Bimekizumab efficacy and safety through two years in patients with moderate psoriasis: Analysis of pooled data from five phase 3/3b clinical trials

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Objectives

To evaluate efficacy and safety of bimekizumab (BKZ) in patients with moderate plaque psoriasis over two years using data from five phase 3/3b trials.

Introduction

- BKZ has demonstrated high levels of efficacy in patients with moderate to severe plaque psoriasis.[1–4]
- Here, we consider BKZ efficacy and safety in patients with moderate psoriasis.

Materials and Methods

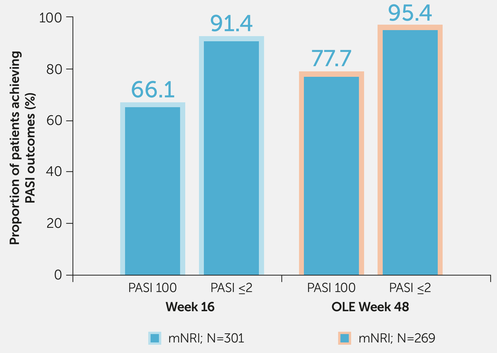
- Moderate psoriasis was defined as body surface area (BSA) ≥10%–≤15%, Psoriasis Area and Severity Index (PASI) ≥12, and Investigators Global Assessment (IGA)=3 at baseline.
- Data were pooled from BE SURE, BE VIVID, BE READY, the first year of the BE BRIGHT open label extension (OLE), and BE RADIANT (48-week double-blinded period and ongoing OLE).[1–5]
- Patients received BKZ 320 mg every 4 weeks (Q4W) to Week 16, then either BKZ Q4W or every 8 weeks (Q8W) maintenance dosing (**Figure 1**).
- Efficacy outcomes are reported through two years for all BKZ treated patients, regardless of dosing regimen.
- Data are reported using modified non-responder imputation (mNRI), NRI, and as the observed case (OC)
  - For mNRI, patients who discontinued due to lack of efficacy, entered the BE READY open-label escape arm, or discontinued treatment due to an adverse event (AE) prior to OLE entry were considered non-responders at subsequent timepoints; multiple imputation was used for all other missing data.
- Treatment-emergent AEs (TEAEs), evaluated as exposure-adjusted incidence rates (EAIRs) per 100 patient-years, are reported for patients with moderate psoriasis who received ≥1 BKZ dose. The percentage of patients who experienced a TEAE is also reported.

Results

- At baseline, 301 patients with moderate psoriasis were randomised to BKZ; 269 continued to the OLEs.
- Baseline characteristics for patients with moderate psoriasis were similar to the BKZ-randomised study population with moderate to severe plaque psoriasis (except for criteria used to distinguish between moderate and moderate to severe psoriasis; **Table 1**).
- High levels of PASI ≤2, PASI 100, and BSA ≤1% responses were observed in BKZ-treated patients at Week 16. Similarly high response levels were reported after two years of treatment (OLE Week 48) among patients who entered the OLEs (**Figure 2**).
- TEAEs occurred in 90.7% of patients and were lower with BKZ Q8W vs Q4W. Serious TEAEs and TEAEs leading to discontinuation were low (**Table 2**).
- The most common TEAEs were nasopharyngitis, oral candidiasis, and upper respiratory tract infections (**Table 2**; **Table 3**).
- Oral candidiasis EAIRs were lower with BKZ Q8W vs Q4W. The majority of oral candidiasis TEAEs were mild/moderate (98.2%). Two patients with oral candidiasis discontinued BKZ.
- Similar to the overall study population,[6] EAIRs of safety topics of interest were low in moderate psoriasis patients (**Table 2**; **Table 3**).
- Occurrence of TEAEs and serious TEAEs generally decreased or remained comparable over time (**Table 3**).

Summary

Percentage of patients achieving PASI outcomes at Week 16 and OLE Week 48 (mNRI)



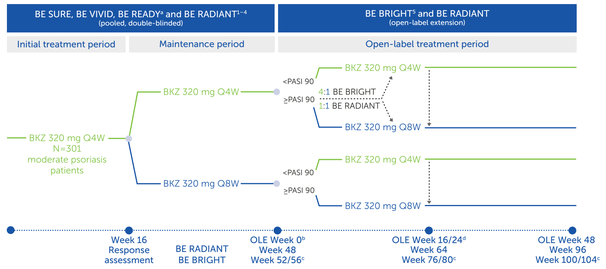
A high proportion of patients with moderate psoriasis achieved PASI 100 at Week 16 and through to two years (OLE Week 48) suggesting that high levels of improvement can be observed regardless of disease severity.

Table 1 Baseline characteristics

	Moderate psoriasis BKZ Total[a] N=301	Moderate to severe psoriasis BKZ-randomised[b] N=1,208
Age (years), mean ± SD	46.3 ± 14.3	45.4 ± 13.8
Male, n (%)	205 (68.1)	844 (69.9)
Caucasian, n (%)	271 (90.0)	1,053 (87.2)
Weight (kg), mean ± SD	87.9 ± 19.6	89.7 ± 22.0
BMI, mean ± SD	29.3 ± 6.1	29.9 ± 6.8
Duration of psoriasis (years), mean ± SD	17.7 ± 13.4	18.3 ± 12.7
PASI, mean ± SD[c]	**15.7 ± 2.9**	**20.7 ± 7.5**
BSA (%), mean ± SD[c]	**12.9 ± 1.6**	**26.2 ± 15.6**
IGA, n (%)[c]		
3: moderate	**301 (100)**	**793 (65.6)**
4: severe	**0.0**	**412 (34.1)**
DLQI, mean ± SD	10.6 ± 6.3	10.6 ± 6.5
Any prior systemic therapy, n (%)	214 (71.1)	933 (77.2)
Prior biologic therapy, n (%)	113 (37.5)	453 (37.5)
anti-TNF	51 (16.9)	187 (15.5)
anti-IL-17	53 (17.6)	241 (20.0)
anti-IL-23	20 (6.6)	64 (5.3)
anti-IL-12/23	19 (6.3)	72 (6.0)

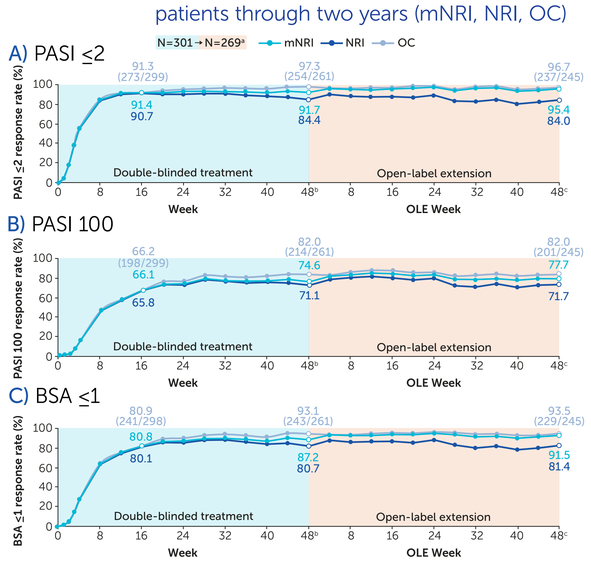
[a]Data are reported for all BKZ-treated patients with moderate psoriasis, regardless of dosing regimen; [b]Data are reported for all patients with moderate to severe psoriasis, randomised to BKZ at baseline of the BE SURE, BE VIVID, BE READY, and BE RADIANT phase 3/3b trials who entered the OLEs; [c]Values in bold are for assessments used to distinguish between moderate and moderate to severe psoriasis.

Figure 1 Study design



[a]Analyses include patients who received open-label escape treatment (BKZ 320 mg Q4W) in BE READY;[2] [b]Patients who achieved ≥PASI 90 at the end of the feeder studies were randomised 4:1 in BE BRIGHT and 1:1 in BE RADIANT to BKZ 320 mg Q4W or Q8W; [c]Week numbers correspond to feeder study baseline; OLE Week 48 (two years) corresponds to BE RADIANT Week 96, BE VIVID/BE BRIGHT Week 100, and BE READY/BE BRIGHT and BE SURE/BE BRIGHT Week 104; [d]In BE BRIGHT, at OLE Week 24, patients achieving ≥PASI 90 could switch to Q8W at the investigator's discretion; in BE RADIANT, at OLE Week 16 or the next scheduled clinic visit, patients switched to BKZ Q8W after the implementation of a protocol amendment.

Figure 2 Efficacy responses for moderate psoriasis patients through two years (mNRI, NRI, OC)



For patients in the BE READY escape arm who then entered BE BRIGHT, their OC assessments were used for OC only, whilst an NRI record which was created at the same visit, even if an OC assessment was present, was used for NRI. [a]Number of patients who entered the OLEs; [b]BE SURE, BE VIVID, and BE READY extended beyond 48 weeks; Week 48 was the last common timepoint; [c]OLE Week 48 (two years) corresponds to BE RADIANT Week 96, BE VIVID/BE BRIGHT Week 100, and BE READY/BE BRIGHT and BE SURE/BE BRIGHT Week 104.

Table 2 Summary of TEAEs in moderate psoriasis patients

	BKZ Total patients[a] N=539		BKZ Q8W patients N=395		BKZ Q4W patients N=499	
	EAIR (95% CI)	**n (%)[b]**	**EAIR (95% CI)**	**n (%)[b]**	**EAIR (95% CI)**	**n (%)[b]**
Any TEAE	224.0 (204.6, 244.7)	489 (90.7)	164.8 (144.9, 186.7)	247 (62.5)	258.1 (233.8, 284.2)	412 (82.6)
Serious TEAEs	7.6 (5.9, 9.6)	67 (12.4)	7.9 (5.4, 11.3)	30 (7.6)	7.3 (5.2, 10.0)	38 (7.6)
Discontinuation due to TEAEs	3.4 (2.3, 4.8)	31 (5.8)	2.8 (1.4, 5.1)	11 (2.8)	3.7 (2.3, 5.8)	20 (4.0)
Severe TEAEs	6.6 (5.0, 8.5)	59 (10.9)	7.1 (4.7, 10.3)	27 (6.8)	6.7 (4.7, 9.3)	35 (7.0)
Deaths[c]	0.3 (0.1, 0.9)	3 (0.6)	0.3 (0.0, 1.4)	1 (0.3)	0.4 (0.0, 1.3)	2 (0.4)
Most common TEAEs						
Nasopharyngitis	21.2 (17.9, 24.8)	154 (28.6)	20.0 (15.4, 25.6)	64 (16.2)	24.4 (20.0, 29.4)	108 (21.6)
Oral candidiasis	13.3 (10.9, 16.1)	106 (19.7)	11.8 (8.5, 16.0)	42 (10.6)	17.6 (14.0, 21.9)	83 (16.6)
Upper respiratory tract infection	7.8 (6.1, 10.0)	66 (12.2)	8.0 (5.3, 11.4)	29 (7.3)	8.4 (6.1, 11.4)	42 (8.4)
Safety topics of interest						
Serious infections	1.5 (0.8, 2.6)	14 (2.6)	1.0 (0.3, 2.6)	4 (1.0)	2.1 (1.0, 3.7)	11 (2.2)
IBD	0.1 (0.0, 0.6)	1 (0.2)	0.0	0.0	0.2 (0.0, 1.0)	1 (0.2)
Adjudicated SIB	0.0	0.0	0.0	0.0	0.0	0.0
Malignancies	1.1 (0.5, 2.0)	10 (1.9)	0.8 (0.2, 2.2)	3 (0.8)	1.3 (0.5, 2.7)	7 (1.4)
Serious hypersensitivity reactions	0.1 (0.0, 0.6)	1 (0.2)	0.3 (0.0, 1.4)	1 (0.3)	0.0	0.0
Adjudicated MACE	0.3 (0.1, 0.9)	3 (0.6)	0.5 (0.1, 1.9)	2 (0.5)	0.2 (0.0, 1.0)	1 (0.2)
Elevated liver enzymes	2.7 (1.7, 3.9)	24 (4.5)	2.9 (1.4, 5.1)	11 (2.8)	2.8 (1.6, 4.7)	15 (3.0)

TEAEs were assigned to the dose most recently received prior to the TEAE's date of onset. Patients who received both BKZ 320 mg Q4W and Q8W at different times in the trials were included in the population count of both groups, but only once in the BKZ Total group. BE RADIANT data cut-off was 20 April 2021; BE BRIGHT data cut-off was 09 Nov 2020. [a]Data reported for all patients with moderate psoriasis who received ≥1 BKZ dose; [b]Proportion of patients reporting at least one TEAE in that category; [c]No deaths were assessed as treatment-related.

Table 3 Incidence rates of TEAEs by time period

EAIR (95% CI)	Weeks 0–16 N=539	Weeks 16–52 N=525	Weeks 52–104 N=443
Any TEAE	339.7 (304.3, 378.2)	226.7 (204.3, 251.0)	170.6 (151.1, 192.0)
Serious TEAEs	7.9 (4.2, 13.6)	7.3 (4.7, 10.9)	8.2 (5.4, 12.0)
Discontinuation due to TEAEs	4.3 (1.7, 8.8)	3.6 (1.9, 6.3)	3.4 (1.7, 6.1)
Severe TEAEs	5.5 (2.5, 10.4)	7.7 (5.0, 11.3)	8.2 (5.3, 12.0)
Deaths	0.6 (0.0, 3.4)	0.3 (0.0, 1.7)	0.3 (0.0, 1.7)
Most common TEAEs			
Nasopharyngitis	34.0 (25.4, 44.4)	27.6 (22.0, 34.2)	21.0 (16.1, 27.0)
Oral candidiasis	31.6 (23.5, 41.7)	19.1 (14.5, 24.6)	12.2 (8.6, 16.8)
Upper respiratory tract infection	10.5 (6.1, 16.7)	12.0 (8.5, 16.5)	6.7 (4.2, 10.2)

Data are reported for all patients with moderate psoriasis who received ≥1 BKZ dose (BKZ Total).

Conclusions

Results demonstrate that continuously high levels of skin clearance were seen with BKZ over two years in patients with moderate psoriasis.

BKZ was well-tolerated over two years in patients with moderate psoriasis.

AEs: adverse events; **BKZ:** bimekizumab; **BMI:** body mass index; **BSA:** body surface area; **DLQI:** Dermatology Life Quality Index; **EAIR:** exposure-adjusted incidence rate; **IBD:** inflammatory bowel disease; **IGA:** Investigators Global Assessment; **IL:** interleukin; **MACE:** major adverse cardiac events; **mNRI:** modified non-responder imputation; **NRI:** non-responder imputation; **OC:** observed case; **OLE:** open-label extension; **PASI 75/90/100:** ≥75%/≥90%/100% improvement from baseline in the Psoriasis Area and Severity Index; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SD:** standard deviation; **SIB:** suicidal ideation and behaviour; **TEAE:** Treatment-emergent adverse event; **TNF:** tumour necrosis factor.

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