Bimekizumab Treatment in Patients with Active PsA and Prior Inadequate Response to TNF Inhibitors: Sustained Efficacy and Safety Results from a Phase 3 Study and its Open-Label Extension up to 1 Year

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Objective

To assess the long-term efficacy and safety of bimekizumab (BKZ) treatment up to 52 weeks in patients with active psoriatic arthritis (PsA) and prior inadequate response or intolerance to tumor necrosis factor-α inhibitors (TNFi-IR).

Background

- BKZ is a humanized monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- BKZ has shown superior efficacy to 16 weeks versus placebo (PBO) and tolerability in patients with active PsA in two phase 3 studies, BE OPTIMAL (naïve to biologic disease-modifying antirheumatic drugs [bDMARDs]) and BE COMPLETE (TNFi-IR).[1,2]
- The efficacy and tolerability of BKZ to 52 weeks has also been demonstrated in BE OPTIMAL.[3]
- Patients with PsA and TNFi-IR typically exhibit reduced treatment responses compared with bDMARD-naive patients,[4,5] so identifying treatments that effectively manage the long-term clinical needs of these patients is important.

Methods

- BE COMPLETE (NCT03896581) included a 16-week double-blind, PBO-controlled period.[2]
- Patients were randomized 2:1 to subcutaneous BKZ 160 mg or PBO every 4 weeks (Q4W).
- Patients who completed Week 16 were eligible for entry into an open-label extension, BE VITAL (NCT04009499). Upon entry, PBO-randomized patients switched to receive BKZ (PBO/BKZ).
- BE VITAL included patients from BE OPTIMAL and BE COMPLETE; we report here patients randomized at baseline (Week 0) of BE COMPLETE, up to 1 year (**Figure 1**).
- Efficacy data reported are observed case or have imputed missing data using non-responder imputation (binary) or multiple imputation (continuous).
- The number of treatment-emergent adverse events (TEAEs) to Week 52 are reported for patients who received ≥1 dose of BKZ, including patients who switched from PBO to BKZ at Week 16.

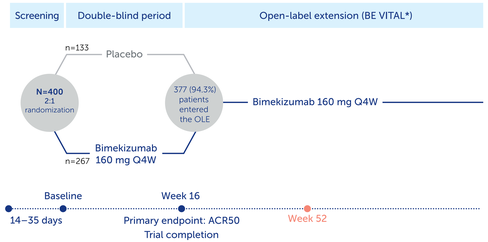
Results

- 388/400 (97.0%) patients completed Week 16; 377 (94.3%) entered BE VITAL and 347 (86.8%) completed Week 52.*
- Baseline characteristics were comparable between groups (**Table 1**).
- Improvements in joint and skin responses with BKZ treatment at Week 16 were sustained to Week 52. Patients who switched to BKZ at Week 16 demonstrated improvements in efficacy responses to Week 52 (**Figure 2**, **Table 2**).
- Improvements from baseline in all ACR components were seen at Week 16 and sustained to Week 52 in BKZ-treated patients (**Figure 3**).
- To Week 52, 243/388 (62.6%) patients had ≥1 TEAE whilst receiving BKZ (exposure-adjusted incident rate [EAIR]: 126.0 per 100 patient-years; **Table 3**).
- The most frequent TEAEs were SARS-CoV-2 (COVID-19), oral candidiasis, nasopharyngitis and urinary tract infection (**Table 3**).
- All *Candida* infections were mild or moderate and none were systemic. Two cases of oral candidiasis led to study discontinuation.
- There was one death, considered unrelated to study treatment by the investigator (BKZ-treated patient with a history of cardiac events).

Conclusions

In patients with PsA and prior TNFi-IR, bimekizumab treatment demonstrated sustained improvements across joints and skin from Week 16 to Week 52. Patients who switched to bimekizumab at Week 16 also displayed meaningful improvements in efficacy responses at Week 52. The safety profile was consistent with previous reports.[1–3]

Figure 1 BE COMPLETE and BE VITAL study design



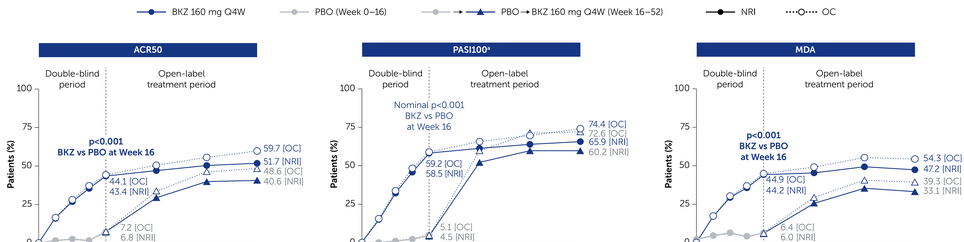
*BE VITAL includes patients from the BE OPTIMAL and BE COMPLETE studies; results are only presented for patients from BE COMPLETE. BKZ-treated patients were eligible to receive rescue therapy from Week 16 at the discretion of the investigator, while continuing to receive BKZ.

Table 1 Baseline patient demographics and disease characteristics

	PBO n=133	BKZ 160 mg Q4W n=267
Age, years, mean (SD)	51.3 (12.9)	50.1 (12.4)
Male, n (%)	60 (45.1)	130 (48.7)
BMI, kg/m², mean (SD)	29.0 (5.4)	30.1 (6.5)
Time since first PsA diagnosis,[a] years, mean (SD)	9.2 (8.1)	9.6 (9.9)
BSA affected by psoriasis ≥3%, n (%)	88 (66.2)	176 (65.9)
PASI score,[b] mean (SD)	8.5 (6.6)	10.1 (9.1)
TJC (of 68 joints), mean (SD)	19.3 (14.2)	18.4 (13.5)
SJC (of 66 joints), mean (SD)	10.3 (8.2)	9.7 (7.5)
Enthesitis (LEI >0),[c] n (%)	36 (27.1)	106 (39.7)
LEI score,[d] mean (SD)	2.9 (1.6)	2.6 (1.5)
Dactylitis (LDI >0),[c] n (%)	14 (10.5)	34 (12.7)
LDI score,[e] mean (SD)	66.4 (127.6)	72.7 (114.4)
Nail psoriasis (mNAPSI >0),[c] n (%)	83 (62.4)	159 (59.6)
mNAPSI score,[f] mean (SD)	4.5 (2.8)	4.3 (2.8)
hs-CRP ≥6 mg/L, n (%)	59 (44.4)	118 (44.2)
HAQ-DI score, mean (SD)	1.04 (0.69)	0.97 (0.59)
SF-36 PCS score, mean (SD)	35.9 (10.2)	36.4 (9.0)

Randomized set. [a] Data missing for 1 PBO patient; 1 BKZ patient; [b] In patients with psoriasis involving at least 3% of BSA at baseline; [c] Data missing for 1 PBO patient; [d] In patients with enthesitis at baseline (LEI >0); [e] In patients with dactylitis at baseline (LDI >0); [f] In patients with nail psoriasis at baseline (mNAPSI >0).

Figure 2 ACR, PASI and MDA response rates over time to Week 52 (NRI and OC)



Randomized set. For binary variables, p values were calculated using a logistic regression model with treatment, prior TNFi exposure, and region as stratification factors. Nominal p values are not powered or adjusted for multiplicity and should not be used to assess statistical significance. N values are NRI/OC at Week 0 and OC at Week 16 and Week 52. [a] In patients with psoriasis involving at least 3% of BSA at baseline.

Figure 3 ACR components change from baseline at Week 16 and Week 52 (MI)

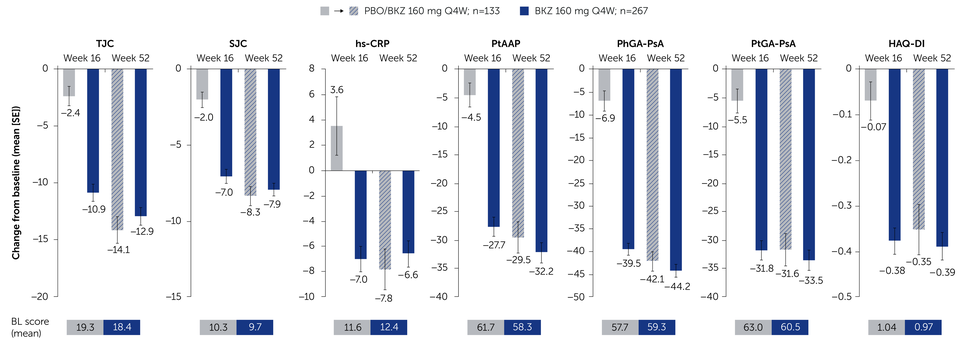


Table 2 Additional efficacy endpoints at Week 16 and Week 52 (NRI)

NRI, n/N (%), unless otherwise specified	PBO (Weeks 0–16) → BKZ 160 mg Q4W (Weeks 16–52) n=133		BKZ 160 mg Q4W n=267	
	Week 16	Week 52	Week 16	Week 52
ACR20 responders	21/133 (15.8)	80/133 (60.2)	179/267 (67.0)	182/267 (68.2)
ACR70 responders	1/133 (0.8)	34/133 (25.6)	71/267 (26.6)	95/267 (35.6)
PASI75 responders[a]	9/88 (10.2)	71/88 (80.7)	145/176 (82.4)	148/176 (84.1)
PASI90 responders[a]	6/88 (6.8)	65/88 (73.9)	121/176 (68.8)	131/176 (74.4)
Enthesitis resolution[b]	8/36 (22.2)	21/36 (58.3)	52/106 (49.1)	60/106 (56.6)
Dactylitis resolution[c]	6/14 (42.9)	12/14 (85.7)	24/34 (70.6)	29/34 (85.3)
Nail psoriasis resolution[d]	12/83 (14.5)	51/83 (61.4)	73/159 (45.9)	107/159 (67.3)
	Week 16	**Week 40***	**Week 16**	**Week 40***
SF-36 PCS CfB, MI, mean (SE)	1.4 (0.7)	7.3 (0.9)	7.3 (0.5)	8.4 (0.6)

Randomized set. Previously reported data through Week 16 included for reference. *Data not collected at Week 52 for SF-36 PCS. [a] In patients with psoriasis involving at least 3% of BSA at baseline; [b] In patients with enthesitis at baseline (LEI >0); [c] In patients with dactylitis at baseline (LDI >0); [d] In patients with nail psoriasis at baseline (mNAPSI >0).

Table 3 Safety to Week 16 and Week 52

n (%) [EAIR]	Weeks 0–16[c] (Double-blind period)		Weeks 16–52 (Open-label period)	Weeks 0–52 (Overall study period)	
	PBO n=132 (PYAR: 42.5)	BKZ 160 mg Q4W n=267 (PYAR: 87.1)	PBO/BKZ 160 mg Q4W[c] n=121 (PYAR: 80.3)	BKZ 160 mg Q4W n=267 (PYAR: 259.5)	BKZ 160 mg Q4W Total[d] n=388 (PYAR: 339.8)
Any TEAE	44 (33.3)	108 (40.4)	68 (56.2) [127.7]	175 (65.5) [125.4]	243 (62.6) [126.0]
Severe TEAEs	0	5 (1.9)	3 (2.5)[c]	14 (5.2)[c]	17 (4.4)[c]
Study discontinuation due to TEAEs	0	2 (0.7)	6 (5.0) [7.6]	10 (3.7) [3.9]	16 (4.1) [4.8]
Drug-related TEAEs	4 (3.0)	35 (13.1)	21 (17.4)[c]	66 (24.7)[c]	87 (22.4)[c]
Serious TEAEs	0	5 (1.9)	8 (6.6) [10.2]	15 (5.6) [6.0]	23 (5.9) [7.0]
Deaths	0	0	1 (0.8)[c,d]	0	1 (0.3)[c,d]
Most frequent TEAEs*					
SARS-CoV-2 (COVID-19)	6 (4.5)	5 (1.9)	7 (5.8) [8.9]	21 (7.9) [8.4]	28 (7.2) [8.5]
Oral candidiasis	0	7 (2.6)	7 (5.8) [9.0]	17 (6.4) [6.8]	24 (6.2) [7.3]
Nasopharyngitis	1 (0.8)	10 (3.7)	4 (3.3) [5.0]	19 (7.1) [7.7]	23 (5.9) [7.0]
Urinary tract infection	3 (2.3)	5 (1.9)	4 (3.3) [5.1]	19 (7.1) [7.7]	23 (5.9) [7.0]
Serious infections	0	2 (0.7)	3 (2.5) [3.8]	4 (1.5) [1.6]	7 (1.8) [2.1]
Opportunistic infections	0	0	2 (1.7) [2.5][f]	0	2 (0.5) [0.6][f]
Neutropenia	0	4 (1.5)[g]	0	5 (1.9) [2.0][h]	5 (1.3) [1.5][h]
Hypersensitivity	1 (0.8)	7 (2.6)	4 (3.3) [5.1]	15 (5.6) [6.0]	19 (4.9) [5.8]
Dermatitis and eczema	0	4 (1.5)	2 (1.7) [2.5]	6 (2.2) [2.4]	8 (2.1) [2.4]
Injection site reactions	0	3 (1.1)	0	6 (2.2) [2.4]	6 (1.5) [1.8]
Adjudicated MACE	0	0	2 (1.7) [2.5][i]	0	2 (0.5) [0.6][i]
Malignancies excluding non-melanoma skin cancer	0	0	1 (0.8) [1.3]	2 (0.7) [0.8][j]	3 (0.8) [0.9][j,k]
Non-melanoma skin cancer	1 (0.8)[l]	0	0	0	0

Safety set. No cases of active tuberculosis, definite or probable adjudicated IBD, suicidal ideation and behavior, or uveitis were reported. [a] EAIRs not available for double-blind period; [b] Includes patients who switched from PBO to BKZ and only includes TEAEs occurring whilst receiving BKZ; [c] EAIRs not available; [d] Sudden death in 54-year old patient with a history of hypertension, aortic regurgitation, electrocardiogram changes of coronary artery disease; no further information available; no autopsy was performed; [e] Most frequent adverse events are those occurring in ≥5% of patients in any study arm; [f] 2 esophageal candidiasis; [g] 3 neutropenia; 1 neutrophil count decreased; [h] 4 neutropenia; 1 neutrophil count decreased; [i] 1 sudden death; 1 cerebral hemorrhage; [j] 1 prostate cancer; [k] 1 endometrial cancer stage I; 1 gastric cancer recurrent; [l] 1 basal cell carcinoma.

*Of the 347 patients remaining in the study at Week 52, 4 (1.0%) were not on randomized treatment. **ACR20/50/70:** ≥20/50/70% improvement from baseline in American College of Rheumatology criteria; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **BL:** baseline; **BMI:** body mass index; **BSA:** body surface area; **CfB:** change from baseline; **EAIR:** exposure-adjusted incident rate per 100 patient-years; **HAQ-DI:** Health Assessment Questionnaire–Disability Index; **hs-CRP:** high-sensitivity C-reactive protein; **IBD:** inflammatory bowel disease; **IL:** interleukin; **LDI:** Leeds Dactylitis Index; **LEI:** Leeds Enthesitis Index; **MACE+:** major adverse cardiovascular event; **MDA:** minimal disease activity; **MI:** multiple imputation; **mNAPSI:** modified Nail Psoriasis Severity Index; **NRI:** non-responder imputation; **OC:** observed case; **OLE:** open-label extension; **PASI:** Psoriasis Area and Severity Index; **PBO:** placebo; **PhGA-PsA:** Physician Global Assessment – PsA; **PsA:** psoriatic arthritis; **PtAAP:** Patient's Assessment of Arthritis Pain; **PtGA-PSA:** Patient Global Assessment – PsA; **PYAR:** patient years at risk; **Q4W:** every four weeks; **SD:** standard deviation; **SE:** standard error; **SF-36 PCS:** Short-Form 36-item Health Survey Physical Component Summary; **SJC:** swollen joint count; **TEAE:** treatment-emergent adverse event; **TJC:** tender joint count; **TNFi:** tumor necrosis factor-α inhibitor; **TNFi-IR:** prior inadequate response or intolerance to tumor necrosis factor-α inhibitors.

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