# 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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# Disclosures and Acknowledgments

## Disclosures

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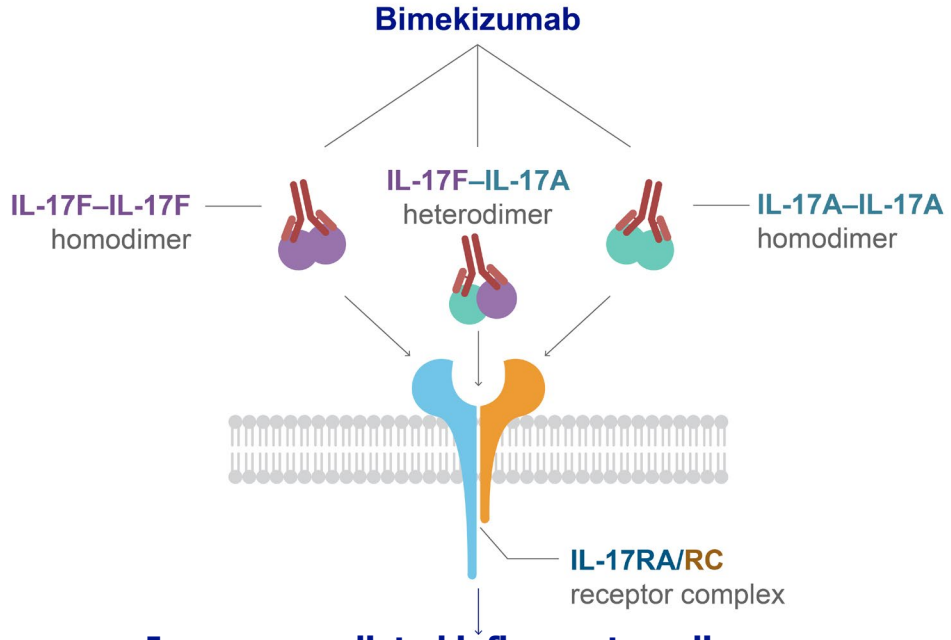
# Background and Objective

- **Pre-clinical data** suggest that inhibition of interleukin (IL)-17A and IL-17F may more effectively **inhibit** new bone formation in axial spondyloarthritis (axSpA) vs inhibition of IL-17A alone[1]
- **Bimekizumab** is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A
- Bimekizumab has demonstrated **consistent and sustained efficacy** to 2 years in patients with non-radiographic (nr-) and radiographic (r-)axSpA, in the parallel phase 3 studies BE MOBILE 1 and BE MOBILE 2, respectively, and their combined open-label extension (OLE)[2,3]
- Bimekizumab has also demonstrated **long-term sustained efficacy** in patients with r-axSpA up to 5 years[4]
- However, the impact of bimekizumab on **structural radiographic progression** in the spine in patients with r-axSpA has **not yet been demonstrated**

## IL-17A and IL-17F[5]



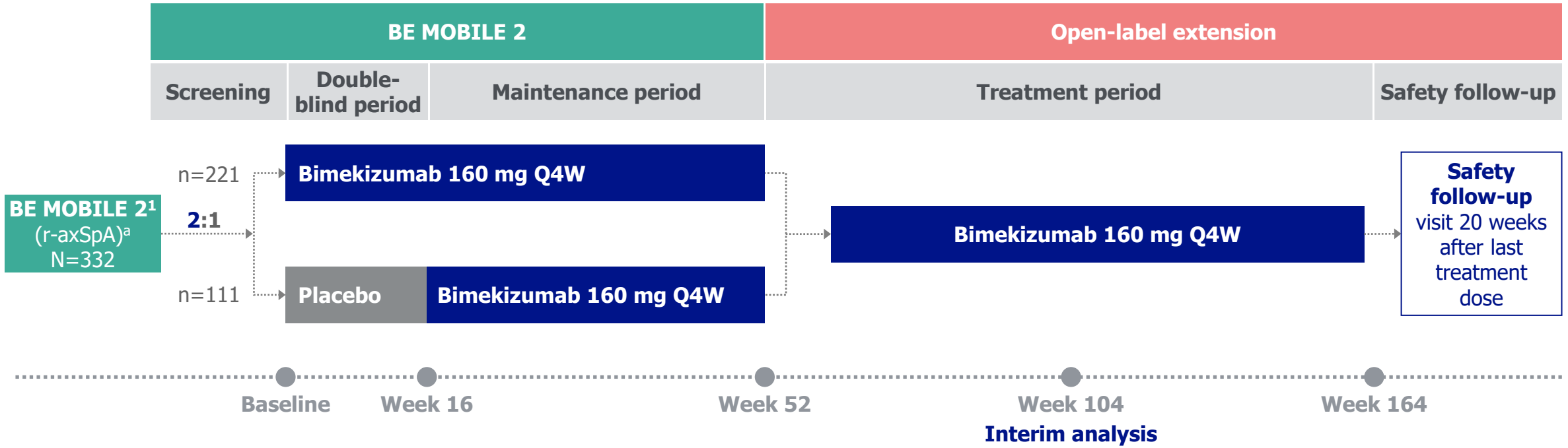

**OBJECTIVE: To evaluate the impact of bimekizumab treatment on spinal radiographic progression and new syndesmophyte formation in patients with r-axSpA at 2 years in the open-label extension (OLE) of the phase 3 BE MOBILE 2 study**

1. Shah M. RMD Open 2020;6:e001306; 2. Baraliakos X. Ann Rheum Dis 2024;83:199–213; 3. Baraliakos X. Presented at EULAR 2024. POS0806; 4. Deodhar A. Arthritis Rheumatol 2023;75(suppl 9); 5. Yang XO. J Exp Med. 2008;1063–75; 6. Glatt S. Ann Rheum Dis. 2018;77:523–32; 7. Navarro-Compán V. Front Immunol 2023;14:1191782. BE MOBILE 1: NCT03928704; BE MOBILE 2: NCT03928743; OLE: NCT04436640. axSpA: axial spondyloarthritis; Ig: immunoglobulin; IL: interleukin; OLE: open-label extension; RA: receptor A; r-axSpA: radiographic axial spondyloarthritis; RC: receptor C.

# Methods (1/4)

## Study Design

- BE MOBILE 2 (r-axSpA) comprised a 16-week double-blind placebo-controlled period followed by a 36-week maintenance period
- Patients were randomized 2:1 to receive subcutaneous bimekizumab 160 mg every 4 weeks (Q4W) or placebo; from Weeks 16 to 52, all patients received bimekizumab 160 mg Q4W
- At Week 52 of BE MOBILE 2, eligible patients could enroll in an ongoing OLE, where all patients continued bimekizumab

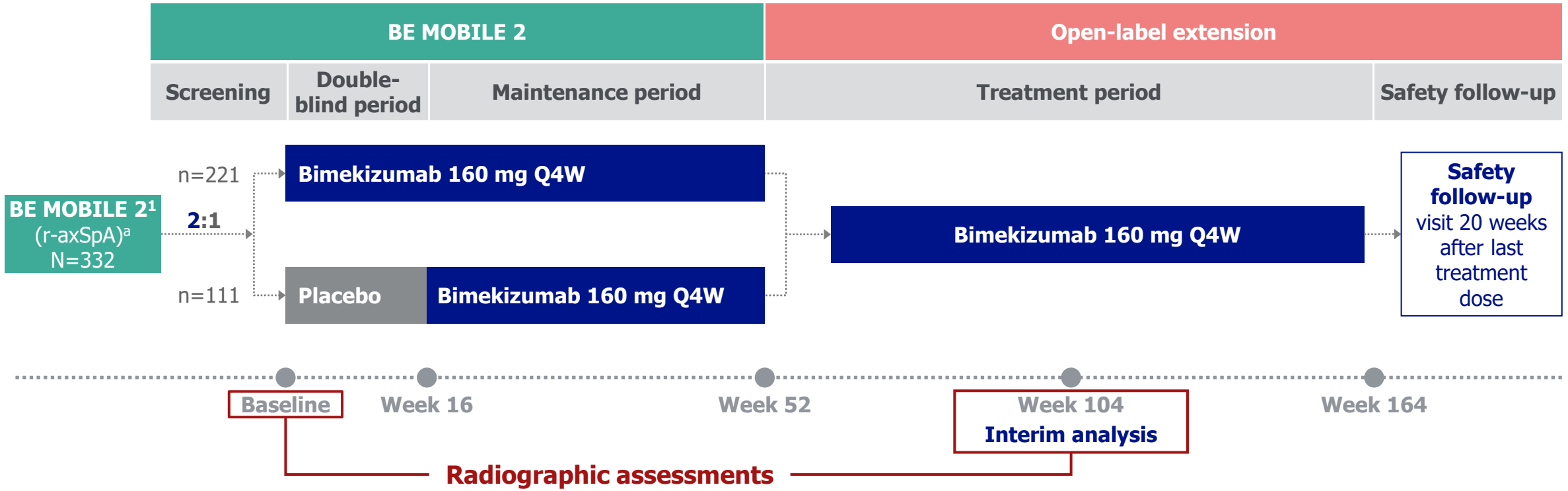



[a] Included patients had radiographic evidence of r-axSpA fulfilling modified New York criteria. 1. van der Heijde D, et al. Ann Rheum Dis. 2023;82:515–26. BE MOBILE 2: NCT03928743; OLE: NCT04436640. axSpA: axial spondyloarthritis; OLE: open-label extension; Q4W: every 4 weeks; r-axSpA: radiographic axSpA.

# Methods (2/4)

## Spinal Radiographic Assessments

- Modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) was assessed at baseline and Week 104
- Spinal radiographs were read centrally by two independent experts (adjudicated if change scores differed by ≥5 points)
- The average change score was determined for each radiograph; if adjudicated, the average of the two closest change scores was calculated
- All readers were blinded to timepoint and any clinical data

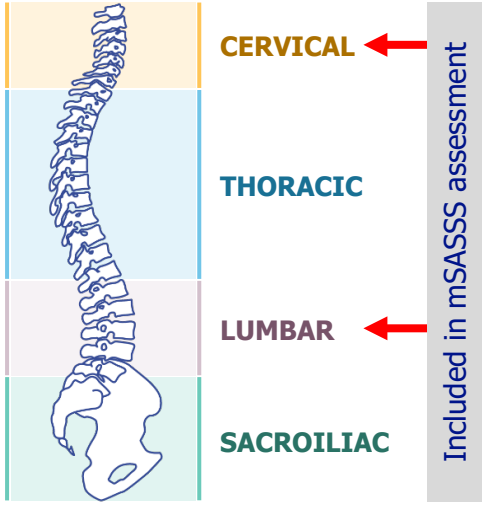



[a] Included patients had radiographic evidence of r-axSpA fulfilling modified New York criteria. 1. van der Heijde D, et al. Ann Rheum Dis. 2023;82:515–26. BE MOBILE 2: NCT03928743; OLE: NCT04436640. axSpA: axial spondyloarthritis; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score; OLE: open-label extension; Q4W: every 4 weeks; r-axSpA: radiographic axSpA.

# Methods (3/4)

## Evaluation of Radiographic Changes in the Spine Using mSASSS[1–3]

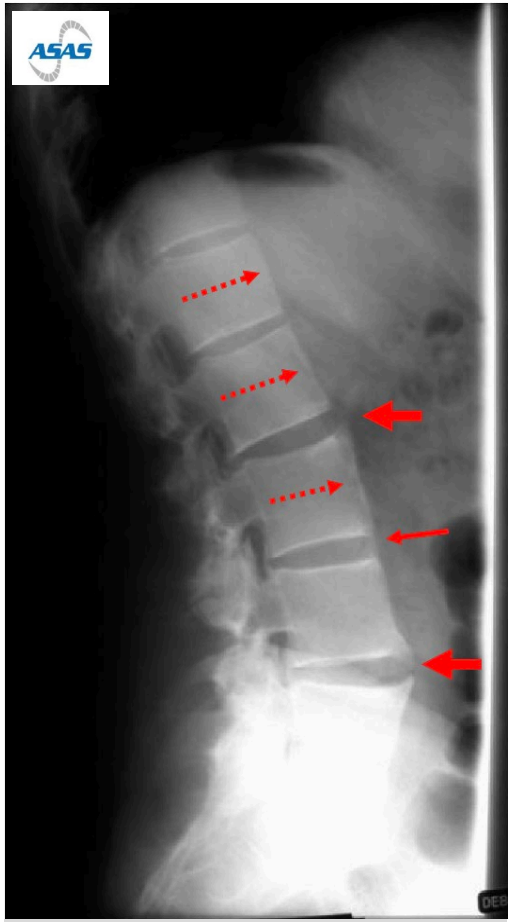
Each vertebral corner (VC) of the **cervical** and **lumbar** spine (a total of 24 VCs) is scored 0–3:




- **0** No abnormality
- **1** Erosion/sclerosis/squaring
- **2** Syndesmophyte
- **3** Bridging syndesmophytes/ankylosis

Scores are added together to give a total **possible score range of 0–72**

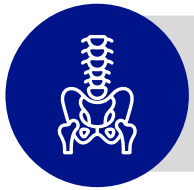
In this study, syndesmophytes were considered present if **two reviewers recorded an mSASSS of 2 or 3 at a given anatomical site,**
**or at least two of the three reviewers** if mSASSS adjudication was required




1. Creemers MCW et al. Ann Rheum Dis. 2005:64(1):127–9; 2. van der Heijde D, et al. Rheumatology. 2019;58:388–400; 3. Image adapted from ASAS Educational Slide Kits. 2013. Available at: https://www.asas-group.org/education/asas-slide-library/ [Accessed June 2024]. mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score; VC: vertebral corner.

# Methods (4/4)

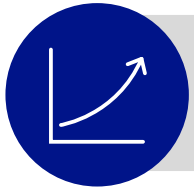
For patients with an mSASSS available at both timepoints (baseline and Week 104), the following parameters are reported:



Mean and cumulative probability of change from baseline (CfB) in mSASSS

Proportion of non-progressors, using definitions mSASSS CfB ≤0.5 and mSASSS CfB <2

Number of patients with new syndesmophytes, including in those with existing syndesmophytes at baseline[a]

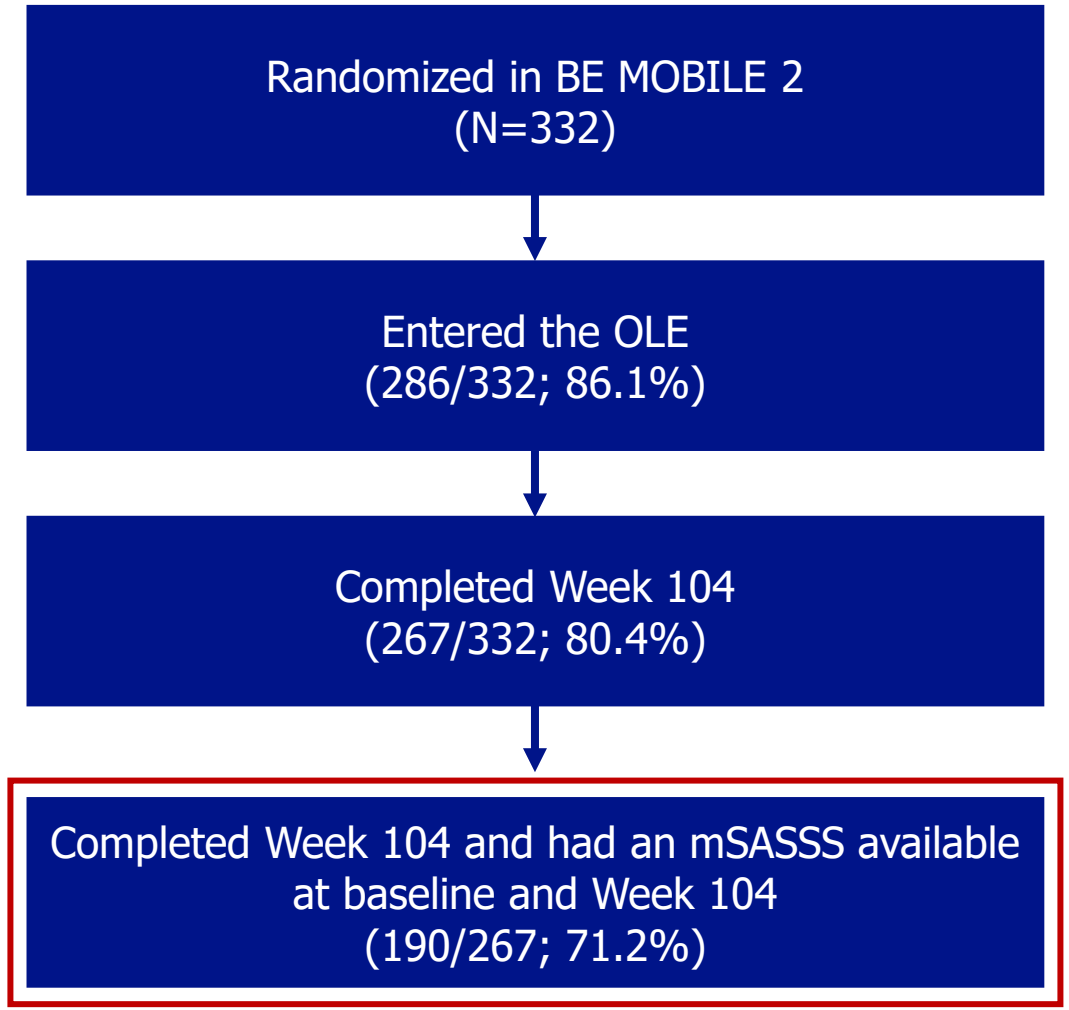


Potential predictive factors for spinal radiographic progression (mSASSS CfB ≥2) at Week 104, assessed using univariable and multivariable logistic regression models[b]

[a] New syndesmophytes were defined as syndesmophytes declared present at Week 104 but not at baseline at the same site. [b] Potential predictive factors in the univariable model were baseline mSASSS, age, sex, BMI (<30 vs ≥30), race, smoking status, prior TNFi use, HLA-B27 status, and average ASDAS score. Potential predictive factors in the multivariable model were baseline mSASSS and HLA-B27 status. ASDAS: Axial Spondylarthritis Disease Activity Score; BMI: body mass index; CfB: change from baseline; HLA-B27: human leukocyte antigen-B27; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score; TNFi: tumor necrosis factor inhibitor.

# Patient Disposition and Baseline Characteristics

- Of patients with r-axSpA who completed Week 104, ~70% had an mSASSS available at baseline and Week 104




**Baseline Characteristics**

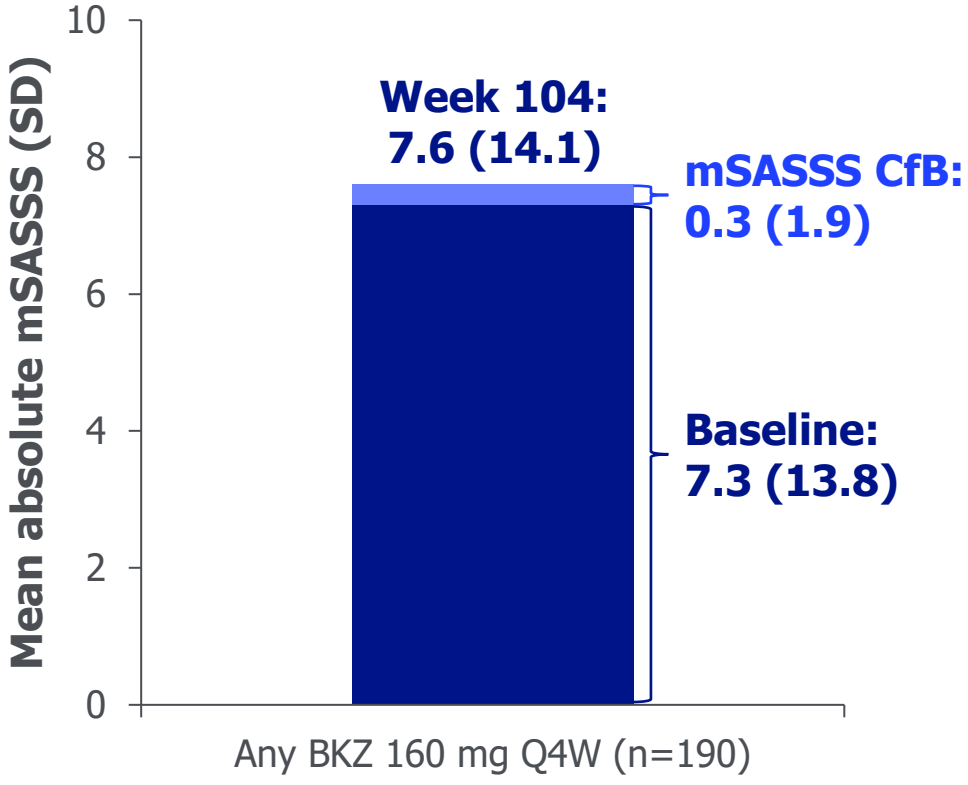
| Mean (SD), unless otherwise specified | Completed Week 104 n=267 | X-ray population[a] n=190 |
|---|---|---|
| **Age,** years | 40.4 (12.3) | 39.8 (11.9) |
| **Sex, male,** n (%) | 192 (71.9) | 135 (71.1) |
| **BMI, kg/m²** | 27.1 (5.9) | 26.7 (5.6) |
| **Race, White,** n (%) | 221 (82.8)[b] | 163 (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 three patients was reported as missing at baseline. [c] Race for one patient was reported as missing at baseline. ASDAS: Axial Spondyloarthritis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BMI: body mass index; CV: co-efficient of variation; HLA-B27: human leukocyte antigen-B27; hs-CRP: high-sensitivity C-reactive protein; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score; OLE: open-label extension; r-axSpA: radiographic axial spondyloarthritis; SD: standard deviation; TNFi: tumor necrosis factor inhibitor.

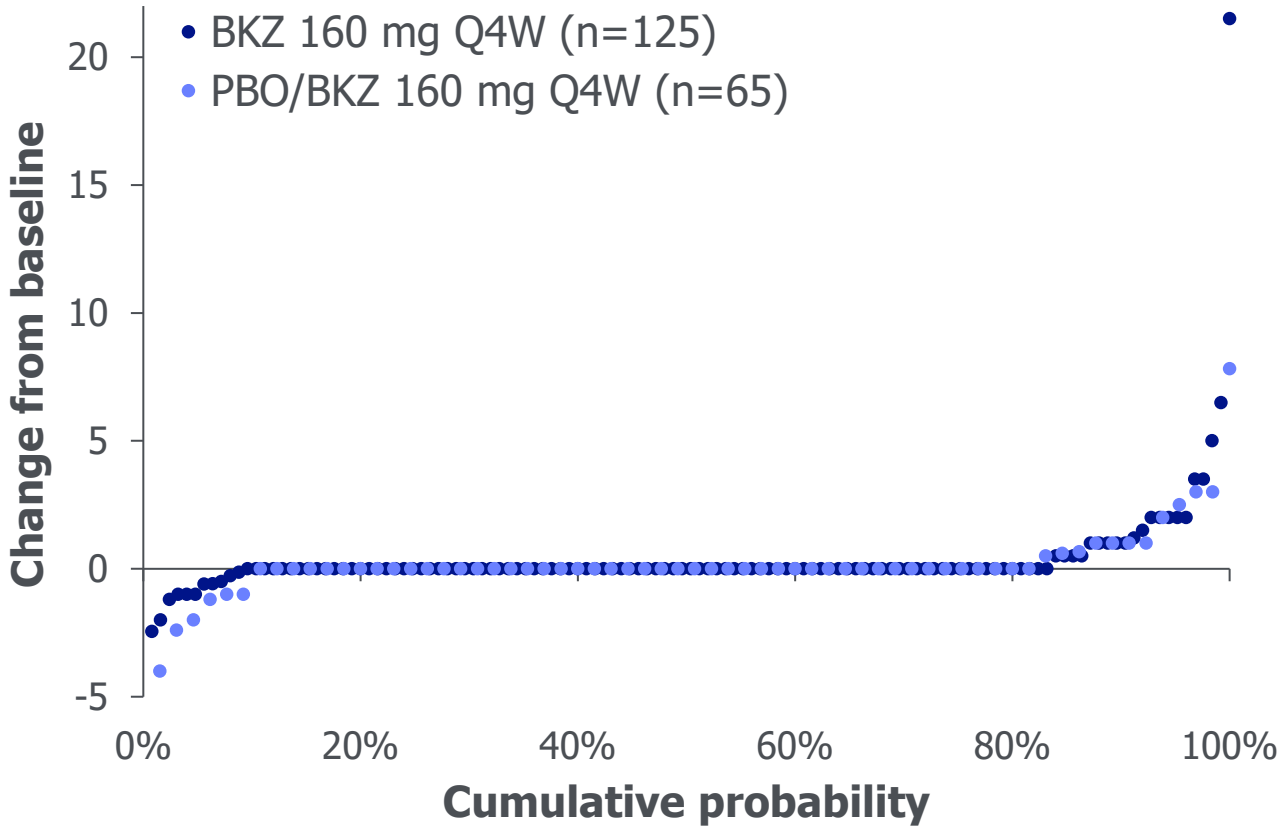
# mSASSS Change from Baseline at Week 104 (OC)

- Patients with r-axSpA had minimal spinal radiographic progression at 2 years with bimekizumab

## Absolute mSASSS




## Cumulative probability of change from baseline in mSASSS, by patient

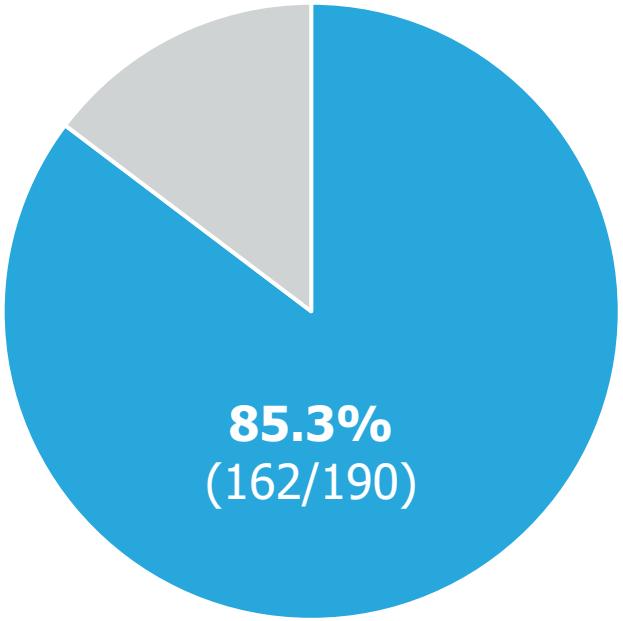



Includes patients in the X-ray sub-study with valid X-ray assessments at baseline and Week 104 (n=190). All patients received bimekizumab 160 mg Q4W from Week 16. mSASSS ranges from 0–72, with lower scores indicating less structural damage. BKZ: bimekizumab; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score; OC: observed case; PBO: placebo; Q4W; every 4 weeks; SD: standard deviation.

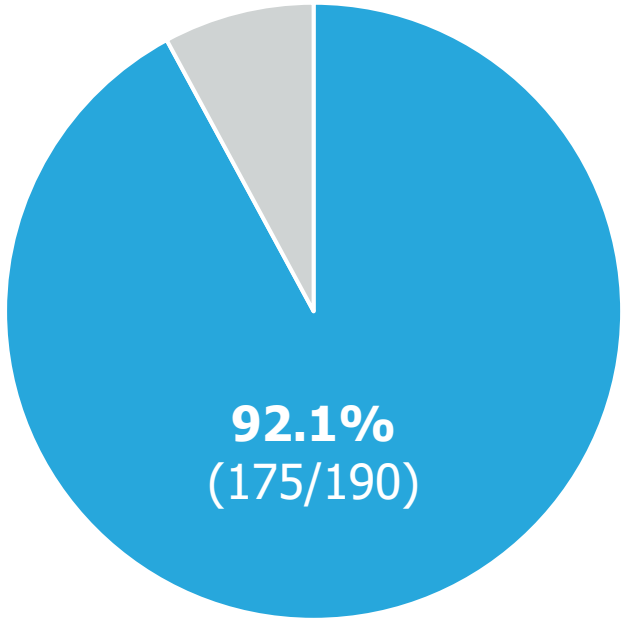
# Proportion of Non-Progressors at Week 104 (OC)

- The majority of patients treated with bimekizumab were non-progressors, including those with existing structural damage at baseline

**Non-progression defined as mSASSS CfB ≤0.5**




**Non-progression defined as mSASSS CfB <2**




Patients with **no** spinal radiographic progression

Patients with spinal radiographic progression

Of patients with **existing structural damage** (mSASSS ≥2) at baseline, **83.1% (69/83)** were **non-progressors** at Week 104 (mSASSS CfB <2)

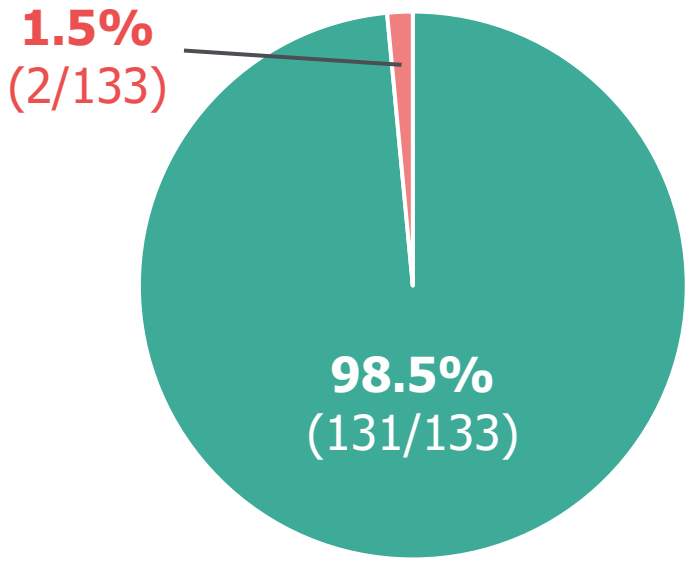
Includes patients in the X-ray sub-study with valid X-ray assessments at baseline and Week 104 (n=190). All patients received bimekizumab 160 mg Q4W from Week 16. mSASSS ranges from 0–72, with lower scores indicating less structural damage. CfB: change from baseline; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score; OC: observed case; Q4W; every 4 weeks.

# New Syndesmophytes at Week 104 (OC)

- A minor fraction of patients had new syndesmophytes at 2 years of treatment with bimekizumab, including almost one fifth of patients who had existing syndesmophytes at baseline

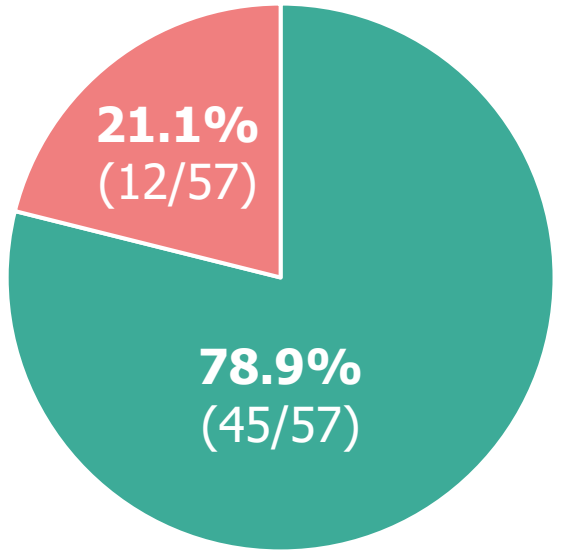
## New syndesmophytes in patients without syndesmophytes at baseline

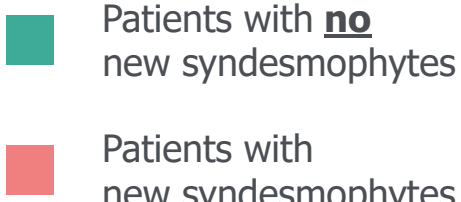
At baseline, 133/190 patients (70.0%) had **no** syndesmophytes present




## New syndesmophytes in patients with syndesmophytes at baseline

At baseline, 57/190 patients (30.0%) had syndesmophytes present




Includes patients in the X-ray sub-study with valid X-ray assessments at baseline and Week 104 (n=190). New syndesmophytes were defined as syndesmophytes declared present at Week 104 but not at baseline at the same site.
OC: observed case.

# Predictive Factors for Spinal Radiographic Progression (OC)

- 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

| Predictive factor (non-ref vs ref)[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 [one 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 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). ASDAS: Axial Spondylarthritis Disease Activity Score; BMI: body mass index; CfB: change from baseline; CI: confidence interval; HLA-B27: human leukocyte antigen-B27; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score; OC: observed case; TNFi: tumor necrosis factor inhibitor.

# Conclusions

After 2 years of treatment with bimekizumab, the following was observed in patients with r-axSpA:

**Minimal** spinal radiographic progression

A high proportion of **non-progressors,** including in patients with baseline spinal damage

**Limited new syndesmophyte formation,** with new syndesmophyte formation primarily occurring in patients with existing syndesmophytes

These findings suggest that dual inhibition of IL-17A and IL-17F with bimekizumab may have a **positive impact on spinal progression and irreversible damage** in patients with r-axSpA

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IL: interleukin; r-axSpA: radiographic axial spondyloarthritis.