Bimekizumab Maintains Improvements in Efficacy Endpoints and has a Consistent Safety Profile Through 52 Weeks in Patients with Non-Radiographic Axial Spondyloarthritis and Ankylosing Spondylitis: Results from Two Parallel Phase 3 Studies

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Objective

To report efficacy and safety of bimekizumab (BKZ) in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) and ankylosing spondylitis (AS) up to Week 52 in the pivotal phase 3 studies, BE MOBILE 1 and 2, respectively.

Background

- BKZ, a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, met all primary and ranked secondary endpoints at Week 16 in patients with active nr-axSpA and AS (i.e. radiographic axSpA) in the phase 3 BE MOBILE 1 and 2 studies, respectively.[1,2]

Methods

- BE MOBILE 1 (NCT03928704; nr-axSpA) and 2 (NCT03928743; AS) were conducted in parallel; each comprised a 16-week double-blind, placebo (PBO)-controlled period followed by a 36-week maintenance period (**Figure 1**).
- Primary and secondary efficacy endpoints were assessed at Week 16, and are presented in this analysis to Week 52 (randomized set).
- Treatment-emergent adverse events (TEAEs; MedDRA v19.0) following first BKZ exposure are reported at the Week 52 data cut (safety set).

Results

Patients

- 220/254 (86.6%) randomized patients with nr-axSpA and 298/332 (89.8%) with AS completed Week 52.
- Baseline characteristics were reflective of patient population with moderate-to-severe nr-axSpA and AS (**Table 1**).

Efficacy

- In both studies, in BKZ-randomized patients, the primary and ranked secondary efficacy outcomes were sustained to Week 52 (**Table 2**); among patients who switched from PBO to BKZ at Week 16 (PBO/BKZ), efficacy at Week 52 was similar to that seen in BKZ-randomized patients.
  - ASAS40 responses in BKZ-randomized patients increased from Week 16 to Week 52 (**Figure 2**).
- ASAS40 responses at Week 52 were consistent across both TNFi-naïve and TNFi-inadequate responder populations (**Table 2**).
- At Week 52, ASDAS <2.1 was achieved by >50% of BKZ-randomized patients with nr-axSpA and AS (**Figure 3**).
- The Week 16 reductions from baseline in objective signs of inflammation (MRI, hs-CRP; **Figure 4**), and improvements in function (BASFI), and AS Quality-of-Life, were maintained through 52 Weeks.
- Complete resolution of enthesitis (MASES=0 in patients with baseline MASES >0, NRI) at Week 52 was achieved by 54.3% and 50.8% of BKZ vs 44.6% and 46.3% PBO/BKZ-treated patients with nr-axSpA and AS, respectively.

Safety

- At the Week 52 data cut, 75.0% (183/244) of patients with nr-axSpA and 75.5% (249/330) of patients with AS had ≥1 TEAE with BKZ exposure; including those who switched from PBO to BKZ at Week 16 (**Table 3**).
- The most frequent TEAEs were nasopharyngitis, upper respiratory tract infection and oral candidiasis.
- Most incidences of fungal infection were *candidiasis* and mild to moderate (none were serious or systemic); two patients with nr-axSpA and two with AS discontinued the study due to *Candida* infections.
- Few COVID-19 infections were reported (nr-axspA: 7.0%; AS: 2.1%); none were serious.
- No major adverse cardiovascular events, active tuberculosis cases, or deaths were reported. Incidence of inflammatory bowel disease and uveitis were low (**Table 3**).

Summary

- In patients with active non-radiographic axial spondyloarthritis and ankylosing spondylitis respectively, subcutaneous bimekizumab 160 mg Q4W:
  - Achieved the primary and all ranked secondary endpoints at Week 16.
  - Showed sustained efficacy to Week 52.
- Bimekizumab resulted in clinically meaningful and sustained improvements in:

Disease activity
ASDAS, ASDAS-MI, ASDAS <2.1, BASDAI

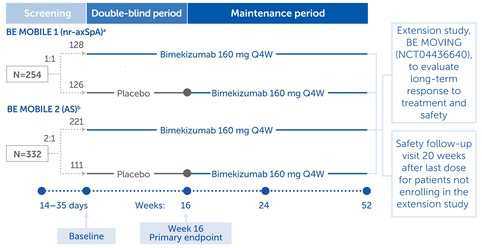
Objective signs of inflammation
SPARCC MRI SIJ score, hs-CRP, Berlin MRI spine score

Signs and symptoms
ASAS40, ASAS40 in TNFi-naïve patients, ASAS20, ASAS 5/6, ASAS PR, nocturnal spinal pain, MASES (enthesitis)

Safety
No new safety signals were observed

Mobility, physical function and HRQoL
BASMI, BASFI, SF-36 PCS, ASQoL

Figure 1 BE MOBILE 1 and 2 study designs



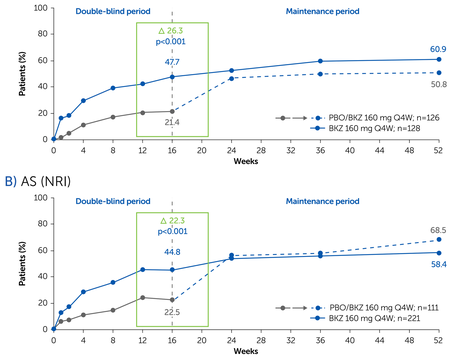
Patients were eligible to receive non-biologic rescue therapy from Week 20 at the discretion of the investigator, while continuing to receive BKZ. All patients had active nr-axSpA or AS at baseline (BASDAI ≥4 and spinal pain ≥4). [a]Included patients had adult-onset nr-axSpA fulfilling ASAS classification criteria and objective signs of inflammation (active sacroiliitis on MRI and/or elevated CRP (≥6 mg/L)). [b]Included patients had radiographic evidence of AS fulfilling Modified New York criteria.

Table 1 Baseline characteristics

	BE MOBILE 1 (nr-axSpA) N=254	BE MOBILE 2 (AS) N=332
Age, mean (SD)	39.4 (11.5)	40.4 (12.3)
Sex, male, n (%)	138 (54.3)	240 (72.3)
HLA-B27 positive, n (%)	197 (77.6)	284 (85.5)
Symptom duration, years, mean (SD)	9.0 (8.8)	13.5 (10.3)
Time since first diagnosis of nr-axSpA/AS, years, mean (SD)	3.6 (5.8)	6.4 (7.9)
ASDAS, mean (SD)	3.7 (0.7)	3.7 (0.8)[a]
BASDAI, mean (SD)	6.8 (1.3)	6.5 (1.3)
hs-CRP, mg/L, median (min, max)	6.3 (0.1, 79.1)	7.4 (0.1, 105.4)
hs-CRP >ULN,[b] n (%)	141 (55.5)	204 (61.4)
Total spinal pain score, mean (SD)	7.2 (1.5)	7.2 (1.5)
BASFI, mean (SD)	5.4 (2.3)	5.2 (2.1)
Prior TNFi exposure, n (%)	27 (10.6)	54 (16.3)

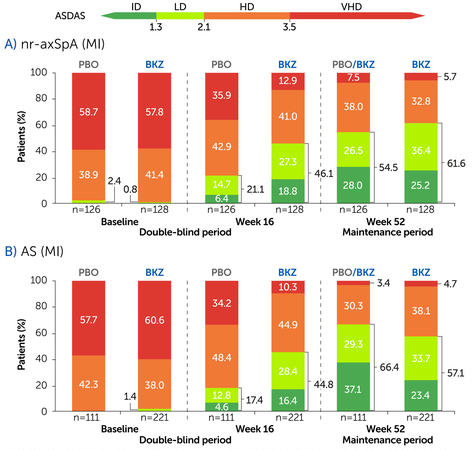
Randomized set. [a]n=333; [b]ULN value for hs-CRP is 5 mg/L.

Figure 2 ASAS40 to Week 52



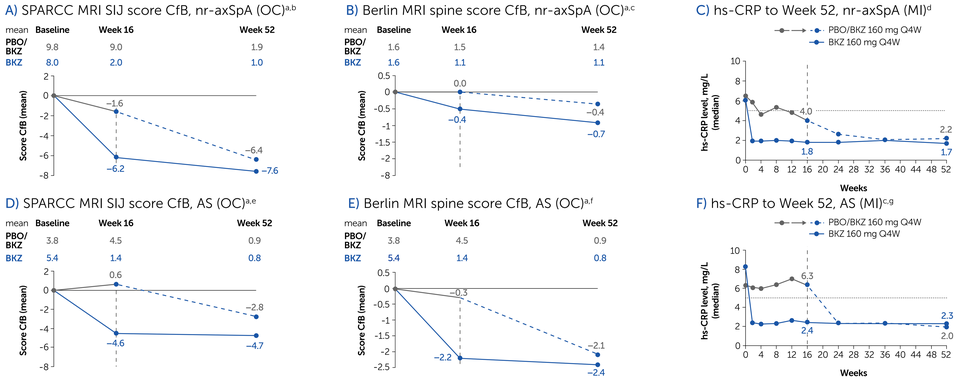
Randomized set. Missing data were imputed using NRI. p values were calculated using logistic regression with treatment, prior MRI/CRP status (BE MOBILE 1) or TNFi exposure (BE MOBILE 2), and region as factors.

Figure 3 ASDAS states over time



Randomized set. Data reported using MI where patients that discontinued treatment due to loss of efficacy or safety were considered as non-responders. 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.

Figure 4 Objective signs of inflammation



Randomized set. Data reported using OC (SPARCC MRI SIJ; Berlin MRI spine score) or MI (hs-CRP), where patients that discontinued treatment due to loss of efficacy or safety were considered as non-responders. Tables report mean absolute values. [a]Only includes pts enrolled in the SIJ and spine MRI sub-study. [b]At baseline n=70 (PBO/BKZ), n=82 (BKZ); [c]At baseline n=67 (PBO/BKZ), n=79 (BKZ); [d]n=126 (PBO/BKZ), n=128 (BKZ); [e]At baseline n=48 (PBO/BKZ), n=90 (BKZ); [f]At baseline n=48 (PBO/BKZ), n=89 (BKZ); [g]n=111 (PBO/BKZ), n=221 (BKZ).

Table 2 Efficacy endpoints at Week 52

	BE MOBILE 1 (nr-axSpA)		BE MOBILE 2 (AS)	
	Week 52		Week 52	
	PBO→BKZ 160 mg Q4W N=126	BKZ 160 mg Q4W N=128	PBO→BKZ 160 mg Q4W N=111	BKZ 160 mg Q4W N=221
ASAS40[a] [NRI], n (%)	64 (50.8)	78 (60.9)	76 (68.5)	129 (58.4)
ASAS40 in TNFi-naïve[i] [NRI], n (%)	58 (53.2)[a]	73 (61.9)[b]	67 (71.3)[c]	108 (58.7)[d]
ASAS40 in TNFi-IR[e] [NRI], n (%)	6 (35.3)[f]	5 (50.0)[g]	9 (52.9)[f]	21 (56.8)[h]
ASAS20[b] [NRI], n (%)	88 (69.8)	94 (73.4)	89 (80.2)	158 (71.5)
ASAS PR[c] [NRI], n (%)	38 (30.2)	38 (29.7)	41 (36.9)	66 (29.9)
ASAS 5/6[d] [NRI], n (%)	65 (51.6)	71 (55.5)	74 (66.7)	124 (56.1)
BASDAI CfB[e] [MI], mean (SE)	−3.5 (0.2)	−3.9 (0.2)	−4.0 (0.2)	−3.6 (0.1)
BASFI CfB[e] [MI], mean (SE)	−2.6 (0.2)	−3.0 (0.2)	−2.8 (0.2)	−2.8 (0.1)
ASDAS-MI[e] [NRI], n (%)	37 (29.4)	47 (36.7)	49 (44.1)	71 (32.1)
ASDAS-CRP CfB [MI], mean (SE)	−1.6 (0.1)	−1.8 (0.1)	−1.9 (0.1)	−1.7 (0.1)
Nocturnal spinal pain CfB[e] [MI], mean (SE)	−4.1 (0.2)	−4.3 (0.3)	−4.6 (0.3)	−4.1 (0.2)
ASQoL CfB[e] [MI], mean (SE)	−5.3 (0.4)	−5.9 (0.4)	−5.6 (0.4)	−5.7 (0.3)
SF-36 PCS CfB[e] [MI], mean (SE)	11.4 (0.9)	12.2 (0.9)	12.3 (0.9)	12.0 (0.6)
BASMI CfB[e] [MI], mean (SE)	−0.4 (0.1)	−0.6 (0.1)	−0.7 (0.1)	−0.7 (0.1)

Randomized set. *Primary endpoint; †Secondary endpoint in BE MOBILE 1; ‡Secondary endpoint in BE MOBILE 2. Missing data were imputed using NRI for binary endpoints and MI (based on the missing at random assumption) for all continuous endpoints, for which a reference-based MI approach was applied for the Week 16 timepoint (based on data from the placebo group). [a]n=109; [b]n=118; [c]n=94; [d]n=184. [e]Patients received maximum of one TNFi; [f]n=17; [g]n=10; [h]n=37.

Table 3 Safety overview

n (%) [EAIR]	BE MOBILE 1 (nr-axSpA) BKZ 160 mg Q4W Total[a] n=244	BE MOBILE 2 (AS) BKZ 160 mg Q4W Total[a] n=330
Any TEAE	183 (75.0) [202.1]	249 (75.5) [200.8]
Most frequently reported TEAEs[b]		
Nasopharyngitis	30 (12.3) [15.7]	30 (9.1) [11.0]
Upper respiratory tract infection	23 (9.4) [11.9]	21 (6.4) [7.5]
Oral candidiasis	18 (7.4) [9.0]	20 (6.1) [7.2]
Severe TEAEs	8 (3.3)	14 (4.2)
Serious TEAEs[c]	9 (3.7) [4.4]	20 (6.1) [7.1]
Study discontinuation due to TEAEs	6 (2.5) [2.9]	15 (4.5) [5.2]
Drug-related TEAEs	81 (33.2)	135 (40.9)
Any fungal infections	37 (15.2) [19.6]	40 (12.1) [14.9]
Adjudicated IBD[d]	2 (0.8) [1.0]	3 (0.9) [1.0]
Crohn's disease	1 (0.4) [0.5]	2 (0.6) [0.7]
Ulcerative colitis	1 (0.4) [0.5]	1 (0.3) [0.3]
Uveitis event[e,f]	3 (1.2) [1.5]	7 (2.1) [2.4]

Safety set. MedDRA (Version 19.0). [a]Includes patients who switched from PBO to BKZ (events after switch only); [b]TEAEs >5% in patients receiving BKZ are reported by preferred term; [c]Includes TEAEs that are fatal; life threatening; requiring in-patient hospitalisation or prolongation of existing hospitalisation; resulting in persistent or significant disability or incapacity; or any other medically important serious event. [d]At baseline, 4/244 (1.6%) patients with nr-axSpA, and 4/330 (1.2%) patients with AS had a medical history of IBD; [e]At baseline, 39/244 (16.0%) patients with nr-axSpA and 56/330 (17.0%) patients with AS had a medical history of uveitis; [f]Includes the preferred terms autoimmune uveitis, uveitis, iridocyclitis and iritis.

Conclusions

Across the full axSpA disease spectrum, dual inhibition of IL-17F in addition to IL-17A with bimekizumab resulted in sustained efficacy, including suppression of inflammation and improvements in function and quality of life, to Week 52. No new safety signals were observed, consistent with the safety profile established in prior studies.[3,4]

AS: ankylosing spondylitis; **ASAS20/40:** Assessment of SpondyloArthritis international Society 20/40 response; **ASAS 5/6:** ASAS 5/6 response; **ASAS PR:** ASAS partial remission; **ASDAS-CRP:** Ankylosing Spondylitis Disease Activity Score C-reactive protein; **ASDAS-MI:** ASDAS major improvement; **ASQoL:** Ankylosing Spondylitis Quality of Life; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BASFI:** Bath Ankylosing Spondylitis Functional Index; **BASMI:** Bath Ankylosing Spondylitis Metrology Index. **BKZ:** bimekizumab; **CfB:** change from baseline; **CRP:** C-reactive protein; **EAIR:** exposure adjusted incidence rate; **HLA-B27:** human leukocyte antigen B27; **hs-CRP:** high sensitivity-C-reactive protein; **IR:** inadequate responders; **MASES:** Maastricht Ankylosing Spondylitis Enthesitis Score; **MI:** multiple imputation; **MRI:** magnetic resonance imaging; **n:** number; **nr-axSpA:** non-radiographic axial spondyloarthritis; **NRI:** non-responder imputation; **OC:** observed case; **PBO:** placebo; **pts:** patients; **Q4W:** every four weeks; **SE:** standard error; **SF-36 PCS:** Short Form-36 Physical Component Summary; **SIJ:** Sacroiliac Joints; **SPARCC:** Spondyloarthritis Research Consortium of Canada; **TNFi:** tumor necrosis factor inhibitor; **ULN:** upper limit of normal.

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