Long-Term Sustained Efficacy and Safety of Bimekizumab Across the Full Spectrum of Axial Spondyloarthritis: 2-Year Results from Two Phase 3 Studies

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Objective

To assess the 2-year efficacy and safety of bimekizumab (BKZ) across the full disease spectrum of axial spondyloarthritis (axSpA).

Background

- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- BKZ demonstrated efficacy and safety to 1 year in patients with active non-radiographic (nr-) and radiographic axSpA (r-axSpA; or ankylosing spondylitis)[1] in the phase 3 studies, BE MOBILE 1 and 2, respectively.[2,3]
- Here we report 2-year data from the combined open-label extension (OLE) study, BE MOVING.

Methods

- BE MOBILE 1 (NCT03928704) and 2 (NCT03928743) both comprised a 16-week double-blind period followed by a 36-week maintenance period (**Supplementary Figure 1**; QR code).
- At Week 52, all patients who completed either study without meeting any withdrawal criteria were eligible to be enrolled into the BE MOVING OLE (NCT04436640).
- Efficacy outcomes are reported for patients with nr-axSpA and r-axSpA from BE MOBILE 1 and 2 and the combined OLE up to 2 years.
  - Data are reported for the randomised set using non-responder imputation (NRI; binary outcomes), multiple imputation (MI; continuous outcomes) and observed cases (OC). Patients not enrolled in the OLE were imputed as non-responders.
  - MRI outcomes are presented for patients who were enrolled in the sacroiliac joint (SIJ) and spine MRI sub-studies. MRI remission, defined as MRI SIJ Spondyloarthritis Research Consortium of Canada (SPARCC) score of <2 (patients with nr-axSpA) or a Berlin MRI spine score ≤2 (patients with r-axSpA), is reported among patients with a baseline score of ≥2 or >2, respectively.
- Pooled safety data are reported up to 2 years for all patients who received ≥1 dose BKZ (N=574); safety data split by study year are also reported.

Results

Patients

- Of the patients originally randomised to BKZ or placebo in BE MOBILE 1 (nr-axSpA) and BE MOBILE 2 (r-axSpA), 81.9% (208/254) and 86.1% (286/332) patients entered BE MOVING at Week 52, respectively. At the July 2023 data cut, 189 patients with nr-axSpA and 267 patients with r-axSpA had completed Week 104 (**Supplementary Figure 1**; QR code).
  - Baseline characteristics were similar across both patient populations.[3]

Efficacy

- 1-yr efficacy was sustained to 2 years in both nr-/r-axSpA populations (**Figure 1–2**; **Table 1**).[3]
- ASAS40 responses were maintained from Week 52 to 104 (nr-axSpA: 49.2% [NRI]; 58.9% [MI]; 66.1% [125/189; OC]; r-axSpA: 53.9% [NRI]; 61.0% [MI]; 67.0% [179/267; OC]).
- At Week 104, ASDAS low disease activity (LDA; <2.1) was achieved by 61.2% and 63.4% of patients with nr-/r-axSpA, respectively (MI). ASDAS inactive disease (ASDAS <1.3) and ASAS partial remission were achieved by roughly a third of patients (**Table 1**; **Figure 2**).
- BKZ treatment led to sustained suppression of inflammation, demonstrated by hs-CRP levels (median hs-CRP [baseline to Week 104]: 6.3 to 2.1 in patients with nr-axSpA; 7.4 to 2.3 in patients with r-axSpA), total resolution of enthesitis and improvements in MRI inflammation scores in both patient populations, with more than 57% of patients achieving MRI remission at Week 104 (**Table 1**; **Figure 3**).

Safety

- To Week 104, 89.5% (514/574) of patients with axSpA had ≥1 treatment-emergent adverse event (TEAE) on BKZ.
- Most frequent TEAEs by preferred term (exposure-adjusted incidence rate per 100 patient-years [EAIR/100 PY]; MedDRA v19.0) were SARS-CoV-2 infection (COVID-19; 13.2), nasopharyngitis (10.2) and upper respiratory tract infection (6.0).
- EAIR/100 PY of serious TEAEs was low (5.4). No major adverse cardiovascular events, active tuberculosis cases, serious SARS-CoV-2 infections, anaphylaxis or deaths were reported.
- Of 122 patients who experienced fungal infections (21.3%; EAIR/100 PY: 10.0), 76 had *Candida* infections (13.2%; EAIR/100 PY: 5.8 – mostly oral); almost all *Candida* infections were mild–moderate and none were serious/systemic – 6 cases led to study discontinuation.
- Incidence of adjudicated suicidal ideation and behaviour (EAIR/100 PY: 0.1), adjudicated inflammatory bowel disease (EAIR/100 PY: 0.6) and uveitis (EAIR/100 PY: 1.6) was low.
- 72 (12.5%; EAIR/100 PY: 5.5) patients had a hepatic TEAE; most had liver function test elevations or transient abnormalities (n=53; no confirmed Hy's law cases). None resulted in study or treatment discontinuation.
- The incidence of most TEAEs was broadly similar across both study years, with the notable exception of SARS-CoV-2 (COVID-19) infections, which were more common in Year 2 of the study (**Table 2**). The safety profile of BKZ was also similar across patients with nr-axSpA and r-axSpA to Week 104.

Conclusions

Across the full disease spectrum of axSpA, bimekizumab treatment demonstrated sustained clinical efficacy up to 2 years. No new safety signals were observed; data were consistent with the safety profile established in prior studies.[3]

Summary

BKZ showed **sustained efficacy**, across the full disease spectrum of axSpA, **up to 2 years**. At Week 104:

>60% of patients achieved ASDAS <2.1

>57% of patients who were enrolled in the MRI sub-studies achieved MRI remission[a]

No new safety signals were detected

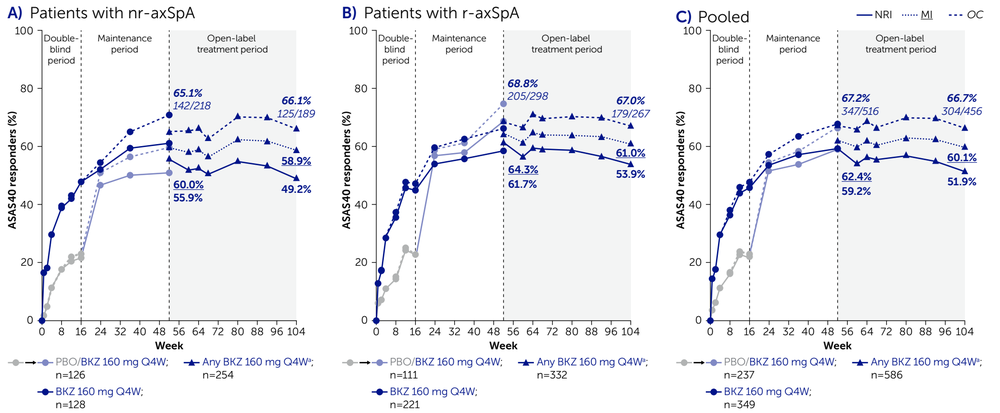
[a] MRI remission is defined as MRI SIJ SPARCC <2 (patients with nr-axSpA) or Berlin MRI spine score ≤2 (patients with r-axSpA). Includes patients who had a baseline MRI SIJ SPARCC (patients with nr-axSpA) score of ≥2 or a baseline Berlin MRI spine (patients with r-axSpA) score of >2 and with recorded MRI data at Week 16, Week 52 and Week 104.

Table 1 Efficacy to 2 years (Week 104)

	nr-axSpA	r-axSpA
	BKZ 160 mg Q4W N=254	**BKZ 160 mg Q4W N=332**
ASAS40		
[OC] n/N (%)	125/189 (66.1)	179/267 (67.0)
[MI] Mean proportion (%)	58.9	61.0
[NRI] n (%)	125 (49.2)	179 (53.9)
ASAS Partial Remission [NRI] n (%)	78 (30.7)	104 (31.3)
ASDAS [MI]		
Mean at baseline (SE)	3.7 (0.1)	3.7 (0.0)
Mean at Week 104 (SE)	1.9 (0.1)	1.9 (0.1)
Mean CfB at Week 104 (SE)	−1.8 (0.1)	−1.9 (0.1)
BASDAI [MI]		
Mean at baseline (SE)	6.8 (0.1)	6.5 (0.1)
Mean at Week 104 (SE)	2.9 (0.1)	2.6 (0.1)
Mean CfB at Week 104 (SE)	−4.0 (0.1)	−3.9 (0.1)
Total resolution of enthesitis[a] [NRI] n (%)	78 (41.9)[b]	106 (53.3)[c]
SPARCC MRI SIJ score [OC][d]		
Mean at baseline (SD)	8.8 (11.3)[e]	–
Mean at Week 104 (SD)	2.5 (4.2)[f]	–
Mean CfB at Week 104 (SD)	−5.4 (9.5)[f]	–
Berlin MRI spine score [OC][d]		
Mean at baseline (SD)	–	3.2 (4.4)[g]
Mean at Week 104 (SD)	–	1.6 (2.8)[f]
Mean CfB at Week 104 (SD)	–	−1.5 (3.9)[f]

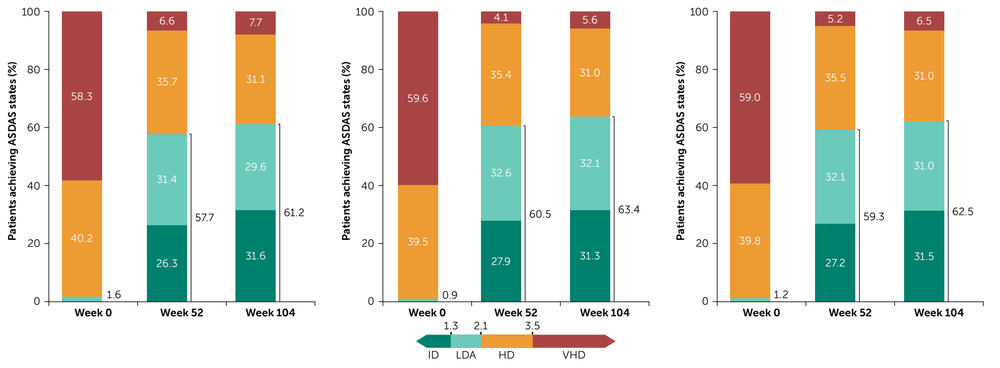
Randomised set. Includes patients originally randomised to placebo. [a] MASES=0 in patients with MASES >0 at baseline; [b] n=186; [c] n=199; [d] MRI sub-studies – SPARCC MRI SIJ data were collected for the nr-axSpA patient cohort to Week 104, Berlin MRI spine data were collected for the r-axSpA patient cohort to Week 104; [e] n=152; [f] n=95; [g] n=137.

Figure 1 Achievement of ASAS40 to 2 years (NRI, MI, OC)



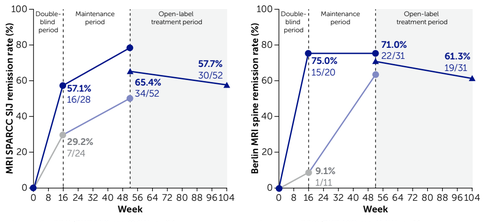
Randomised set; all patients treated with BKZ 160 mg Q4W from Week 16. Data reported using NRI and OC from Week 0–104, in addition to MI from Week 52–104. A dotted line is used to indicate entry into the combined open-label treatment period (BE MOVING) following Week 52 of BE MOBILE 1 and BE MOBILE 2. [a] Includes patients originally randomised to placebo.

Figure 2 ASDAS states over time (MI)



Randomised set. Patients treated with BKZ 160 mg Q4W; includes patients originally randomised to placebo. ASDAS LDA (<2.1) values shown next to bars are manually calculated from the sum of the proportion of patients achieving ASDAS <1.3 and ≥1.3–<2.1.

Figure 3 MRI remission (SPARCC <2; Berlin MRI spine ≤2) to 2 years (OC)



Only study participants enrolled in the SIJ and spine MRI sub-studies and with baseline MRI SIJ SPARCC (nr-axSpA) ≥2, or baseline Berlin MRI spine (r-axSpA) score >2 and with recorded data at each of the timepoints shown, are included in this analysis. MRI remission is defined as having a SPARCC <2 or Berlin MRI spine score ≤2. [a] Includes patients originally randomised to placebo.

Table 2 Safety overview to 2 years (Week 104)

	Any BKZ 160 mg Q4W[a]	
n (%) [EAIR/100 PY]	**Year 1 (N=574; 552 PY)**	**Year 2 (N=518; 478 PY)**
Any TEAE	451 (78.6) [196.4]	367 (70.8) [150.6]
Serious TEAEs	32 (5.6) [6.0]	28 (5.4) [6.0]
TEAEs leading to study discontinuation	21 (3.7) [3.9]	8 (1.5) [1.7]
Drug-related TEAEs[b]	226 (39.4) [57.3]	137 (26.4) [34.5]
Severe TEAEs	23 (4.0) [4.3]	16 (3.1) [3.4]
Death	0	0
Most frequently reported TEAEs by preferred term[c]		
SARS-CoV-2 (COVID-19) infection	35 (6.1) [6.5]	108 (20.8) [25.2]
Nasopharyngitis	61 (10.6) [11.9]	50 (9.7) [11.0]
Upper respiratory tract infection	47 (8.2) [9.0]	24 (4.6) [5.1]
Oral candidiasis	42 (7.3) [8.0]	25 (4.8) [5.4]
Key TEAEs of special monitoring		
Serious infections	10 (1.7) [1.8]	6 (1.2) [1.3]
Opportunistic infections	8 (1.4) [1.5]	4 (0.8) [0.8]
Active tuberculosis	0	0
Fungal infections	83 (14.5) [16.5]	53 (10.2) [11.8]
Candida infections	52 (9.1) [10.0]	31 (6.0) [6.8]
Neutropenia[d]	4 (0.7) [0.7]	4 (0.8) [0.8]
Hypersensitivity reactions[e]	64 (11.1) [12.4]	41 (7.9) [9.1]
Adjudicated suicidal ideation and behaviour	2 (0.3) [0.4]	0
Adjudicated MACE	0	0
Hepatic events	54 (9.4) [10.4]	22 (4.2) [4.7]
Liver function analyses	39 (6.8) [7.4]	19 (3.7) [4.1]
Malignancies	2 (0.3) [0.4]	2 (0.4) [0.4]
Adjudicated IBD (definite or probable)[f]	5 (0.9) [0.9]	4 (0.8) [0.8]
With prior history	1 (12.5) [13.7]	0
Without prior history	4 (0.7) [0.7]	4 (0.8) [0.9]
Uveitis[g,h]	14 (2.4) [2.6]	6 (1.2) [1.3]
With prior history	10 (10.5) [11.4]	6 (6.6) [7.2]
Without prior history	4 (0.8) [0.9]	0
Injection site reactions[i]	22 (3.8) [4.1]	4 (0.8) [0.8]

Safety set. Year 1: >0–52 weeks; Year 2: >52–104 weeks. MedDRA (Version 19.0). [a] Includes patients who switched from placebo to BKZ (events after switch only). [b] Per study investigator assessment. [c] Most common TEAEs in patients receiving BKZ are reported by preferred term. [d] Includes the preferred term neutropenia; [e] Most instances were dermatitis and eczema; there were no anaphylactic reactions to BKZ. [f] At baseline, 8/574 (1.4%) patients had a medical history of IBD. In Year 2 (>52 weeks), 7/518 (1.4%) patients had a medical history of IBD. [g] At baseline, 99/574 (16.6%) patients had a medical history of uveitis. In Year 2 (>52 weeks), 91/518 (17.6%) patients had a medical history of uveitis; [h] Includes the preferred terms autoimmune uveitis, uveitis, iridocyclitis and iritis; [i] Includes the high-level term injection site reactions.

ASAS: Assessment of SpondyloArthritis international Society; **ASAS40:** ASAS 40% response; **ASDAS:** Axial Spondyloarthritis Disease Activity Score; **axSpA:** axial spondyloarthritis; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BKZ:** bimekizumab; **CfB:** change from baseline; **EAIR:** exposure-adjusted incidence rate; **HD:** high disease; **hs-CRP:** high-sensitivity C-reactive protein; **IBD:** inflammatory bowel disease; **ID:** inactive disease; **LDA:** low disease activity; **MACE:** major adverse cardiovascular event; **MASES:** Maastricht Ankylosing Spondylitis Enthesitis Score; **MI:** multiple imputation; **MRI:** magnetic resonance imaging; **nr-axSpA:** non-radiographic axSpA; **NRI:** non-responder imputation; **OC:** observed case; **PBO:** placebo; **PY:** patient-years; **Q4W:** every 4 weeks; **r-axSpA:** radiographic axial spondyloarthritis; **SD:** standard deviation; **SE:** standard error; **SIJ:** sacroiliac joint; **SPARCC:** Spondyloarthritis Research Consortium of Canada; **TEAE:** treatment-emergent adverse event; **VHD:** very high disease.

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