Bimekizumab efficacy and safety in patients with psoriatic arthritis who had skin and nail psoriasis at baseline: Up to 2-year results from two phase 3 studies

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Synopsis

- Bimekizumab (BKZ), a humanized monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated efficacy and tolerability to 1 year in patients with PsA and psoriasis (≥3% body surface area [BSA]),[1] and in patients with moderate-to-severe plaque psoriasis.[2]
- Among patients with psoriasis, nail involvement is associated with increased risk of PsA, more severe disease, and decreased quality of life.[3,4] Therefore, it is clinically important to evaluate the efficacy and tolerability of new treatments in patients with PsA who also have skin and nail psoriasis.

Objective

To assess the efficacy and safety of BKZ to 2 years in patients with psoriatic arthritis (PsA) who also had skin and nail psoriasis, and were biologic disease-modifying antirheumatic drug (bDMARD)-naïve or had prior inadequate response or intolerance to tumor necrosis factor inhibitors (TNFi-IR).

Methods

- BE OPTIMAL (NCT03895203; bDMARD-naïve) and BE COMPLETE (NCT03896581; TNFi-IR), both placebo (PBO)-controlled to Week 16, assessed subcutaneous BKZ 160 mg every 4 weeks (Q4W) in patients with PsA; PBO-randomized patients switched to BKZ at Week 16.
- BE OPTIMAL included a reference arm (adalimumab [ADA] 40 mg Q2W); these patients switched to BKZ at Week 52 with no washout between treatments.
- BE OPTIMAL Week 52 and BE COMPLETE Week 16 completers were eligible for the open-label extension BE VITAL (NCT04009499).
- Post hoc data are reported for patients with baseline skin psoriasis (≥3% BSA) and nail psoriasis (modified Nail Psoriasis Severity Index [mNAPSI] >0).
- Efficacy outcomes are reported to Week 104 (BE OPTIMAL) and Week 100 (BE COMPLETE).
- Missing data were imputed using non-responder (binary), multiple (continuous) or worst-category (categorical) imputation.
- Safety data are reported for all BKZ-treated patients with baseline skin and nail psoriasis.

Results

Patient characteristics

- Among patients with baseline skin and nail psoriasis, 230/263 (87.5%) bDMARD-naïve and 136/159 (85.5%) TNFi-IR patients completed Week 104/100.
- Baseline characteristics were generally similar across treatment arms and studies (**Supplementary Table 1**; accessible via QR code).

Efficacy

- Improvements seen with BKZ treatment at Week 52 were sustained to Week 104/100, with high proportions of bDMARD-naïve and TNFi-IR patients achieving ≥50% improvement from baseline in American College of Rheumatology response criteria (ACR50) and 100% improvement from baseline in Psoriasis Area and Severity Index (PASI100; **Figure 1**).
- The proportion of patients achieving Minimal Disease Activity (MDA), a composite outcome spanning joint, skin, and patient-reported outcomes, at Week 52 was sustained to Week 104/100 (**Figure 1**).*
- ACR50 and MDA responses were sustained in bDMARD-naïve patients who switched from ADA to BKZ at Week 52, with further improvement seen in PASI100 achievement following the switch.
- Similar trends were observed for additional joint, skin, nail, physical function, and composite outcomes (**Supplementary Table 2**; accessible via QR code).

Safety

- The **Table** reports safety data for BKZ-treated patients with baseline skin and nail psoriasis.
- Exposure-adjusted incidence rates per 100 patient-years (EAIR/100 PY) to Week 104 for ≥1 treatment-emergent adverse event (TEAE) were 154.9 for bDMARD-naïve and 78.8 for TNFi-IR patients; incidence rates (EAIR/100 PY) of serious TEAEs were 6.6 and 5.2, respectively.
- To Week 104, 2 deaths occurred in bDMARD-naïve patients and 1 death occurred in a TNFi-IR patient; all were deemed unrelated to treatment.

Conclusions

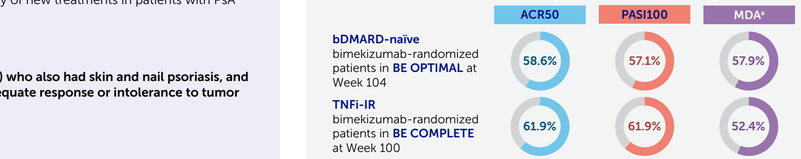
Bimekizumab treatment resulted in sustained clinical efficacy up to 2 years in patients with PsA who also had skin and nail psoriasis, regardless of prior exposure to bDMARDs.

Bimekizumab was well tolerated; no new safety signals were observed.[1,2]

Summary

Efficacy and **safety** of **bimekizumab** treatment were assessed **up to 2 years** in patients with **PsA** who also had **skin and nail psoriasis**, and were bDMARD-naïve (BE OPTIMAL) or TNFi-IR (BE COMPLETE).

The high levels of treatment responses across **joint, skin, and composite outcomes** observed at 1 year were **sustained up to 2 years** with **bimekizumab** treatment (NRI):



In bDMARD-naïve patients **switching from adalimumab to bimekizumab** at Week 52, **ACR50** and **MDA responses were sustained** and **PASI100 responses further improved** to Week 104.

Bimekizumab was well tolerated to 2 years with **no new safety signals observed**.

Bimekizumab treatment demonstrated **sustained clinical efficacy** up to **2 years** in patients with **PsA** who also had **skin and nail psoriasis**.

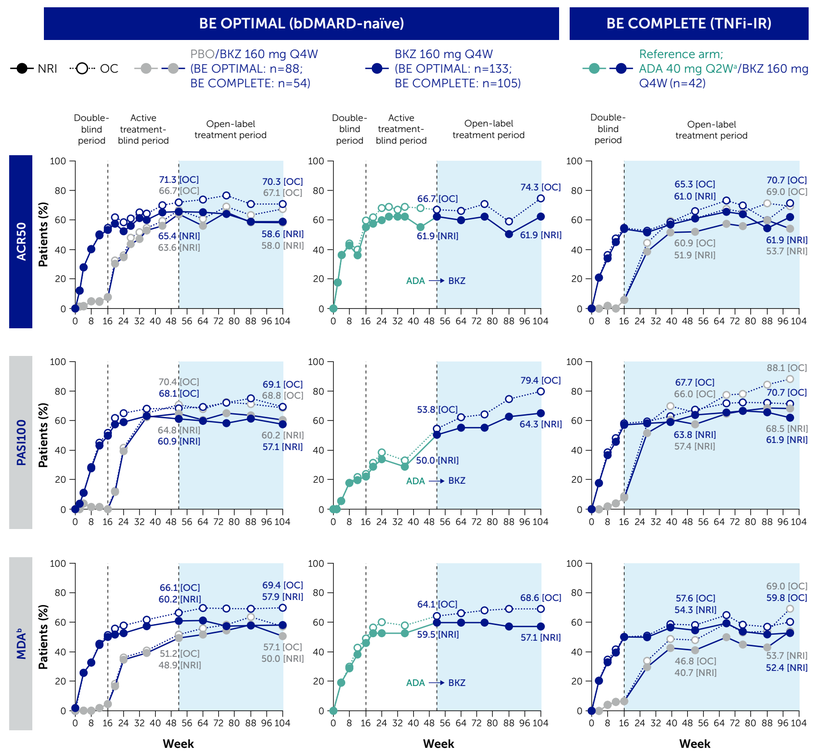
[a] MDA response defined as achievement of ≥5 of the following 7 criteria: TJC ≤1, SJC ≤1, PASI ≤1 or BSA ≤3%, PtAAP ≤15 mm, PGA-PsA ≤20 mm, HAQ-DI ≤0.5, and tender entheseal points ≤1.

Table 1 Safety to Week 104

EAIR/100 PY (95% CI)	BE OPTIMAL (bDMARD-naïve) Week 0–104 BKZ 160 mg Q4W Total[a] (n=260) 431.9 PY	BE COMPLETE (TNFi-IR) Week 0–104 BKZ 160 mg Q4W Total[a] (n=155) 281.0 PY
Any TEAEs	154.9 (135.2, 176.7)	78.8 (64.8, 94.9)
Serious TEAEs	6.6 (4.3, 9.5)	5.2 (2.9, 8.8)
Severe TEAEs	5.0 (3.1, 7.7)	4.0 (2.0, 7.2)
Study discontinuation due to TEAEs	4.2 (2.5, 6.7)	3.2 (1.5, 6.1)
Drug-related TEAEs	28.2 (22.7, 34.7)	17.4 (12.4, 23.7)
Deaths, n (%)	2 (0.8)[b]	1 (0.6)[c]
Most common TEAEs[d]		
Nasopharyngitis	10.1 (7.2, 13.8)	2.6 (1.0, 5.3)
SARS-CoV-2 (COVID-19) infection	8.3 (5.8, 11.6)	7.7 (4.7, 11.8)
Upper respiratory tract infection	5.4 (3.4, 8.1)	3.3 (1.5, 6.3)
Oral candidiasis	4.6 (2.8, 7.2)	2.2 (0.8, 4.7)
Urinary tract infection	4.3 (2.6, 6.9)	3.7 (1.8, 6.9)
Safety topics of interest[e]		
Adjudicated MACE	0.5 (0.1, 1.7)[f]	0.7 (0.1, 2.6)[g]
Neutropenia	1.7 (0.7, 3.4)[h]	2.6 (1.0, 5.3)[i]
Serious infections	0.7 (0.1, 2.0)[j]	1.5 (0.4, 3.7)[k]
Opportunistic infections	1.4 (0.5, 3.1)[l]	0.4 (0.0, 2.0)[m]
Serious hypersensitivity	0.2 (0.0, 1.3)[n]	0.4 (0.0, 2.0)[n]
Injection site reactions	1.7 (0.7, 3.4)	1.1 (0.2, 3.2)
Adjudicated SIB	0.5 (0.1, 1.7)	0.0
Hepatic adverse events or hepatic enzyme elevations	0.7 (0.1, 2.0)	0.4 (0.0, 2.0)
Malignancies, excluding non-melanoma skin cancer	0.5 (0.1, 1.7)[o]	0.7 (0.1, 2.6)[p]
Adjudicated IBD[q]	0.5 (0.1, 1.7)	0.0

Safety set, in patients with baseline skin psoriasis ≥3% BSA and mNAPSI >0. **[a]** BKZ Total includes PBO/BKZ Week 16 switchers (for both BE OPTIMAL and BE COMPLETE), includes events during BKZ treatment only; BE OPTIMAL also includes patients who switched from ADA to BKZ at Week 52, includes events during BKZ treatment only; **[b]** 1 death due to a motorcycle accident occurred before Week 52, reported as unrelated to the study treatment; 1 death due to cardiac arrest occurred after Week 52, reported as unrelated to the study treatment; **[c]** Sudden death in 54-year old patient with a history of hypertension, aortic regurgitation, and electrocardiogram changes of coronary artery disease occurred before Week 52, reported as unrelated to the study treatment; no further information available as no autopsy was performed; **[d]** Top 5 most common TEAEs in any BKZ-treated group at the Week 104 data cut; **[e]** No cases of active tuberculosis or uveitis were reported; **[f]** 1 thrombotic cerebral infarction, 1 acute myocardial infarction; **[g]** 1 cerebral hemorrhage, 1 sudden death; **[h]** 6 neutropenia, 1 decreased neutrophil count; **[i]** 4 neutropenia, 3 decreased neutrophil count; **[j]** 1 pneumonia, 1 extradural abscess, 1 SARS-CoV-2 (COVID-19) infection; **[k]** 1 bursitis infective, 1 pneumonia, 1 post-operative wound infection, 1 pyelonephritis acute; **[l]** 3 *Candida* infections, 3 fungal infections not elsewhere classified; **[m]** 1 *Candida* infection; **[n]** No anaphylactic reactions associated with BKZ were reported; **[o]** 1 breast cancer, 1 ovarian cancer; **[p]** 1 gastric cancer, 1 gastric cancer recurrent; **[q]** Cases deemed definite or probable IBD by the investigator.

Figure 1 Proportion of patients with baseline skin and nail psoriasis achieving ACR50, PASI100, and MDA over time to Week 104/100 (NRI, OC)



Randomized set, in patients with baseline skin psoriasis ≥3% BSA and mNAPSI >0. In BE OPTIMAL patients were randomized 3:2:1 to BKZ 160 mg Q4W:PBO:reference arm (ADA 40 mg Q2W), in BE COMPLETE patients were randomized 2:1 to BKZ 160 mg Q4W:PBO. In both studies, patients on PBO switched to BKZ 160 mg Q4W at Week 16. In BE OPTIMAL, patients on ADA switched to BKZ 160 mg Q4W at Week 52. **[a]** Reference arm; study not powered for statistical comparisons of ADA to BKZ or PBO; **[b]** 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.

*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. **ACR50:** 50% improvement from baseline in American College of Rheumatology response criteria; **ADA:** adalimumab; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **BSA:** body surface area; **EAIR:** exposure-adjusted incidence rate; **HAQ-DI:** Health Assessment Questionnaire-Disability Index; **IBD:** inflammatory bowel disease; **IL:** interleukin; **MACE:** major adverse cardiovascular event; **MDA:** Minimal Disease Activity; **mNAPSI:** modified Nail Psoriasis Severity Index; **NRI:** non-responder imputation; **OC:** observed case; **PASI:** Psoriasis Area and Severity Index; **PASI100:** 100% improvement from baseline in Psoriasis Area and Severity Index; **PBO:** placebo; **PGA-PsA:** Patient's Global Assessment of Psoriatic Arthritis; **PsA:** psoriatic arthritis; **PtAAP:** Patient's Assessment of Arthritis Pain; **PY:** patient-years; **Q2W:** every two weeks; **Q4W:** every four weeks; **SIB:** suicidal ideation and behavior; **SJC:** swollen joint count; **TEAE:** treatment-emergent adverse event; **TJC:** tender joint count; **TNFi-IR:** prior inadequate response or intolerance to tumor necrosis factor inhibitors.

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References: [1]Thaçi et al. EADV 2023; Abstract 2959. [2]Gordon et al. Lancet 2021;397:475–86. [3]Zabotti et al. Ann Rheum Dis 2023;82:1162–70. [4]Cengiz et al. Int J Rheum Dis 2023;26:43–50. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **DT**, **AA**, **W-HB**, **ABG**, **ML**, **RBW**, **BI**, **RB**, **JC**, **JFM**; Drafting of the publication, or reviewing it critically for important intellectual content: **DT**, **AA**, **W-HB**, **ABG**, **ML**, **RBW**, **BI**, **RB**, **JC**, **JFM**; Final approval of the publication: **DT**, **AA**, **W-HB**, **ABG**, **ML**, **RBW**, **BI**, **RB**, **JC**, **JFM**. **Author Disclosures: DT:** Investigator and/or consultant/advisor for AbbVie, Almirall, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly and Company, Galderma, Janssen-Cilag, Kyowa Kirin, LEO Pharma, L'Oreal, New Bridge, Novartis, Pfizer, Regeneron, Samsung, Sanofi, Target-RWE, UCB, and Vichy; received grants from AbbVie, LEO Pharma, and Novartis. **AA:** Honoraria and/or research grants from AbbVie, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Eisai, Eli Lilly and Company, Janssen, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Sun Pharma, Taiho Pharma, Torii Pharmaceutical Co., and UCB. **W-HB:** Received honoraria as a speaker and/or advisor from AbbVie, Almirall, Bristol Myers Squibb, Eli Lilly and Company, Janssen, LEO Pharma, Novartis, and UCB; **ABG:** Research/educational grants from Bristol Myers Squibb, Highlights Therapeutics, Janssen, and UCB (all paid to Mount Sinai School of Medicine); honoraria as an advisory board member and consultant for Amgen, AnaptysBio, Avotres Therapeutics, Bristol Myers Squibb, Boehringer Ingelheim, DiCE Therapeutics, Eli Lilly and Company, Highlights Therapeutics, Janssen, Novartis, Sanofi, Teva, UCB, and Xbiotech (stock options for RA). **ML:** Employee of Mount Sinai; research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Dermavant Sciences, Eli Lilly and Company, Incyte, Inozyme, Janssen Research & Development, LLC, Ortho Dermatologics, Pfizer, Sanofi-Regeneron, and UCB; consultant for Almirall, AltruBio Inc., AnaptysBio, Apogee, Arcutis Inc., AstraZeneca, Atomwise, Avotres, Bristol Myers Squibb, Boehringer-Ingelheim, Brickell Biotech, Castle Biosciences, Celltrion, CorEvitas, Dermavant Sciences, EPI, Evommune Inc., Facilitation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Galderma, Genentech, Incyte, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Sanofi-Regeneron, Seanergy, Strata, Takeda, Trevi, and Verrica. **RBW:** Consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, DiCE Therapeutics, Eli Lilly and Company, GSK, Janssen, LEO Pharma, Meiji Pharma, Novartis, Pfizer, RAPT Therapeutics, Sanofi, Sun Pharma, UCB, and Union; research grants to his institution from AbbVie, Almirall, Amgen, Celgene, Eli Lilly and Company, Janssen, LEO Pharma, Novartis, Pfizer, and UCB; honoraria from AbbVie, Almirall, Bristol Myers Squibb, Eli Lilly and Company, Galderma, Janssen, and Novartis. **BI:** Employee of UCB; shareholder of AbbVie, GSK, and UCB. **RB, JC:** Employees and shareholders of UCB. **JFM:** Consultant and/or investigator for AbbVie, Amgen, AstraZeneca, Biogen, Bristol Myers Squibb, Boehringer Ingelheim, Dermavant, Eli Lilly and Company, Incyte, Janssen, LEO Pharma, MoonLake Immunotherapeutics, Novartis, Pfizer, Sanofi-Regeneron, Sun Pharma, and UCB.

Acknowledgments: This study was funded by UCB. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Heather Edens, PhD, UCB, Smyrna, GA, USA for publication coordination, Alice Di Vincenzo, MSc, Costello Medical, Manchester, UK for medical writing and editorial assistance, and the Costello Medical Creative team for graphic design assistance. All costs associated with development of this poster were funded by UCB.

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