.3)
Cellulitis	0.1 (0.0, 0.4)	0.0	0.2 (0.0, 0.4)	0.0	0.1 (0.0, 0.3)

[a]Year 1 includes data from Weeks 0–52 of treatment; [b]Year 2 includes data from Weeks 52–104 of treatment.

Table 4 Fungal infections

	Year 1[a]	Year 2[b]	Cumulative over two years		
	BKZ Total N=2,186	BKZ Total N=1,710	BKZ 320 mg Q4W N=2,025	BKZ 320 mg Q8W N=1,576	BKZ Total N=2,186
Summary of fungal infection TEAEs, EAIR/100 PY (95% CI)					
Fungal infections	29.8 (27.3, 32.5)	22.7 (20.0, 25.6)	27.4 (25.1, 29.9)	19.0 (16.7, 21.6)	21.9 (20.2, 23.6)
Candida infections	21.5 (19.4, 23.7)	15.5 (13.4, 17.9)	19.9 (18.0, 21.9)	11.9 (10.1, 13.9)	15.0 (13.6, 16.4)
Oral candidiasis	18.4 (16.5, 20.5)	13.3 (11.3, 15.5)	17.1 (15.4, 19.0)	10.5 (8.9, 12.4)	13.0 (11.8, 14.3)
Oropharyngeal candidiasis	1.2 (0.8, 1.8)	0.2 (0.0, 0.7)	1.0 (0.7, 1.5)	0.2 (0.0, 0.6)	0.7 (0.5, 1.0)
Vulvovaginal candidiasis	1.1 (0.7, 1.6)	0.5 (0.2, 1.0)	1.0 (0.6, 1.4)	0.3 (0.1, 0.8)	0.7 (0.5, 1.0)
Skin candidiasis	0.8 (0.5, 1.3)	1.1 (0.6, 1.8)	0.9 (0.5, 1.3)	0.8 (0.4, 1.4)	0.9 (0.6, 1.2)
Esophageal candidiasis	0.2 (0.1, 0.6)[c]	0.0	0.2 (0.0, 0.4)[c]	0.1 (0.0, 0.4)	0.1 (0.0, 0.3)[c]
Tinea infections	3.8 (3.0, 4.7)	2.4 (1.6, 3.4)	3.2 (2.5, 4.1)	2.9 (2.1, 4.0)	2.9 (2.4, 3.5)
Fungal infections NEC	4.5 (3.6, 5.5)	4.7 (3.6, 6.0)	4.2 (3.4, 5.2)	3.4 (2.5, 4.5)	3.7 (3.1, 4.3)

[a]Year 1 includes data from Weeks 0–52 of treatment; [b]Year 2 includes data from Weeks 52–104 of treatment; [c]There was one serious, severe case of esophageal candidiasis in a patient receiving BKZ 320 mg Q4W during the first year of treatment which led to discontinuation.

For patients who received both BKZ 320 mg Q4W and Q8W doses during the trials, 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 were included in the population count of both treatment groups, but only once in each BKZ Total group.

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; **PY:** patient-years; **Q4W:** every four weeks; **Q8W:** every eight weeks; **TEAE:** treatment-emergent adverse event.

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Conclusions

Over two years of BKZ treatment, EAIRs of infection TEAEs and pre-defined infections of interest, including oral candidiasis, were generally lower in patients treated with BKZ Q8W compared with Q4W.

Infection rates decreased with longer duration of BKZ exposure.

Rates of discontinuation due to infections were low.

There were no new safety findings with long-term exposure to BKZ.