Bimekizumab in Patients with Active Non-Radiographic Axial Spondyloarthritis: 24-Week Efficacy & Safety from BE MOBILE 1, a Phase 3, Multicentre, Randomised, Placebo-Controlled Study

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Objective

To assess efficacy and safety of subcutaneous bimekizumab (BKZ) vs placebo (PBO) in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) up to Week 24 in the ongoing pivotal phase 3 study, BE MOBILE 1.

Background

- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A. In a phase 2b study, BKZ showed rapid and sustained efficacy and was well tolerated up to 156 weeks in patients with active ankylosing spondylitis (AS).[1,2]
- Similarly, recent results from the ongoing BE MOBILE 2 phase 3 study demonstrate rapid, clinically meaningful improvements in efficacy outcomes in patients with active AS treated with BKZ vs PBO.[3]
- Here, we present the first results on the efficacy and safety of BKZ in patients with active nr-axSpA and objective signs of inflammation.

Methods

- BE MOBILE 1 (NCT03928704) is comprised of a 16-week double-blind, PBO-controlled period followed by a 36-week maintenance period **(Figure 1)**.
- At baseline, patients were randomised 1:1 to subcutaneous BKZ 160 mg or PBO every four weeks (Q4W); from Week 16, all patients received BKZ 160 mg Q4W.
- Primary and secondary efficacy endpoints were assessed at Week 16; selected endpoints are also presented in this analysis to Week 24 (randomised set).
- Treatment-emergent adverse events (TEAEs; MedDRA v19.0) are reported to Week 16 by treatment group, and to Week 24 for exposure to BKZ (safety set).

Results

Patients

- Of 254 randomised patients (BKZ: 128; PBO: 126), 244 (96.1%) completed Week 16 and 240 (94.5%) completed Week 24.
- Baseline characteristics were comparable between groups **(Table 1)**.

Efficacy

- At Week 16, the primary (ASAS40: 47.7% BKZ vs 21.4% PBO; p<0.001) and all ranked secondary endpoints were met (p<0.001), with rapid separation of the BKZ arm from PBO as early as Week 1 for ASAS40 **(Figure 2)**.
- Similar kinetics of response to Week 24 were observed in patients switching from PBO to BKZ at Week 16 **(Figure 2A)**.
- ASAS40 responses at Week 16 were consistent across both TNFi-naïve (46.6% BKZ vs 22.9% PBO) and TNFi-experienced (60.0% BKZ vs 11.8% PBO) patients.
- Substantial reductions of MRI SIJ inflammation by Week 16 and hs-CRP by Week 2 were achieved with BKZ vs PBO **(Figure 3)**.
- At Week 24, >50% of patients initially randomised to BKZ had achieved ASDAS <2.1 **(Figure 4)**.
- BKZ was associated with complete resolution of enthesitis (non-ranked secondary endpoint: MASES=0 in patients with baseline MASES >0, non-responder imputation), which was achieved by 51.1% of BKZ-treated patients vs 23.9% on PBO at Week 16.

Safety

- Up to Week 24, 124/244 (50.8%) patients had ≥1 TEAE on BKZ, including those who switched from PBO to BKZ at Week 16 **(Table 2)**.
- The most common TEAEs were upper respiratory tract infection, nasopharyngitis, pharyngitis and oral candidiasis. All cases of oral candidiasis were non-severe and non-systemic, and none led to study discontinuation.
- Up to Week 24 in patients on BKZ, incidence of serious TEAEs was low (0.4%). No IBD, active tuberculosis, MACE or deaths were reported, and incidence of uveitis was low (0.8%).

Conclusion

Dual inhibition of IL-17F in addition to IL-17A with BKZ in patients with active nr-axSpA resulted in rapid and clinically meaningful improvements of key signs and symptoms of disease and reduction of disease activity. Objective signs of inflammation, measured by CRP and MRI, were markedly reduced with BKZ, and no new safety signals were observed.[1,2]

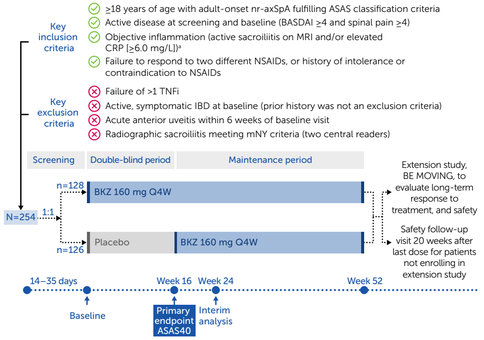
These findings, in combination with the phase 3 results of BKZ in active AS,[3] demonstrate the consistency of BKZ efficacy across the axSpA disease spectrum.

Summary

In patients with active nr-axSpA, subcutaneous BKZ 160 mg Q4W achieved the primary and all ranked secondary endpoints. BKZ resulted in clinically meaningful improvements in:

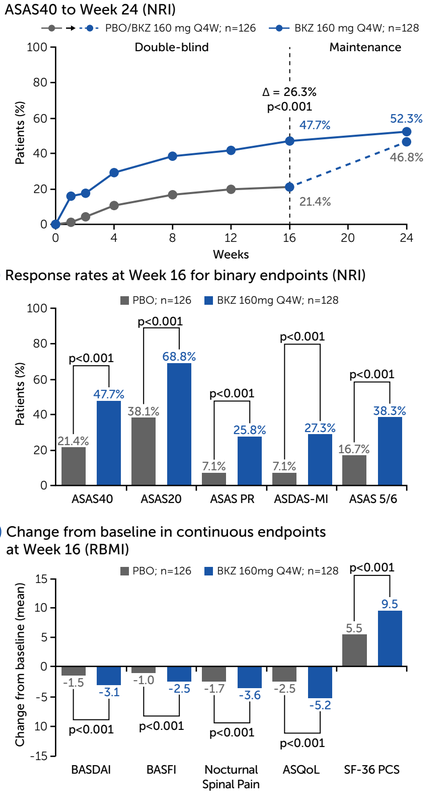
- **Signs and symptoms**: ASAS40, ASAS20, ASAS PR, ASAS 5/6, nocturnal spinal pain, MASES
- **Disease activity**: ASDAS, BASDAI, ASDAS-MI, ASDAS <2.1
- **Quality of life**: ASQoL, SF-36 PCS
- **Objective signs of inflammation**: SPARCC MRI SIJ score, hs-CRP
- **Physical function**: BASFI
- **Safety**: No new safety signals were observed

Figure 1 Study design



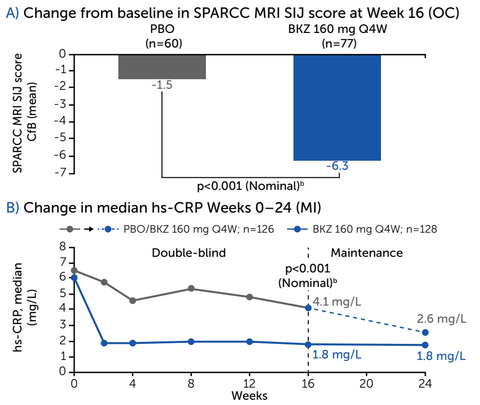
Enrolled patients were eligible to receive non-biologic rescue therapy from Week 20, at the discretion of the investigator, while continuing to receive BKZ. [a] Patients who are MRI negative must have elevated CRP and be HLA-B27 positive at screening.

Figure 2 Ranked primary and secondary efficacy endpoints[a]



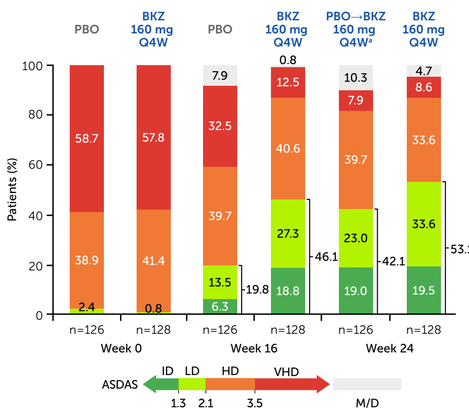
Randomised set. Missing data were imputed using non-responder imputation for binary endpoints and reference-based multiple imputation for continuous endpoints (based on data from the PBO group). [a] All tests performed at a 2-sided alpha level of 0.05 (for binary variables, p values were calculated by logistic regression with treatment, MRI/CRP classification and region as factors; for continuous variables, p values were obtained by ANCOVA with treatment, MRI/CRP classification and region as fixed effects, and baseline values as covariates).

Figure 3 Objective signs of inflammation[a]



Randomised set. MRI data are reported as observed case; for hs-CRP, missing data were imputed using multiple imputation (based on the missing at random assumption). SPARCC MRI SIJ score ranges from 0 to 72 with lower scores indicating less SIJ inflammation, and a negative change representing improvement. [a] Only patients enrolled in the MRI sub-study are included in this analysis; [b] Nominal p values were not controlled for multiplicity and were obtained by ANCOVA with treatment, MRI/CRP classification and region as fixed effects, and baseline values as covariates.

Figure 4 ASDAS states



Randomised set. Data reported as observed case. [a] At Week 16, patients on PBO switched to BKZ. VHD: ASDAS >3.5; HD: ASDAS ≥2.1–≤3.5; LD: ASDAS ≥1.3–<2.1; ID: ASDAS <1.3.

Table 1 Patient demographics and baseline characteristics

	PBO n=126	BKZ 160 mg Q4W n=128
Age, years, mean (SD)	39.4 (11.8)	39.5 (11.1)
Male, n (%)	65 (51.6%)	73 (57.0%)
HLA-B27 positive, n (%)	94 (74.6%)	103 (80.5%)
Symptom duration, years, mean (SD)	9.0 (9.0)	9.1 (8.7)
Time since first diagnosis, years, mean (SD)	3.6 (5.4)	3.7 (6.2)
MRI/CRP status,[a] n (%)		
MRI+/CRP+	39 (31.0%)	39 (30.5%)
MRI+/CRP–	56 (44.4%)	53 (41.4%)
MRI–/CRP+	31 (24.6%)	36 (28.1%)
ASDAS, mean (SD)	3.7 (0.7)	3.7 (0.8)
BASDAI, mean (SD)	6.7 (1.3)	6.9 (1.2)
hs-CRP, mg/L, median (min, max)	6.5 (0.1, 56.1)	6.1 (0.1, 79.1)
hs-CRP >ULN,[b] n (%)	71 (56.3%)	70 (54.7%)
Total spinal pain, mean (SD)	7.1 (1.6)	7.3 (1.5)
SPARCC MRI SIJ score,[c] mean (SD) [Nsub]	10.5 (13.8) [68]	8.5 (10.3) [79]
Patients with MASES >0, n (%)	92 (73.0%)	94 (73.4%)
Prior TNFi exposure, n (%)	17 (13.5%)	10 (7.8%)

Randomised set. [a] Patients categorised by the stratum to which they belong, which may differ from the stratum they were randomised to; [b] ULN value for hs-CRP is 5 mg/L; [c] Only patients enrolled in the MRI sub-study are included in this analysis.

Table 2 Safety overview

	Double-blind period (Weeks 0–16)		Overall (Weeks 0–24)
n (%)	PBO n=126	BKZ 160 mg Q4W n=128	BKZ 160 mg Q4W Total[a] N=244
Any TEAE	71 (56.3)	80 (62.5)	124 (50.8)
Most frequently reported TEAEs (>3%) by preferred term on BKZ			
Upper respiratory tract infection	9 (7.1)	9 (7.0)	17 (7.0)
Nasopharyngitis	6 (4.8)	12 (9.4)	16 (6.6)
Pharyngitis	1 (0.8)	4 (3.1)	7 (2.9)
Oral candidiasis[b]	0	4 (3.1)	7 (2.9)
Serious TEAEs	1 (0.8)	0	1 (0.4)
Discontinuation due to TEAEs	5 (4.0)	2 (1.6)	2 (0.8)[c]
Drug-related TEAEs	18 (14.3)	32 (25.0)	53 (21.7)
Severe TEAEs	1 (0.8)	0	1 (0.4)
Deaths	0	0	0
Adjudicated MACE	0	0	0
Adjudicated IBD[d]			
Definite ulcerative colitis	1 (0.8)	0	0
Uveitis[e,f]	6 (4.8)	2 (1.6)	2 (0.8)

Safety set. MedDRA (Version 19.0). [a] Includes patients who switched from PBO to BKZ (events after switch only); [b] All cases of oral candidiasis were non-severe and non-systemic, and none led to study discontinuation; [c] Of the 2 discontinuations from BKZ, 1 had neurological signs and symptoms NEC and 1 had psychiatric evaluation abnormal; [d] Definite or probable IBD reported, patient had no medical history of IBD; [e] At baseline, 21/126 (16.7%) patients on PBO and 19/128 (14.8%) patients on BKZ had a medical history of uveitis; [f] Includes the preferred terms uveitis, autoimmune uveitis, iridocyclitis and iritis.

ANCOVA: analysis of covariance; AS: ankylosing spondylitis; ASAS: Assessment in Spondyloarthritis international Society; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-MI: ASDAS major improvement; ASQoL: Ankylosing Spondylitis Quality of Life; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; BMI: body mass index; CfB: change from baseline; CI: confidence interval; CRP: C-reactive protein; HD: high disease; HLA-B27: human leukocyte antigen–B27; hs-CRP: high-sensitivity C-reactive protein; IBD: inflammatory bowel disease; ID: inactive disease; IL: interleukin; LD: low disease; MACE: major adverse cardiovascular event; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; MI: major improvement; MRI: magnetic resonance imaging; mNY: modified New York; M/D: missing data; n: number; NEC: not elsewhere classified; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; NSAID: non-steroidal anti-inflammatory drug; Nsub: number of patients in subgroup; OC: observed case; PBO: placebo; PCS: Physical Component Summary; PR: partial remission; PY: patient years; Q4W: every 4 weeks; RBMI: reference-based multiple imputation; SD: standard deviation; SF-36: Short-Form 36-item Health Survey; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada; TEAE: treatment-emergent adverse event; TNFi: tumour necrosis factor inhibitor; ULN: upper limit of normal; VHD: very high disease.

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