Bimekizumab Treatment in Patients with Active Axial Spondyloarthritis: 52-Week Efficacy and Safety From the Randomised Parallel Phase 3 BE MOBILE 1 and BE MOBILE 2 Studies

Xenofon Baraliakos, MD,[1] Atul Deodhar, MD, MRCP,[2] Désirée van der Heijde, MD,[3] Marina Magrey, MD,[4] Walter P. Maksymowych, MD, FRCP,[5] Tetsuya Tomita, MD,[6] Huji Xu, MD, PhD,[7] Ute Massow, PhD,[8] Carmen Fleurinck, MD,[9] Alicia M. Ellis, PhD,[10] Thomas Vaux, MSc,[11] Julie Shepherd-Smith, BPharm,[11] Alexander Marten, MD,[8] Lianne S. Gensler, MD[12]

[1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Bochum, Germany; [2]Division of Arthritis & Rheumatic Diseases, Oregon Health & Science University, Portland, OR, USA; [3]Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands; [4]University Hospitals, Case Western Reserve University, Cleveland, OH, USA; [5]Department of Medicine, University of Alberta, Edmonton, Alberta, Canada; [6]Graduate School of Health Science, Morinomiya University of Medical Science, Osaka City, Osaka, Japan; [7]Department of Rheumatology and Immunology, Shanghai Changzheng Hospital, Affiliated to Second Military Medical University, Shanghai, People's Republic of China; [8]UCB Pharma, Monheim am Rhein, Germany; [9]UCB Pharma, Brussels, Belgium; [10]UCB Pharma, Raleigh, NC, USA; [11]UCB Pharma, Slough, UK; [12]Department of Medicine/Rheumatology, University of California, San Francisco, CA, USA

Correspondence to: Xenofon Baraliakos (Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Bochum, Germany; xenofon.baraliakos@elisabethgruppe.de)

Baraliakos X, *et al. Ann Rheum Dis* 2024; 83:199–213. doi: 10.1136/ard-2023-224803

SUPPLEMENTARY METHODS

Study design

Randomisation was performed using interactive response technology, stratified by region (Asia, Eastern Europe, Western Europe, and North America), MRI/CRP classification (BE MOBILE 1 only) and TNFi exposure (BE MOBILE 2 only).

Patient and public involvement

Patients with axSpA were consulted during development of the BKZ in axSpA clinical trial programme to understand treatment needs and recommend ways to facilitate trial participation while minimising burden of trial visits. Most efficacy endpoints were derived from existing patient-reported outcome measures which were originally developed with patient input to capture the experience of patients with axSpA. Trial participants were recruited by the trial sites and provided written consent to participate.

MRI scoring

Inflammation of the SIJ was measured using the MRI SPARCC SIJ scoring method due to its favourable inter-reader reliability and sensitivity compared with other scoring methods.[1] Inflammation of the spine was measured using a modified MRI Berlin spine method as this method is widely used in clinical studies of axSpA.[2]

MRI endpoints are presented for the subset of patients in the MRI sub studies.[3] MRIs were assessed using central reading by two independent expert readers, with a third adjudicator in cases of disagreement. MRIs from all time points were read in a single reading campaign with readers blinded to time point and treatment arm.

Baraliakos X, *et al. Ann Rheum Dis* 2024; 83:199–213. doi: 10.1136/ard-2023-224803

Safety endpoint definitions

TEAEs were defined as adverse events with an onset date on or after the first dose of the study drug and within 20 weeks of the final dose. Treatment-emergent SAEs were defined as any TEAE meeting ≥1 of the following: death, life-threatening illness, medically significant or persistent disability or incapacity, congenital anomaly, or birth defect (including that occurring in a foetus), important medical event, and initial inpatient hospitalisation or prolongation of hospitalisation.

Statistical analysis

Sample size calculations and statistical analyses were performed as described previously.[3]

For continuous ranked endpoints reported at Week 16, missing data to Week 16 were imputed with reference-based multiple imputation (RBMI), with the MI model based on PBO group data only. Missing data for non-ranked continuous endpoints and continuous ranked endpoints before and after Week 16 were handled with MI using data from both BKZ and PBO groups. OC data are reported for MRI SPARCC SIJ and Berlin spine inflammation scores, as only a subset of patients underwent MRI.

For binary endpoints, an intercurrent event (IE) was defined as discontinuation of study treatment prior to Week 16 due to any reason. Study participants with missing data at Week 16 preceded by an intercurrent event were counted as non-responders, as well as study participants with missing data at Week 16 that were not preceded by an intercurrent event. For continuous endpoints, an IE was defined as discontinuation due to lack of efficacy or AE. Continuous ranked endpoints with missing data at Week 16 and non-missing data after IE (which are reset to missing),

were imputed using MI based on a reference-based approach, in which the MI model is based on data from the PBO group. For non-ranked continuous endpoints and continuous ranked endpoints, missing data at Week 16 were imputed using MI based on Markov Chain Monte Carlo followed by monotone regression.

SUPPLEMENTARY RESULTS

Patients were screened for both studies from 25 April 2019. The last Week 52 visits were 1 July 2022 (BE MOBILE 1) and 31 May 2022 (BE MOBILE 2).

Covid-19 impact

COVID-19 had minimal impact on the trials despite both trials being conducted during the COVID-19 pandemic. Across all study participants (both BKZ and PBO/BKZ groups), only 8 (3.1%) patients in BE MOBILE 1 and 17 (5.1%) patients in BE MOBILE 2 had visits classed as 'not done' to Week 52; visits classed as not done were deemed related to COVID-19 and could include discontinuation of treatment or termination of study participation. To Week 52, only 13 (5.1%) doses in BE MOBILE 1 and 22 doses (6.6%) were missed in BE MOBILE 2 (either BKZ or PBO) due to COVID-19.

The number of confirmed corona virus infections in both trials during the DBTP have been reported previously.[3] During the overall period (Weeks 0–52), there were 17 (8.3/100 PY) and 7 cases (2.4/100 PY) in BE MOBILE 1 and BE MOBILE 2, respectively. All corona virus cases were mild to moderate and none were serious. Supportive analyses demonstrated that the pandemic had a negligible impact on the results of the BE MOBILE trials and the treatment effect for ASAS40 in the COVID-19 free set aligned with that of the overall population (data not reported).

Enthesitis and peripheral arthritis

Among patients with enthesitis at baseline (MASES >0), mean MASES at baseline was 4.8 (BKZ) and 4.9 (PBO/BKZ) for patients with nr-axSpA and 4.2 (BKZ) and 4.4 (PBO/BKZ) for patients with r-axSpA. Reductions (mean CfB) in MASES observed at Week 16 were sustained to Week 52 for patients initially randomised to BKZ (nr-axSpA: −3.6; r-axSpA: −2.9 [MI]); to Week 52, reductions in MASES were also observed in patients switching from PBO at Week 16 (nr-axSpA: −2.9; r-axSpA: −3.2 [MI]; **Table S4**). It should be noted that MASES is measure of entheseal tenderness and therefore may overestimate the proportion of patients with active enthesitis at baseline.

Among patients with SJC >0 or TJC >0 at baseline, reductions in SJC and TJC score were observed to Week 52 both for patients originally randomised to BKZ (CfB [baseline mean]: SJC: nr-axSpA: −2.5 [4.2]; r-axSpA: −4.2 [4.7]; TJC: nr-axSpA: −4.0 [6.0]; r-axSpA: −4.0 [5.3]; MI) and patients switching from PBO to BKZ at Week 16 (SJC: nr-axSpA: −2.9 [3.8]; r-axSpA: −3.6 [3.9]; TJC: nr-axSpA: −3.5 [6.3]; r-axSpA: −4.5 [5.4]; MI; **Table S4**).

SUPPLEMENTARY TABLES AND FIGURES

Table S1. Individual ASAS components of the primary endpoint at Week 16 and Week 52

		Baseline[a]		Change from baseline				
				Week 16[b]			Week 52[a]	
		PBO	BKZ 160 mg Q4W	PBO	BKZ 160 mg Q4W	BKZ vs PBO difference, mean (95% CI)	PBO→BKZ 160 mg Q4W	BKZ 160 mg Q4W
nr-axSpA (BE MOBILE 1) **r-axSpA (BE MOBILE 2)**		**n=126** **n=111**	**n=128** **n=221**	**n=126** **n=111**	**n=128** **n=221**		**n=126** **n=111**	**n=128** **n=221**
PtGADA [RBMI/MI], mean (SE)	nr-axSpA	6.9 (0.2)	7.1 (0.2)	−1.4 (0.2)	−3.2 (0.2)	−1.8 (−2.4, −1.2)	−3.8 (0.2)	−4.1 (0.2)
	r-axSpA	6.7 (0.2)	6.6 (0.1)	−1.6 (0.2)	−2.7 (0.2)	−1.3 (−1.8, −0.8)	−4.2 (0.2)	−3.6 (0.2)
Total spinal pain [RBMI/MI], mean (SE)	nr-axSpA	7.1 (0.1)	7.3 (0.1)	−1.7 (0.2)	−3.4 (0.2)	−1.6 (−2.2, −1.0)	−3.9 (0.2)	−4.2 (0.2)
	r-axSpA	7.2 (0.1)	7.1 (0.1)	−1.9 (0.2)	−3.3 (0.2)	−1.4 (−1.9, −0.9)	−4.5 (0.2)	−4.1 (0.2)
BASFI [RBMI/MI], mean (SE)	nr-axSpA	5.3 (0.2)	5.5 (0.2)	−1.0 (0.2)	−2.5 (0.2)	−1.5 (−2.0, −1.0)	−2.6 (0.2)	−3.0 (0.2)
	r-axSpA	5.2 (0.2)	5.3 (0.2)	−1.1 (0.2)	−2.2 (0.1)	−1.1 (−1.5, −0.6)	−2.8 (0.2)	−2.8 (0.1)
BASDAI Q5&6 mean score (morning stiffness) [RBMI/MI], mean (SE)	nr-axSpA	6.9 (0.1)	7.0 (0.2)	−1.9 (0.2)	−3.6 (0.3)	−1.7 (−2.3, −1.1)	−4.1 (0.2)	−4.5 (0.2)
	r-axSpA	6.8 (0.2)	6.7 (0.1)	−2.1 (0.2)	−3.2 (0.2)	−1.1 (−1.6, −0.7)	−4.4 (0.2)	−3.9 (0.2)

Randomised set. Least squares mean differences between BKZ and PBO are reported from the ANCOVA model in which treatment, MRI/CRP classification and region (BE MOBILE 1) or treatment, prior TNFi exposure and region (BE MOBILE 2) were included as fixed effects, and baseline values as covariates. [a]Missing data were imputed using MI; [b]Missing data were imputed using RBMI. ANCOVA: analysis of covariance; ASAS: Assessment of SpondyloArthritis international Society; BKZ: bimekizumab; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CI: confidence interval; CRP: C-reactive protein; MI: multiple imputation; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; PtGADA: Patient's Global Assessment of Disease Activity; Q: question; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; RBMI: reference-based multiple imputation; SE: standard error; TNFi: tumour necrosis factor inhibitor.

Table S2. ASAS40 responses in TNF-naïve and –IR patients at Week 16 and Week 52

		Week 16			Week 52	
		PBO	BKZ 160 mg Q4W	p value	PBO→BKZ 160 mg Q4W	BKZ 160 mg Q4W
	nr-axSpA (BE MOBILE 1)	**n=109**	**n=118**		**n=109**	**n=118**
	r-axSpA (BE MOBILE 2)	**n=94**	**n=184**		**n=94**	**n=184**
ASAS40 in TNFi-naïve[a] [NRI], n (%)	nr-axSpA	25 (22.9)	55 (46.6)	<0.001[b]	58 (53.2)	73 (61.9)
	r-axSpA	22 (23.4)	84 (45.7)	<0.001	67 (71.3)	108 (58.7)
	nr-axSpA (BE MOBILE 1)	**n=17**	**n=10**		**n=17**	**n=10**
	r-axSpA (BE MOBILE 2)	**n=17**	**n=37**		**n=17**	**n=37**
ASAS40 in TNFi-IR[c] [NRI], n (%)	nr-axSpA	2 (11.8)	6 (60.0)	-	6 (35.3)	5 (50.0)
	r-axSpA	3 (17.6)	15 (40.5)	-	9 (52.9)	21 (56.8)

Randomised set. [a]Ranked secondary endpoint in BE MOBILE 2 only; [b]Outcome was not part of the statistical hierarchy, therefore p values are nominal (no multiplicity adjustment) and should not be used as an indicator of statistical significance; [c]Exploratory endpoint. ASAS40: Assessment of SpondyloArthritis international Society 40 Response; BKZ: bimekizumab; IR: inadequate responder; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; PBO: placebo; Q4W: every four weeks; r-axSpA: radiographic axial spondyloarthritis; TNFi: tumour necrosis factor inhibitor.

Table S3. Change from baseline in BASDAI Q1 (fatigue) scores at Week 16 and Week 52

		Baseline		Change from baseline			
				Week 16		Week 52	
		PBO	BKZ 160 mg Q4W	PBO	BKZ 160 mg Q4W	PBO→BKZ 160 mg Q4W	BKZ 160 mg Q4W
nr-axSpA (BE MOBILE 1) **r-axSpA (BE MOBILE 2)**		**n=126** **n=111**	**n=128** **n=221**	**n=126** **n=111**	**n=128** **n=221**	**n=126** **n=111**	**n=128** **n=221**
BASDAI Q1, mean (SE)	nr-axSpA	6.4 (0.2)	6.7 (0.1)	−1.1 (0.2)	−2.6 (0.2)	−2.7 (0.2)	−3.2 (0.2)
	r-axSpA	6.4 (0.1)	6.4 (0.1)	−1.7 (0.2)	−2.5 (0.2)	−3.4 (0.2)	−3.1 (0.2)

Randomised set. Data reported are MI. BKZ: bimekizumab; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; MI: multiple imputation; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; Q: question; r-axSpA: radiographic axial spondyloarthritis; Q4W: every 4 weeks; SE: standard error.

Table S4. Change from baseline in enthesitis (MASES) and peripheral arthritis (SJC and TJC) score at Week 16 and Week 52

Mean (SE)		Baseline		Change from baseline				
				Week 16			Week 52	
		PBO	BKZ 160 mg Q4W	PBO	BKZ 160 mg Q4W	Nominal p value	PBO→BKZ 160 mg Q4W	BKZ 160 mg Q4W
MASES[a]	nr-axSpA[b]	4.9 (0.4)	4.8 (0.3)	−1.3 (0.3)	−2.4 (0.3)	0.013	−2.9 (0.4)	−3.6 (0.3)
	r-axSpA[c]	4.4 (0.3)	4.2 (0.3)	−1.5 (0.3)	−2.4 (0.3)	0.003	−3.2 (0.3)	−2.9 (0.3)
SJC[d]	nr-axSpA[e]	3.8 (0.5)	4.2 (0.8)	−1.3 (0.6)	−3.1 (0.7)	0.007	−2.9 (0.4)	−2.5 (0.8)
	r-axSpA[f]	3.9 (0.7)	4.7 (0.6)	−2.1 (0.5)	−3.6 (0.5)	0.074	−3.6 (0.8)	−4.2 (0.6)
TJC[g]	nr-axSpA[h]	6.3 (0.6)	6.0 (0.8)	−1.1 (0.5)	−3.0 (0.7)	0.008	−3.5 (0.6)	−4.0 (0.8)
	r-axSpA[i]	5.4 (0.6)	5.3 (0.6)	−2.9 (0.5)	−2.5 (0.4)	0.401	−4.5 (0.6)	−4.0 (0.5)

Randomised set. Data reported are MI. Assessed in pts with: [a]MASES >0 at BL: [b]PBO n=92; BKZ n=94; [c]PBO n=67; BKZ n=132; [d]SJC >0 at BL: [e]PBO n=43; BKZ n=45; [f]PBO n=22; BKZ n=44; [g]TJC >0 at BL: [h]PBO n=85; BKZ n=78; [i]PBO n=61; BKZ n=116. p values without any multiplicity adjustment are indicated as nominal p values and should not be used as an indicator of statistical significance. p value for the comparison of BKZ to PBO (LS mean difference) were calculated using ANCOVA with treatment, region, MRI/CRP classification (BE MOBILE 1 only), prior TNFi exposure (BE MOBILE 2 only) as fixed effects, and baseline scores as covariate. ANCOVA: analysis of covariance; BKZ: bimekizumab; BL: baseline; CRP: C-reactive protein; LS: least squares; MASES: Maastricht ankylosing spondylitis enthesitis score; MI: multiple imputation; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; r-axSpA: radiographic axial spondyloarthritis; Q4W: every 4 weeks; SE: standard error; SJC: swollen joint count; TJC: tender joint count; TNFi: tumour necrosis factor inhibitor.

Table S5. TEAEs leading to discontinuation of study drug by preferred term

n (%), overall period: [EAIR/100 PY]		Double-blind treatment period Weeks 0–16		Overall Weeks 0–52
		PBO	BKZ 160 mg Q4W	BKZ 160 mg Q4W Total[a]
	nr-axSpA (BE MOBILE 1) r-axSpA (BE MOBILE 2)	n=126 (38.1 PYAR) n=111 (34.6 PYAR)	n=128 (40.4 PYAR) n=221 (68.3 PYAR)	n=244 (208.2 PYAR) n=330 (290.9 PYAR)
Any TEAE leading to discontinuation of study drug	nr-axSpA	5 (4.0)	2 (1.6)	8 (3.3) [3.9]
	r-axSpA	0	7 (3.2)	16 (4.8) [5.6]
Iridocyclitis	nr-axSpA	0	0	1 (0.4) [0.5][b]
	r-axSpA	0	0	0
Uveitis	nr-axSpA	2 (1.6)	0	0
	r-axSpA	0	0	0
Colitis ulcerative	nr-axSpA	1 (0.8)	0	0
	r-axSpA	0	1 (0.5)	1 (0.3) [0.3]
Crohn's disease	nr-axSpA	0	0	0
	r-axSpA	0	1 (0.5)	2 (0.6) [0.7]
Cellulitis	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Psychiatric evaluation abnormal	nr-axSpA	2 (1.6)	1 (0.8)	1 (0.4) [0.5]
	r-axSpA	0	2 (0.9)	3 (0.9) [1.0]
Peripheral arthritis	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Dizziness	nr-axSpA	0	1 (0.8)	1 (0.4) [0.5][b]
	r-axSpA	0	0	0
Anxiety	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Hypoaesthesia	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Clear cell renal cell carcinoma	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Lymphoid tissue hyperplasia[c]	nr-axSpA	0	0	0
	r-axSpA	0	1 (0.5)	1 (0.3) [0.3]
Oesophageal candidiasis	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Oral candidiasis	nr-axSpA	0	0	3 (1.2) [1.5][b]

n (%), overall period: [EAIR/100 PY]		Double-blind treatment period Weeks 0–16		Overall Weeks 0–52
		PBO	BKZ 160 mg Q4W	BKZ 160 mg Q4W Total[a]
		nr-axSpA (BE MOBILE 1) n=126 (38.1 PYAR) r-axSpA (BE MOBILE 2) n=111 (34.6 PYAR)	n=128 (40.4 PYAR) n=221 (68.3 PYAR)	n=244 (208.2 PYAR) n=330 (290.9 PYAR)
	r-axSpA	0	1 (0.5)	1 (0.3) [0.3]
Dermatitis allergic	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Rash	nr-axSpA	0	0	0
	r-axSpA	0	1 (0.5)	1 (0.3) [0.3]
Suicidal ideation	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Pleural effusion	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]

Safety set. MedDRA (Version 19.0), preferred terms reported. [a]Includes patients who switched from PBO to BKZ (events after switch only); [b]Assessed as related to study medication by the investigator; [c]Lymphoid tissue hyperplasia was a TEAE related to gastrointestinal disorders and not related to lymphoid blood cells – the TEAE was diagnosed and reported as 'lymphoid nodular hyperplasia'. BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; MedDRA: medical dictionary for regulatory activities; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; PY: patient-years; PYAR: patient-years at risk; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; TEAE: treatment-emergent adverse event.

Table S6. Serious treatment-emergent adverse events by preferred term

n (%), overall period: [EAIR/100 PY]		Double-blind treatment period Weeks 0–16		Overall Weeks 0–52
		PBO	BKZ 160 mg Q4W	BKZ 160 mg Q4W Total[a]
	nr-axSpA (BE MOBILE 1) r-axSpA (BE MOBILE 2)	n=126 (38.1 PYAR) n=111 (34.6 PYAR)	n=128 (40.4 PYAR) n=221 (68.3 PYAR)	n=244 (208.2 PYAR) n=330 (290.9 PYAR)
Any SAE	nr-axSpA	1 (0.8)	0	9 (3.7) [4.4]
	r-axSpA	1 (0.9)	5 (2.3)	20 (6.1) [7.1]
Sinus node dysfunction	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Deafness unilateral	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Goitre	nr-axSpA	0	0	0
	r-axSpA	0	1 (0.5)	1 (0.3) [0.3]
Abdominal adhesions	nr-axSpA	1 (0.8)	0	0
	r-axSpA	0	0	0
Colitis ulcerative	nr-axSpA	0	0	0
	r-axSpA	0	1 (0.5)	1 (0.3) [0.3]
Crohn's disease	nr-axSpA	0	0	0
	r-axSpA	0	1 (0.5)	1 (0.3) [0.3]
Hiatus hernia	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Ileus paralytic	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Cholelithiasis	nr-axSpA	0	0	0
	r-axSpA	0	1 (0.5)	1 (0.3) [0.3]
Appendicitis	nr-axSpA	0	0	2 (0.8) [1.0][b]
	r-axSpA	0	0	0
Diverticulitis	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3][c]
Cellulitis	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3][c]
Tonsillitis bacterial	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Otitis media	nr-axSpA	0	0	0

n (%), overall period: [EAIR/100 PY]		Double-blind treatment period Weeks 0–16		Overall Weeks 0–52
		PBO	BKZ 160 mg Q4W	BKZ 160 mg Q4W Total[a]
	nr-axSpA (BE MOBILE 1) r-axSpA (BE MOBILE 2)	n=126 (38.1 PYAR) n=111 (34.6 PYAR)	n=128 (40.4 PYAR) n=221 (68.3 PYAR)	n=244 (208.2 PYAR) n=330 (290.9 PYAR)
	r-axSpA	0	0	1 (0.3) [0.3][c]
Hepatitis A	nr-axSpA	0	0	0
	r-axSpA	0	1 (0.5)	1 (0.3) [0.3]
Infectious pleural effusion	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Erysipelas	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	1 (0.3) [0.3][c]
Viral infection	nr-axSpA	0	0	0
	r-axSpA	1 (0.9)[c]	0	0
Radius fracture	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Osteoarthritis	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Clear cell renal cell carcinoma[e]	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Superficial spreading melanoma stage I	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Uterine leiomyoma	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Syncope	nr-axSpA	0	0	0
	r-axSpA	0	0	4 (1.2) [1.4][d]
Depression	nr-axSpA	0	0	0
	r-axSpA	1 (0.9)	0	0
Suicidal ideation	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3][c]
Intentional self-injury	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Nasal crusting	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Rhinoplasty	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]

Safety set. MedDRA (Version 19.0), preferred terms reported. [a]Includes patients who switched from PBO to BKZ (events after switch only); [b]One event in one patient assessed as related to study medication by the investigator; [c]Assessed as related to study medication by the investigator; [d]One event assessed as related to study medication by the investigator; [e]SAE occurred 132 days after treatment initiation. BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; MedDRA: medical dictionary for regulatory activities; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; PY: patient-years; PYAR: patient-years at risk; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; SAE: treatment-emergent serious adverse event.

Table S7. Fungal infections

n (%), overall period: [EAIR/100 PY]		Double-blind treatment period Weeks 0–16		Overall Weeks 0–52
		PBO	BKZ 160 mg Q4W	BKZ 160 mg Q4W Total[a]
	nr-axSpA (BE MOBILE 1) / r-axSpA (BE MOBILE 2)	n=126 (38.1 PYAR) / n=111 (34.6 PYAR)	n=128 (40.4 PYAR) / n=221 (68.3 PYAR)	n=244 (208.2 PYAR) / n=330 (290.9 PYAR)
Fungal infections, n (%)	nr-axSpA	0	9 (7.0)	37 (15.2) [19.6]
	r-axSpA	0	14 (6.3)	40 (12.1) [14.9]
Candida infections	nr-axSpA	0	5 (3.9)	25 (10.2) [12.8]
	r-axSpA	0	11 (5.0)	23 (7.0) [8.3]
Oral candidiasis	nr-axSpA	0	4 (3.1)	18 (7.4) [9.0]
	r-axSpA	0	10 (4.5)	20 (6.1) [7.2]
Anal candidiasis	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Genital candidiasis	nr-axSpA	0	0	0
	r-axSpA	0	1 (0.5)	1 (0.3) [0.3]
Oesophageal candidiasis[b]	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Oropharyngeal candidiasis[b]	nr-axSpA	0	1 (0.8)	4 (1.6) [1.9]
	r-axSpA	0	0	1 (0.3) [0.3]
Vulvovaginal candidiasis	nr-axSpA	0	0	3 (1.2) [1.5]
	r-axSpA	0	0	0
Skin candida	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Fungal infections NEC	nr-axSpA	0	4 (3.1)	13 (5.3) [6.4]
	r-axSpA	0	5 (2.3)	14 (4.2) [5.0]
Fungal skin infection	nr-axSpA	0	2 (1.6)	4 (1.6) [1.9]
	r-axSpA	0	0	4 (1.2) [1.4]
Tongue fungal infection	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Oral fungal infection	nr-axSpA	0	1 (0.8)	3 (1.2) [1.5]
	r-axSpA	0	0	3 (0.9) [1.0]
Onychomycosis	nr-axSpA	0	0	2 (0.8) [1.0]
	r-axSpA	0	0	2 (0.6) [0.7]

n (%), overall period: [EAIR/100 PY]		Double-blind treatment period Weeks 0–16		Overall Weeks 0–52
		PBO	BKZ 160 mg Q4W	BKZ 160 mg Q4W Total[a]
	nr-axSpA (BE MOBILE 1) r-axSpA (BE MOBILE 2)	n=126 (38.1 PYAR) n=111 (34.6 PYAR)	n=128 (40.4 PYAR) n=221 (68.3 PYAR)	n=244 (208.2 PYAR) n=330 (290.9 PYAR)
Oropharyngitis fungal[b]	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Fungal oesophagitis	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Vulvovaginal mycotic infection	nr-axSpA	0	1 (0.8)	3 (1.2) [1.5]
	r-axSpA	0	5 (2.3)	7 (2.1) [2.5]
Tinea infections	nr-axSpA	0	0	2 (0.8) [1.0]
	r-axSpA	0	1 (0.5)	6 (1.8) [2.1]
Tinea pedis	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	3 (0.9) [1.0]
Tinea versicolour	nr-axSpA	0	0	0
	r-axSpA	0	1 (0.5)	2 (0.6) [0.7]
Tinea infection	nr-axSpA	0	0	1 (0.4) [0.5]
	r-axSpA	0	0	0
Dermatophytosis of nail	nr-axSpA	0	0	0
	r-axSpA	0	0	1 (0.3) [0.3]
Serious *Candida* infections	nr-axSpA	0	0	0
	r-axSpA	0	0	0
Systemic fungal infections	nr-axSpA	0	0	0
	r-axSpA	0	0	0
Candida infections leading to study discontinuation	nr-axSpA	0	0	2 (0.8) [1.0]
	r-axSpA	0	1 (0.5)	2 (0.6) [0.7]

Safety Set. MedDRA (Version 19.0), preferred terms reported. Overall period includes all data available up to the last Week 52 visit, including data for patients treated beyond Week 24. [a]Includes patients who switched from PBO to BKZ (events after switch only); [b]For BE MOBILE 1, 1 oropharyngeal candidiasis event in the Weeks 0–16 period and 4 oropharyngeal candidiasis events and 1 oropharyngitis fungal event in the Weeks 0–52 period were reported as opportunistic infections. For BE MOBILE 2, 1 oesophageal candidiasis, 1 oropharyngeal candidiasis and 1 fungal oesophagitis event in the Weeks 0–52 period was reported as an opportunistic infection. BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; NEC: not elsewhere classified; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; PY: patient-years; PYAR: patient-years at risk; Q4W: every four weeks; r-axSpA: radiographic axial spondyloarthritis.

Table S8. Supportive observed case data for binary and continuous endpoints

		Week 16		Week 52	
		PBO	BKZ 160 mg Q4W	PBO→BKZ 160 mg Q4W	BKZ 160 mg Q4W
nr-axSpA (BE MOBILE 1)		**n=126**	**n=128**	**n=126**	**n=128**
r-axSpA (BE MOBILE 2)		**n=111**	**n=221**	**n=111**	**n=221**
Binary endpoints					
ASAS40[a], n/N (%)	nr-axSpA	27/118 (22.9)	61/127 (48.0)	64/108 (59.3)	78/110 (70.9)
	r-axSpA	25/109 (22.9)	99/210 (47.1)	76/102 (74.5)	129/196 (65.8)
ASAS20[b], n/N (%)	nr-axSpA	48/118 (40.7)	88/127 (69.3)	88/108 (81.5)	94/110 (85.5)
	r-axSpA	48/109 (44.0)	146/210 (69.5)	89/102 (87.3)	158/196 (80.6)
ASAS PR[b], n/N (%)	nr-axSpA	9/118 (7.6)	33/127 (26.0)	38/108 (35.2)	38/108 (35.2)
	r-axSpA	8/109 (7.3)	53/210 (25.2)	41/102 (40.2)	66/196 (33.7)
ASAS40 in TNFi-naïve patients[c], n/N (%)	nr-axSpA	25/103 (24.3)	55/117 (47.0)	58/95 (61.1)	73/103 (70.9)
	r-axSpA	22/92 (23.9)	84/177 (47.5)	67/85 (78.8)	108/165 (65.5)
ASAS40 in TNFi-IR patients[d], n/N (%)	nr-axSpA	2/15 (13.3)	6/10 (60.0)	6/13 (46.2)	5/7 (71.4)
	r-axSpA	3/17 (17.6)	15/33 (45.5)	9/17 (52.9)	21/31 (67.7)
ASDAS-MI[b], n/N (%)	nr-axSpA	9/116 (7.8)	35/127 (27.6)	37/105 (35.2)	47/106 (44.3)
	r-axSpA	6/108 (5.6)	57/205 (27.8)	49/99 (49.5)	71/189 (37.6)
ASDAS LDA[d], n/N (%)	nr-axSpA	25/116 (21.6)	59/127 (46.5)	60/105 (57.1)	69/106 (65.1)
	r-axSpA	19/108 (17.6)	93/206 (45.1)	68/99 (68.7)	111/189 (58.7)
ASDAS ID[d], n/N (%)	nr-axSpA	8/116 (6.9)	24/127 (18.9)	32/105 (30.5)	29/106 (27.4)

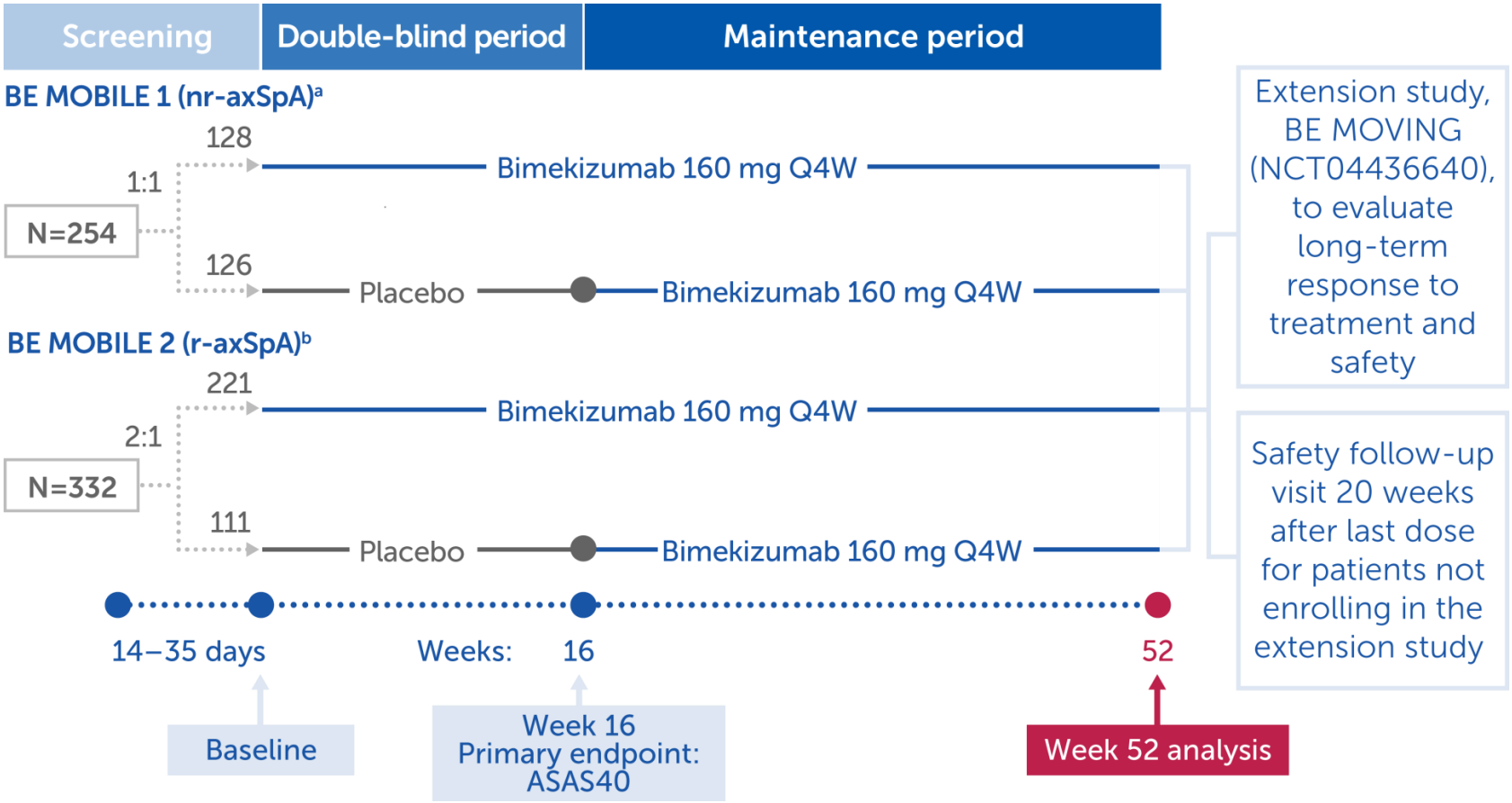
		Week 16		Week 52	
		PBO	BKZ 160 mg Q4W	PBO→BKZ 160 mg Q4W	BKZ 160 mg Q4W
nr-axSpA (BE MOBILE 1)		**n=126**	**n=128**	**n=126**	**n=128**
r-axSpA (BE MOBILE 2)		**n=111**	**n=221**	**n=111**	**n=221**
	r-axSpA	5/108 (4.6)	34/206 (16.5)	39/99 (39.4)	45/189 (23.8)
MASES=0[d,e], n/N (%)	nr-axSpA	22/87 (25.3)	48/93 (51.6)	41/79 (51.9)	51/78 (65.4)
	r-axSpA	22/65 (33.8)	68/123 (55.3)	31/60 (51.7)	67/111 (60.4)
SJC=0[d,f], n/N (%)	nr-axSpA	18/40 (45.0)	26/44 (59.1)	28/34 (82.4)	28/37 (75.7)
	r-axSpA	8/22 (36.4)	28/43 (65.1)	18/21 (85.7)	32/41 (78.0)
TJC=0[d,g], n/N (%)	nr-axSpA	21/80 (26.3)	33/76 (43.4)	40/73 (54.8)	38/65 (58.5)
	r-axSpA	20/59 (33.9)	48/110 (43.6)	35/55 (63.6)	68/101 (67.3)
BASDAI50[d], n/N (%)	nr-axSpA	27/118 (22.9)	60/127 (47.2)	62/108 (57.4)	69/109 (63.3)
	r-axSpA	29/109 (26.6)	103/210 (49.0)	69/102 (67.6)	119/196 (60.7)
Continuous endpoints					
ASDAS CfB[d], mean (SD), N	nr-axSpA	−0.6 (0.9), 116	−1.5 (1.1), 127	−1.7 (0.9), 105	−1.9 (1.1), 106
	r-axSpA	−0.7 (0.7), 108	−1.4 (1.0), 205	−1.9 (0.9), 99	−1.8 (1.0), 189
hs-CRP[d], geometric mean (geometric CV, %), N	nr-axSpA	4.0 (275.3), 116	2.0 (202.4), 128	2.0 (184.3), 105	1.7 (186.5), 109
	r-axSpA	6.0 (189.6), 108	2.4 (209.3), 209	2.1 (186.4), 100	2.2 (193.5), 189
BASDAI CfB[b], mean (SD), N	nr-axSpA	−1.5 (1.9), 118	−3.1 (2.3), 127	−3.6 (1.9), 108	−4.1 (2.1), 109
	r-axSpA	−1.9 (1.9), 109	−2.9 (2.1), 210	−4.0 (2.0), 102	−3.6 (1.9), 196
BASFI CfB[b], mean (SD), N	nr-axSpA	−1.0 (2.0), 118	−2.5 (2.4), 127	−2.6 (2.2), 108	−3.2 (2.3), 110

		Week 16		Week 52	
		PBO	BKZ 160 mg Q4W	PBO→BKZ 160 mg Q4W	BKZ 160 mg Q4W
nr-axSpA (BE MOBILE 1)		**n=126**	**n=128**	**n=126**	**n=128**
r-axSpA (BE MOBILE 2)		**n=111**	**n=221**	**n=111**	**n=221**
	r-axSpA	−1.1 (1.7), 109	−2.2 (2.1), 210	−2.8 (1.8), 102	−2.8 (2.1), 196
BASMI CfB[c], mean (SD), N	nr-axSpA	−0.1 (0.7), 118	−0.4 (0.8), 127	−0.5 (0.8), 106	−0.6 (0.8), 106
	r-axSpA	−0.2 (0.7), 104	−0.5 (0.8), 208	−0.8 (0.9), 97	−0.7 (0.9), 187
Nocturnal spinal pain CfB[b], mean (SD), N	nr-axSpA	−1.7 (2.4), 118	−3.6 (3.0), 127	−4.1 (2.5), 108	−4.6 (2.9), 109
	r-axSpA	−1.9 (2.4), 109	−3.4 (2.4), 210	−4.5 (2.7), 102	−4.2 (2.2), 196
Total spinal pain CfB[d], mean (95% CI), N	nr-axSpA	−1.7 (−2.1, −1.3), 118	−3.4 (−3.9, −2.9), 127	−4.0 (−4.4, −3.6), 108	−4.5 (−4.9, −4.0), 109
	r-axSpA	−1.9 (−2.4, −1.5), 109	−3.3 (−3.7, −3.0), 210	−4.5 (−5.0, −4.1), 102	−4.1 (−4.4, −3.8), 196
ASQoL CfB[b], mean (SD), N	nr-axSpA	−2.6 (4.2), 118	−5.2 (4.8), 127	−5.5 (4.5), 108	−6.2 (4.8), 110
	r-axSpA	−3.2 (3.6), 109	−5.0 (4.4), 210	−5.5 (4.3), 102	−5.8 (4.6), 196
SF-36 PCS CfB[b], mean (SD), N	nr-axSpA	5.6 (7.6), 118	9.5 (8.3), 127	11.8 (9.3), 108	12.5 (9.6), 110
	r-axSpA	5.8 (7.9), 109	9.4 (8.5), 209	12.1 (9.1), 102	12.3 (9.1), 196
Morning stiffness CfB[d], mean (95% CI), N	nr-axSpA	−1.9 (−2.3, −1.5), 118	−3.7 (−4.1, −3.2), 127	−4.2 (−4.6, −3.8), 108	−4.7 (−5.2, −4.2), 109
	r-axSpA	−2.1 (−2.5, −1.7), 109	−3.3 (−3.6, −2.9), 210	−4.5 (−4.9, −4.0), 102	−4.0 (−4.3, −3.6), 196
MASES CfB[d], mean (SD), N	nr-axSpA	−1.3 (2.7), 87	−2.4 (3.3), 93	−2.9 (3.4), 79	−3.6 (2.9), 78
	r-axSpA	−1.5 (2.3), 65	−2.5 (2.8), 123	−3.4 (2.7), 60	−3.0 (2.9), 111
SJC CfB[d], mean (SD), N	nr-axSpA	−1.4 (3.9), 40	−3.1 (4.5), 44	−3.0 (2.6), 34	−3.0 (5.5), 38
	r-axSpA	−2.1 (2.5), 22	−3.6 (3.6), 43	−3.5 (3.8), 21	−4.3 (4.0), 41

		Week 16		Week 52	
		PBO	**BKZ 160 mg Q4W**	**PBO→BKZ 160 mg Q4W**	**BKZ 160 mg Q4W**
	nr-axSpA (BE MOBILE 1)	**n=126**	**n=128**	**n=126**	**n=128**
	r-axSpA (BE MOBILE 2)	**n=111**	**n=221**	**n=111**	**n=221**
TJC CfB[d], mean (SD), N	nr-axSpA	−1.1 (4.9), 80	−3.0 (5.8), 76	−3.5 (5.0), 73	−3.9 (6.8), 66
	r-axSpA	−3.0 (4.0), 59	−2.5 (4.5), 111	−4.6 (4.5), 55	−4.2 (5.7), 101

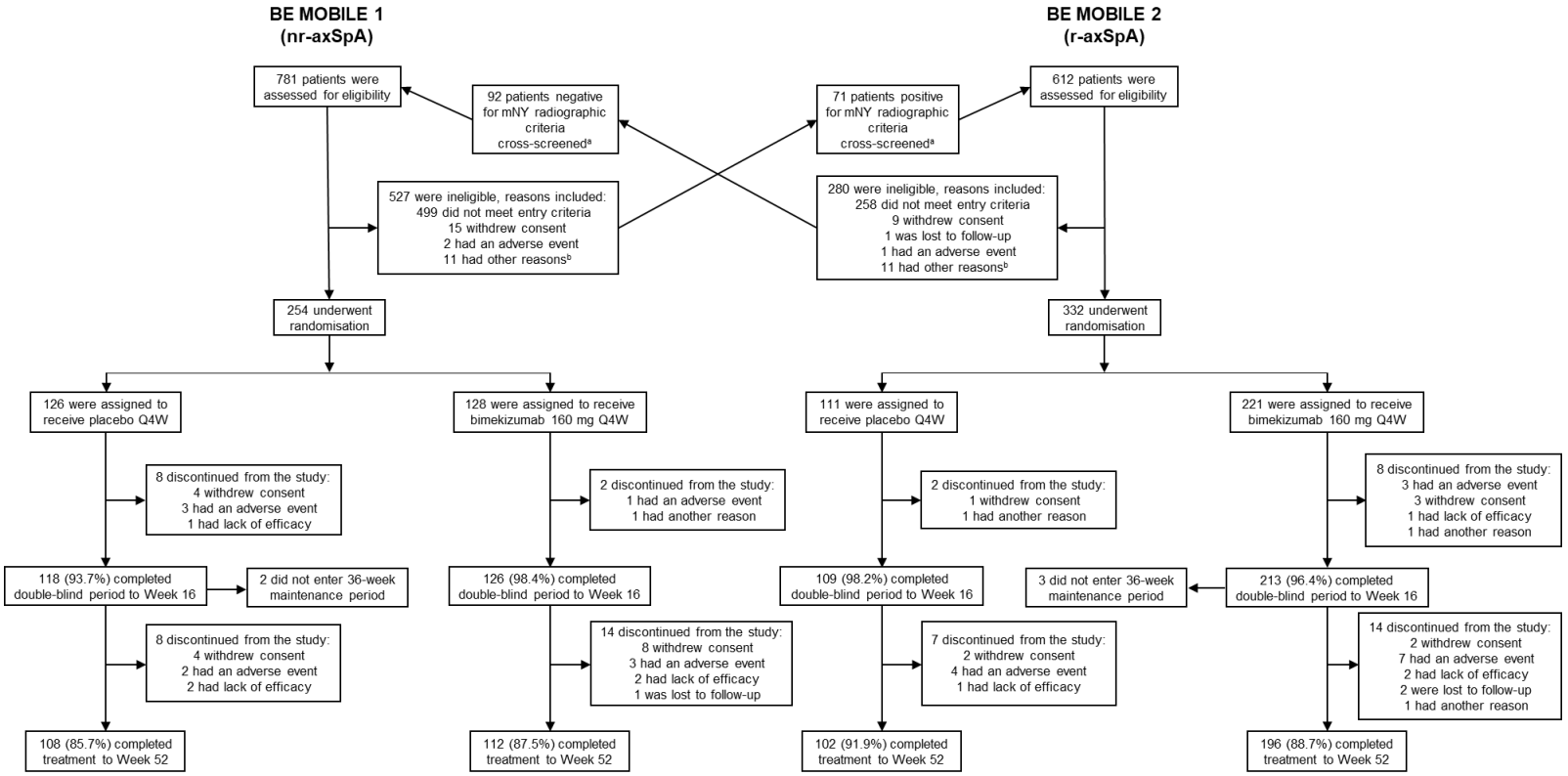
Randomised set. [a]Primary endpoint; [b]Secondary endpoints; [c]Ranked secondary endpoint in BE MOBILE 2; [d]Exploratory endpoints; [e]In patients with MASES >0 at baseline; [f]In patients with SJC >0 at baseline; [g]In patients with TJC >0 at baseline. ASAS20/40/PR: Assessment of Spondyloarthritis international Society 20%/40% response/partial remission; ASDAS-ID/MI: Ankylosing Spondylitis Disease Activity Score inactive disease/major improvement; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASDAI50: BASDAI 50% response; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BKZ: bimekizumab; CfB: change from baseline; CI: confidence interval; CV: coefficient of variation; hs-CRP: CRP: high sensitivity C-reactive protein; LDA: low disease activity; MASES: Maastricht ankylosing spondylitis enthesitis score; MI: multiple imputation; N: number of participants with a non-missing measurement for that timepoint; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; OC: observed case; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; TNFi: tumour necrosis factor inhibitor; SD: standard deviation; SE: standard error; SF-36 PCS: Short-Form 36-item Health Survey Physical Component Summary; SJC: swollen joint count; TJC: tender joint count; TNFi: tumour necrosis factor inhibitor.

Figure S1. Study design



Patients were eligible to receive non-biologic rescue therapy from Week 20 at the discretion of the investigator while continuing to receive BKZ. [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 nr-axSpA fulfilling modified New York criteria. ASAS: Assessment of SpondyloArthritis international Society; ASAS40: ASAS 40% response; BKZ: bimekizumab; CRP: C-reactive protein; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.

Figure S2. Enrollment, randomisation and treatment



[a]Patients who failed screening in both studies could not be re-screened; [b]Screen failure reasons noted as 'other' mainly related to the COVID-19 pandemic (e.g. hospital closures or the halt in enrolment early in the pandemic). mNY: modified New York; nr-axSpA: non-radiographic axial spondyloarthritis; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.

REFERENCES

1. Landewé, RB; Hermann, K-GA; van der Heijde, DM *et al.* Scoring sacroiliac joints by magnetic resonance imaging. A multiple-reader reliability experiment. The Journal of Rheumatology. 2005;32(10):2050-2055.
2. Hededal, P; Østergaard, M; Sørensen, IJ *et al.* Development and validation of MRI sacroiliac joint scoring methods for the semiaxial scan plane corresponding to the Berlin and SPARCC MRI scoring methods, and of a new global MRI sacroiliac joint method. The Journal of Rheumatology. 2018;45(1):70-77.
3. van der Heijde, D; Deodhar, A; Baraliakos, X *et al.* Efficacy and safety of bimekizumab in axial spondyloarthritis: results of two parallel phase 3 randomised controlled trials. Annals of the Rheumatic Diseases. 2023;82:515–526.