Minimal Spinal Radiographic Progression in Patients with Radiographic Axial Spondyloarthritis Over 2 Years of Bimekizumab Treatment: Results from a Phase 3 Open-Label Extension Study

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Objective

To evaluate the impact of bimekizumab (BKZ) treatment on spinal radiographic progression and new syndesmophyte formation in patients with radiographic axial spondyloarthritis (r-axSpA) at 2 years in the open-label extension (OLE) of the phase 3 BE MOBILE 2 study.

Background

- Pre-clinical data suggest that dual inhibition of interleukin (IL)-17A and IL-17F may have stronger inhibitory effects on new bone formation in axSpA versus IL-17A inhibition alone.[1]
- BKZ, a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has demonstrated consistent and sustained efficacy to 2 years in patients with non-radiographic (nr)-axSpA and r-axSpA in the parallel phase 3 studies BE MOBILE 1 and BE MOBILE 2, respectively, and their combined OLE.[2,3]
- BKZ has also demonstrated long-term sustained efficacy in patients with r-axSpA up to 5 years.[4]
- The impact of BKZ on structural progression in the spine, as assessed by radiography, has not been previously reported in patients with r-axSpA.

Methods

- The BE MOBILE 2 (r-axSpA; NCT03928743) study comprised a 16-week double-blind period followed by a 36-week maintenance period.[5] At Week 52, eligible patients could enrol in an ongoing OLE (NCT04436640) to receive subcutaneous BKZ 160 mg every 4 weeks (Q4W).
- Spinal radiographs were taken at baseline and Week 104, with spinal radiographic progression assessed using modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS).
- At both timepoints, 2 central readers were used, with an adjudicator if change scores differed by ≥5 mSASSS points; all readers were blinded to timepoint. The average of change scores across readers was determined for each radiograph; if 3 readers were used, an average of the 2 closest change scores was calculated.
- Mean and cumulative probability of change from baseline (CfB) in mSASSS at Week 104, the proportion of non-progressors (using definitions mSASSS CfB ≤0.5 and mSASSS CfB <2), and the number of patients with new syndesmophytes are reported.
- Potential predictive factors for spinal radiographic progression (mSASSS CfB ≥2) at Week 104 were assessed using logistic regression models.

Results

Patient Disposition

- Of 332 patients randomised in BE MOBILE 2, 286 (86.1%) entered the OLE and 267 (80.4%) completed Week 104.
  - Of these, 71.9% (192/267) of patients were male and 16.1% (43/267) were tumour necrosis factor inhibitor (TNFi)-inadequate responders (**Table 1**).
- At Week 104, 71.2% (190/267) of patients with r-axSpA had an mSASSS available.

Radiographic Progression

- The mean (standard deviation [SD]) mSASSS score at baseline was 7.3 (13.8); CfB at Week 104 was 0.3 (1.9); the majority (157/190) of patients had no spinal radiographic progression at Week 104 (**Figure 1**).
- The proportion of non-progressors at Week 104, defined as mSASSS CfB ≤0.5, was 85.3% (162/190). The proportion of non-progressors at Week 104, defined as mSASSS CfB <2, was 92.1% (175/190; **Figure 2**).
- Non-White race (comprising Asian, Black, and Other) and negative HLA-B27 status were associated with a significantly increased likelihood of spinal radiographic progression (mSASSS CfB ≥2) at Week 104 in the univariable model (**Table 2**).

Syndesmophytes

- At baseline, 30.0% (57/190) of patients had syndesmophytes; at Week 104, just one-fifth of these patients had new syndesmophytes. Of the patients with no syndesmophytes at baseline, 1.5% (2/133) had new syndesmophytes at Week 104 (**Figure 3**).

Conclusions

After 2 years of treatment with bimekizumab, patients with r-axSpA showed minimal spinal radiographic progression, and a high proportion were non-progressors, including in those with baseline spinal damage. New syndesmophyte formation was limited in patients treated with bimekizumab, and primarily occurred in patients with existing syndesmophytes at baseline.

These findings suggest that bimekizumab may have a positive impact on spinal progression and irreversible damage in patients with r-axSpA.

Summary

In patients with r-axSpA, dual inhibition of **IL-17A and IL-17F** with **bimekizumab** resulted in the following:

Minimal spinal radiographic progression

Mean mSASSS CfB: **0.3**

A high proportion of non-progressors

mSASSS CfB <2: **92.1%** of patients

Limited new syndesmophyte formation

98.5% of patients had no new syndesmophytes[a]

These findings suggest that bimekizumab may have a positive impact on spinal progression and irreversible damage in patients with r-axSpA

(a) In patients without syndesmophytes at baseline.

Table 1 Baseline characteristics

Mean (SD), unless otherwise specified	Completed Week 104 n=267	X-ray population[a] n=190
Age, years	40.4 (12.3)	39.8 (11.9)
Sex, male, n (%)	192 (71.9)	135 (71.1)
BMI, kg/m^2	27.1 (5.9)	26.7 (5.6)
Race, White, n (%)	221 (82.8)[b]	163 (85.8)[c]
Symptom duration, years	13.3 (10.0)	12.9 (9.4)
HLA-B27 positive, n (%)	230 (86.1)	165 (86.8)
ASDAS	3.7 (0.8)	3.7 (0.8)
BASDAI	6.5 (1.3)	6.6 (1.2)
hs-CRP, mg/L, geometric mean (geometric CV, %)	6.8 (214.6)	6.3 (201.4)
Current smoker, n (%)	69 (25.8)	51 (26.8)
Prior TNFi exposure, n (%)	43 (16.1)	28 (14.7)

[a] Patients who completed Week 104 and had an mSASSS available at baseline and Week 104. **[b]** Race for 3 patients was reported as missing at baseline. **[c]** Race for 1 patient was reported as missing at baseline.

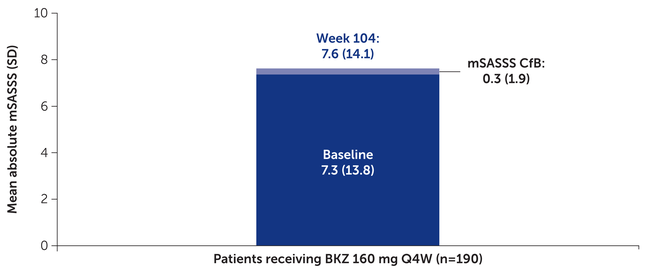
Table 2 Predictive factors for spinal radiographic progression (OC)

Predictive factor non-reference vs. reference[a]	Odds ratio (95% CI)	P value
Univariable model		
Baseline mSASSS[b]	1.03 (1.00, 1.06)	0.069
Age	0.99 (0.95, 1.04)	0.720
Sex (male vs female)	3.83 (0.68, 21.51)	0.127
BMI (≥30 vs <30)	1.22 (0.40, 3.69)	0.724
Race (non-White vs White)[c]	3.25 (1.01, 10.45)	0.048*
HLA-B27 status (positive vs negative)	0.26 (0.08, 0.82)	0.022*
Average ASDAS score[d]	1.71 (0.82, 3.57)	0.155
Smoking status (current smoker vs never/former smoker)	0.74 (0.21, 2.55)	0.630
Prior TNFi use (yes vs no)	2.30 (0.69, 7.59)	0.174
Multivariable model[e]		
Baseline mSASSS[f]	1.03 (1.00, 1.06)	0.084
HLA-B27 status (positive vs negative)	0.25 (0.08, 0.79)	0.018*

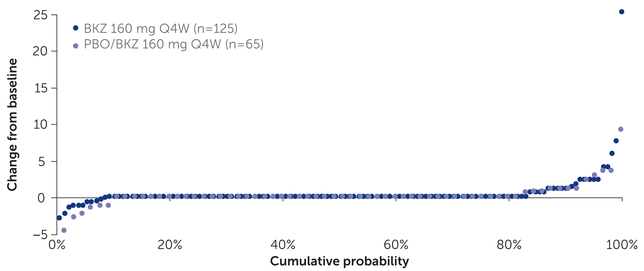
Predictive factors assessed using univariable and multivariable logistic regression models. **[a]** Univariable and multivariable analyses were performed on the X-ray population (univariable analyses: n=190; multivariable analyses: n=189 [1 patient with missing race was excluded from the multivariable analysis]). Except **[b]**, all other univariable models were adjusted for mSASSS at baseline. **[c]** 'Non-White' comprises the race categories Asian, Black, and Other. **[d]** Average ASDAS score derived as a mean of ASDAS score at all visits except the Week 104 visit. **[e]** Firth logistic model was used. Factors in the final model were selected using backward elimination with a significance level of 0.05. Baseline mSASSS was kept in the model selection process. **[f]** mSASSS at baseline was forced in each backward step. *Indicates significance (p value <0.05).

Figure 1 Change from baseline in mSASSS at Week 104

A) Absolute mSASSS



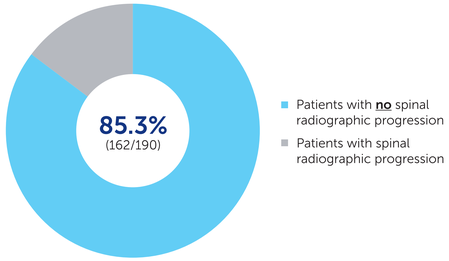
B) Cumulative probability of change from baseline in mSASSS, by patient (OC)



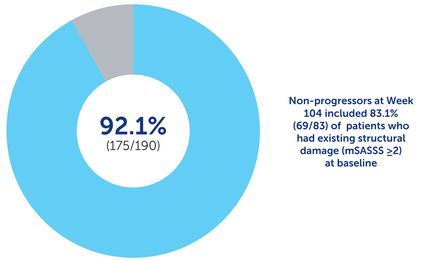
Includes patients in the X-ray sub-study with valid X-ray assessments at baseline and Week 104 (n=190). All patients received BKZ 160 mg Q4W from Week 16. mSASSS ranges from 0–72, with lower scores indicating less structural damage.

Figure 2 Patients with no spinal radiographic progression at Week 104 by mSASSS change from baseline thresholds (OC)

A) Non-progression defined as mSASSS CfB ≤0.5



B) Non-progression defined as mSASSS Cfb <2

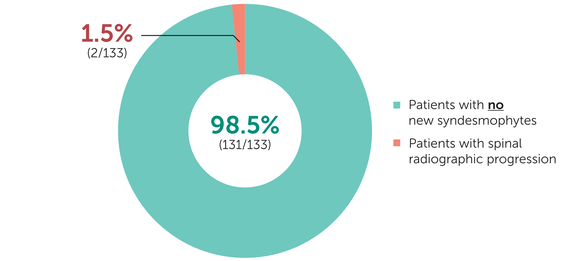


Non-progressors at Week 104 included 83.1% (69/83) of patients who had existing structural damage (mSASSS ≥2) at baseline

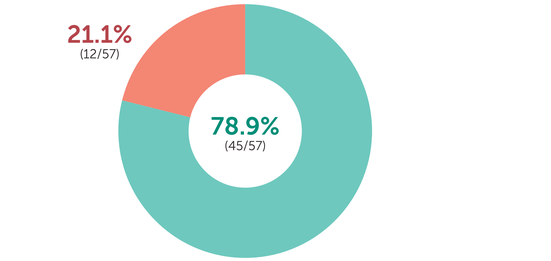
Includes patients in the X-ray sub-study with valid X-ray assessments at baseline and Week 104 (n=190). All patients received BKZ 160 mg Q4W from Week 16. mSASSS ranges from 0–72, with lower scores indicating less structural damage.

Figure 3 New syndesmophytes at Week 104 in patients with and without syndesmophytes at baseline (OC)

A) New syndesmophytes in patients without syndesmophytes at baseline



B) New syndesmophytes in patients with syndesmophytes at baseline



Includes patients in the X-ray sub-study with valid X-ray assessments at baseline and Week 104 (n=190). All patients received BKZ 160 mg Q4W from Week 16. New syndesmophytes were defined as syndesmophytes declared present at Week 104 but not at baseline at the same site.

ASDAS: Axial Spondylarthritis Disease Activity Score; **axSpA:** axial spondyloarthritis; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BKZ:** bimekizumab; **BMI:** body mass index; **CfB:** change from baseline; **CI:** confidence interval; **CV:** coefficient of variation; **HLA-B27:** human leukocyte antigen-B27; **hs-CRP:** high-sensitivity C-reactive protein; **Ig:** immunoglobulin; **IL:** interleukin; **mSASSS:** modified Stoke Ankylosing Spondylitis Spinal Score; **nr-axSpA:** non-radiographic axial spondyloarthritis; **OC:** observed case; **OLE:** open-label extension; **PBO:** placebo; **Q4W:** every 4 weeks; **r-axSpA:** radiographic axial spondyloarthritis; **SD:** standard deviation; **TNFi:** tumour necrosis factor inhibitor.

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