"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**).

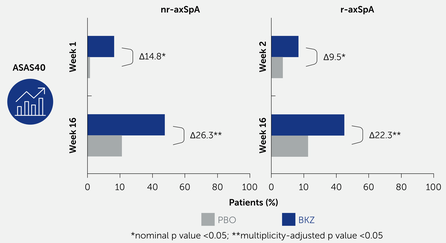
Conclusions

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.

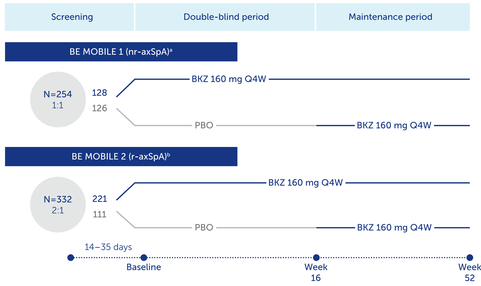
Early separation from placebo was achieved with bimekizumab at **Week 1** for patients with **nr-axSpA** and **Week 2** for patients with **r-axSpA**, and sustained to Week 16.



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

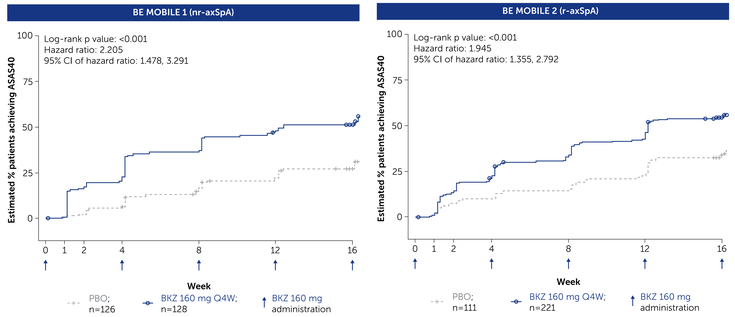
Across other outcome measures of disease activity, pain, physical function, enthesitis, and inflammation, separation from placebo was also observed as early as **1–2 weeks** after a **single dose of bimekizumab** at baseline.

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)



Randomized 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.

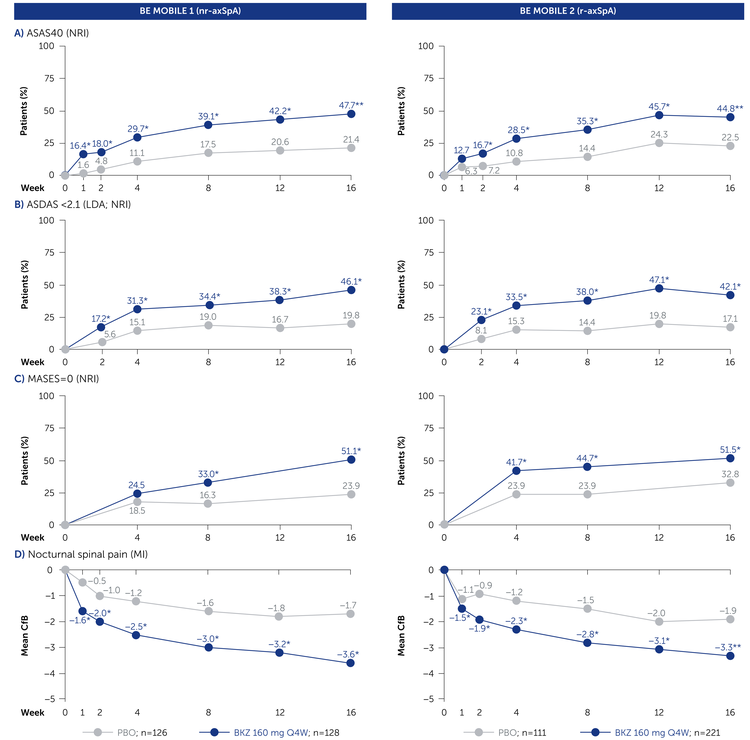
Table Efficacy responses to Week 16 (MI, NRI)

	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, 6.7)

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

Randomized 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.

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



Randomized 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.

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; **CI:** confidence interval; **CfB:** change from baseline; **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.

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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 revising 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 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; grant/research support from Novartis and UCB.
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