Bimekizumab 3-year maintenance of response in Week 16 responders with moderate to severe plaque psoriasis: Results from five phase 3/3b trials

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Synopsis

- Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A,[1] has demonstrated rapid and superior efficacy in the treatment of patients with moderate to severe plaque psoriasis in head-to-head studies versus ustekinumab, adalimumab, and secukinumab, with established long-term durability of response.[2–6]
- As psoriasis is a chronic disease and loss of response to therapies can occur over time, studying long-term efficacy of new treatments is important.[7]
- Maintenance of responses through 3 years of BKZ 320 mg treatment, in psoriasis patients who achieved disease control after 16 weeks, has been shown previously in patients from four phase 3 trials.[6]
- Here, we report maintenance of response from the largest available data pool through 3 years, with patients included across five phase 3/3b trials.

Objective

To report maintenance of response over 3 years in patients who achieved complete or near-complete skin clearance after 16 weeks of BKZ treatment from five phase 3/3b trials.

Methods

- Data were pooled from the 52-week BE VIVID, 56-week BE READY, and 56-week BE SURE phase 3 trials, their ongoing open-label extension (OLE), BE BRIGHT, as well as the BE RADIANT phase 3b trial (48-week double-blinded period, 96-week OLE; **Figure 1**).[2–6]
- Included patients were randomized to BKZ 320 mg every 4 weeks (Q4W) at baseline to Week 16. Patients then received either BKZ Q4W or every 8 weeks (Q8W) through the maintenance and OLE periods.
  - All patients still receiving BKZ Q4W were re-assigned to BKZ Q8W at OLE Week 16/48 (BE RADIANT/BE BRIGHT) or next scheduled visit, via protocol amendment.
- Maintenance of ≥90/100% improvement from baseline in Psoriasis Area and Severity Index (PASI 90/100), and Investigator's Global Assessment (IGA) 0/1 responses through Year 3 (Week 144/OLE Week 96) are reported in Week 16 PASI 90, PASI 100, and IGA 0/1 responders, respectively.
- Dermatology Life Quality Index (DLQI) 0/1 responses (indicating no impact of skin disease on patient's life)[8] are also reported in Week 16 PASI 100 responders.
- Data are reported for the combined BKZ dosing groups (BKZ Total) and for the subset of patients who received BKZ Q4W/Q8W/Q8W (initial/maintenance/OLE) dosing.
- Data are reported using modified non-responder imputation (mNRI): patients who discontinued due to lack of efficacy or treatment-related adverse events were considered non-responders at subsequent timepoints; multiple imputation was used for all other missing data (NRI/observed case [OC] data in **Table 2** only).

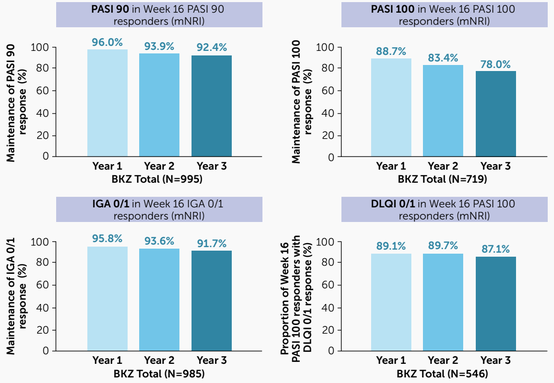
Results

- Across the phase 3/3b trials, 1,362 patients were randomized to BKZ Q4W for the initial treatment periods.
- Among these, 86.9% achieved PASI 90, 62.4% achieved PASI 100, and 86.9% achieved IGA 0/1 at Week 16 (**Figure 2**). 995 PASI 90 responders, 719 PASI 100 responders, and 985 IGA 0/1 responders entered the OLE.
  - Baseline characteristics of these patients are presented in **Table 1**.
- Among Week 16 PASI 90, PASI 100, and IGA 0/1 responders, 96.0%, 88.7%, and 95.8% maintained their responses at Year 1 (Week 48; **Figure 2A–C**; **Table 2**).
- Among Week 16 PASI 100 responders, DLQI 0/1 response rates increased through the first year of BKZ treatment, with 89.1% achieving DLQI 0/1 at Year 1 (**Figure 2D**).
- These high levels of response continued to be sustained up to Year 3 (Week 144; **Figure 2**; **Table 2**).
- Similarly high responses were maintained over 3 years in Week 16 responders who received BKZ Q4W/Q8W/Q8W (**Figure 2**; **Table 2**).
- Study discontinuation in Week 16 PASI 90, PASI 100, and IGA 0/1 responders due to loss of efficacy and adverse events during the maintenance period and OLE was low (n=8/1,102 [0.7%] and n=77/1,102 [7.0%], respectively).

Conclusions

Pooled data from five trials found that, among Week 16 responders, high clinical responses were maintained through 3 years of BKZ 320 mg treatment. High levels of response were also maintained in those who received BKZ Q4W/Q8W/Q8W, the approved dosing regimen for most patients with psoriasis.[9]

Summary



BKZ provided **long-term maintenance of disease control up to 3 years** in patients with moderate to severe plaque psoriasis

Table 1 Baseline characteristics

	Week 16 PASI 90 responders		Week 16 PASI 100 responders		Week 16 IGA 0/1 responders	
	BKZ Total (N=995)	BKZ Q4W/Q8W/Q8W (N=348)	BKZ Total (N=719)	BKZ Q4W/Q8W/Q8W (N=267)	BKZ Total (N=985)	BKZ Q4W/Q8W/Q8W (N=345)
Age (years), mean ± SD	45.0 ± 13.5	44.8 ± 14.1	45.1 ± 13.3	44.5 ± 13.8	45.1 ± 13.5	45.1 ± 14.0
Male, n (%)	695 (69.8)	247 (71.0)	497 (69.1)	185 (69.3)	692 (70.3)	246 (71.3)
White, n (%)	872 (87.6)	330 (94.8)	642 (89.3)	254 (95.1)	871 (88.4)	328 (95.1)
Weight (kg), mean ± SD	89.1 ± 20.8	88.9 ± 20.7	87.9 ± 19.6	87.4 ± 19.0	89.4 ± 20.8	88.9 (20.7)
Duration of psoriasis (years), mean ± SD	18.2 ± 12.6	18.6 ± 12.4	18.2 ± 12.6	19.2 ± 12.8	18.3 ± 12.5	19.0 ± 12.5
PASI, mean ± SD	21.2 ± 7.7	20.6 ± 7.5	20.8 ± 7.3	20.4 ± 7.4	21.0 ± 7.6	20.4 ± 7.5
BSA (%), mean ± SD	26.9 ± 16.0	24.5 ± 13.6	25.8 ± 15.0	23.8 ± 13.2	26.5 ± 15.7	24.1 ± 13.3
IGA, n (%)						
3: moderate	652 (65.5)	240 (69.0)	476 (66.2)	181 (67.8)	648 (65.8)	239 (69.3)
4: severe	341 (34.3)	107 (30.7)	242 (33.7)	86 (32.2)	334 (33.9)	104 (30.1)
DLQI total score, mean ± SD	10.7 ± 6.4	10.7 ± 6.3	10.9 ± 6.5	10.9 ± 6.4	10.7 ± 6.4	10.6 ± 6.3
Any prior systemic therapy, n (%)	772 (77.6)	266 (76.4)	568 (79.0)	209 (78.3)	760 (77.2)	262 (75.9)
Prior biologic therapy, n (%)	383 (38.5)	125 (35.9)	282 (39.2)	98 (36.7)	378 (38.4)	123 (35.7)

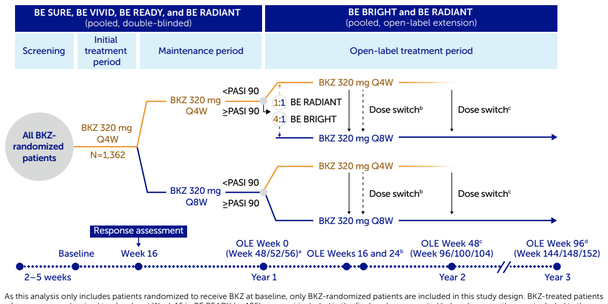
Data were pooled for all patients who were randomized to BKZ at the start of the study in BE SURE, BE READY, BE VIVID, and BE RADIANT, achieved a PASI 90, PASI 100, or IGA 0/1 response, respectively, at Week 16 and entered the relevant OLE (BKZ Total). Data are also presented for the subsets of these patients who received BKZ Q4W during the initial treatment periods, BKZ Q8W during the maintenance treatment periods and BKZ Q8W during the OLE periods (the approved dosing regimen for the majority of patients). The BE VIVID study design did not include a Q4W/Q8W/Q8W treatment arm, therefore patients from BE VIVID are not included in the Q4W/Q8W/Q8W subset.

Table 2 Summary of efficacy outcomes (NRI, OC)

	All BKZ-treated Week 16 responders (BKZ Total)		BKZ Q4W/Q8W/Q8W	
	NRI, n (%)	OC, n/N (%)	NRI, n (%)	OC, n/N (%)
PASI 90 in Week 16 PASI 90 responders	N=995		N=348	
Year 1	934 (93.9)	934/962 (97.1)	337 (96.8)	337/340 (99.1)
Year 2	875 (87.9)	881/916 (96.2)	313 (89.9)	313/321 (97.5)
Year 3	819 (82.3)	826/862 (95.8)	290 (83.3)	290/295 (98.3)
PASI 100 in Week 16 PASI 100 responders	N=719		N=267	
Year 1	632 (87.9)	632/704 (89.8)	240 (89.9)	240/262 (91.6)
Year 2	575 (80.0)	576/660 (87.3)	218 (81.6)	218/247 (88.3)
Year 3	527 (73.3)	528/626 (84.3)	194 (72.7)	194/229 (84.7)
IGA 0/1 in Week 16 IGA 0/1 responders	N=985		N=345	
Year 1	923 (93.7)	923/952 (97.0)	332 (96.2)	332/337 (98.5)
Year 2	857 (87.0)	864/905 (95.5)	308 (89.3)	308/319 (96.6)
Year 3	800 (81.2)	808/852 (94.8)	285 (82.6)	285/294 (96.9)
DLQI 0/1 in Week 16 PASI 100 responders[a]	N=546		N=267	
Year 1	480 (87.9)	480/534 (89.9)	238 (89.1)	238/262 (90.8)
Year 2	459 (84.1)	460/501 (91.8)	226 (84.6)	226/247 (91.5)
Year 3	420 (76.9)	420/467 (89.9)	210 (78.7)	210/229 (91.7)

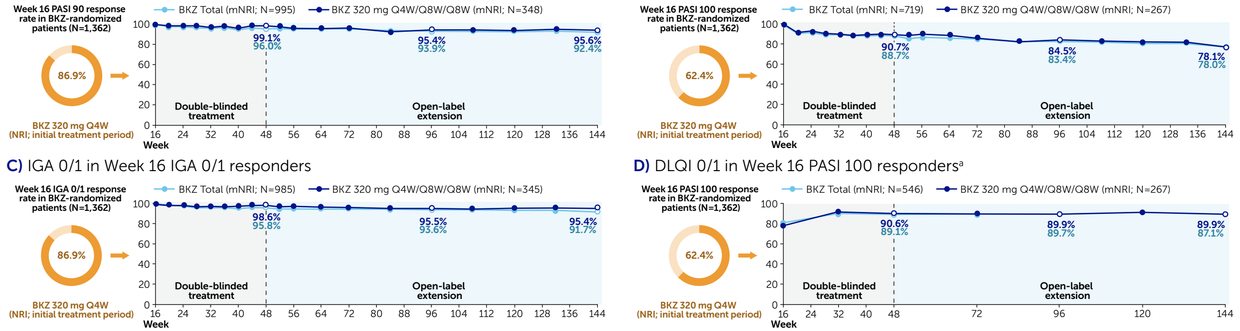
Data were pooled for all patients who were randomized to BKZ at the start of the study in BE SURE, BE READY, BE VIVID, and BE RADIANT, achieved a PASI 90, PASI 100, or IGA 0/1 response, respectively, at Week 16 and entered the relevant OLE (BKZ Total). Data are also presented for the subsets of these patients who received BKZ Q4W during the initial treatment periods, BKZ Q8W during the maintenance treatment periods and BKZ Q8W during the OLE periods. Year 1 data were recorded at Week 48, the last common timepoint for PASI, IGA, and DLQI assessment across BE VIVID, BE READY, BE SURE, and BE RADIANT before OLE entry. Year 2 refers to Week 96, and Year 3 refers to Week 144. [a]DLQI assessment was performed on a different schedule in BE VIVID compared to BE SURE, BE READY, and BE RADIANT; this table only presents DLQI responses at visits common to BE SURE, BE READY, and BE RADIANT.

Figure 1 Study design (included patients)



As this analysis only includes patients randomized to receive BKZ at baseline, only BKZ-randomized patients are included in this study design. BKZ-treated patients who were re-randomized to placebo at Week 16 in BE READY (n=105) were not included in the final analyses reported below, however they are included in the randomized patient numbers shown above (N=1,362). [a]Patients receiving BKZ 320 mg Q4W who achieved ≥PASI 90 at the end of the feeder studies (BE RADIANT: Week 48; BE VIVID: Week 52; BE READY and BE SURE: Week 56) were randomized 1:1 in BE RADIANT and 4:1 in BE BRIGHT to BKZ 320 mg Q4W or Q8W; patients receiving BKZ 320 mg Q8W who achieved ≥PASI 90 at the end of the feeder studies remained on Q8W dosing; [b]In BE RADIANT, at OLE Week 16 or the next scheduled clinic visit, all patients switched to BKZ Q8W after the implementation of a protocol amendment; in BE BRIGHT, at OLE Week 24, patients achieving ≥PASI 90 could switch to Q8W at the investigator's discretion, and all patients were re-assigned to BKZ Q8W at OLE Week 48 or the next scheduled visit via protocol amendment; [c]OLE Week 48 (the end of Year 2) 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]OLE Week 96 (the end of Year 3) corresponds to BE RADIANT Week 144, BE VIVID/BE BRIGHT Week 148, and BE READY/BE BRIGHT and BE SURE/BE BRIGHT Week 152.

Figure 2 Maintenance of PASI 90, PASI 100, IGA 0/1, and DLQI 0/1 in Week 16 BKZ-treated responders who entered the BE BRIGHT or BE RADIANT OLEs (mNRI)



Week 16 responses are reported for all BKZ-randomized patients; response rates from Week 16 up to Year 3 (Week 144) are reported among patients who were randomized to BKZ at the start of the study in BE SURE, BE READY, BE VIVID, and BE RADIANT, achieved a PASI 90, PASI 100, or IGA 0/1 response, respectively, at Week 16 and entered the relevant OLE. Week 48 was the last common timepoint for PASI, IGA, and DLQI assessment across BE VIVID, BE READY, BE SURE, and BE RADIANT before OLE entry; therefore, data are only shown up to this point before the OLE. The BE SURE and BE READY feeder studies had a duration of 56 weeks, while BE VIVID had a duration of 52 weeks and BE RADIANT had a duration of 48 weeks; to pool the data across all three studies, Week 52 and 56 data from the feeder studies were not included. Therefore, time points after Week 48 in this figure are from the BE BRIGHT and BE RADIANT OLEs. [a]DLQI assessment was performed on a different schedule in BE VIVID compared to BE SURE, BE READY, and BE RADIANT; this figure only presents DLQI responses at visits common to BE SURE, BE READY, and BE RADIANT.

BKZ: bimekizumab; **BSA:** body surface area; **DLQI:** Dermatology Life Quality Index; **Ig:** immunoglobulin; **IGA:** Investigator's Global Assessment; **IL:** interleukin; **mNRI:** modified non-responder imputation; **NRI:** non-responder imputation; **OC:** observed case; **OLE:** open-label extension; **PASI 90/100:** ≥90%/100% improvement from baseline in Psoriasis Area and Severity Index; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SD:** standard deviation.

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