“How quickly will I feel better with this new drug?” – Rapidity of Treatment Response in Patients with Axial Spondyloarthritis Treated with Bimekizumab: Analysis from Two Phase 3 Studies

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Objective

To assess the rapidity of response to treatment after a single dose, and subsequent doses, of bimekizumab (BKZ) in patients with axial spondyloarthritis (axSpA), using data from two phase 3 studies.

Background

- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- Two phase 3 studies were conducted where treatment with BKZ demonstrated efficacy and was shown to be well tolerated to 52 weeks across the full disease spectrum of axSpA: BE MOBILE 1 (non-radiographic [nr-]axSpA) and BE MOBILE 2 (radiographic [r-]axSpA i.e., ankylosing spondylitis).[1,2]
- One of the most common questions patients ask their healthcare providers is, “how quickly will I feel better after starting this new drug?”

Methods

- The BE MOBILE 1 (NCT03928704) and 2 (NCT03928743) studies were double-blind, consisting of a 16-week placebo-controlled period and a 36-week maintenance period (**Figure 1**).
- We present treatment responses over the first 16 weeks for the BKZ and placebo treatment arms, including Kaplan-Meier analyses of Assessment of SpondyloArthritis international Society 40% (ASAS40) response, using observed case (OC).
  - Non-responder imputation (NRI) and multiple imputation (MI) were applied for missing binary and continuous outcomes, respectively
  - Aside from p values reported at Week 16 for the ranked primary (ASAS40) and secondary endpoints of each study, all other p values are nominal.

Results

Patient Population

- Of the 254 patients enrolled in BE MOBILE 1 (BKZ: 128; placebo: 126) and 332 in BE MOBILE 2 (BKZ: 221; placebo: 111), 96.1% (244/254) and 97.0% (322/332) completed treatment to Week 16, respectively.
- Baseline characteristics were similar across both patient populations.[1]

Rapidity of Treatment Response

- Kaplan-Meier analyses showed early separation between BKZ and placebo for ASAS40 (**Figure 2**), with a greater proportion of patients achieving ASAS40 after a single dose of BKZ at baseline, from Week 1 for patients with nr-axSpA and from Week 2 for patients with r-axSpA (**Figure 3**).
  - ASAS40 response rates continued to increase to Week 16 in both populations.
- Across the full disease spectrum of axSpA, from Week 1 onwards, patients treated with BKZ demonstrated greater improvements in total and nocturnal spinal pain and physical function, as assessed by Bath Ankylosing Spondylitis Functional Index (BASFI), than those receiving placebo (**Figure 3** and **Table**).
- Similar separation from placebo was observed for improvements in inflammation as demonstrated by hs-CRP levels from first measurement at Week 2 (**Table**).
- Resolution of enthesitis indicated by a Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)=0 was achieved by a greater percentage of patients receiving BKZ than placebo, with separation from placebo observed by Week 8 in patients with nr-axSpA and Week 4 in patients with r-axSpA (**Figure 3**).

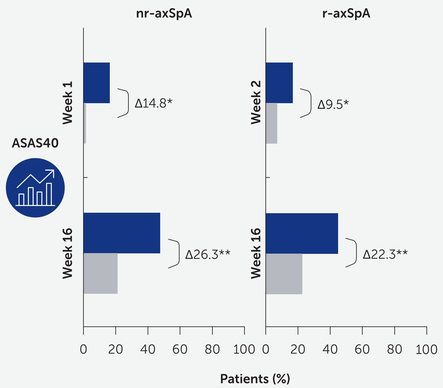
Conclusions

Patients across the full disease spectrum of axSpA treated with bimekizumab achieved rapid treatment responses, with early separation from placebo as early as 1–2 weeks after a single dose of bimekizumab at baseline. These results are of practical importance for counseling patients with axSpA.

Summary

Achieving **rapid treatment response** is an important predictor for long-term disease control.

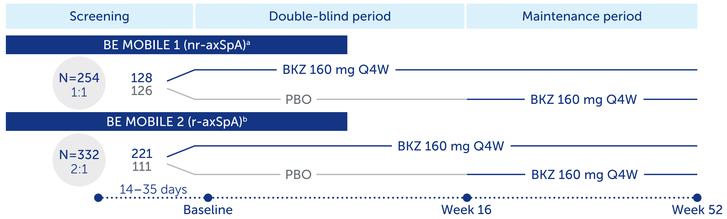
Early separation from placebo was achieved with bimekizumab at **Week 1** for patients with **nr-axSpA** and **Week 2** for patients with **r-axSpA**, and sustained to Week 16.



*nominal p value <0.05; **multiplicity-adjusted p value <0.05

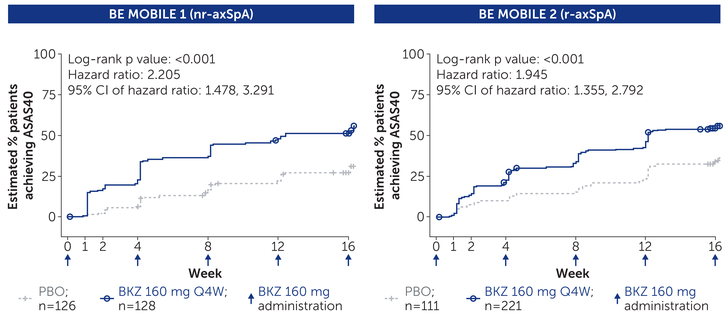
Across other outcome measures of disease activity, pain, physical function, enthesitis and inflammation, separation from placebo was also observed as early as **1–2 weeks** after a **single dose of bimekizumab** at baseline.

Figure 1 Study design



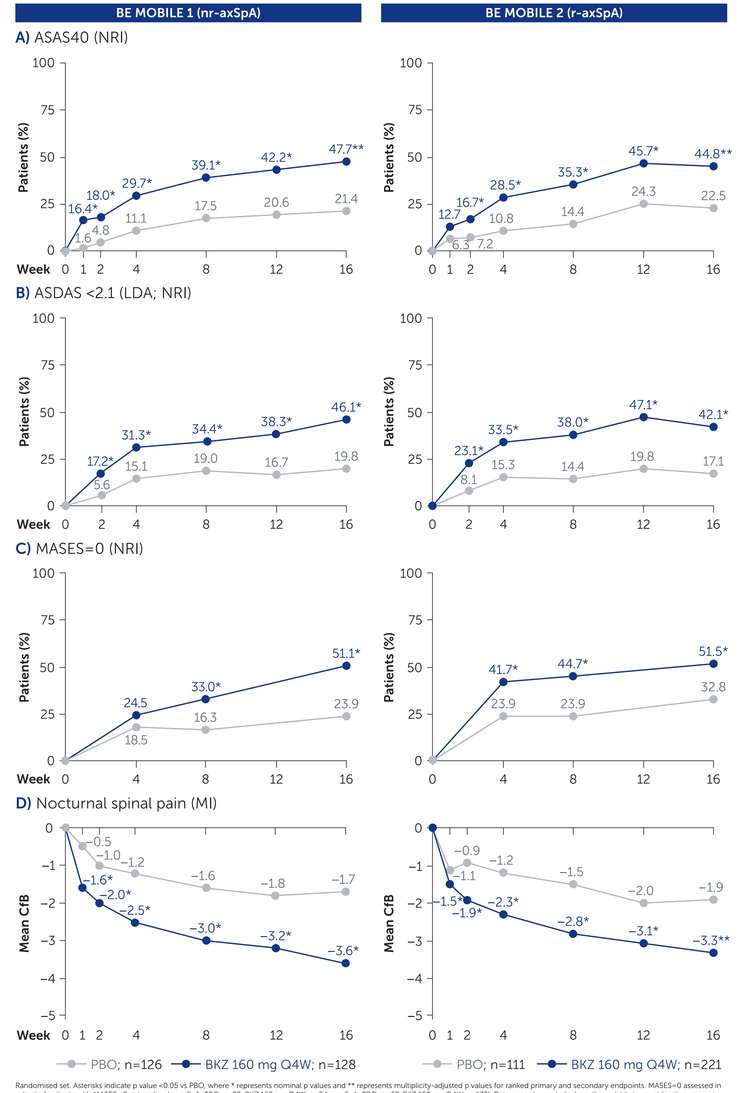
Patients were eligible to receive non-biologic rescue therapy from Week 20 at the discretion of the investigator, while continuing to receive BKZ. **[a]** Included patients had adult-onset nr-axSpA fulfilling ASAS classification criteria and objective signs of inflammation (active sacroiliitis on MRI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

Figure 2 Kaplan-Meier analyses: Time to ASAS40 response to Week 16 (OC)



Randomised set. ASAS40 was the primary outcome in BE MOBILE 1 and 2. Nominal p values are reported for the analysis; they are not multiplicity-adjusted and should not be used as an indication of statistical significance. Time to ASAS40 response: time in days from treatment start date until the first date when response is achieved. The comparison was made using a log-rank test. Missing ASAS response data were not imputed. Study participants who discontinued treatment prior to achieving a response at Week 16 were censored at the earliest date between the date of treatment discontinuation and Week 16. Study participants who reached the end of the double-blind treatment period without achieving the given response were censored at the date of the end of double-blind treatment period.

Figure 3 Efficacy responses to Week 16 (MI, NRI)



Randomised set. Asterisks indicate p value <0.05 vs PBO, where * represents nominal p values and ** represents multiplicity-adjusted p values for ranked primary and secondary endpoints. MASES=0 assessed in subset of patients with MASES >0 at baseline (nr-axSpA: PBO: n=92; BKZ 160 mg Q4W: n=94; r-axSpA: PBO: n=67; BKZ 160 mg Q4W: n=132). Data are not reported where the variable in consideration was not assessed at the visit.

Table Efficacy responses to Week 16 (MI, NRI)

	Week 1		Week 2		Week 4		Week 8		Week 16	
	BE MOBILE 1 (nr-axSpA)									
	PBO	**BKZ 160 mg Q4W**	PBO	**BKZ 160 mg Q4W**	PBO	**BKZ 160 mg Q4W**	PBO	**BKZ 160 mg Q4W**	PBO	**BKZ 160 mg Q4W**
ASAS-PR [NRI], %	2.4	3.9	2.4	5.5	4.8	10.2	6.3	16.4	7.1	25.8
Total spinal pain CfB [MI], mean (SE)	−0.6 (0.1)	−1.6 (0.2)	−1.0 (0.2)	−1.9 (0.2)	−1.2 (0.2)	−2.3 (0.2)	−1.5 (0.2)	−2.8 (0.2)	−1.7 (0.2)	−3.4 (0.2)
BASFI CfB [MI], mean (SE)	−0.1 (0.1)	−0.9 (0.2)	−0.2 (0.1)	−1.1 (0.2)	−0.4 (0.2)	−1.6 (0.2)	−0.8 (0.2)	−2.1 (0.2)	−1.0 (0.2)	−2.5 (0.2)
hs-CRP (mg/L) [MI], median (Q1, Q3)	–	–	5.8 (1.7, 12.1)	1.9 (0.7, 6.8)	4.6 (1.8, 11.7)	1.9 (0.7, 5.5)	5.3 (2.1, 9.4)	2.0 (1.0, 5.1)	4.1 (1.6, 11.4)	1.8 (0.8, 5.7)
	BE MOBILE 2 (r-axSpA)									
ASAS-PR [NRI], %	1.8	5.0	2.7	4.5	6.3	10.4	5.4	15.8	7.2	24.0
Total spinal pain CfB [MI], mean (SE)	−0.9 (0.2)	−1.6 (0.1)	−1.0 (0.2)	−2.0 (0.1)	−1.2 (0.2)	−2.4 (0.1)	−1.4 (0.2)	−2.8 (0.2)	−1.9 (0.2)	−3.3 (0.2)
BASFI CfB [MI], mean (SE)	−0.3 (0.1)	−0.9 (0.1)	−0.2 (0.1)	−1.0 (0.1)	−0.4 (0.1)	−1.4 (0.1)	−0.7 (0.2)	−1.8 (0.1)	−1.1 (0.2)	−2.2 (0.1)
hs-CRP (mg/L) [MI], median (Q1, Q3)	–	–	6.1 (2.2, 15.5)	2.4 (1.0, 7.0)	6.0 (2.3, 14.0)	2.3 (1.0, 5.3)	6.4 (2.7, 15.6)	2.3 (1.1, 5.9)	6.3 (2.8, 16.5)	2.4 (1.0, 6.6)

nominal p value <0.05 | multiplicity-adjusted p value <0.05

Randomised set. BE MOBILE 1: PBO n=126, BKZ 160 mg Q4W n=128. BE MOBILE 2: PBO n=111, BKZ 160 mg Q4W n=221. Shaded cells indicate p value <0.05 vs PBO, where green represents nominal p values and blue represents multiplicity-adjusted p values for ranked primary and secondary endpoints. Data are not reported where the variable in consideration was not assessed at the visit.

ASAS40: Assessment of SpondyloArthritis international Society 40% response; **ASAS-PR:** ASAS partial remission; **ASDAS:** Axial Spondyloarthritis Disease Activity Score; **BASFI:** Bath Ankylosing Spondylitis Functional Index; **BKZ:** bimekizumab; **CfB:** change from baseline; **CI:** confidence interval; **hs-CRP:** high sensitivity C-reactive protein; **IL:** interleukin; **LDA:** low disease activity; **MASES:** Maastricht Ankylosing Spondylitis Enthesitis Score; **MI:** multiple imputation; **MRI:** magnetic resonance imaging; **nr-axSpA:** non-radiographic axial spondyloarthritis; **NRI:** non-responder imputation; **OC:** observed case; **PBO:** placebo; **Q4W:** every 4 weeks; **r-axSpA:** radiographic axial spondyloarthritis; **SE:** standard error.

References: [1]Baraliakos X. Ann Rheum Dis 2024;83:199–213; [2]Boel A. Ann Rheum Dis 2019;78(11):1545–49. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **ADe**, **EN**, **ADa**, **SH**, **VT**, **DV**, **MM**, **XB**. Drafting of the publication, or reviewing it critically for important intellectual content: **ADe**, **EN**, **ADa**, **SH**, **VT**, **DV**, **MM**, **XB**. Final approval of the publication: **ADe**, **EN**, **ADa**, **SH**, **VT**, **DV**, **MM**, **XB**. **Author Disclosures: ADe:** Speaker for Eli Lilly, Janssen, Novartis, Pfizer and UCB; consultant for BMS, Eli Lilly, Janssen, MoonLake, Novartis, Pfizer and UCB; grant/research support from BMS, Celgene, Eli Lilly, Novartis, Pfizer and UCB. **EN:** Speakers honoraria/participated in advisory boards for AbbVie, Alfasigma, Eli Lilly, Fresenius, Gilead, Galapagos, Pfizer and UCB; research grants from Eli Lilly and Pfizer. **ADa:** Research grants from Eli Lilly and Novartis, advisor for AbbVie, Amgen, Janssen, and Novartis; speaker for Amgen and Janssen. **SH:** Grant/research support from and/or consulting fees from AbbVie, Eli Lilly, Novartis and UCB. **VT:** Employee and shareholder of UCB. **DV:** Contractor for UCB and employee of Veramed. **MM:** Consultancy fees from AbbVie, BMS, Eli Lilly, Novartis, Pfizer and UCB; research grants from AbbVie, BMS and UCB. **XB:** Speakers bureau from AbbVie, BMS, Chugai, Eli Lilly, Galapagos, MSD, Novartis, Pfizer and UCB; paid instructor for AbbVie, BMS, Chugai, Eli Lilly, Galapagos, MSD, Novartis, Pfizer and UCB; consultant of AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, Novartis, Pfizer and UCB; grant/research support from Abbvie, Celltrion, Janssen and Novartis. **AB:** Employee of UCB. **Acknowledgements:** We would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to these studies. The authors acknowledge Celia Menckeberg, PhD, UCB, Breda, The Netherlands, for publication coordination, Rebecca Light, BSc, Costello Medical, London, UK, for medical writing and editorial assistance, Charlotte Frail, BSc, Costello Medical, Bristol, UK for editorial assistance and the Costello Medical Creative team for graphic design support. These studies were funded by UCB. All costs associated with development of this presentation were funded by UCB.

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