P3321

Bimekizumab long-term efficacy in patients with moderate to severe plaque psoriasis after switching from adalimumab, ustekinumab, or secukinumab: Results from up to 4 years of total treatment from BE BRIGHT and BE RADIANT

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Objective

To investigate efficacy and health-related quality of life responses after switch to bimekizumab (BKZ) from adalimumab (ADA), ustekinumab (UST), or secukinumab (SEC) through 3 or 4 years of total treatment in the BE RADIANT and BE BRIGHT phase 3/3b studies, respectively.

Introduction

- To achieve improvements in psoriasis management, patients and clinicians may choose to switch biologics, particularly in cases of suboptimal response and due to patient preference.[1]
- It has been reported previously that, among patients with psoriasis who achieved ≥90% improvement from baseline in Psoriasis Area and Severity Index (PASI 90) with biologic therapy, approximately one-quarter lost their response at 6 months and half lost response at 18 months.[2]
- Interleukin (IL)-17A and IL-17F have been identified as pivotal drivers of psoriasis and may be differentially regulated;[3] therefore, inhibiting both may offer additional benefits for patients.
- Rapid skin clearance after switching to BKZ has previously been reported in patients who did not adequately respond to either ADA, UST, or SEC, and these responses were maintained for up to 80 weeks after switch (2 years' total treatment).[1]
- Here, we investigate the impact of switching to BKZ on efficacy and health-related quality of life responses, and how they evolve in the long term following switch.

Methods

- Included patients from BE BRIGHT were initially randomised to ADA to Week 24 followed by BKZ every 4 weeks (Q4W) to Week 56 (BE SURE), or to UST to Week 52 (BE VIVID), and then entered the BE BRIGHT open-label extension (OLE; 4 years' total treatment) where they received BKZ Q4W or every 8 weeks (Q8W; **Figure 1**).[4–6]
- Included patients from BE RADIANT (3 years' total treatment) received SEC to Week 48, followed by BKZ Q4W or Q8W during its OLE (**Figure 1**).[7,8]
- Here, PASI 90/PASI 100 and Dermatology Life Quality Index (DLQI) 0/1 responses are reported by number of weeks after switch to BKZ, in the long term, grouped by observed PASI 90 response status at switch (regardless of BKZ dosing regimen).
- 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 (modified non-responder imputation; mNRI). Observed case (OC) data are also reported.

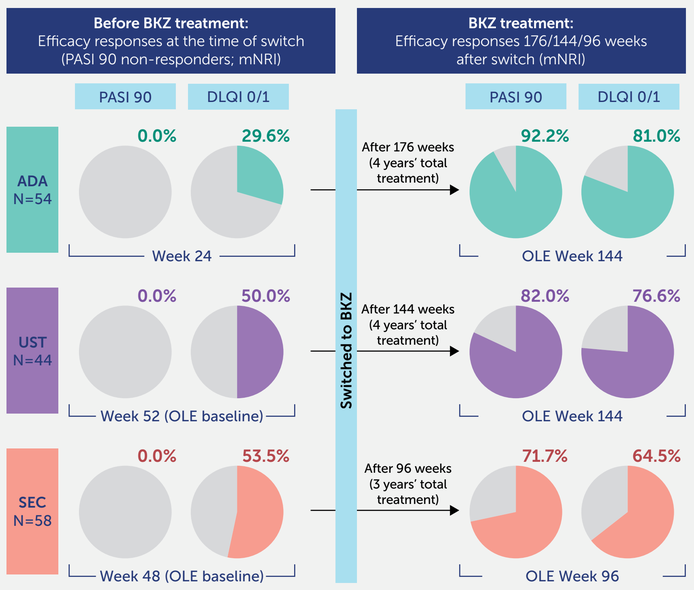
Results

- Baseline characteristics are shown in **Table 1**.
- Of patients randomised to ADA, UST, and SEC at baseline who entered the respective OLEs, 54/129 (41.9%) ADA, 44/132 (33.3%) UST, and 58/314 (18.5%) SEC patients did not achieve PASI 90 at the time of switch to BKZ (Week 24, 52, and 48 respectively; OC).
  - At the time of switch, 29.6%, 50.0%, and 53.5% of PASI 90 non-responders had DLQI 0/1, respectively (mNRI).
- In PASI 90 non-responders, following switch to BKZ, rapid responses were observed and maintained in the long term (mNRI; **Figure 2**):
  - Following switch from ADA and after 176 weeks of BKZ, 92.2%, 74.4%, and 81.0% achieved PASI 90, PASI 100, and DLQI 0/1, respectively;
  - Following switch from UST and after 144 weeks of BKZ, 82.0%, 58.8%, and 76.6% achieved PASI 90, PASI 100, and DLQI 0/1, respectively;
  - Following switch from SEC and after 96 weeks of BKZ, 71.7%, 39.8%, and 64.5% achieved PASI 90, PASI 100, and DLQI 0/1, respectively.
- Switching ADA, UST, and SEC PASI 90 responders to BKZ resulted in maintained PASI 90, PASI 100, and DLQI 0/1 responses through 3 or 4 years of total treatment (**Figure 3**).

Conclusions

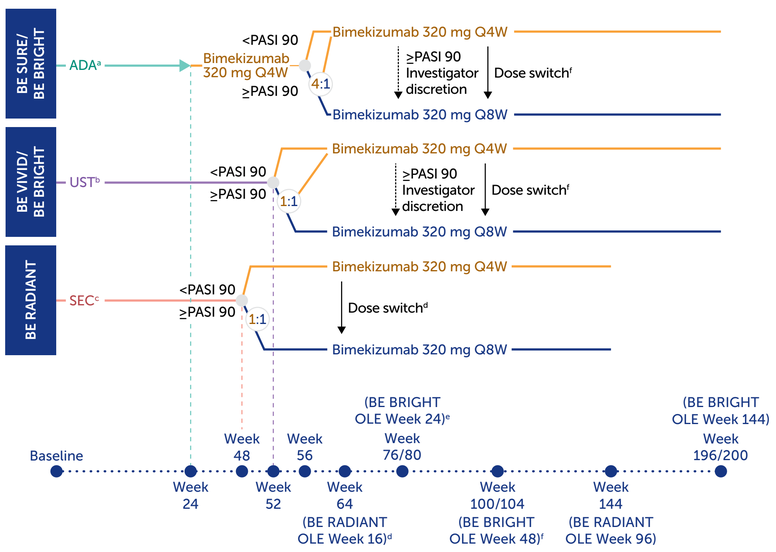
Switching adalimumab, ustekinumab, or secukinumab PASI 90 non-responders to bimekizumab led to rapid achievement and long-term maintenance of clinical responses, through 3 or 4 years of total treatment. In adalimumab, ustekinumab, or secukinumab PASI 90 responders, response rates were maintained in the long term following switch to bimekizumab.

Summary



Switching patients who did not adequately respond to adalimumab, ustekinumab, or secukinumab **to bimekizumab resulted in patients achieving and maintaining PASI 90 and DLQI 0/1 responses through 3 or 4 years** of total treatment.

Figure 1 Study design (included patients)



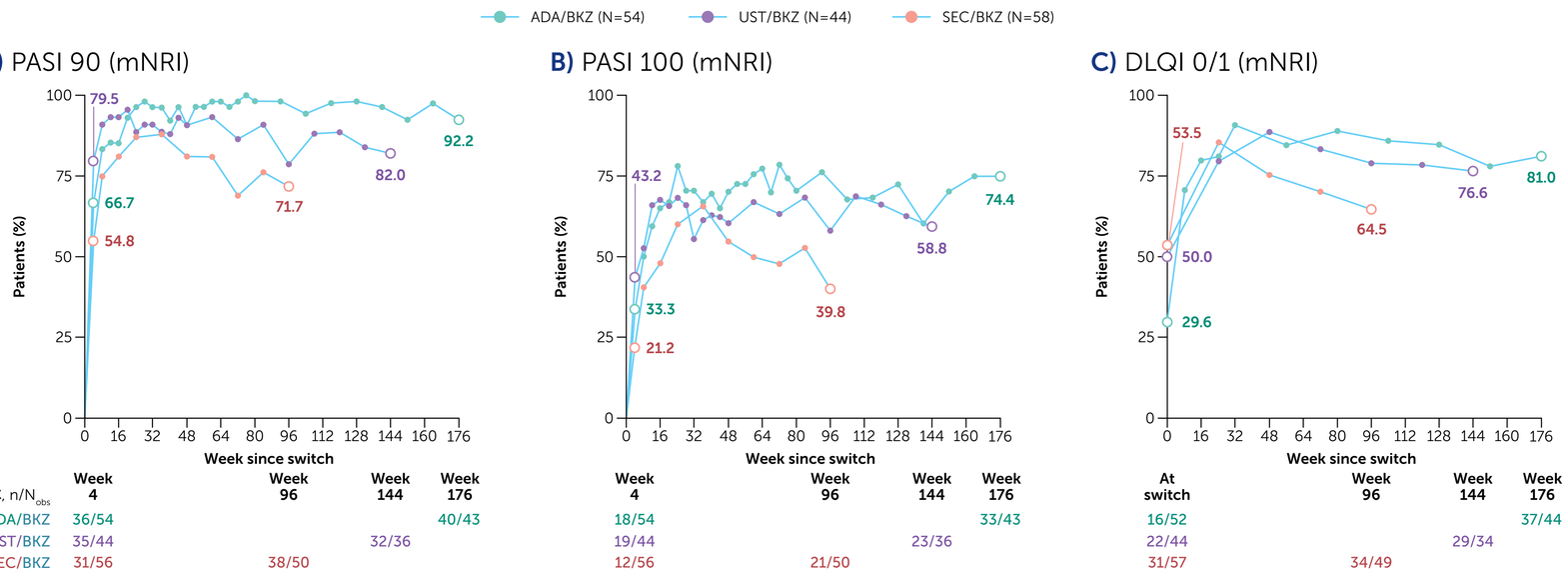
Patients completing BE SURE or BE VIVID could enrol in the BE BRIGHT OLE, and those completing BE RADIANT could enter the BE RADIANT OLE. Patients received BKZ Q4W or Q8W depending on PASI response on completion of the feeder trials (BE SURE/ BE VIVID) or at Week 48 (BE RADIANT). In these analyses, BKZ Q4W and Q8W treatment arms for each trial are pooled. **[a]** Dosed 80 mg at baseline, 40 mg at Week 1, then 40 mg Q2W; **[b]** Dosing based on bodyweight at baseline: 45 mg for patients weighing ≤100 kg, and 90 mg for patients weighing >100 kg, received at baseline and Week 4, then Q12W; **[c]** Dosed 300 mg weekly to Week 4, then Q4W; **[d]** At BE RADIANT Week 64, or the next scheduled clinic visit, patients receiving BKZ Q4W switched to Q8W after the implementation of a protocol amendment; **[e]** At BE BRIGHT OLE Week 24, patients receiving BKZ Q4W who achieved PASI 90 could switch to Q8W, at the investigator's discretion; **[f]** Following a protocol amendment, at BE BRIGHT OLE Week 48 or the next scheduled clinic visit, all patients receiving BKZ Q4W switched to Q8W dosing.

Table 1 Baseline characteristics

	BE SURE/BE BRIGHT ADA/BKZ		BE VIVID/BE BRIGHT UST/BKZ		BE RADIANT SEC/BKZ	
	Week 24 PASI 90 non-responders N=54	Week 24 PASI 90 responders N=75	Week 52 PASI 90 non-responders N=44	Week 52 PASI 90 responders N=88	Week 48 PASI 90 non-responders N=58	Week 48 PASI 90 responders N=256
Age (years), mean ± SD	45.7 ± 14.0	45.3 ± 14.4	52.0 ± 12.0	44.3 ± 13.5	47.1 ± 13.2	44.1 ± 14.7
Sex, male, n (%)	41 (75.9)	53 (70.7)	29 (65.9)	66 (75.0)	36 (62.1)	170 (66.4)
Racial group, white, n (%)	48 (88.9)	68 (90.7)	31 (70.5)	69 (78.4)	55 (94.8)	242 (94.5)
Weight (kg), mean ± SD	96.6 ± 20.3	85.4 ± 18.5	89.8 ± 21.4	86.6 ± 20.7	95.1 ± 20.3	88.1 ± 19.0
Disease duration (years), mean ± SD	15.4 ± 11.3	17.7 ± 12.5	19.9 ± 12.6	17.3 ± 11.4	19.8 ± 12.0	17.1 ± 12.1
PASI, mean ± SD	19.5 ± 6.1	19.1 ± 5.9	20.3 ± 8.2	21.5 ± 8.5	17.8 ± 4.9	19.8 ± 6.3
BSA (%), mean ± SD	26.3 ± 17.1	25.3 ± 13.8	26.7 ± 20.4	27.2 ± 15.3	20.5 ± 13.0	23.6 ± 13.4
IGA, n (%)						
3: moderate	35 (64.8)	55 (73.3)	26 (59.1)	56 (63.6)	42 (72.4)	190 (74.2)
4: severe	19 (35.2)	20 (26.7)	18 (40.9)	32 (36.4)	16 (27.6)	66 (25.8)
DLQI total, mean ± SD	11.9 ± 7.5	9.7 ± 7.0	10.8 ± 5.7	10.8 ± 7.4	11.0 ± 7.6	11.2 ± 7.2
Any prior systemic therapy, n (%)	34 (63.0)	59 (78.7)	38 (86.4)	69 (78.4)	47 (81.0)	187 (73.0)
Any prior biologic therapy, n (%)	21 (38.9)	26 (34.7)	20 (45.5)	30 (34.1)	23 (39.7)	82 (32.0)
Anti-TNF	4 (7.4)	8 (10.7)	6 (13.6)	12 (13.6)	13 (22.4)	49 (19.1)
Anti-IL-17	17 (31.5)	15 (20.0)	12 (27.3)	19 (21.6)	9 (15.5)	38 (14.8)

Data presented for patients who entered the OLE period by initial treatment group (ADA, UST, or SEC) and whether they achieved PASI 90 response at the time of switch, regardless of BKZ OLE dosing regimen following switch.

Figure 2 PASI 90, PASI 100, and DLQI 0/1 responses in PASI 90 non-responders following switch to BKZ (mNRI, OC)



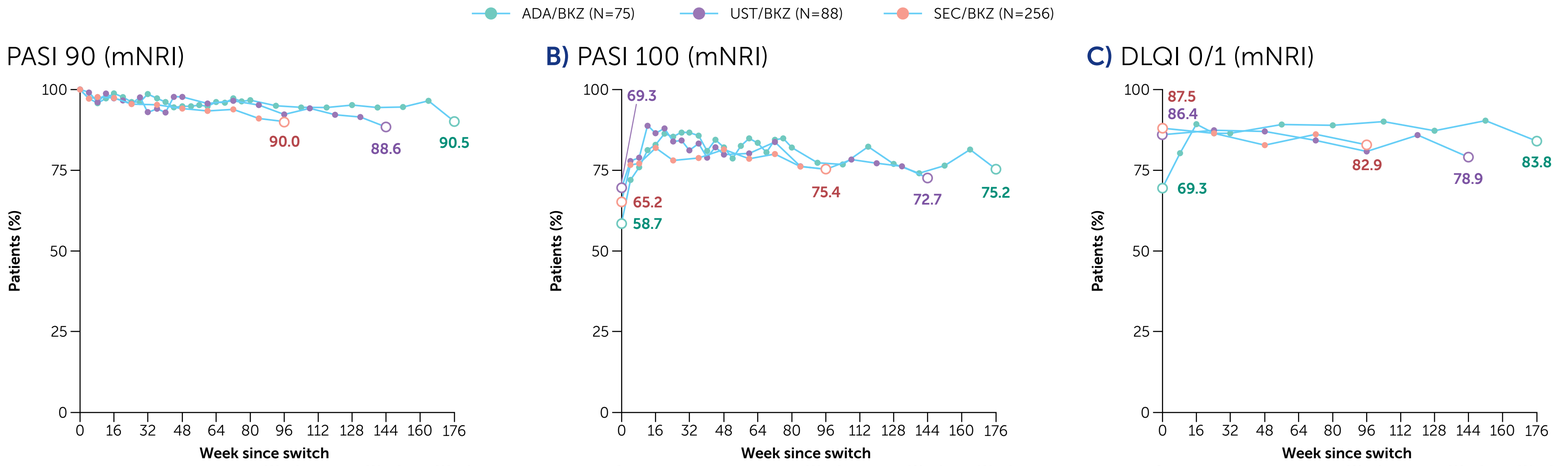
OC, n/N_{obs}	Week 4	Week 96	Week 144	Week 176
ADA/BKZ	36/54			40/43
UST/BKZ	35/44		32/36	
SEC/BKZ	31/56	38/50		

	Week 4	Week 96	Week 144	Week 176
ADA/BKZ	18/54			33/43
UST/BKZ	19/44		23/36	
SEC/BKZ	12/56	21/50		

	At switch	Week 96	Week 144	Week 176
ADA/BKZ	16/52			37/44
UST/BKZ	22/44		29/34	
SEC/BKZ	31/57	34/49		

Data reported according to weeks since switch to BKZ up to 3 years (SEC/BKZ) and 4 years (ADA/BKZ and UST/BKZ) of total treatment. Upon entering the OLE, patients received either BKZ 320 mg Q4W or Q8W based on PASI 90 response at Week 56, 52, or 48 for patients initially randomised to ADA, UST, or SEC, respectively. Due to differences in scheduling between the trials, efficacy assessments were performed at different timepoints after switch from ADA, UST, and SEC to BKZ.

Figure 3 PASI 90, PASI 100, and DLQI 0/1 responses in PASI 90 responders following switch to BKZ (mNRI, OC)



OC, n/N_{obs}	Week 96	Week 144	Week 176
ADA/BKZ			56/59
UST/BKZ		72/76	
SEC/BKZ	205/215		

	At switch	Week 96	Week 144	Week 176
ADA/BKZ	44/75			49/59
UST/BKZ	61/88		60/76	
SEC/BKZ	167/256	180/215		

	At switch	Week 96	Week 144	Week 176
ADA/BKZ	52/75			54/59
UST/BKZ	76/88		65/75	
SEC/BKZ	224/256	196/218		

Data reported according to weeks since switch to BKZ up to 3 years (SEC/BKZ) and 4 years (ADA/BKZ and UST/BKZ) of total treatment. Upon entering the OLE, patients received either BKZ 320 mg Q4W or Q8W based on PASI 90 response at Week 56, 52, or 48 for patients initially randomised to ADA, UST, or SEC, respectively. Due to differences in scheduling between the trials, assessments were performed at different timepoints after switch from ADA, UST, and SEC to BKZ.

ADA: adalimumab; **BKZ:** bimekizumab; **BSA:** body surface area; **DLQI:** Dermatology Life Quality Index; **IGA:** Investigator's Global Assessment; **IL:** interleukin; **mNRI:** modified non-responder imputation; N_{obs}: N observed; **OC:** observed case; **OLE:** open-label extension; **PASI 90/100:** ≥90%/100% improvement from baseline in Psoriasis Area and Severity Index; **Q2W:** every 2 weeks; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **Q12W:** every 12 weeks; **SD:** standard deviation; **SEC:** secukinumab; **TNF:** tumour necrosis factor; **UST:** ustekinumab.

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