Bimekizumab improves key patient-reported symptoms of axial spondyloarthritis including spinal pain and fatigue: Results from two phase 3 studies

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Objective

To report the impact of bimekizumab (BKZ) versus placebo (PBO) on spinal pain, stiffness, and fatigue in patients with axial spondyloarthritis (axSpA).

Introduction

- Spinal pain, morning stiffness, and fatigue are major contributors to disease burden in patients with active non-radiographic axSpA (nr-axSpA) and radiographic axSpA (r-axSpA; i.e., ankylosing spondylitis) from the patient perspective.[1]
- BKZ, a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated sustained efficacy and was well tolerated up to 24 Weeks in patients with nr-axSpA and AS in the phase 3 studies BE MOBILE 1 and 2.[2,3]
- In both studies all primary and ranked secondary endpoints at Week 16 were met, including change from baseline (CfB) in nocturnal spinal pain.

Methods

- BE MOBILE 1 (NCT03928704; nr-axSpA) and BE MOBILE 2 (NCT03928743; r-axSpA) were conducted in parallel and comprised a 16-week double-blind period followed by a 36-week maintenance period (**Figure 1**).[2,3]
- Here we report, for the Week 24 interim analysis for both studies, the proportion of patients achieving the following outcomes using non-responder imputation (NRI):
  - Increasingly stringent total and nocturnal spinal pain scores (≤4/3/2/1/0) at Week 16
  - Improvements in fatigue, indicated by a ≥4-point increase from baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score at Week 16
- Mean CfB in total and nocturnal spinal pain, BASDAI morning stiffness (mean of BASDAI questions 5 and 6), and FACIT-Fatigue scores to Week 24 are also reported using multiple imputation (MI).

Results

Patients

- 254 patients with nr-axSpA (BKZ: 128; PBO: 126) and 332 with r-axSpA (BKZ: 221; PBO: 111) were randomised; 94.5% and 94.3% completed to Week 24, respectively.
- Across both studies, mean baseline scores for all reported outcomes indicated high symptom severity (**Table 1**).

Pain, Stiffness, and Fatigue

- At Week 16, a greater proportion of nr-axSpA and r-axSpA patients treated with BKZ compared with PBO achieved:
  - Low total and nocturnal spinal pain scores (**Figure 2**)
  - ≥4-point improvement in FACIT-Fatigue score (nr-axSpA: 70.3% vs 45.2%; r-axSpA: 66.1% vs 49.5%).
- Greater mean improvement at Week 16 with BKZ vs PBO was achieved in: total spinal pain, nocturnal spinal pain, BASDAI morning stiffness and FACIT-Fatigue scores, with separation from PBO at the first post-baseline assessment.
- Improvements continued with BKZ to Week 24 and, for patients who switched from PBO to BKZ at Week 16, mean CfB at Week 24 approached or reached similar levels to those seen in BKZ-randomised patients (**Figure 3**).

Conclusions

Inhibition of IL-17F in addition to IL-17A with BKZ resulted in rapid, substantial, and clinically relevant improvements in spinal pain, morning stiffness, and fatigue in patients across the spectrum of axSpA, with separation from PBO at the first post-baseline assessment. These findings support the benefit of BKZ for clinical symptoms which are central to the patient experience and have significant impact on patients' daily lives.

Summary

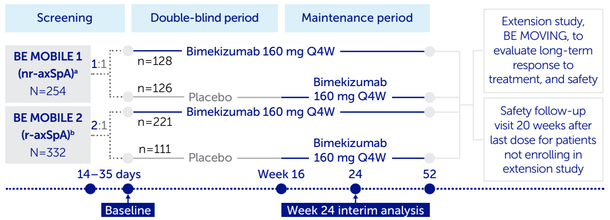
In patients with active non-radiographic and radiographic axial spondyloarthritis, bimekizumab resulted in similar clinically relevant improvements in:

Spinal pain
Total and nocturnal spinal pain scores

Fatigue
FACIT-Fatigue score

Morning stiffness
Mean of BASDAI questions 5 and 6

Figure 1 BE MOBILE 1 and BE MOBILE 2 study designs



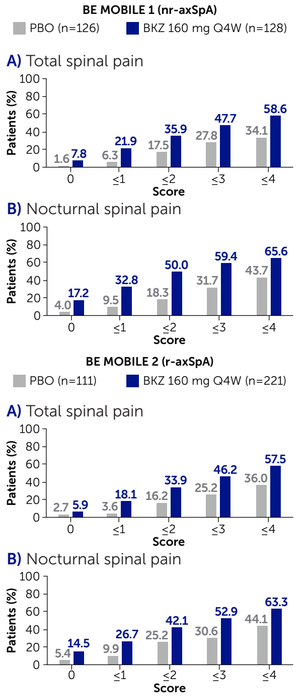
Patients were eligible to receive non-biologic rescue therapy from Week 20 at the discretion of the investigator, while continuing to receive BKZ. [a]Included patients had adult-onset nr-axSpA fulfilling ASAS classification criteria and objective signs of inflammation (active sacroiliitis on MRI and/or elevated CRP [≥6 mg/L]); [b]Included patients had radiographic evidence of axSpA fulfilling modified New York criteria. Patients also fulfilled ASAS classification criteria.

Table 1 Baseline characteristics

	BE MOBILE 1 (nr-axSpA)		BE MOBILE 2 (r-axSpA)	
	PBO N=126	BKZ 160 mg Q4W N=128	PBO N=111	BKZ 160 mg Q4W N=221
Age, years, mean (SD)	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, mean (SD)	9.0 (9.0)	9.1 (8.7)	11.9 (8.6)	14.2 (11.0)
ASDAS-CRP, mean (SD)	3.7 (0.7)	3.7 (0.8)	3.7 (0.8)	3.7 (0.8)[a]
CRP, mg/L, geometric mean (geometric CV %)	5.0 (230.5)	4.6 (297.7)	6.7 (197.4)	6.5 (275.0)
BASDAI, mean (SD)	6.7 (1.3)	6.9 (1.2)	6.5 (1.3)	6.5 (1.3)
Total spinal pain, mean (SD)	7.1 (1.6)	7.3 (1.5)	7.2 (1.2)	7.1 (1.6)
Nocturnal spinal pain, mean (SD)	6.7 (2.1)	6.9 (2.0)	6.8 (1.8)	6.6 (1.9)
Morning stiffness (BASDAI Q5 and 6), mean (SD)	6.9 (1.6)	7.0 (1.8)	6.8 (1.6)	6.7 (1.9)
FACIT-Fatigue, mean (SE)	30.6 (1.0)	29.5 (0.9)	33.1 (1.0)	30.7 (0.7)
TNFi-IR, n (%)	17 (13.5)	10 (7.8)	17 (15.3)	37 (16.7)

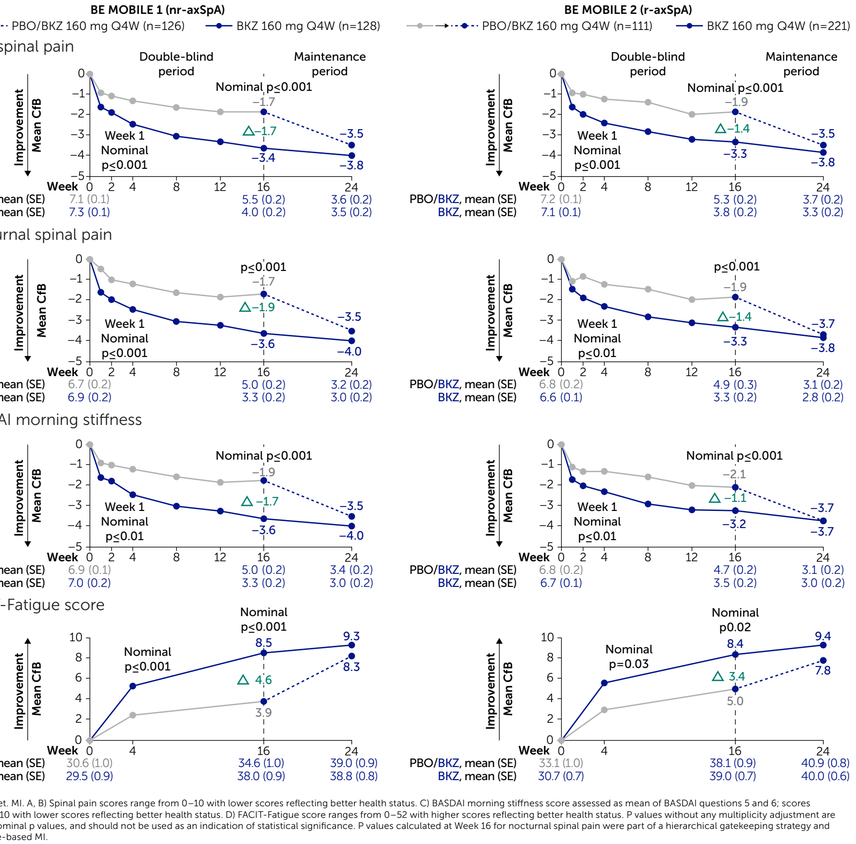
Randomised set. [a]n=220.

Figure 2 Achievement of (A) total and (B) nocturnal spinal pain scores below multiple thresholds at Week 16 (NRI)



Randomised set. NRI. Percentage of patients each week achieving given response who did not discontinue study treatment prior to Week 16. Spinal pain scores range from 0–10 with lower scores reflecting better health status.

Figure 3 Mean change from baseline in (A) total spinal pain, (B) nocturnal spinal pain, (C) BASDAI morning stiffness, and (D) FACIT-Fatigue scores to Week 24 (MI)



Randomised set. MI. A, B) Spinal pain scores range from 0–10 with lower scores reflecting better health status. C) BASDAI morning stiffness score assessed as mean of BASDAI questions 5 and 6; scores range from 0–10 with lower scores reflecting better health status. D) FACIT-Fatigue score ranges from 0–52 with higher scores reflecting better health status. P values without any multiplicity adjustment are indicated as nominal p values, and should not be used as an indication of statistical significance. P values calculated at Week 16 for nocturnal spinal pain were part of a hierarchical gatekeeping strategy and used reference-based MI.

ASAS: Assessment of SpondyloArthritis international Society; **axSpA:** axial spondyloarthritis; **BKZ:** bimekizumab; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **CfB:** change from baseline; **CRP:** C-reactive protein; **FACIT:** Functional Assessment of Chronic Illness Therapy; **HLA-B27:** human leukocyte antigen-B27; **IL:** interleukin; **MI:** multiple imputation; **MRI:** magnetic resonance imaging; **nr-axSpA:** non-radiographic axial spondyloarthritis; **NRI:** non-responder imputation; **PBO:** placebo; **Q4W:** every 4 weeks; **r-axSpA:** radiographic axial spondyloarthritis; **SD:** standard deviation; **SE:** standard error; **TNFi-IR:** tumor necrosis factor inhibitor inadequate responder.

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References: [1]Strand V. J Clin Rheumatol 2017;23:383–91; [2]Boel A. Ann Rheum Dis 2019;78:1545–9; [3]van der Heijde D. Ann Rheum Dis 2023;82:515–26. **Author Contributions:** Substantial contributions to study conception/design or acquisition/analysis/interpretation of data: **PJM**, **AD**, **MDo**, **MDu**, **MM**, **HMO**, **MR**, **CdlL**, **AME**, **CF**, **MO**, **VT**, **LSG**; drafting of the publication or revising it critically for important intellectual content: **PJM**, **AD**, **MDo**, **MDu**, **MM**, **HMO**, **MR**, **CdlL**, **AME**, **CF**, **MO**, **VT**, **LSG**; final approval of the publication: **PJM**, **AD**, **MDo**, **MDu**, **MM**, **HMO**, **MR**, **CdlL**, **AME**, **CF**, **MO**, **VT**, **LSG**. **Author Disclosures: PJM:** Research grants from AbbVie, Acelyrin, 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, UCB Pharma, and Ventyx; speakers' bureau for AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB Pharma; **AD:** Speaker for Janssen, Novartis, and Pfizer; consulting fees from AbbVie, Amgen, Aurinia, BMS, Eli Lilly, Janssen, MoonLake, Novartis, Pfizer, and UCB Pharma; research grants from AbbVie, BMS, Celgene, Eli Lilly, MoonLake, Novartis, Pfizer, and UCB Pharma; **MDo:** Consultancy/speaker fees/research grants from AbbVie, Eli Lilly, Merck, Novartis, Pfizer, and UCB Pharma; **MDu:** Educational grant from Pfizer paid to Institution; consulting fees (e.g. advisory boards) from Amgen, and UCB Pharma; **MM:** Consultancy fees from AbbVie, BMS, Eli Lilly, Novartis, Pfizer, and UCB Pharma; research grants from AbbVie, BMS and UCB Pharma; **HMO:** Research grants from Janssen, Novartis and UCB Pharma; speaking honoraria and/or consultancy fees from AbbVie, Biogen, Eli Lilly, Janssen, Moonlake, Novartis, Pfizer, Takeda and UCB Pharma; **MR:** Speakers bureau from AbbVie, Boehringer Ingelheim, Chugai, Eli Lilly, Janssen, Novartis, Pfizer, and UCB Pharma; consultant of AbbVie, Eli Lilly, Novartis, and UCB Pharma; **CdlL:** Consultant to UCB Pharma; **AME**, **CF:** Employees of UCB Pharma; **MO**, **VT:** Employee and shareholder of UCB Pharma; **LSG:** Grants from Novartis and UCB Pharma, paid to Institution; consulting fees from AbbVie, Acelyrin, Eli Lilly, Fresenius Kabi, Janssen, Novartis, Pfizer, and UCB Pharma. **Acknowledgements:** We would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to this study. The authors acknowledge Celia Menckeberg, PhD, UCB Pharma, for publication coordination, Jane Spingardi, DPhil, Costello Medical, London, UK for medical writing and editorial assistance, and the Costello Medical Creative Team for design support. This study was funded by UCB Pharma. All costs associated with development of this presentation were funded by UCB Pharma.

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