Efficacy and safety of bimekizumab in bDMARD-naïve patients with psoriatic arthritis: 24-week results from BE OPTIMAL, a phase 3, multicentre, randomised, placebo-controlled, active reference study

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Objective

To assess the efficacy and safety of bimekizumab (BKZ) vs placebo (PBO) in biologic DMARD-naïve patients with active psoriatic arthritis (PsA) up to Week 24 in the phase 3 study BE OPTIMAL.

Introduction

- BKZ is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A.
- BKZ has shown rapid and sustained efficacy and was well tolerated up to 152 weeks in the phase 2b BE ACTIVE study in patients with active PsA.[1,2]

Methods

- BE OPTIMAL (NCT03895203) comprised a 16-week double-blind, PBO-controlled period, followed by a 36-week treatment-blind period.
- Patients were randomised 3:2:1, subcutaneous BKZ 160 mg every four weeks (Q4W):PBO:reference arm (subcutaneous adalimumab [ADA] 40 mg Q2W). At Week 16, PBO patients switched to BKZ 160 mg Q4W (**Figure 1**).
- The ADA arm served as an active reference; the study was not powered for statistical comparisons of ADA to BKZ or PBO.
- Efficacy and safety are reported for the PBO-controlled period up to Week 16; additional efficacy is given to Week 24 following the switch from PBO to BKZ.
- Missing data were imputed as non-responder imputation for binary endpoints; multiple imputation for continuous endpoints.

Results

- Of 852 randomised patients, 821 (96.4%) completed Week 16 and 806 (94.6%) completed Week 24.
- Baseline characteristics were generally comparable across treatment arms (**Table 1**).
- At Week 16, BKZ demonstrated superiority vs PBO for the primary endpoint, ACR50 (p<0.001; **Figure 2A**).
- 47.5% patients with psoriasis affecting ≥3% body surface area at baseline achieved complete skin clearance (PASI100) at Week 16 in the BKZ arm (**Figure 2A**).
- Joint and skin outcomes continued to improve to Week 24 (**Figure 2B**).
- In the overall radiographic set, there was greater inhibition of structural damage progression at Week 16 in the BKZ arm compared with the PBO arm: vdHmTSS mean (SE) change from baseline: 0.01 (0.04) BKZ, 0.31 (0.09) PBO; p<0.001; −0.03 (0.07) ADA.
- Up to Week 16, patients who had ≥1 TEAE: BKZ 59.9%; PBO 49.5%; ADA 59.3% (safety set; **Table 2**).
- There were 13 patients with *Candida* infection up to Week 16 (11 [2.6%] BKZ, 2 [0.7%] PBO). All *Candida* infections were mild to moderate and none were systemic; one moderate infection led to discontinuation on the BKZ arm.
- Up to Week 24, there was one case of adjudicated major adverse cardiac event and one adjudicated inflammatory bowel disease in BKZ-treated patients; no deaths were reported.

Summary

- In biologic DMARD-naïve patients with PsA, BKZ treatment resulted in clinically relevant improvements in efficacy outcomes vs PBO at Week 16; efficacy continued to improve up to Week 24.
- BKZ was well tolerated and no new safety signals were observed.[1,2]

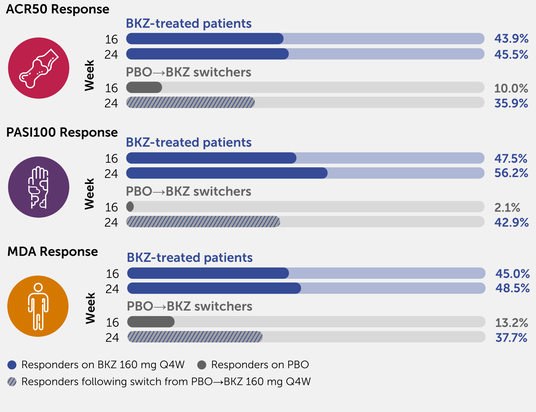


Table 1 Baseline characteristics

	Placebo n=281	BKZ 160 mg Q4W n=431	Reference Arm (ADA 40 mg Q2W) n=140
Age (years), mean (SD)	48.7 (11.7)	48.5 (12.6)	49.0 (12.8)
Male, n (%)	127 (45.2)	201 (46.6)	71 (50.7)
BMI (kg/m^2), mean (SD)	29.6 (6.1)	29.2 (6.8)	28.4 (5.9)
Time since PsA diagnosis (years),[a] mean (SD)	5.6 (6.5)	6.0 (7.3)	6.1 (6.8)
Concomitant methotrexate, n (%)	162 (57.7)	252 (58.5)	82 (58.6)
TJC (of 68 joints), mean (SD)	17.1 (12.5)	16.8 (11.8)	17.5 (13.1)
SJC (of 66 joints), mean (SD)	9.5 (7.3)	9.0 (6.2)	9.6 (7.1)
Psoriasis BSA ≥3%, n (%)	140 (49.8)	217 (50.3)	68 (48.6)
PASI score,[b] mean (SD)	7.9 (5.6)	8.2 (6.8)	8.5 (7.6)
HAQ-DI score,[c] mean (SD)	0.9 (0.6)	0.8 (0.6)	0.9 (0.5)
SF-36 PCS score,[c] mean (SD)	36.9 (9.7)	38.1 (9.4)	37.6 (8.8)
vdHmTSS (at risk subgroup),[d,e] mean (SD)	15.8 (26.6)	15.5 (31.8)	17.2 (29.5)
vdHmTSS (overall),[d,f] mean (SD)	13.4 (25.1)	13.4 (29.9)	14.5 (27.5)

Randomised set. [a]PBO: n=279; BKZ 160 mg Q4W: n=423; reference arm (ADA 40 mg Q2W): n=139; [b]In patients with psoriasis affecting ≥3% BSA at baseline; PBO: n=140; BKZ 160 mg Q4W: n=217; reference arm (ADA 40 mg Q2W): n=68; [c]Data missing for one BKZ patient; [d]Radiographic set; [e]At risk subgroup defined as patients with elevated hs-CRP (≥6 mg/L) and/or ≥1 bone erosion at baseline; PBO: n=227; BKZ: 160 mg Q4W n=361; reference arm (ADA 40 mg Q2W): n=112; [f]Overall radiographic set; PBO: n=269; BKZ 160 mg Q4W: n=420; reference arm (ADA 40 mg Q2W): n=135.

Figure 1 BE OPTIMAL study design

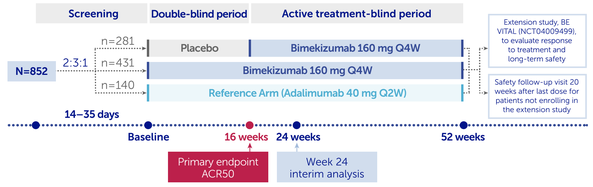
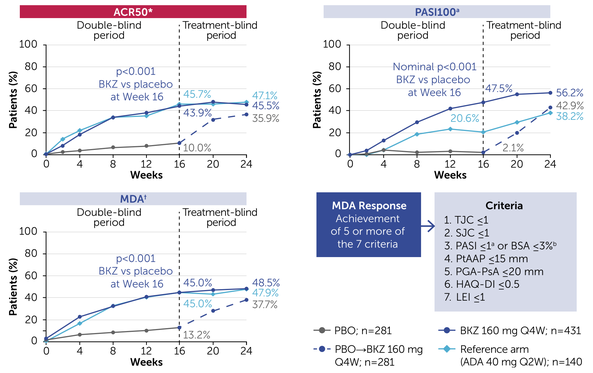


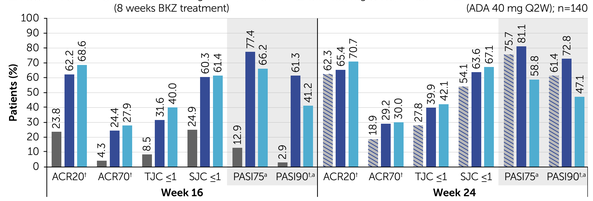
Figure 2 Efficacy at Weeks 16 and 24

A) Joint and skin outcomes to Week 24



Randomised set. Interim analysis. Data reported as NRI. Nominal p values are not powered or adjusted for multiplicity. *Primary endpoint. †Ranked secondary endpoint. [a]In patients with psoriasis affecting ≥3% body surface area at baseline; PBO: n=140; PBO→BKZ 160 mg Q4W: n=140; BKZ 160 mg Q4W: n=217; reference arm (ADA 40 mg Q2W): n=68; [b]Patients with psoriasis involving <3% of BSA at baseline will always meet the criteria PASI ≤1 or BSA ≤3% except in the cases where a BSA score ≥3% is observed.

B) Additional joint and skin outcomes at Week 16 and Week 24



Randomised set. Interim analysis. Data reported as NRI. *PBO→BKZ 160 mg Q4W patients received PBO through Week 16, then switched to BKZ 160 mg Q4W through Week 24 (8 weeks of treatment). †Secondary endpoint. PASI90 BKZ 160 mg Q4W vs PBO p<0.001 at Week 16; all other endpoints BKZ 160 mg Q4W vs PBO nominal p<0.001 at Week 16 (not powered or adjusted for multiplicity). [a]In patients with psoriasis affecting ≥3% body surface area at baseline; PBO: n=140; PBO→BKZ 160 mg Q4W: n=140; BKZ 160 mg Q4W: n=217; reference arm (ADA 40 mg Q2W): n=68.

Table 2 Safety overview to Week 16 and Week 24

n (%)	Week 0–16 Placebo n=281	Week 0–16 BKZ 160mg Q4W n=431	Week 0–16 Reference Arm (ADA 40 mg Q2W) n=140	Week 0–24 BKZ 160 mg Q4W Total n=702[a]	Week 0–24 Reference Arm (ADA 40 mg Q2W) n=140
Any TEAE	139 (49.5)	258 (59.9)	83 (59.3)	395 (56.3)	96 (68.6)
Serious TEAEs	3 (1.1)	7 (1.6)	2 (1.4)	20 (2.8)	5 (3.6)
Study discontinuation due to TEAEs	3 (1.1)	8 (1.9)	3 (2.1)	12 (1.7)	7 (5.0)
Drug-related TEAEs	35 (12.5)	101 (23.4)	34 (24.3)	149 (21.2)	43 (30.7)
Severe TEAEs	0	4 (0.9)	3 (2.1)	10 (1.4)	3 (2.1)
Most frequently reported TEAEs (≥3% in any treatment arm)					
Nasopharyngitis	13 (4.6)	40 (9.3)	7 (5.0)	58 (8.3)	12 (8.6)
Upper respiratory tract infection	18 (6.4)	21 (4.9)	3 (2.1)	31 (4.4)	5 (3.6)
Headache	7 (2.5)	20 (4.6)	2 (1.4)	26 (3.7)	3 (2.1)
Diarrhoea	7 (2.5)	16 (3.7)	5 (3.6)	21 (3.0)	5 (3.6)
Hypertension	11 (3.9)	12 (2.8)	4 (2.9)	19 (2.7)	4 (2.9)
ALT elevation[b]	2 (0.7)	3 (0.7)	7 (5.0)	5 (0.7)	8 (5.7)
Oral herpes	3 (1.1)	5 (1.2)	3 (2.1)	7 (1.0)	6 (4.3)
Injection site erythema	0	1 (0.2)	4 (2.9)	2 (0.3)	5 (3.6)
Serious infections	0	1 (0.2)	1 (0.7)	3 (0.4)	2 (1.4)
Fungal infections[c]	4 (1.4)	20 (4.6)	1 (0.7)	40 (5.7)	1 (0.7)
Candida infections[d]	2 (0.7)	11 (2.6)	0	22 (3.1)	0
Adjudicated MACE	0	0	0	1 (0.1)	0
Adjudicated IBD	0	0	0	1 (0.1)[e]	0

Safety set, MedDRA (Version 19.0). Interim analysis. [a]Includes patients who switched from placebo to BKZ (events after switch only); [b]ALT elevation refers to a reported TEAE and was not based on laboratory criteria; [c]No fungal infections were systemic; [d]All *Candida* infections were mild to moderate and none were serious; one BKZ-treated patient discontinued due to a moderate *Candida* infection; [e]One case of probable IBD in a patient with no prior history of IBD.

Conclusions

In biologic DMARD-naïve patients with PsA, BKZ treatment resulted in rapid and clinically relevant improvements in efficacy outcomes vs PBO at Week 16. Responses continued to increase up to Week 24. BKZ was well tolerated and no new safety signals were observed.[1,2]

Results were similar to patients with PsA and inadequate response to TNFi in the BE COMPLETE study through Week 16.[3]

ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology response criteria; **ADA:** adalimumab; **ALT:** alanine transaminase; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **BMI:** body mass index; **BSA:** body surface area; **DMARD:** disease-modifying antirheumatic drug; **HAQ-DI:** Health Assessment Questionnaire Disability Index; **IBD:** inflammatory bowel disease; **LEI:** Leeds Enthesitis Index; **MACE:** major adverse cardiac event; **MDA:** minimal disease activity; **MedDRA:** Medical Dictionary for Regulatory Activities; **NRI:** non-responder imputation; **PASI75/90/100:** ≥75/90/100% improvement in Psoriasis Area and Severity Index; **PBO:** placebo; **PGA-PsA:** Patient's Global Assessment of Psoriatic Arthritis; **PsA:** psoriatic arthritis; **PSO:** psoriasis; **PtAAP:** patient's assessment of arthritis pain; **Q2W:** every 2 weeks; **Q4W:** every 4 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:** tumour necrosis factor inhibitor; **vdHmTSS:** van der Heijde modified Total Sharp Score.

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References: [1]Ritchlin et al. Lancet 2020;395(10222):427–40; [2]Coates et al. Ann Rheum Dis 2021;80:779–80(POS1022); [3]Merola et al. Ann Rheum Dis 2022;81:167–9. **Author Contributions:** Substantial contributions to study conception/design or acquisition/analysis/interpretation of data: **JFM, AA, FB, ABG, ML, DM, PJM, LP, WB, BI, DA, RB, JC, PG;** drafting of the publication or revising it critically for important intellectual content: **JFM, AA, FB, ABG, ML, DM, PJM, LP, WB, BI, DA, RB, JC, PG;** final approval of the publication: **JFM, AA, FB, ABG, ML, DM, PJM, LP, WB, BI, DA, RB, JC, PG.** **Author Disclosures: JFM:** Consultant/investigator for Abbvie, Amgen, Bayer, Biogen, BMS, Dermavant, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi-Regeneron, Sun Pharma, and UCB Pharma. **AA:** Research grants/honoraria from AbbVie, Amgen, BMS, Boehringer Ingelheim, Eisai, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi Tanabe Pharma, Pfizer, Sun Pharma, Taiho Pharma, Torii Pharmaceutical, and UCB Pharma. **FB:** Consultant and/or speaker and/or investigator for AbbVie, Affibody, Amgen, Boehringer Ingelheim, Celgene, Chugai, Eli Lilly, Genzyme, GSK, Janssen, MSD, MoonLake, Novartis, Pfizer, Roche, Sandoz, and Sanofi. **ABG:** Honoraria as an advisory board member, non-promotional speaker or consultant for: Amgen, AnaptysBio, Avotres Therapeutics, Boehringer Ingelheim, BMS, Dermavant, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi, Sun Pharma, UCB Pharma, and Xbiotech (stock options for an RA project); research/educational grants from: AnaptysBio, BMS, Janssen, Novartis, Ortho Dermatologics, Sun Pharma, and UCB Pharma; all funds go to the Icahn School of Medicine at Mount Sinai. **ML:** Employee of Mount Sinai and receives research funds from: AbbVie, Amgen, Arcutis, Avotres Therapeutics, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen Research & Development, LLC, Ortho Dermatologics, Regeneron, and UCB Pharma; consultant for Aditum Bio, Almirall, AltruBio Inc., AnaptysBio, Arcutis, Inc., Aristea Therapeutics, Arrive Technologies, Avotres Therapeutics, BiomX, Boehringer Ingelheim, BMS, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant, Dr. Reddy's Laboratories, Evelo Biosciences, Evommune, Inc., Facilitatation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Helsinn Therapeutics, Hexima Ltd., LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Seanergy, and Verrica. **DM:** Research grants from AbbVie, Celgene, Janssen, Merck, Pfizer and Novartis; consulting/speaker's fees/honoraria from AbbVie, Celgene, Janssen, Merck, Novartis, Pfizer, and UCB Pharma. **PM:** Research grants from AbbVie, Amgen, BMS, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma; consultancy fees from AbbVie, Acelyrin, Aclaris, Amgen, BMS, Boehringer Ingelheim, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Moonlake Pharma, Novartis, Pfizer, Sun Pharma and UCB Pharma; speakers' bureau from AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer and UCB Pharma. **LP:** Consultancy/speaker's fees from AbbVie, Almirall, Amgen, Baxalta, Biogen, Boehringer Ingelheim, Celgene, Eli Lilly, Gebro, Janssen, JS BIOCAD, LEO Pharma, Merck-Serono, MSD, Mylan, Novartis, Pfizer, Regeneron, Roche, Samsung-Bioepis, Sandoz, Sanofi Genzyme, and UCB Pharma. **WHB:** Speaker/advisor honoraria from Abbvie, Almirall, BMS, Eli Lilly, Janssen, LEO Pharma, Novartis, and UCB Pharma. **BI:** Employee of UCB Pharma; and stockholder of GSK and UCB Pharma. **DA, RB, JC:** Employee and stockholder of UCB Pharma. **PG:** Consultant for AbbVie, Abiogen, Almirall, Celgene, Eli Lilly, Janssen, LEO Pharma, Merck, MSD, Novartis, Otsuka, Pfizer, Pierre Fabre, Sanofi, and UCB Pharma. **Acknowledgements:** This study was funded by UCB Pharma. 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 Pharma, Smyrna, Georgia, USA for publication coordination, Sona Popat, BA, Costello Medical, London, UK for medical writing and editorial assistance and the Design team at Costello Medical for graphic design assistance. All costs associated with development of this poster were funded by UCB Pharma.

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