Efficacy and Safety of 108 Weeks Bimekizumab Treatment in Patients with Psoriatic Arthritis: Interim Results from a Phase 2 Open-Label Extension Study

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Objective

To report 2-year interim results from a phase 2b dose-ranging study and open-label extension (OLE) of bimekizumab (BKZ) in patients with psoriatic arthritis (PsA).

Background

- PsA is a chronic, systemic immune-mediated inflammatory disease that occurs in as many as 25% of patients with psoriasis.[1] In a meta-analysis of data for patients with PsA, only ~35% achieved minimal disease activity (MDA) with currently available therapies.[2]
- BKZ, a monoclonal antibody that selectively neutralizes both interleukin (IL)-17A and IL-17F, has shown clinical improvements in joint and skin outcomes over 48 weeks in patients with active PsA.[3]
- Interim efficacy and safety outcomes of BKZ treatment were assessed over 108 weeks **(Figure 1)**.[3]

Methods

Study Design and Patients

- BE ACTIVE was a phase 2b, dose-ranging study (NCT02969525) with an ongoing OLE (NCT03347110) **(Figure 1)**.[3]
- Eligible patients were aged ≥18 years with diagnosis of active PsA, symptoms for ≥6 months duration, and before entering the OLE completed 48 weeks of BKZ treatment in the dose-ranging study.[3]

Study Assessments

- Data are reported to Week 108 for patients initially randomized to BKZ 160 mg every 4 weeks (Q4W), 160 mg with 320 mg loading dose Q4W, or 320 mg Q4W, and who received ≥1 dose BKZ.
- Efficacy variables reported here include American College of Rheumatology (ACR) 20/50/70, complete skin clearance (body surface area [BSA]=0%), MDA, and enthesitis/dactylitis resolution.
  - Patients with PsA are considered in MDA when they meet 5 out of 7 of the following criteria: tender joint count (TJC) ≤1, swollen joint count (SJC) ≤1, Psoriasis Area Severity Index (PASI) ≤1 or BSA ≤3%, patient pain (visual analogue scale [VAS] ≤15), patient global activity (VAS ≤20), Health Assessment Questionnaire (HAQ) ≤0.5, and tender enthesial points ≤1.
- Efficacy measurements from baseline are reported to allow subsequent determination of ACR response criteria.
- Rates of treatment-emergent adverse events (TEAEs) were reported for all patients who received ≥1 dose of BKZ (Safety Set).

Results

Efficacy Outcomes

- Baseline characteristics were comparable across treatment arms **(Table 1)**.
- Over 108 weeks of BKZ treatment, improvements were observed across all reported efficacy outcomes, including ACR50 (non-responder imputation [NRI]: 53.7%; **Figure 2**), and additional joint and skin outcomes **(Figure 3)**.
- MDA was achieved in 51.2% of patients and >50% of patients reported dactylitis and enthesitis resolution (NRI; **Figure 3B–D**).

Safety

- Serious TEAEs occurred in 9.3% of patients **(Table 2)**; no deaths or major adverse cardiac events were reported. Discontinuation rates due to TEAEs were low (18 [8.8%]).
- One incidence of moderate, non-serious collagenous/microscopic colitis was reported and considered unrelated to treatment. Oral candidiasis occurred in 7.8% of patients (no serious cases; no related discontinuations).

Figure 1 Study design

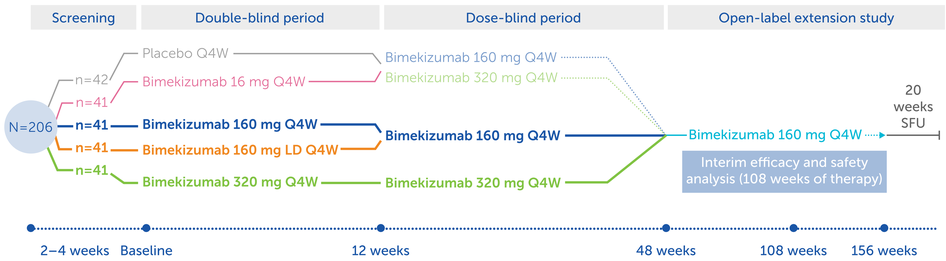


Figure 2 ACR outcomes at Week 108

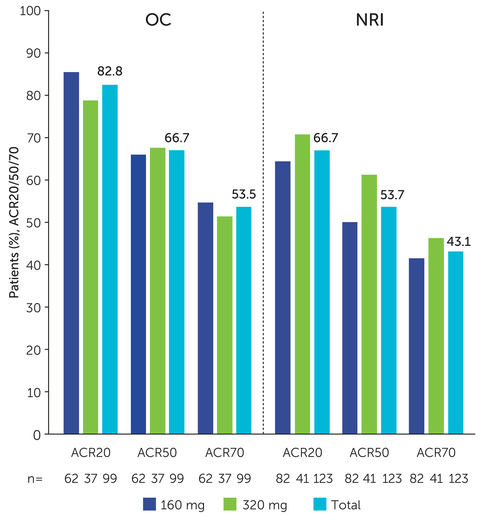
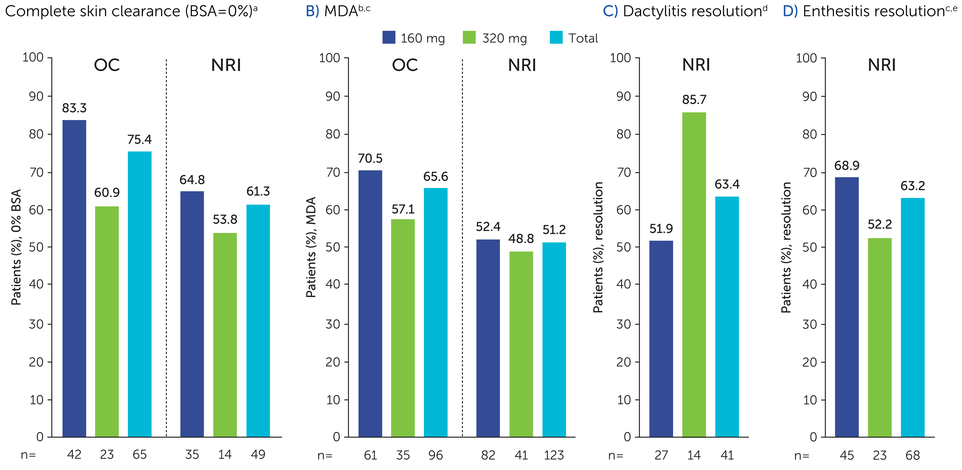


Figure 3 Other efficacy outcomes at Week 108



[a]Due to a data collection error, PASI scores were not collected for all patients with BSA ≥3% at baseline of BE ACTIVE as intended. As such, BSA=0% has been used as a surrogate of complete clearance as it was collected more frequently; [b]MDA achievement of 5/7 of the following criteria: TJC ≤1, SJC ≤1, PASI ≤1 or BSA ≤3%, patient pain (VAS ≤15), patient global activity (VAS ≤20), HAQ ≤0.5, and tender entheseal points ≤1; [c]Data from Week 120; [d]Resolution from patients with dactylitis at baseline. Leeds Dactylitis Index>0; [e]Resolution from patients with enthesitis at baseline. Maastricht Ankylosing Spondylitis Enthesitis Index>0.

Table 1 Demographics and baseline characteristics

	BKZ 160 mg[a] (n=82)	BKZ 320 mg[b] (n=41)	BKZ total[a,b] (N=123)
Age, years, mean (SD)	48.5 (12.3)	50.4 (12.1)	49.2 (12.2)
Gender, female, n (%)	48 (58.5)	18 (43.9)	66 (53.7)
Weight, kg, mean (SD)	82.3 (18.4)	86.8 (19.6)	83.8 (18.9)
TJC, mean (SD)	19.9 (13.8)	25.4 (18.5)	21.7 (15.7)
SJC, mean (SD)	10.7 (8.0)	12.1 (9.4)	11.2 (8.4)
hs-CRP, mg/L, mean (SD)	11.9 (17.3)	12.5 (15.6)	12.1 (16.7)
Psoriasis BSA <3%, n (%)	28 (34.1)	14 (34.1)	42 (34.1)
Dactylitis, n (%)	27 (32.9)	14 (34.1)	41 (33.3)
Enthesitis, n (%)	45 (54.9)	23 (56.1)	68 (55.3)
Prior anti-TNF therapy, n (%)	15 (18.3)	8 (19.5)	23 (18.7)
Concomitant MTX	57 (69.5)	26 (63.4)	83 (67.5)

Baseline characteristics reported from the start of the double-blind period. [a]BKZ 160 mg patients received this dose continuously to Week 108 (includes those originally assigned to 160 mg with loading dose); [b]BKZ 320 mg patients were dose-reduced to 160 mg at OLE entry.

Table 2 Safety at Week 108

Safety (SS) n (%) [EAER/100 PY]	BKZ 160 mg[a] (n=198)	BKZ 320 mg[a] (n=80)	BKZ total[a,b] (N=204)
Any TEAEs	163 (82.3) [160.9]	57 (71.3) [299.8]	179 (87.7) [181.1]
Serious TEAEs	19 (9.6) [4.8]	0	19 (9.3) [4.1]
Discontinuations due to TEAEs[c]	16 (8.1)	2 (2.5)	18 (8.8)
Drug-related TEAEs	72 (36.4)	29 (36.3)	92 (45.1)
Severe TEAEs	11 (5.6)	2 (2.5)	13 (6.4)
Deaths	0	0	0
TEAEs of special interest			
Candida infections	18 (9.1) [8.5]	5 (6.3) [9.3]	22 (10.8) [8.5]
Oral candidiasis	12 (6.1) [6.0]	4 (5.0) [6.2]	16 (7.8) [5.9]
Opportunistic infections[d]	2 (1.0) [0.7]	1 (1.3) [1.6]	3 (1.5) [0.8]
Malignancies[e]	3 (1.5) [0.9]	1 (1.3) [1.6]	4 (2.0) [1.0]
Major adverse cardiac events	0	0	0
Neutropenia	3 (1.5) [0.7]	1 (1.3) [1.6]	4 (2.0) [0.8]
Suicidal and self-injurious behaviour	1 (0.5) [0.2]	0	1 (0.5) [0.2]
Hypersensitivity	25 (12.6) [7.6]	2 (2.5) [3.1]	26 (12.7) [6.9]
Any hepatic events	20 (10.1) [8.5]	6 (7.5) [18.6]	25 (12.3) [9.7]
Increased alanine aminotransferase	9 (4.5) [2.5]	3 (3.8) [4.7]	11 (5.4) [2.8]
Increased aspartate aminotransferase	7 (3.5) [1.6]	2 (2.5) [4.7]	8 (3.9) [2.0]
Increased γ-glutamyltransferase	6 (3.0) [1.6]	2 (2.5) [3.1]	7 (3.4) [1.8]
Increased hepatic enzymes	2 (1.0) [0.5]	1 (1.3) [4.7]	3 (1.5) [1.0]
Other TEAEs reported in ≥7% of patients			
Nasopharyngitis	25 (12.6) [7.1]	11 (13.8) [17.1]	34 (16.7) [8.9]
Upper respiratory tract infection	25 (12.6) [7.6]	8 (10.0) [15.5]	31 (15.2) [8.7]
Pharyngitis	13 (6.6) [3.5]	7 (8.8) [10.9]	17 (8.3) [4.3]
Bronchitis	15 (7.6) [3.9]	3 (3.8) [4.7]	17 (8.3) [4.0]
Sinusitis	12 (6.1) [3.2]	4 (5.0) [9.3]	15 (7.4) [4.0]

[a]Dose received at TEAE onset (patients may be counted in multiple columns); [b]Includes patient time on BKZ 16 mg; [c]Defined as permanent withdrawal of study medication due to TEAEs; [d]Localized fungal events defined as opportunistic infections by internal company conventions; [e]Includes neoplasms benign, malignant, and unspecified.

Conclusions

BKZ shows long-term efficacy for joint and skin manifestations of PsA with >50% patients achieving high thresholds of disease control (ACR50, BSA 0%, MDA) after 108 weeks' treatment. BKZ was well-tolerated, reflecting previous studies.[3]

ACR: American College of Rheumatology; anti-TNF: anti-tumor necrosis factor; BKZ: bimekizumab; BSA: body surface area; EAER/100 PY: exposure-adjusted event rate per 100 patient-years; FAS: full analysis set; HAQ: Health Assessment Questionnaire; hs-CRP: high sensitivity C-reactive protein; IL: interleukin; LD: loading dose; MDA: minimal disease activity; MTX: methotrexate; NRI: non-responder imputation; OC: observed case; OLE: open-label extension; PASI: Psoriasis Area Severity Index; Q4W: every four weeks; SD: standard deviation; SFU: safety follow-up; SJC: swollen joint count; SS: safety set; TEAE: treatment-emergent adverse event; TJC: tender joint count; VAS: visual analogue scale.

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References: [1]Alinaghi F. JAAD 2019;80:251–65; [2]Hagège B. Rheumatol. 2020;doi:10.1093/rheumatology/keaa030; [3]Ritchlin CT. Lancet 2020;395:427–440. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **IBM, JFM, PJM, LCC, PJ, JC, BI, CTR**; Drafting of the publication, or revising it critically for important intellectual content: **IBM, JFM, PJM, LCC, PJ, JC, BI, CTR**; Final approval of the publication: **IBM, JFM, PJM, LCC, PJ, JC, BI, CTR**. **Author Disclosures: IBM:** Consulting fees and honoraria from AbbVie, Janssen, Novartis, Eli Lilly, Celgene, UCB Pharma, Bristol-Myers Squibb, Boehringer Ingelheim; Research support from Celgene, Janssen, Bristol-Myers Squibb, UCB Pharma and Boehringer Ingelheim; **JFM:** Consultant for AbbVie, Amgen, Bayer, Biogen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi-Regeneron, UCB Pharma; Principal investigator for Dermavent, Leo Pharma, UCB Pharma; **PJM:** Speakers' bureau from AbbVie, Amgen Inc., Eli Lilly, Janssen, Novartis, Pfizer, UCB Pharma; Consultancy fees from AbbVie, Amgen Inc., Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, Sun Pharma, UCB Pharma; Research grants from AbbVie, Amgen Inc., Bristol-Myers Squibb, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, UCB Pharma; **LCC:** Shareholder: none to disclose; Speaker's bureau for AbbVie, Amgen, Biogen, Celgene, Gilead, GSK, Janssen, Lilly, Medac, Novartis, Pfizer, UCB Pharma; Paid Instructor: none to disclose; Consulting fees from: Abbvie, Amgen, Biogen, Boehringer Ingelheim, Celgene, Domain, Gilead, Janssen, Eli Lilly; Grant/research support from: AbbVie, Amgen, Celgene, Gilead, Janssen, Lilly, Novartis, Pfizer, UCB Pharma; Employee: none to disclose: **PJ, JC, BI:** Employees of UCB Pharma; **BI:** Shareholder of GlaxoSmithKline and UCB Pharma; **CTR:** Research: UCB Pharma, AbbVie, Amgen Inc.; Consultant: UCB Pharma, Amgen Inc., AbbVie, Lilly, Pfizer, Novartis, Gilead, Janssen. **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, for publication coordination and Hannah Brechka, PhD, Costello Medical, Cambridge, UK, for medical writing and editorial assistance and the Costello Medical Design Team for design support. All costs associated with development of this poster were funded by UCB Pharma.

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