Bimekizumab Demonstrated Comparable One-Year Efficacy in Male and Female Patients with Axial Spondyloarthritis: Results from Two Phase 3 Studies

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Objective

To assess the efficacy of bimekizumab (BKZ) treatment to Week 52 in patients across the full disease spectrum of axial spondyloarthritis (axSpA), focusing on potential sex-based differences in treatment response.

Background

- Female patients with axSpA typically have a higher disease burden and reduced response to treatment compared with male patients.[1]
- BKZ, a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated sustained efficacy to Week 52 in patients with non-radiographic (nr-) and radiographic (r-)axSpA in the phase 3 studies BE MOBILE 1 and 2.[2,3]
- Here, we present BKZ efficacy in male versus female patients with axSpA, up to Week 52 in BE MOBILE 1 and 2.

Methods

- In BE MOBILE 1 (NCT03928704) and BE MOBILE 2 (NCT03928743), patients were randomized to subcutaneous BKZ 160 mg every 4 weeks (Q4W) or placebo for Weeks 0–16 (double-blind period); all received BKZ in Weeks 16–52 (maintenance period).
- We report a post-hoc analysis of the following efficacy outcomes to Week 52, stratified by sex: ASAS40 responders (non-responder imputation [NRI]), patients achieving ASDAS <2.1 (multiple imputation [MI]), and mean absolute BASDAI score (MI); mean absolute values for MRI SPARCC SIJ score, MRI Berlin spine score, and hs-CRP (observed case [OC]); mean CfB in ASQoL score (MI).
- Since all analyses were post-hoc, no formal p values are provided.
  - To compare efficacy in male versus female patients for binary outcomes, adjusted relative odds ratios (rOR), and odds ratios are reported at Week 16 and Week 52, respectively.
  - For most continuous outcomes, adjusted relative differences (RDs) and differences are reported at Week 16 and Week 52, respectively. Due to skewed distribution, adjusted relative ratio to baseline and ratio to baseline, at Week 16 and Week 52, respectively, are reported for hs-CRP.

Results

Baseline characteristics

- 254 patients (male: 138/254; female: 116/254) with nr-axSpA were randomized in BE MOBILE 1 and 332 patients (male: 240/332; female: 92/332) with r-axSpA were randomized in BE MOBILE 2.
  - Of these, 220/254 (male: 124/138 [89.9%]; female: 96/116 [82.8%]) and 298/332 (male: 215/240 [89.6%]; female: 83/92 [90.2%]) completed Week 52.
- Key baseline differences between male and female patients included longer mean symptom duration (years), lower HLA-B27 positivity (%), and worse health-related quality of life (HRQoL, according to higher mean ASQoL scores) in females (**Table**). Mean baseline BASDAI and objective signs of inflammation (OSI) scores are shown in **Figures 1–2**.

Disease activity

- Across ASAS40, ASDAS <2.1, and BASDAI, there was a pattern of higher BKZ versus placebo treatment effect in male versus female patients at Week 16, which was reflected in the rORs and RDs at this timepoint (**Figure 1**).
- At Week 52, treatment responses were higher in males versus females with nr-axSpA but comparable in patients with r-axSpA, which was reflected in the ORs and differences at this timepoint.
- Overall, at Week 52 both males and females responded well in both trials, with >50% of BKZ-randomized patients achieving ASAS40, >40% achieving ASDAS <2.1, and with good overall response in mean improvements in BASDAI scores (**Figure 1**).

Objective signs of inflammation

- For CfB in OSI outcomes, relative differences generally indicated a higher BKZ versus placebo treatment effect in males versus females at Week 16; however, absolute OSI values in males and females at this timepoint were mostly comparable, despite males generally having higher OSI scores at baseline (**Figure 2**). The number of female patients with MRI scores in the r-axSpA placebo group was limited.
- At Week 52, improvements in MRI SPARCC SIJ and MRI Berlin spine scores were comparable between male versus female patients with nr-axSpA or r-axSpA, as reflected in the difference values for CfB at this timepoint.
  - The ratio to baseline for hs-CRP at Week 52 indicated a higher BKZ effect in males versus females in nr-axSpA, but not r-axSpA (**Figure 2**).

Health-related quality of life

- Both male and female patients reported substantial improvements (mean CfB) in ASQoL at Week 16 with BKZ treatment (**nr-axSpA**: –5.5 versus –4.8; **r-axSpA**: –4.8 versus –5.5) compared with placebo (**nr-axSpA**: –2.1 versus –2.9; **r-axSpA**: –3.1 versus –3.7).
- Improvements continued to Week 52 with BKZ (**nr-axSpA**: continuous BKZ: –5.7 versus –6.2, placebo/BKZ-switchers: –5.5 versus –5.1; **r-axSpA**: continuous BKZ: –5.4 versus –6.5, placebo/BKZ-switchers: –5.5 versus –5.8).

Conclusions

In this first analysis comparing efficacy outcomes between sexes in BE MOBILE 1 and 2, the treatment effect of bimekizumab versus placebo at Week 16 tended to be higher among male patients with axSpA compared with their female counterparts, including MRI outcomes (despite higher baseline scores in males versus females).

However, by Week 52, female patients showed improvement in longer-term treatment response to bimekizumab, with efficacy approaching similar levels to those seen in male patients at this timepoint.

Overall, the efficacy of bimekizumab for disease activity, OSI and HRQoL outcomes was demonstrated in both male and female patients across the full disease spectrum of axSpA.

Summary

We assessed the **efficacy of bimekizumab treatment to Week 52** in **male versus female patients**.

Week 16	Week 52
At Week 16, males with axSpA demonstrated a larger treatment effect of bimekizumab versus placebo across all efficacy measures than females.	By Week 52, females showed improvement in longer-term response to bimekizumab, with efficacy approaching similar levels to those seen in males.

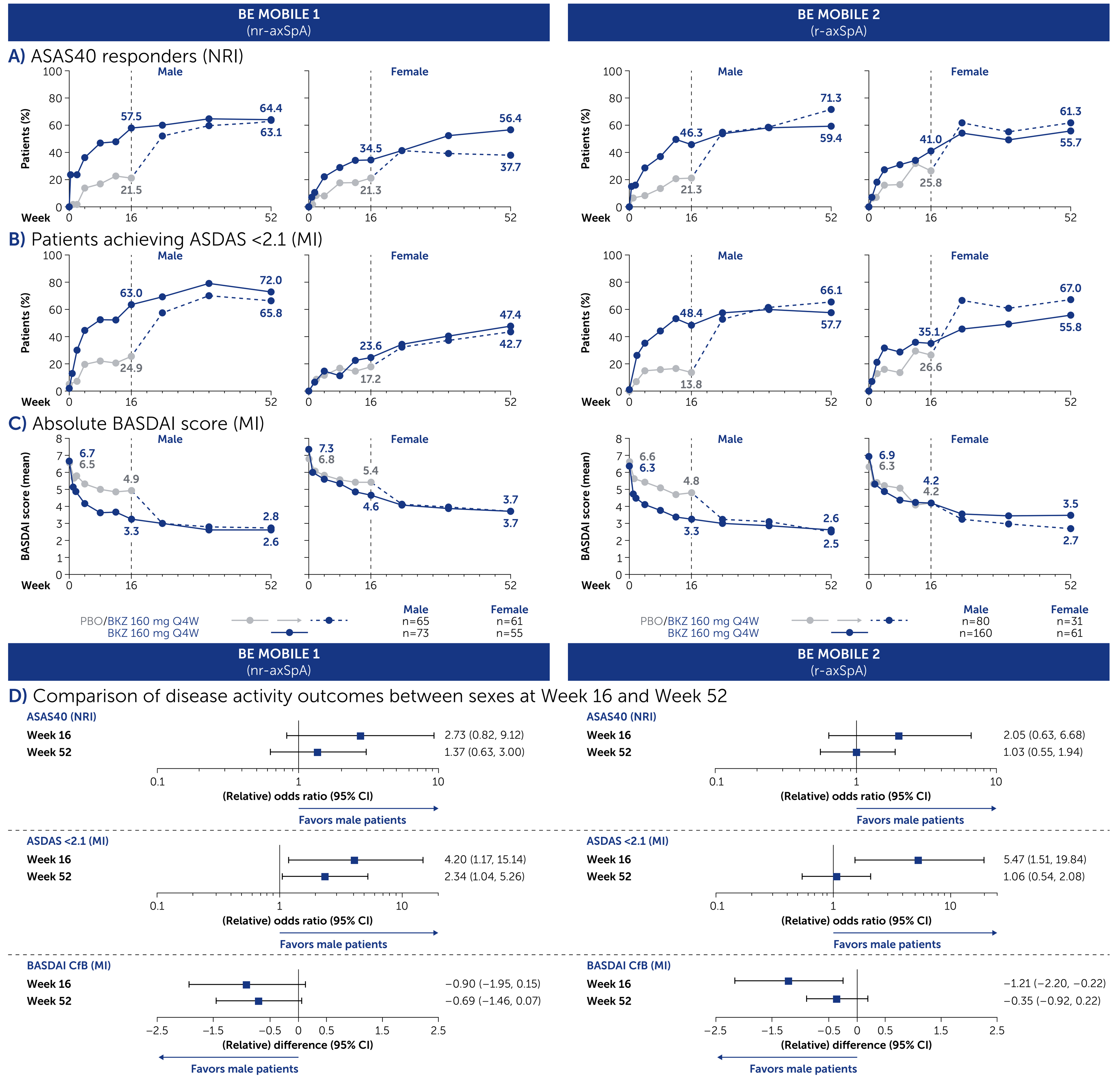
Overall, the efficacy of bimekizumab for disease activity, objective signs of inflammation, and HRQoL outcomes was demonstrated in **both male and female patients across the full disease spectrum of axSpA.**

Table Baseline characteristics in BE MOBILE 1 (nr-axSpA) and BE MOBILE 2 (r-axSpA), stratified by sex

	BE MOBILE 1 (nr-axSpA)				BE MOBILE 2 (r-axSpA)			
	Male		Female		Male		Female	
	PBO n=65	BKZ 160 mg Q4W n=73	PBO n=61	BKZ 160 mg Q4W n=55	PBO n=80	BKZ 160 mg Q4W n=160	PBO n=31	BKZ 160 mg Q4W n=61
Age, years, mean (SD)	36.4 (10.6)	37.8 (10.5)	42.7 (12.3)	41.6 (11.6)	37.0 (11.4)	40.2 (11.8)	45.0 (13.7)	43.3 (12.8)
Symptom duration, years, mean (SD)	6.9 (7.3)	7.6 (7.5)	11.2 (10.0)	11.1 (9.9)	10.8 (7.6)	14.0 (11.2)	14.9 (10.2)	15.0 (10.5)
Time since diagnosis, years, mean (SD)	3.4 (5.7)	3.3 (5.9)	3.7 (5.0)	4.1 (6.6)	5.7 (6.2)	6.7 (8.1)	5.7 (8.6)	6.8 (8.7)
TNFi-naïve, n (%)	57 (87.7)	69 (94.5)	52 (85.2)	49 (89.1)	69 (86.3)	131 (81.9)	25 (80.6)	53 (86.9)
HLA-B27 positive, n (%)	58 (89.2)	59 (80.8)	36 (59.0)	44 (80.0)	72 (90.0)	140 (87.5)	21 (67.7)	51 (83.6)
ASDAS, mean (SD)	3.7 (0.8)	3.6 (0.8)	3.7 (0.7)	3.9 (0.7)	3.8 (0.8)	3.7 (0.8)	3.4 (0.5)	3.7 (0.9)
ASQoL, mean (SE)	8.6 (0.6)	8.5 (0.5)	10.2 (0.5)	10.8 (0.6)	8.4 (0.5)	8.3 (0.4)	9.0 (0.6)	11.1 (0.6)
hs-CRP >ULN,[a] n (%)	39 (60.0)	37 (50.7)	32 (52.5)	33 (60.0)	54 (67.5)	104 (65.0)	13 (41.9)	33 (54.1)

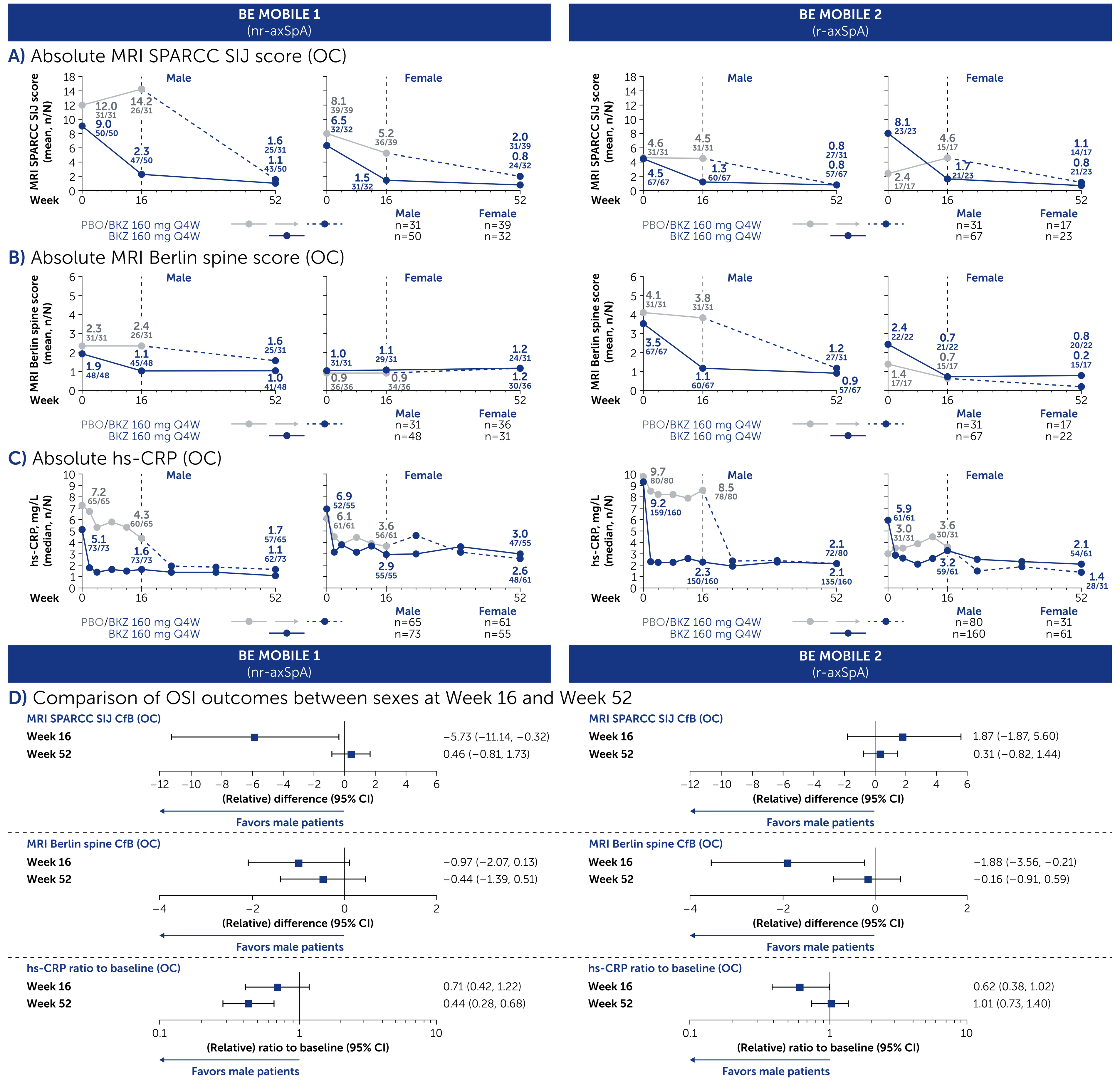
Randomized set. [a] ULN value for hs-CRP is 5 mg/L.

Figure 1 Disease activity outcomes to Week 52, stratified by sex



Randomized set. rOR and RD for the comparison of BKZ versus PBO treatment effect in males versus females at Week 16 were calculated using logistic regression and ANCOVA, respectively. OR and difference for the comparison of males versus females in BKZ-randomized patients at Week 52 were calculated using logistic regression and ANCOVA, respectively. All rOR/OR and RD/difference analyses were adjusted for region, baseline age, HLA-B27 status and, for the continuous endpoints, their baseline values. Additionally, in patients with nr-axSpA, rOR/OR, and RD/difference analyses were adjusted for MRI/CRP classification and, in patients with r-axSpA, for prior TNFi exposure and baseline hs-CRP.

Figure 2 Objective signs of inflammation outcomes to Week 52, stratified by sex



Randomized set. RD for the comparison of BKZ versus PBO treatment effect in males versus females at Week 16 was calculated using ANCOVA. Difference for the comparison of males versus females in BKZ-randomized patients at Week 52 was calculated using ANCOVA. All RD/difference analyses were adjusted for region, baseline age, HLA-B27 status, and MRI baseline values. Additionally, in patients with nr-axSpA, RD/difference analyses were adjusted for MRI/CRP classification and, in patients with r-axSpA, for prior TNFi exposure and baseline hs-CRP. For MRI outcomes, only study participants enrolled in the MRI sub-studies are included. Due to skewed distribution, hs-CRP data are presented in panel C using median of absolute values to Week 52, and ratio to baseline values of the geometric mean were used for ANCOVA relative ratio analyses, shown in panel D.

ANCOVA: analysis of covariance; **ASAS40:** Assessment in SpondyloArthritis international Society 40% improvement; **ASDAS:** axial spondyloarthritis disease activity score; **ASQoL:** Ankylosing Spondylitis Quality of Life Questionnaire; **axSpA:** axial spondyloarthritis; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BKZ:** bimekizumab; **CfB:** change from baseline; **CI:** confidence interval; **CRP:** C-reactive protein; **HLA-B27:** human leukocyte antigen B27; **HRQoL:** health-related quality of life; **hs-CRP:** high-sensitivity C-reactive protein; **IL:** interleukin; **MI:** multiple imputation; **MRI:** magnetic resonance imaging; **nr-axSpA:** non-radiographic axial spondyloarthritis; **NRI:** non-responder imputation; **OC:** observed case; **OR:** odds ratio; **OSI:** objective signs of inflammation; **PBO:** placebo; **Q4W:** every 4 weeks; **r-axSpA:** radiographic axial spondyloarthritis; **RD:** relative difference; **rOR:** relative odds ratio; **SD:** standard deviation; **SE:** standard error; **SIJ:** sacroiliac joint; **SPARCC:** Spondyloarthritis Research Consortium of Canada; **TNFi:** tumor necrosis factor inhibitor; **ULN:** upper limit of normal.

References: [1]van der Horst-Bruinsma I. Ann Rheum Dis 2013;72:1221–4; [2]van der Heijde D. Ann Rheum Dis 2023;82:515–26; [3]Baraliakos X. Ann Rheum Dis 2024;83:199–213.
Author Contributions: Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **LSG**, **SR**, **DP**, **MM**, **IvdHB**, **AD**, **VT**, **DV**, **NdP**, **MR**; Drafting of the publication, or reviewing it critically for important intellectual content: **LSG**, **SR**, **DP**, **MM**, **IvdHB**, **AD**, **VT**, **DV**, **NdP**, **MR**; Final approval of the publication: **LSG**, **SR**, **DP**, **MM**, **IvdHB**, **AD**, **VT**, **DV**, **NdP**, **MR**. **Disclosures: LSG:** Grants from UCB paid to institution; consulting fees from Acelyrin, Eli Lilly, Janssen, Novartis, Pfizer, and UCB. **SR:** Consultant for AbbVie, Eli Lilly, Galapagos/Alfasigma, Janssen, Novartis, Pfizer, Sanofi, and UCB; grants from AbbVie, Galapagos/Alfasigma, MSD, Novartis, Pfizer, and UCB. **DP:** Speaker for AbbVie, BMS, Eli Lilly, MSD, Novartis, Pfizer, and UCB; consultant for AbbVie, Biocad, Eli Lilly, Gilead, GSK, Moonlake, MSD, Novartis, Pfizer, Samsung Bioepis, and UCB; grant/research support from AbbVie, Lilly, MSD, Novartis, and Pfizer. **MM:** Consultancy fees from AbbVie, BMS, Eli Lilly, Novartis, Pfizer, and UCB; research grants from AbbVie, BMS, and UCB. **IvdHB:** Consultant for AbbVie, Eli Lilly, MSD, Novartis, and UCB; unrestricted grants received for investigator-initiated studies from AbbVie, MSD, Pfizer, and UCB; fees received for Lectures from AbbVie, BMS, MSD, and Pfizer. **AD:** Speaker for Eli Lilly, J&J, Novartis, Pfizer, and UCB; consultant for BMS, Eli Lilly, J&J, MoonLake, Novartis, Pfizer, and UCB; grant/research support from BMS, Eli Lilly, J&J, Novartis, Pfizer, and UCB. **VT:** Employee and shareholder of UCB. **DV:** Former contractor for UCB and former employee of Veramed. **NdP:** Employee of UCB. **MR:** Speakers bureau from AbbVie, Boehringer Ingelheim, Eli Lilly, Janssen, Novartis, Pfizer, and UCB; consultant of AbbVie, Eli Lilly, Janssen, Novartis, and UCB. **Acknowledgments:** 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, Breda, the Netherlands, for publication coordination, Georgina Gregory, PhD, Costello Medical, Manchester, UK for medical writing and editorial assistance, Roshni Patel, BSc, Costello Medical, London, UK, for editorial assistance, and the Costello Medical Creative team for design support. These studies were funded by UCB. All costs associated with development of this poster were funded by UCB.

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