# Bimekizumab in patients with active non-radiographic axial spondyloarthritis and active ankylosing spondylitis: 24-week efficacy and safety from the BE MOBILE phase 3 studies

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## Objective

***To assess the efficacy and safety of subcutaneous bimekizumab (BKZ) versus placebo in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) and active ankylosing spondylitis (AS; i.e. radiographic axSpA) up to Week 24 in the ongoing, pivotal, BE MOBILE 1 and BE MOBILE 2 phase 3 studies.***

## Introduction

- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- Like plaque psoriasis and psoriatic arthritis, axSpA is an IL-17-driven inflammatory disease. Although axSpA mainly affects the axial skeleton (typically the sacroiliac joints (SIJ) and spine), patients can present with uveitis (16–23%), enthesitis (29–35%), and plaque psoriasis (16.7%).[1,2]
- The axSpA spectrum encompasses patients with definitive structural damage to the SIJ visible on pelvic radiographs (AS) and patients without such structural damage (nr-axSpA).

## Methods

- BE MOBILE 1 (nr-axSpA; NCT03928704) and BE MOBILE 2 (AS; NCT03928743) each comprised a 16-week double-blind, placebo controlled period followed by a 36-week maintenance period (**Figure 1**).[3,4]
- Patients were ≥18 years of age with active disease at screening and baseline (BASDAI ≥4 and spinal pain ≥4), fulfilling the ASAS classification (nr-axSpA) or modified New York (AS) criteria.
- Primary (ASAS40) and secondary endpoints were assessed at Week 16, with efficacy and safety, including incidence of treatment-emergent adverse events (TEAEs), reported to Week 24.

# Results

## Patients

- A total of 244/254 (96.1%) patients with nr-axSpA, and 322/332 (97.0%) patients with AS completed Week 16, respectively; 240/254 (94.5%) nr-axSpA patients and 313/332 (94.3%) AS patients completed Week 24.
- Baseline characteristics were comparable between treatment groups (placebo vs BKZ 160 mg Q4W) in patients with both nr-axSpA and AS (**Table 1**).

## Efficacy

- At Week 16, the primary endpoint (ASAS40) was met in patients with nr-axSpA (47.7% BKZ vs 21.4% placebo; p<0.001) and AS (44.8% BKZ vs 22.5% placebo; p<0.001; **Figure 2**).
  - Rapid separation of the BKZ arm from placebo was seen as early as Week 1 and Week 2 in the nr-axSpA and AS studies, respectively.
  - At Week 24, similar responses were seen in patients switching from placebo to BKZ at Week 16 and the BKZ randomisation arm.
- All ranked secondary endpoints were met at Week 16 in both studies, including change from baseline (CfB) in BASDAI (nr-axSpA: −3.1 BKZ vs −1.5 placebo; AS: −2.9 BKZ vs −1.9 placebo) and nocturnal spinal pain (nr-axSpA: −3.6 BKZ vs −1.7 placebo; AS: −3.3 BKZ vs −1.9 placebo).
- A marked reduction in objective measures of inflammation, including hs-CRP (**Figure 3**), and an increase in the proportion of patients with complete resolution of enthesitis were observed (**Figure 4**); at Week 16, clinically meaningful CfB in SPARCC MRI SIJ scores were achieved in patients with nr-axSpA (placebo: −1.5; BKZ: −6.3) and AS (placebo: 1.1; BKZ: −5.6) treated with BKZ.

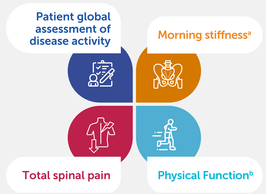
## Safety

- Up to Week 24, 124/244 (50.8%) patients with nr-axSpA, and 183/330 (55.5%) patients with AS had ≥1 TEAE (**Table 2**); few patients had serious adverse events (SAEs; nr-axSpA: 0.4%; AS: 3.6%).
- Most frequent TEAEs by preferred term with BKZ were upper respiratory tract infection (7.0%) and nasopharyngitis (6.6%) in patients with nr-axSpA, and nasopharyngitis (6.4%) and diarrhoea (3.9%) in patients with AS.
- All fungal infections were mild to moderate, localised and mucocutaneous; incidence of opportunistic infections (nr-axSpA: 1.2%; AS: 0.6%) and neutropenia (nr-axSpA: 0.8%; AS: 0.6%) were low.
- No systemic candidiasis, tuberculosis, adjudicated major adverse cardiovascular events (MACE), or deaths were reported. Incidence of inflammatory bowel disease (IBD) and uveitis were low (**Table 2**).

## Summary

**Primary Endpoint: ASAS40**

Defined as an improvement of at least 40%, and an absolute improvement of at least two units (0–10 points NRS) in at least three of the following four measures, and no worsening in the remaining measure:




**Key Outcomes:**

In patients with active nr-axSpA and AS, subcutaneous BKZ 160 mg Q4W provided clinically meaningful improvements in:

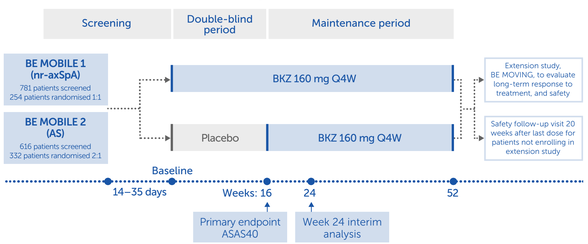
**Signs and symptoms**
ASAS40, BASDAI[c], nocturnal spinal pain, MASES (enthesitis)[d]

**Objective measures of inflammation**
SPARCC MRI SIJ score, hs-CRP

**Safety**
BKZ was well tolerated with no new safety signals observed

[a]Mean of BASDAI Q5 and 6; [b]BASFI; [c]A six item patient-reported outcome measures-based composite index; [d]MASES score ranges from 0 to 13 with lower scores indicating less severe enthesitis, and a negative change representing improvement.

**Figure 1** BE MOBILE 1 and BE MOBILE 2 study designs



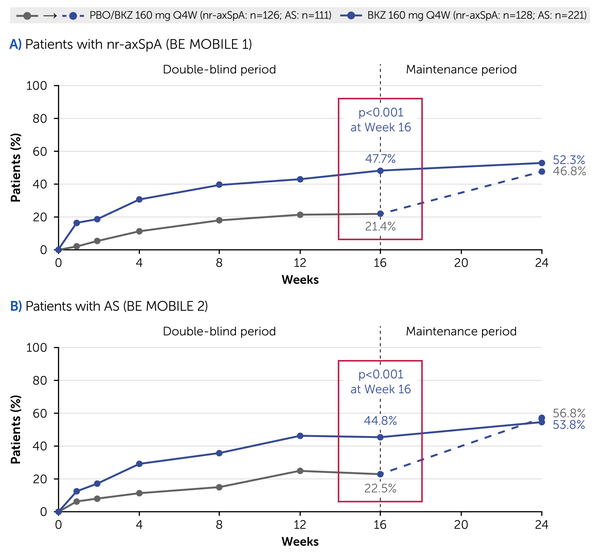

Patients were eligible to receive non-biologic rescue therapy from Week 20 at the discretion of the investigator, while continuing to receive BKZ.

**Table 1** Baseline characteristics

| Baseline characteristics, mean (SD) unless otherwise stated | nr-axSpA (BE MOBILE 1) | | AS (BE MOBILE 2) | |
|---|---|---|---|---|
| | Placebo n=126 | BKZ 160 mg Q4W n=128 | Placebo n=111 | BKZ 160 mg Q4W n=221 |
| Age, years | 39.4 (11.8) | 39.5 (11.1) | 39.2 (12.6) | 41.0 (12.1) |
| Sex, male, n (%) | 65 (51.6) | 73 (57.0) | 80 (72.1) | 160 (72.4) |
| HLA-B27 positive, n (%) | 94 (74.6) | 103 (80.5) | 93 (83.8) | 191 (86.4) |
| Symptom duration, years | 9.0 (9.0) | 9.1 (8.7) | 11.9 (8.6) | 14.2 (11.0) |
| BASDAI | 6.7 (1.3) | 6.9 (1.2) | 6.5 (1.3) | 6.5 (1.3) |
| ASDAS-CRP | 3.7 (0.7) | 3.7 (0.8) | 3.7 (0.8) | 3.7 (0.8) |
| Nocturnal spinal pain | 6.7 (2.1) | 6.9 (2.0) | 6.8 (1.8) | 6.6 (1.9) |
| hs-CRP, mg/L, geometric mean (geometric CV) | 5.0 (230.5) | 4.6 (297.7) | 6.7 (197.4) | 6.5 (275.0) |
| SPARCC MRI SIJ score[a] | 10.5 (13.8)[b] | 8.5 (10.3)[c] | 5.8 (7.7)[a] | 7.4 (10.7)[a] |
| Current enthesitis[i], n (%) | 92 (73.0) | 94 (73.4) | 67 (60.4) | 132 (59.7) |
| Prior TNFi therapy, n (%) | 17 (13.5) | 10 (7.8) | 17 (15.3) | 37 (16.7) |
| Previous and ongoing psoriasis, n (%) | 7 (5.6) | 9 (7.0) | 10 (9.0) | 16 (7.2) |

Randomised set. Data reported for patients with nr-axSpA (BE MOBILE 1) and patients with AS (BE MOBILE 2). [a]Includes only patients in the MRI sub-study; [b]n=68; [c]n=79; [d]n=45; [e]n=83; [f]Patients with MASES >0 at BL.

**Figure 2** ASAS40 response (Weeks 0–24)



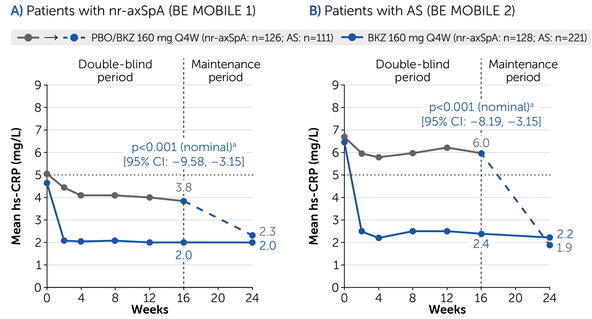

Randomised set. Missing data were imputed using non-responder imputation (NRI). P values for the primary endpoints (ASAS40 at Week 16) were calculated using logistic regression with (A) treatment, MRI/CRP classification and region or (B) treatment, prior TNFi exposure and region as factors in BE MOBILE 1 and BE MOBILE 2, respectively.

**Table 2** Safety overview

| Safety overview n (%) | nr-axSpA (BE MOBILE 1) | | | AS (BE MOBILE 2) | | |
|---|---|---|---|---|---|---|
| | Double-blind period (Weeks 0–16) | | Overall (Weeks 0–24)[a] | Double-blind period (Weeks 0–16) | | Overall (Weeks 0–24)[a] |
| | Placebo n=126 | BKZ 160 mg Q4W n=128 | BKZ 160 mg Q4W n=244 | Placebo n=111 | BKZ 160 mg Q4W n=221 | BKZ 160 mg Q4W n=330 |
| Any TEAE | 71 (56.3) | 80 (62.5) | 124 (50.8) | 48 (43.2) | 120 (54.3) | 183 (55.5) |
| Serious TEAEs | 1 (0.8) | 0 | 1 (0.4) | 1 (0.9) | 4 (1.8) | 12 (3.6) |
| Study discontinuation due to TEAEs | 5 (4.0) | 2 (1.6) | 2 (0.8) | 0 | 6 (2.7) | 11 (3.3) |
| Drug-related TEAEs | 18 (14.3) | 32 (25.0) | 53 (21.7) | 19 (17.1) | 65 (29.4) | 96 (29.1) |
| Severe TEAEs | 1 (0.8) | 0 | 1 (0.4) | 0 | 3 (1.4) | 9 (2.7) |
| Deaths | 0 | 0 | 0 | 0 | 0 | 0 |
| Adjudicated IBD[b] | 1 (0.8) | 0 | 0 | 0 | 2 (0.9) | 2 (0.6)[c] |
| Uveitis[d] | 6 (4.8)[e] | 2 (1.6)[e] | 2 (0.8) | 5 (4.5)[f] | 0[f] | 2 (0.6) |

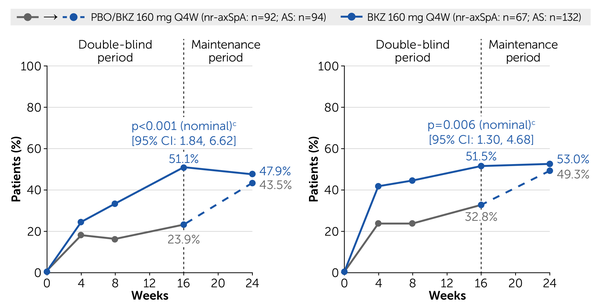
Safety set. MedDRA (Version 19.0). [a]Includes patients who switched from placebo to BKZ (events after switch only); [b]Definite or probable IBD reported, patients had no medical history of IBD. [c]n=326; [d]Includes the preferred terms uveitis, autoimmune uveitis, iridocyclitis and iritis; [e]At baseline, 21/126 (16.7%) patients on PBO and 19/128 (14.8%) patients on BKZ had a medical history of uveitis; [f]At baseline, 24/111 (21.6%) patients on PBO and 33/221 (14.9%) patients on BKZ had a medical history of uveitis.

**Figure 3** Mean hs-CRP (Weeks 0–24)




Randomised set. Data reported for patients with nr-axSpA (BE MOBILE 1) and patients with AS (BE MOBILE 2). Missing data were imputed using multiple imputation (MI). [a]Nominal p values were not adjusted for multiplicity.

**Figure 4** Complete resolution of enthesitis (Weeks 0–24)




Randomised set. Data reported for patients with nr-axSpA (BE MOBILE 1) and patients with AS (BE MOBILE 2). Missing data were imputed using NRI. MASES score ranges from 0 to 13 with lower scores indicating less severe enthesitis, and a negative change representing improvement. [a]MASES=0 in patients with BL MASES >0; [b]Assessed in the subgroup of patients with enthesitis at BL (MASES >0); [c]Nominal p values were not adjusted for multiplicity.

## Conclusions

***Dual inhibition of IL-17A and IL-17F with BKZ in patients across the full axSpA disease spectrum (nr-axSpA and AS) resulted in consistently rapid and robust improvement over placebo in ASAS40 response, as well as objective measures of inflammation (hs-CRP and MRI) and resolution of enthesitis. These results reflect overall improvements in core symptoms, functional impact, and disease activity. BKZ was well tolerated in both studies and the safety profile was consistent with prior observations.[5,6]***

**AS:** ankylosing spondylitis; **ASAS40:** Assessment of SpondyloArthritis international Society 40% response; **ASDAS-CRP:** Ankylosing Spondylitis Disease Activity Score C-reactive protein; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BKZ:** bimekizumab; **BL:** baseline; **CfB:** change from baseline; **CI:** confidence interval; **CRP:** C-reactive protein; **CV:** coefficient of variation; **HLA-B27:** human leukocyte antigen B27; **hs-CRP:** high-sensitivity CRP; **IBD:** inflammatory bowel disease; **IL:** interleukin; **MACE:** Major Adverse Cardiovascular Event; **MASES:** Maastricht Ankylosing Spondylitis Enthesitis Score; **MI:** multiple imputation; **MRI:** magnetic resonance imaging; **n:** number; **nr-axSpA:** non-radiographic axial spondyloarthritis; **NRI:** non-responder imputation; **Q4W:** every four weeks; **SAEs:** serious adverse events; **SD:** standard deviation; **SPARRC:** Spondyloarthritis Research Consortium of Canada; **SIJ:** Sacroiliac Joints; **TEAE:** treatment-emergent adverse event; **TNFi:** tumour necrosis factor inhibitor.

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**References:** [1]de Winter J. Arthritis Res 2016;18:196; [2]Lucasson F. RMD Open 2022;8:e001986; [3]van der Heijde D. Ann Rheum Dis 2022;OP0019; [4]Deodhar A. Ann Rheum Dis 2022;OP0016; [5]Gensler L. Arthritis Rheumatol 2021;73(suppl 10):0491; [6]van der Heijde D. Ann Rheum Dis 2020;79:595–604. **Author Contributions:** Substantial contributions to study conception/design or acquisition/analysis/interpretation of data: **DT, XB, JFM, DP, FvdB, MO, CF, AME, TV, JSS, AM, DvdH**; drafting of the publication or revising it critically for important intellectual content: **DT, XB, JFM, DP, FvdB, MO, CF, AME, TV, JSS, AM, DvdH;** final approval of the publication: **DT, XB, JFM, DP, FvdB, MO, CF, AME, TV, JSS, AM, DvdH.** **Author Disclosures: DT:** Honoraria for participation on advisory boards, as a speaker and consultancy fees from AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, BMS, Celltrion, Eli Lilly, Galapagos, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron, Samsung, Sanofi Genzyme and UCB Pharma; Research grants received from LEO Pharma and Novartis. **XB:** Speaker for AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer and UCB Pharma; Paid instructor for AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer and UCB Pharma; Consultancy fees from AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, 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. **DP:** Speaker for AbbVie, BMS, Eli Lilly, MSD, Novartis, Pfizer and UCB Pharma; Consultancy fees from AbbVie, Biocad, Eli Lilly, Gilead, GSK, MSD, Moonlake, Novartis, Pfizer, Samsung Bioepis and UCB Pharma; Grant/research support from AbbVie, Eli Lilly, MSD, Novartis and Pfizer. **FvdB:** Consultancy fees from AbbVie, Amgen, Eli Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer and UCB Pharma; Speaker for AbbVie, BMS, Celgene, Janssen, Merck, Novartis, Pfizer and UCB Pharma. **MO:** Employee and stockholder of UCB Pharma. **CF, AME, TV, JSS, AM:** Employees of UCB Pharma. **DvdH**: Consultancy fees from AbbVie, Bayer, BMS, Cyxone, Eisai, Galapagos, Gilead, GSK, Janssen, Eli Lilly, Novartis, Pfizer and UCB Pharma; Director of Imaging Rheumatology BV. **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 Celia Menckeberg, PhD, UCB Pharma, Brussels, Belgium, for publication coordination, Alexandra Quinn-Savory, MPH, Costello Medical, Cambridge, 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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