Bimekizumab-Treated Patients with Active Psoriatic Arthritis Showed Sustained Achievement of Minimal Disease Activity and Remission: Up to 2-Year Results from Two Phase 3 Studies

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Objective

To assess the efficacy of bimekizumab (BKZ) using composite outcomes, including Minimal Disease Activity (MDA) and Disease Activity Index for Psoriatic Arthritis (DAPSA) remission, up to 2 years in patients with active psoriatic arthritis (PsA) who were biologic disease-modifying antirheumatic drug (bDMARD)-naïve or had prior inadequate response or intolerance to tumour necrosis factor inhibitors (TNFi-IR).

Background

- BKZ, a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated clinically meaningful, sustained joint and skin efficacy responses at Week 52 in patients with PsA.[1,2]
- PsA is a clinically heterogenous inflammatory disease characterised by multiple domains, including skin and joint disease.[3] Treatment efficacy can therefore be comprehensively evaluated using composite outcome measures that assess disease activity across the multiple affected domains.[3]
- MDA and DAPSA remission have been recommended as key treatment targets.[4]

Methods

- BE OPTIMAL (NCT03895203) and BE COMPLETE (NCT03896581) assessed subcutaneous BKZ 160 mg every 4 weeks (Q4W) in bDMARD-naïve and TNFi-IR patients with active PsA, respectively.
- Patients completing Week 52 of BE OPTIMAL and Week 16 of BE COMPLETE were eligible for the open-label extension BE VITAL (NCT04009499; **Figure 1**).[1,2]
- MDA and Very Low Disease Activity (VLDA) responses and components and DAPSA remission or low disease activity (REM ≤4; REM+LDA ≤14) responses and change from baseline were evaluated.
- Data are reported as observed case (OC) and using multiple imputation (MI; continuous), non-responder imputation (NRI; binary) or worst-category imputation (categorical; missing data are set to the most severe category).

Results

- Overall, 710/852 (83.3%) and 322/400 (80.5%) patients completed Week 104/100 of BE OPTIMAL and BE COMPLETE.
- Achievement of MDA by Week 52 was sustained to Week 104/100 in both BKZ-randomised and PBO/BKZ patients. Similarly, in bDMARD-naïve ADA/BKZ patients, the MDA responder rate at Week 52 was sustained to Week 104 (**Figure 2A**).
- Trends were similar to Week 104/100 for achievement of VLDA (bDMARD-naïve: 26.0% PBO/BKZ, 30.6% BKZ, 29.3% ADA/BKZ; TNFi-IR: 17.3% PBO/BKZ, 24.0% BKZ), DAPSA REM+LDA (bDMARD-naïve: 50.2% PBO/BKZ, 52.9% BKZ, 55.0% ADA/BKZ; TNFi-IR: 53.4% PBO/BKZ, 46.1% BKZ) and improvements in DAPSA scores (**Figure 2B**).
- At baseline, MDA components were generally comparable between treatment groups within trials (**Figure 3**).
- BKZ treatment led to improvements to Week 104/100 in most MDA components across all treatment arms in both trial populations, including objective clinical measures (swollen and tender joint count; skin improvements) and patient-reported components (pain; physical function; **Figure 3**).
- Joint and skin responses were also sustained to Week 104/100, including ≥50% improvement from baseline in American College of Rheumatology response criteria (ACR50; bDMARD-naïve: 50.5% PBO/BKZ, 51.5% BKZ, 50.7% ADA/BKZ; TNFi-IR: 48.1% PBO/BKZ, 50.6% BKZ) and Psoriasis Area and Severity Index 100% improvement from baseline in patients with baseline psoriasis ≥3% body surface area (bDMARD-naïve: 60.0% PBO/BKZ, 59.4% BKZ, 60.3% ADA/BKZ patients; TNFi-IR: 65.9% PBO/BKZ, 63.1% BKZ).
- To Week 104, the exposure-adjusted incidence rate (EAIR) per 100 patient-years for ≥1 treatment-emergent adverse event (TEAE) on BKZ was 179.9 in bDMARD-naive patients and 100.3 in TNFi-IR patients (**Table**).

Conclusions

Bimekizumab-treated patients with PsA achieved sustained MDA responses and DAPSA improvements from baseline up to 2 years, regardless of prior bDMARD use. Improvements were observed across all patient-reported and most clinical components of MDA, with robust improvements observed in joint and skin outcomes. Bimekizumab was well tolerated; no new safety signals were observed.[1,2]

Summary

Composite outcome measures assess **treatment efficacy** across multiple domains of **PsA**.

MDA achievement[a]

49.8%–52.4%[c]
bDMARD-naïve patients in BE OPTIMAL at Week 104

44.9%–46.6%[d]
TNFi-IR patients in BE COMPLETE at Week 100

DAPSA REM+LDA achievement[b]

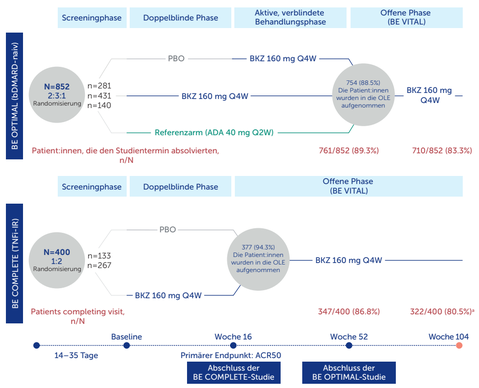
50.2%–55.0%[c]
bDMARD-naïve patients in BE OPTIMAL at Week 104

46.1%–53.4%[d]
TNFi-IR patients in BE COMPLETE at Week 100

Bimekizumab treatment demonstrated **sustained MDA** and **DAPSA improvements** up to 2 years in patients with PsA who were bDMARD-naïve or TNFi-IR.

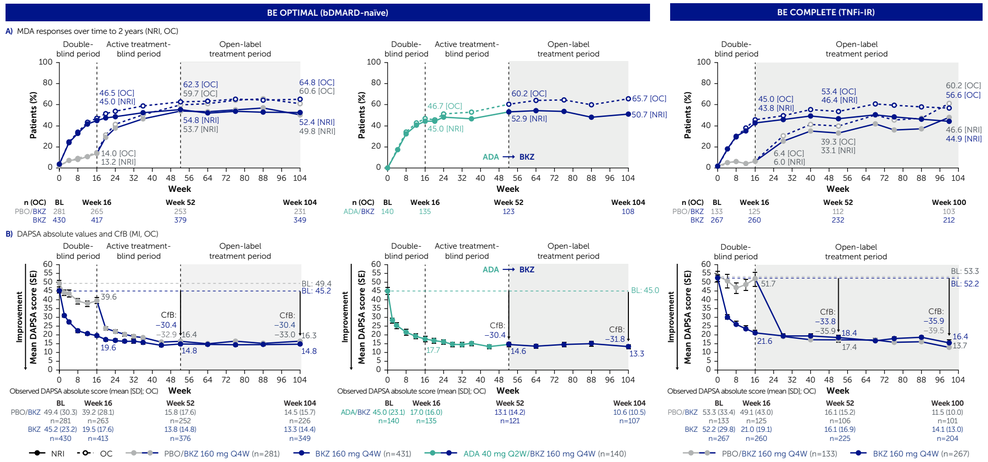
[a] Values shown here use NRI; [b] Values shown here use WCI; [c] Values represent 3 treatment arms (placebo/bimekizumab, bimekizumab, and adalimumab/bimekizumab); [d] Values represent 2 treatment arms (placebo/bimekizumab and bimekizumab).

Figure 1 BE OPTIMAL and BE COMPLETE study designs



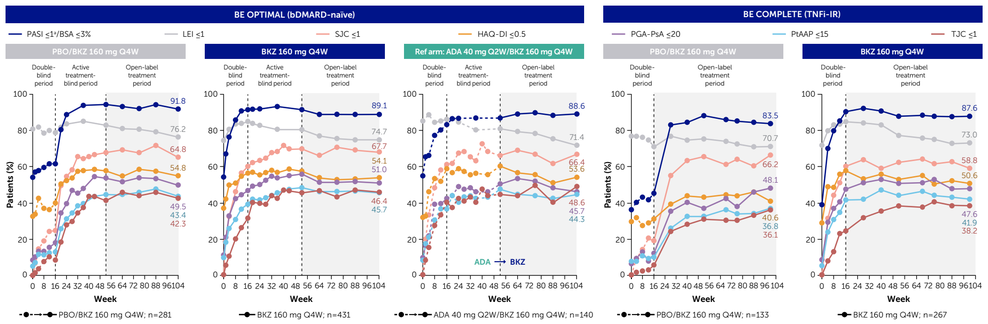
In both studies, PBO-randomised patients switched to BKZ 160 mg Q4W at Week 16 (PBO/BKZ). The ADA 40 mg Q2W treatment arm served as an active reference. There was no washout period for patients who switched from ADA to BKZ (ADA/BKZ) at Week 52 of BE OPTIMAL. The BE OPTIMAL study was not powered for statistical comparisons of ADA to BKZ or PBO. [a] Patients who completed to Week 100 of BE COMPLETE (not including 2 ongoing patients). There were no ongoing patients in BE OPTIMAL at Week 104.

Figure 2 Improvements in MDA and DAPSA to Weeks 104/100



Randomised set. BE OPTIMAL reference arm; study not powered for statistical comparison of ADA with BKZ of PBO. MDA response defined as achievement of ≥5 of the following 7 criteria: TJC ≤1, SJC ≤1, PASI ≤1 or BSA ≤3%, PtAAP ≤15 mm, PGA-PsA ≤20 mm, HAQ-DI ≤0.5, and tender entheseal points ≤1.

Figure 3 MDA component responses to Weeks 104/100 (NRI)



Randomised set. The ADA 40 mg Q2W treatment arm served as an active reference. The BE OPTIMAL study was not powered for statistical comparisons of ADA to BKZ or PBO. [a] For patients with psoriasis affecting ≥3% body surface area at baseline.

Table Safety to Week 52 and Week 104

	BE OPTIMAL (bDMARD-naïve)				BE COMPLETE (TNFi-IR)	
	Week 0–52		Week 52–104		Week 0–52	Week 52–104
EAIR /100 PY (95% CI)	BKZ 160 mg Q4W[a] n=702 595.6 PY	ADA 40 mg Q2W n=140 136.8 PY	ADA/BKZ 160 mg Q4W n=121 117.2 PY	BKZ 160 mg Q4W Total[a] n=773 738.0 PY	BKZ 160 mg Q4W Total[a] n=388 340.0 PY	BKZ 160 mg Q4W Total[a] n=361 335.2 PY
TEAEs	223.0 (204.8, 242.3)	209.4 (172.6, 251.7)	164.5 (132.1, 202.4)	152.2 (139.6, 165.5)	125.2 (110.0, 142.0)	87.3 (75.3, 100.6)
Serious TEAEs	7.8 (5.7, 10.4)	7.5 (3.6, 13.9)	4.3 (1.4, 10.1)	8.2 (6.2, 10.6)	7.0 (4.4, 10.4)	4.9 (2.8, 7.9)
Study discontinuation due to TEAEs	4.1 (2.6, 6.1)	5.2 (2.1, 10.8)	3.4 (0.9, 8.8)	3.0 (1.9, 4.6)	5.1 (3.0, 8.1)	1.8 (0.7, 3.9)
Drug-related TEAEs	47.8 (41.7, 54.5)	53.6 (40.3, 69.9)	36.0 (24.9, 50.2)	29.7 (25.5, 34.3)	29.8 (23.9, 36.9)	16.6 (12.3, 21.8)
Severe TEAEs	3.9 (2.5, 5.9)	6.8 (3.1, 12.9)	3.4 (0.9, 8.8)	3.8 (2.6, 5.6)	4.8 (2.7, 7.8)	2.7 (1.2, 5.1)
Deaths	0.2 (0.0, 0.9)[b]	0	0.9 (0.0, 4.8)[c]	0.1 (0.0, 0.8)[c]	0.3 (0.0, 1.6)[d]	0
Most frequent TEAEs[e]						
SARS-CoV-2 (COVID-19) infection	3.4 (2.1, 5.2)	2.9 (0.8, 7.5)	18.9 (11.6, 29.2)	18.6 (15.4, 22.1)	8.5 (5.6, 12.3)	7.4 (4.7, 10.9)
Nasopharyngitis	15.4 (12.3, 19.1)	9.4 (4.8, 16.3)	5.3 (1.9, 11.5)	5.3 (3.7, 7.2)	7.0 (4.5, 10.6)	4.3 (2.3, 7.2)
Upper respiratory tract infection	8.8 (6.6, 11.6)	6.1 (2.6, 12.0)	6.2 (2.5, 12.7)	6.3 (4.6, 8.4)	3.6 (1.9, 6.3)	4.6 (2.6, 7.6)
Oral candidiasis[f]	6.7 (4.8, 9.2)	0.7 (0.0, 4.1)	4.4 (1.4, 10.2)	5.5 (3.9, 7.5)	7.6 (4.9, 11.3)	3.3 (1.7, 5.9)
Urinary tract infection	7.3 (5.2, 9.8)	3.7 (1.2, 8.7)	4.4 (1.4, 10.3)	4.2 (2.8, 6.0)	7.0 (4.5, 10.5)	4.0 (2.1, 6.8)
Adjudicated MACE[g]	0.7 (0.2, 1.7)	0	1.7 (0.2, 6.2)	0.4 (0.1, 1.2)	0.6 (0.1, 2.1)	0
Neutropenia	1.7 (0.8, 3.1)	1.5 (0.2, 5.3)	0	1.2 (0.6, 2.3)	1.8 (0.7, 3.9)	1.8 (0.7, 3.9)
Serious infections	1.0 (0.4, 2.2)	1.5 (0.2, 5.3)	1.7 (0.2, 6.2)	1.8 (0.9, 3.0)	2.1 (0.8, 4.3)	0.6 (0.1, 2.2)
Opportunistic infections	1.5 (0.7, 2.9)	0.7 (0.0, 4.1)	0	0.8 (0.3, 1.8)	0.6 (0.1, 2.1)	0
Hypersensitivity	10.4 (7.9, 13.4)	5.3 (2.1, 10.9)	9.0 (4.3, 16.5)	6.9 (5.1, 9.1)	5.8 (3.5, 9.0)	3.6 (1.9, 6.4)
Dermatitis and eczema	4.1 (2.6, 6.1)	1.5 (0.2, 5.3)	4.4 (1.4, 10.3)	3.6 (2.4, 5.3)	2.4 (1.0, 4.7)	1.2 (0.3, 3.1)
Injection site reactions	2.7 (1.6, 4.4)	10.2 (5.4, 17.4)	2.6 (0.5, 7.6)	1.8 (1.0, 3.1)	1.8 (0.7, 3.9)	0.3 (0.0, 1.7)
Adjudicated suicidal ideation and behaviour	0	0	0	0.1 (0.0, 0.8)	0	0
Malignancies excluding non-melanoma skin cancer	0.7 (0.2, 1.7)	0	0	0.4 (0.1, 1.2)	0.9 (0.2, 2.6)	0.6 (0.1, 2.2)
Non-melanoma skin cancer	0.5 (0.1, 1.5)	0	0	0	0	0.3 (0.0, 1.7)
Definite or probable adjudicated IBD	0.7 (0.2, 1.7)	0	1.7 (0.2, 6.2)	0.4 (0.1, 1.2)	0	0
Hepatic adverse events or hepatic enzyme elevations	0.5 (0.1, 1.5)	0	0	0.3 (0.0, 1.0)	0.3 (0.0, 1.6)	0
AST or ALT >3x ULN, n/N (%)	21/701 (3.0%)	9/139 (6.5%)	4/121 (3.3%)	15/764 (2.0%)	11/388 (2.8%)	8/354 (2.3%)

Safety set. No cases of active tuberculosis or uveitis were reported. [a] BKZ Total includes PBO/BKZ Week 16 switchers, includes events after switch only; BE OPTIMAL Weeks 52–104 also includes ADA/BKZ switchers, includes events after switch only; [b] One death due to a motorcycle accident; [c] One death due to acute myocardial infarction, reported as unrelated to the study drug; [d] Sudden death in 54-year old patient with a history of hypertension, aortic regurgitation and electrocardiogram changes of coronary artery disease; no further information available as no autopsy was performed; [e] Five most common TEAEs in any BKZ-treated group at the Week 104 data cut; [f] All infections were mild or moderate and none were serious, nine patients discontinued the study after an oral candidiasis event whilst receiving BKZ (one in BE OPTIMAL and two in BE COMPLETE during Week 0–52, four in BE OPTIMAL and two in BE COMPLETE during Week 52–104); [g] Events whilst receiving BKZ: one case each of myocardial infarction, cerebrovascular accident, ischaemic stroke and thrombotic cerebral infarction during Week 0–52 of BE OPTIMAL; two cases of acute myocardial infarction, and one case of ischaemic stroke (deemed by the investigator to be related to study medication), during Week 52–104 of BE OPTIMAL; one case of cerebral hemorrhage and one sudden death during Week 0–52 of BE COMPLETE; no MACE events during Week 52–104 of BE COMPLETE.

ACR50: ≥50% improvement from baseline in American College of Rheumatology response criteria; **ADA:** adalimumab; **ALT:** alanine aminotransferase; **AST:** aspartate aminotransferase; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **BL:** baseline; **BSA:** body surface area; **CfB:** change from baseline; **CI:** confidence interval; **DAPSA:** Disease Activity Index for Psoriatic Arthritis; **EAIR:** exposure-adjusted incident rate; **HAQ-DI:** Health Assessment Questionnaire-Disability Index; **IBD:** inflammatory bowel disease; **IL:** interleukin; **LDA:** low disease activity; **LEI:** Leeds Enthesitis Index; **MACE:** major adverse cardiovascular event; **MDA:** Minimal Disease Activity; **MI:** multiple imputation; **NRI:** non-responder imputation; **OC:** observed case; **OLE:** open-label extension; **PASI:** Psoriasis Area and Severity Index; **PBO:** placebo; **PGA-PsA:** Patient's Global Assessment of PsA; **PsA:** psoriatic arthritis; **PtAAP:** Patient's Assessment of Arthritis Pain; **PY:** patient-years; **Q2W:** every 2 weeks; **Q4W:** every 4 weeks; **REM:** remission; **SD:** standard deviation; **SE:** standard error; **SJC:** swollen joint count; **TEAE:** treatment-emergent adverse event; **TJC:** tender joint count; **TNFi-IR:** prior inadequate response or intolerance to tumour necrosis factor inhibitors; **ULN:** upper limit of normal; **VLDA:** Very Low Disease Activity; **WCI:** worst category imputation.

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