Efficacy and safety of bimekizumab in patients with active psoriatic arthritis and inadequate response to tumour necrosis factor inhibitors: 16-week results from BE COMPLETE, a phase 3, randomised, double-blind placebo-controlled study

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Objective

To assess the efficacy and safety of bimekizumab (BKZ) vs placebo (PBO) in patients with active psoriatic arthritis (PsA) and prior inadequate response or intolerance to tumour necrosis factor inhibitor (TNFi) in the 16-week phase 3 study BE COMPLETE.

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 a phase 2b study in patients with active PsA.[1,2]

Methods

- BE COMPLETE (NCT03896581) comprised a 16-week double-blind, PBO-controlled period.
- Patients with adult-onset PsA with ≥3 tender and ≥3 swollen joint counts, ≥1 active psoriatic lesions and/or a documented history of psoriasis, and inadequate response or intolerance to TNFi were randomised 2:1 to subcutaneous BKZ every 4 weeks or PBO (**Figure 1**).
- The primary endpoint was a ≥50% improvement in the American College of Rheumatology response criteria (ACR50) at Week 16.
- We report joint and skin efficacy outcomes and safety outcomes through 16 weeks.
- Missing data for binary endpoints were imputed with non-responder imputation (NRI).

Results

- Of 400 randomised patients (267 BKZ; 133 PBO), 388 (97.0%) completed Week 16 (263 [98.5%] BKZ; 125 [94.0%] PBO).
- Baseline demographics were generally comparable between treatment arms (**Table 1**).
- At Week 16, BKZ demonstrated superiority vs PBO for the primary endpoint, ACR50 (p<0.001; **Figure 2A**).
- 58.5% BKZ-treated patients with psoriasis affecting ≥3% body surface area at baseline achieved complete skin clearance, defined as PASI100, at Week 16, versus 4.5% PBO-treated patients (**Figure 2A**).
- The improvements with BKZ treatment in joints and skin were shown in a range of additional outcomes (**Figure 2B**).
- Up to Week 16, 108/267 (40.4%) patients on BKZ had ≥1 treatment-emergent adverse event (TEAE) vs 44/132 (33.3%) patients on PBO (safety set; **Table 2**).
- There were seven (2.6%) patients with *Candida* infection in BKZ-treated patients. All *Candida* infections were mild to moderate and none were systemic; one moderate infection led to discontinuation.
- No cases of inflammatory bowel disease, major adverse cardiac events, serious hypersensitivity reactions, anaphylactic reactions, or deaths were reported.

Summary

- Bimekizumab treatment in patients with PsA and inadequate response to TNFi resulted in clinically relevant improvements across the manifestations of PsA at Week 16, including joints and skin.
- BKZ was well tolerated and no new safety signals were observed.[1,2]

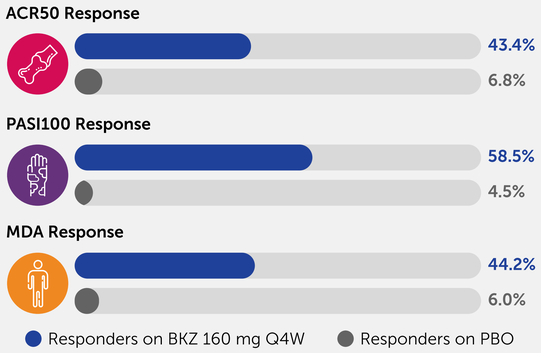


Table 1 Baseline characteristics

	Placebo 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/m^2), mean (SD)	29.0 (5.4)	30.1 (6.5)
Time since PsA diagnosis (years), mean (SD)	9.2 (8.1)	9.6 (9.9)
Concomitant methotrexate, n (%)	51 (38.3)	119 (44.6)
Prior TNFi exposure, n (%)		
Inadequate response to 1 TNFi	103 (77.4)	203 (76.0)
Inadequate response to 2 TNFi	15 (11.3)	30 (11.2)
Intolerance to TNFi	15 (11.3)	34 (12.7)
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)
Psoriasis BSA ≥3%, n (%)	88 (66.2)	176 (65.9)
PASI score,[a] mean (SD)	8.5 (6.6)	10.1 (9.1)
HAQ-DI score, mean (SD)	1.0 (0.7)	1.0 (0.6)
SF-36 PCS score, mean (SD)	35.9 (10.2)	36.4 (9.0)
PtAAP score, mean (SD)	61.7 (24.6)	58.3 (24.2)

Randomised set. [a]In patients with psoriasis affecting ≥3% BSA at baseline; PBO: n=88; BKZ 160 mg Q4W: n=176.

Figure 1 BE COMPLETE study design

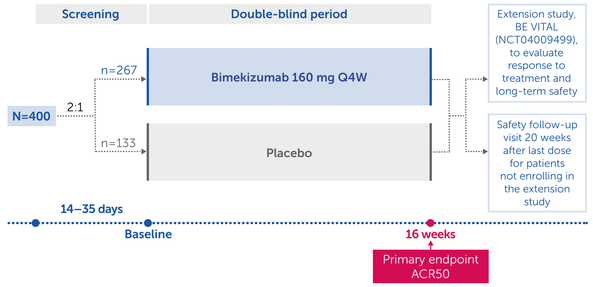


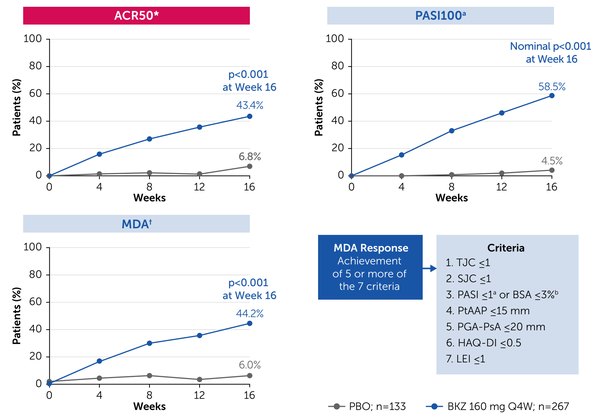
Table 2 Safety overview at Week 16

n (%)	Placebo n=132[a]	BKZ 160 mg Q4W n=267
Any TEAE	44 (33.3)	108 (40.4)
Serious TEAEs	0	5 (1.9)
Discontinuation due to TEAEs	0	2 (0.7)
Drug-related TEAEs	4 (3.0)	35 (13.1)
Severe TEAEs	0	5 (1.9)
Deaths	0	0
Most frequently reported TEAEs on the BKZ arm		
Nasopharyngitis	1 (0.8)	10 (3.7)
Oral candidiasis[b]	0	7 (2.6)
Upper respiratory tract infection	2 (1.5)	6 (2.2)
Serious infections	0	2 (0.7)
Fungal infections[c]	0	12 (4.5)
Systemic fungal infections	0	0
Neutropenia[d]	0	4 (1.5)
Serious hypersensitivity	0	0
Anaphylactic reactions	0	0
Injection site reactions	0	3 (1.1)
Liver function test changes/enzyme elevations		
ALT >3x ULN	0	2 (0.7)
AST or ALT >3x ULN	0	4 (1.5)

Safety set, MedDRA (Version 19.0). [a]One patient included in the randomised set was not counted in the safety set. [b]Six cases were classified by investigator as mild in intensity; one case classified as moderate in intensity; one moderate case resulted in discontinuation. [c]All fungal infections were mild to moderate; none were systemic/disseminated. [d]Neutropenia were generally transient and not associated with serious infections; three patients had neutropenia and one had decreased neutrophil count.

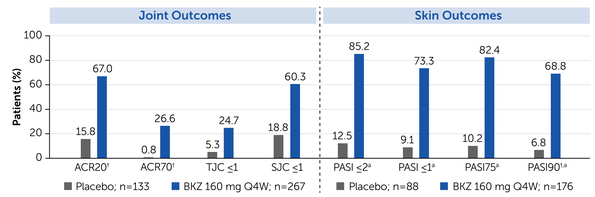
Figure 2 Efficacy to Week 16

A) Joint and skin endpoints to Week 16



Randomised set. Data reported as NRI. *Primary endpoint. †Secondary endpoint. Nominal p values are not powered or adjusted for multiplicity. [a]In patients with psoriasis affecting ≥3% BSA at baseline; PBO: n=88; BKZ 160 mg Q4W: n=176. [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 endpoints at Week 16



Randomised set. Data reported as NRI. †Secondary endpoint. PASI90 BKZ 160 mg Q4W vs PBO p<0.001; all other endpoints nominal p<0.001 (not powered or adjusted for multiplicity). [a]In patients with psoriasis affecting ≥3% BSA at baseline.

Conclusions

BKZ treatment in patients with PsA and inadequate response to TNFi resulted in rapid and clinically relevant improvements in efficacy outcomes vs PBO at Week 16. BKZ was well tolerated and no new safety signals were observed.[1,2]

Results were similar to biologic DMARD-naïve patients with PsA in the BE OPTIMAL study through Week 16.[3]

ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology response criteria; **ALT:** alanine transaminase; **AST:** aspartate transaminase; **BKZ:** bimekizumab; **BMI:** body mass index; **BL:** baseline; **BSA:** body surface area; **CASPAR:** Classification Criteria for PsA; **HAQ-DI:** Health Assessment Questionnaire Disability Index; **DMARD:** disease-modifying antirheumatic drug; **IBD:** inflammatory bowel disease; **LEI:** Leeds Enthesitis Index; **MDA:** minimal disease activity; **MedDRA:** Medical Dictionary for Regulatory Activities; **NRI:** non-responder imputation; **PASI 75/90/100:** ≥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; **Q4W:** every 4 weeks; **SD:** standard deviation; **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; **ULN:** upper limit of normal.

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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]McInnes et al. Ann Rheum Dis 2022;81:206–7. **Author Contributions:** Substantial contributions to study conception/design or acquisition/analysis/interpretation of data: **RBW, AA, PG, LEK, DM, PJM, JFM, BS, DT, BI, DA, RB, JC, ABG;** drafting of the publication or revising it critically for important intellectual content: **RBW, AA, PG, LEK, DM, PJM, JFM, BS, DT, BI, DA, RB, JC, ABG;** final approval of the publication: **RBW, AA, PG, LEK, DM, PJM, JFM, BS, DT, BI, DA, RB, JC, ABG.** **Author Disclosures: RBW:** Consultant for AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; research grants to his institution from AbbVie, Almirall, Janssen, LEO Pharma, Novartis, and UCB Pharma; honoraria from Astellas, DiCE, GSK, and Union. **AA:** Received honoraria and/or research grants 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. **PG:** Consultant for AbbVie, Abiogen, Almirall, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck, MSD, Novartis, Otsuka, Pfizer, Pierre Fabre, Sanofi, and UCB Pharma. **LEK:** Received consulting/speaking fees from AbbVie, Amgen, Biogen, BMS, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer, UCB Pharma; IIT research grants from AbbVie, Eli Lilly, Novartis, Novo, and UCB Pharma. **DM:** Received research grants from AbbVie, Celgene, Janssen, Merck, Pfizer and Novartis; consulting and speaker's fees/honoraria from AbbVie, Celgene, Janssen, Merck, Novartis, Pfizer, and UCB Pharma. **PJM:** 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. **JFM:** Consultant and/or investigator for AbbVie, Amgen, Biogen, BMS, Dermavant, Eli Lilly, Janssen, LEO Pharma, Pfizer, Novartis, Regeneron, Sanofi, Sun Pharma, and UCB Pharma. **BS:** Consultant for AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, BMS, Boehringer Ingelheim, Connect Biopharma, Dermavant, Eli Lilly, EPI Health, Evelo Biosciences, Immunic Therapeutics, Janssen, LEO Pharma, Maruho, Meiji Seika Pharma, Mindera Health, Novartis, Ono, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, UCB Pharma, Union, Ventyxbio, and vTv Therapeutics; Stock Options: Connect Biopharma and Mindera Health; Speaker: AbbVie, Eli Lilly, Janssen, Regeneron, and Sanofi Genzyme; Scientific Co-Director (consulting fee): CorEvitas (formerly Corrona) Psoriasis Registry; Investigator: AbbVie, Cara, CorEvitas Psoriasis Registry, Dermavant, Dermira, and Novartis; Editor-in-Chief (honorarium): Journal of Psoriasis and Psoriatic Arthritis. **DT:** Received honoraria for consulting/speaking/ad boards from AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, BMS, Celltrion, Eli Lilly, Galapagos, Galderma, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma; research grants received from LEO Pharma, and Novartis. **BI:** Employee of UCB Pharma and a shareholder of GSK and UCB Pharma. **DA, RB, JC:** Employee and stockholder of UCB Pharma. **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, Ocrito Dermatologics, Sun Pharma, and UCB Pharma; all funds go to the Icahn School of Medicine at Mount Sinai. **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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