Bimekizumab Achieved Sustained Improvements in Efficacy Outcomes in Patients with Axial Spondyloarthritis, Regardless of Prior TNF Inhibitor Treatment: Week 52 Pooled Results from Two Phase 3 Studies

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Objective

To report the efficacy of bimekizumab (BKZ) over multiple efficacy endpoints to Week 52 in tumor necrosis factor inhibitor (TNFi)-naïve or -inadequate responder (IR) patients across the full disease spectrum of axial spondyloarthritis (axSpA), pooled across two phase 3 studies.

Background

- In patients with non-radiographic (nr-) axSpA and radiographic (r-) axSpA (i.e., ankylosing spondyloarthritis),[1] TNFis are commonly used as a first-line biologic treatment.
- However, many patients experience loss of response over time, and some patients have intolerance or contraindication to TNFis.[2] Efficacy of second-line biologics is typically limited in TNFi-IRs compared with TNFi-naïve patients.[3]
- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- In the phase 3 BE MOBILE 1 and 2 studies, BKZ demonstrated efficacy across the disease spectrum of axSpA and ASAS40 responses at Week 52 were similar in TNFi-naïve and TNFi-IR patients receiving BKZ.[4]

Materials and Methods

- The parallel BE MOBILE 1 (nr-axSpA; NCT03928704) and 2 (r-axSpA; NCT03928743) studies each comprised a 16-week double-blind, placebo-controlled period followed by a 36-week maintenance period (**Figure 1**).[4]
- This post hoc analysis reports pooled efficacy data, through Week 52, stratified by prior TNFi exposure (naive or IR, i.e., those who have experienced loss of efficacy, contraindication or intolerance to TNFi treatment). Only one prior TNFi use was permitted per patient.
  - From Week 16, data reported only for patients continuously treated with BKZ.
- Data are reported with non-responder imputation, observed case methodology, or multiple imputation.
- Treatment-emergent adverse events (TEAEs; MedDRA v19.0) in BKZ-randomized TNFi-naïve and TNFi-IR patients are reported to Week 52 for patients who had received at least one dose of BKZ.

Results

Patients

- This pooled analysis included 505 TNFi-naïve (nr-axSpA: 227; r-axSpA: 278) and 81 TNFi-IR (nr-axSpA: 27; r-axSpA: 54) patients.
  - 302 (59.8%) TNFi-naive and 47 (58.0%) TNFi-IR patients were randomized to BKZ.
- Baseline characteristics are shown in **Table 1**.

Efficacy

- At Week 16, the proportion of patients achieving ASAS40 and ASDAS low disease activity (<2.1) was higher in BKZ-randomized vs placebo-randomized patients, regardless of prior TNFi exposure (**Figure 2**, **Figure 3**).
  - Responses in continuous BKZ-treated patients increased to Week 52.
- Substantial reductions from baseline in BASDAI and MRI inflammation in the sacroiliac joints and spine were also achieved with BKZ vs placebo in both TNFi-naïve and TNFi-IR patients at Week 16; in continuous BKZ-treated patients, this was sustained or further improved at Week 52 (**Table 2**).
- Comparable improvements in physical functioning (BASFI), nocturnal spinal pain, and health-related quality of life (ASQoL) were observed through 52 weeks with BKZ in TNFi-naïve and TNFi-IR patients (**Table 2**).

Safety

- From baseline to Week 52, exposure-adjusted incidence rates (EAIRs) per 100 patient years (PY) for any TEAEs were 197.8 and 233.6 for TNFi-naïve and TNFi-IR patients who received at least one dose of BKZ, respectively. No deaths occurred (**Table 3**).
- Most frequently reported TEAEs were nasopharyngitis, upper respiratory tract and oral candidiasis for both subgroups.

Conclusions

Across the full disease spectrum of axSpA, bimekizumab treatment resulted in clinically relevant improvements in signs and symptoms, disease activity, suppression of inflammation, physical functioning and health-related quality of life. These improvements were seen regardless of prior TNFi exposure and sustained to Week 52. Similar results have been demonstrated in phase 3 studies of bimekizumab in psoriatic arthritis.[5]

Summary

In patients with axSpA, bimekizumab treatment resulted in clinically relevant improvements, regardless of prior TNFi-exposure, in:

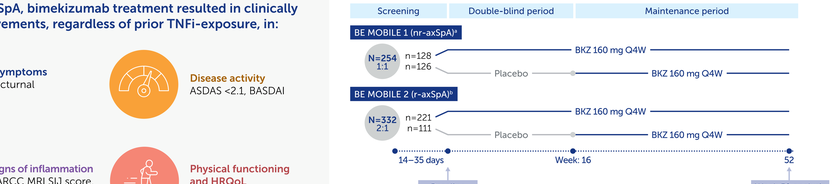
Signs and symptoms
ASAS40, nocturnal spinal pain

Disease activity
ASDAS <2.1, BASDAI

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

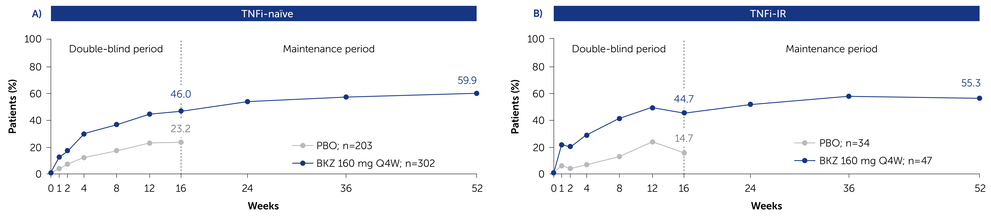
Physical functioning and HRQoL
BASFI, ASQoL

Figure 1 BE MOBILE 1 and 2 study designs



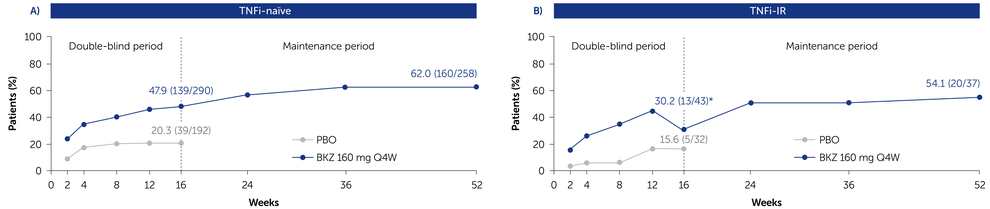
Patients were eligible to receive non-biologic rescue therapy from Week 20 at the discretion of the investigator, while continuing to receive BKZ. All patients had active nr-axSpA or r-axSpA at baseline (BASDAI ≥4 and spinal pain ≥4). [a] Included patients had adult-onset nr-axSpA fulfilling ASAS classification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

Figure 2 Achievement of ASAS40 over 52 weeks in pooled TNFi-naïve and TNFi-IR patients from BE MOBILE 1 and 2 (NRI)



Data are pooled from BE MOBILE 1 and 2. Data from PBO-randomized patients not included from Week 16 onwards.

Figure 3 Achievement of ASDAS <2.1 (low disease activity) over 52 weeks in pooled TNFi-naïve and TNFi-IR patients from BE MOBILE 1 and 2 (OC)



Data are pooled from BE MOBILE 1 and 2. ***In Figure 3B, 7 continuously BKZ-treated patients were identified as being responders at Week 12 and non-responders at Week 16; all were male and the 6 patients were patients with r-axSpA. Of these 7 patients, the 6 patients with r-axSpA all achieved ASDAS<2.1 again at Week 24.** All ASDAS differences in these patients between Week 12 and Week 16 were less than 1. Data from PBO-randomized patients not included from Week 16 onwards.

Table 1 Pooled baseline characteristics across BE MOBILE 1 and 2 in TNFi-naïve and TNFi-IR patients

	TNFi-naïve		TNFi-IR	
Mean (SD), unless otherwise specified	PBO n=203	**BKZ 160 mg Q4W n=302**	PBO n=34	**BKZ 160 mg Q4W n=47**
Age, years	38.4 (12.2)	40.4 (11.7)	44.7 (10.5)	40.7 (12.8)
Male, n (%)	126 (62.1)	200 (66.2)	19 (55.9)	33 (70.2)
HLA-B27 positive, n (%)	159 (78.3)	252 (83.4)	28 (82.4)	42 (89.4)
r-axSpA, n (%)	94 (46.3)	184 (60.9)	17 (50.0)	37 (78.7)
Disease duration ≥2 years, n (%)	86 (42.4)	141 (46.7)	31 (91.2)	42 (89.4)
ASDAS	3.7 (0.7)	3.7 (0.8)[a]	3.8 (0.7)	3.9 (0.8)
BASDAI	6.5 (1.3)	6.6 (1.3)	6.9 (1.3)	6.6 (1.3)
BASFI	5.2 (2.1)	5.4 (2.2)	5.6 (2.5)	5.4 (2.2)
hs-CRP, mg/L, geometric mean (geometric CV, %)	5.8 (212.3)	5.4 (285.2)	5.4 (250.8)	8.8 (269.5)
hs-CRP >ULN,[a] n (%)	120 (59.1)	174 (57.6)	18 (52.9)	33 (70.2)
Total spinal pain	7.1 (1.4)	7.2 (1.6)	7.5 (1.4)	7.1 (1.4)
ASQoL, mean (SE)	8.8 (0.3)	9.4 (0.3)	10.0 (0.7)	7.8 (0.6)
MRI SIJ SPARCC[b]	8.0 (11.4)[d]	6.5 (8.7)[e]	3.9 (6.5)[f]	8.5 (13.4)[g]
MRI spine Berlin[c]	2.1 (3.3)[h]	2.5 (4.0)[i]	3.2 (5.0)[j]	1.9 (2.2)[k]
Concomitant medication use, n (%)				
NSAIDs	152 (74.9)	238 (78.8)	26 (76.5)	39 (83.0)
csDMARDs	46 (22.7)	63 (20.9)	5 (14.7)	13 (27.7)
Oral corticosteroids	21 (10.3)	21 (7.0)	1 (2.9)	1 (2.1)

Data are pooled from BE MOBILE 1 and 2. [a] ULN value for hs-CRP is 5 mg/L; [b] n=301; [c] Only patients enrolled in the SIJ and spine MRI substudy and with ≥1 post-baseline record for the respective variable are included; [d] n=100; [e] n=152; [f] n=15; [g] n=18; [h] n=99; [i] n=148; [j] n=14.

Table 2 Change from baseline in pooled efficacy endpoints across BE MOBILE 1 and 2 in TNFi-naïve and TNFi-IR patients at Week 16 and 52 (MI and OC)

	Week 16						Week 52	
	TNFi-naïve			TNFi-IR			TNFi-naïve	TNFi-IR
CfB [MI], mean (SE), unless otherwise specified	PBO n=203	**BKZ 160 mg Q4W n=302**	**Δ**	PBO n=34	**BKZ 160 mg Q4W n=47**	**Δ**	**BKZ 160 mg Q4W n=302**	**BKZ 160 mg Q4W n=47**
ASDAS	−0.7 (0.1)	−1.5 (0.1)	0.8	−0.6 (0.1)	−1.6 (0.1)	1.0	−1.8 (0.1)	−1.9 (0.2)
BASDAI	−1.7 (0.1)	−3.0 (0.1)	1.3	−1.6 (0.4)	−2.7 (0.3)	1.1	−3.6 (0.1)	−3.7 (0.3)
BASFI	−1.1 (0.1)	−2.3 (0.1)	1.2	−0.5 (0.3)	−2.2 (0.3)	1.7	−2.8 (0.1)	−2.9 (0.3)
MRI SIJ SPARCC (OC),[a] mean (SD)	−0.9 (7.3)[b]	−5.3 (8.4)[c]	4.4	1.4 (6.0)[d]	−5.6 (13.4)[e]	4.2	−5.9 (9.1)[f]	−6.9 (12.2)[e]
MRI spine Berlin (OC),[a] mean (SD)	−0.2 (1.5)[g]	−1.4 (3.2)[h]	1.2	0.4 (1.3)[i]	−0.5 (1.9)[e]	0.9	−1.7 (3.6)[j]	−1.2 (2.1)[e]
Nocturnal spinal pain	−1.7 (0.2)	−3.4 (0.2)	1.7	−2.1 (0.5)	−3.3 (0.3)	1.2	−4.1 (0.2)	−3.9 (0.3)
ASQoL	−2.8 (0.3)	−5.1 (0.3)	2.3	−4.2 (0.6)	−5.8 (0.3)	1.8	−5.8 (0.3)	−4.7 (0.6)

Data are pooled from BE MOBILE 1 and 2. Week 52 data shown only for continuous BKZ patients. [a] Only patients enrolled in the SIJ and spine MRI substudy and with ≥1 post-baseline record for the respective variable are included; [b] n=95; [c] n=144; [d] n=13; [e] n=15; [f] n=130; [g] n=94; [h] n=140; [i] n=12; [j] n=127.

Table 3 Pooled safety overview to Week 52 across BE MOBILE 1 and 2 in TNFi-naïve and TNFi-IR patients

System Organ Class **High Level Term** **Preferred Term** **n (%) [EAIR/100 PY]**	**TNFi-naïve[a]** **BKZ 160 mg Q4W n=495 (432 PY)**	**TNFi-IR[a]** **BKZ 160 mg Q4W n=79 (68 PY)**
Any TEAEs	373 (75.4) [197.8]	61 (77.2) [233.6]
Severe TEAEs	21 (4.2)	3 (3.8)
Study discontinuation due to TEAEs	16 (3.2)	5 (6.3)
Drug-related TEAEs	185 (37.4)	33 (41.8)
Serious TEAEs[b]	24 (4.8)	6 (7.6)
Deaths	0	0
Most frequently reported TEAEs (>5%) by preferred term[c]		
Nasopharyngitis	48 (9.7) [11.9]	12 (15.2) [19.6]
Upper respiratory tract infection	38 (7.7) [9.3]	6 (7.6) [9.3]
Oral candidiasis	33 (6.7) [8.0]	5 (6.3) [7.7]
Headache	28 (5.7) [6.8]	4 (5.1) [6.0]
TEAEs of special monitoring		
Fungal infections[d]	74 (14.9)	9 (11.4)
Colitis (excluding infective)		
Crohn's disease	2 (0.4) [0.5]	0
Ulcerative colitis	2 (0.4) [0.5]	0
Colitis	0	1 (1.3) [1.5]
Uveitis[e]	7 (1.4) [1.6]	3 (3.8) [4.6]

MedDRA (Version 19.0). n is the number of patients reporting at least one TEAE in that category. [a] Data reported for both BKZ-randomized patients and patients who had switched from PBO to BKZ at Week 16 and who received at least one dose of BKZ; [b] Includes TEAEs that were fatal, life threatening, required in-patient hospitalisation or prolongation of existing hospitalisation resulting in persistent or significant disability or incapacity; or any other medically important serious event; [c] >5% in both TNFi-naive and TNFi-IR patients only; [d] Calculated as the sum of patients reporting at least one TEAE within the high level terms *Candida* infections, *Tinea* infections and fungal infections not elsewhere classified; [e] Includes the preferred terms uveitis, autoimmune uveitis, iridocyclitis and iritis.

ASAS40: Assessment of SpondyloArthritis international Society 40 response; **ASDAS:** Ankylosing Spondylitis Disease Activity Score; **ASQoL:** Ankylosing Spondylitis Quality of Life; **axSpA:** axial spondyloarthritis; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BASFI:** Bath Ankylosing Spondylitis Functional Index; **BKZ:** bimekizumab; **CfB:** change from baseline; **CRP:** C-reactive protein; **csDMARD:** conventional synthetic disease-modifying antirheumatic drug; **CV:** coefficient of variation; **EAIR:** exposure-adjusted incidence rate; **IL:** interleukin; **HLA-B27:** human leukocyte antigen B27; **HRQoL:** health-related quality of life; **hs-CRP:** high sensitivity CRP; **IBD:** inflammatory bowel disease; **IR:** inadequate responder; **LDA:** low disease activity; **MI:** multiple imputation; **MRI:** magnetic resonance imaging; **n:** number; **nr-axSpA:** non-radiographic axSpA; **NRI:** non-responder imputation; **NSAID:** non-steroidal anti-inflammatory drug; **OC:** observed case; **PBO:** placebo; **PY:** patient years; **Q4W:** every four weeks; **r-axSpA:** radiographic axSpA; **SD:** standard deviation; **SE:** standard error; **SIJ:** sacroiliac joints; **SPARCC:** SpondyloArthritis Research Consortium of Canada; **TEAE:** treatment-emergent adverse event; **TNFi:** tumor necrosis factor inhibitor; **ULN:** upper limit of normal.

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