Bimekizumab in Patients with Active Ankylosing Spondylitis: 24-Week Efficacy & Safety from BE MOBILE 2, a Phase 3, Multicentre, Randomised, Placebo-Controlled Study

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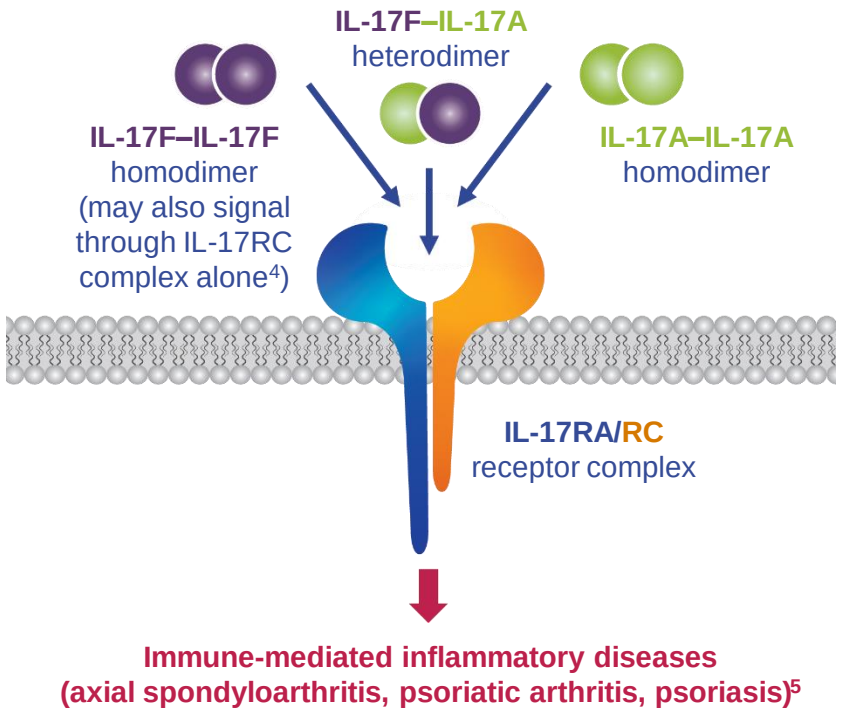
Background & Objective

- **Bimekizumab** (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- In a phase 2b study, bimekizumab showed rapid and sustained efficacy and was well tolerated up to 156 weeks in patients with active ankylosing spondylitis (AS), also known as radiographic axial spondyloarthritis (r-axSpA).[1,2]

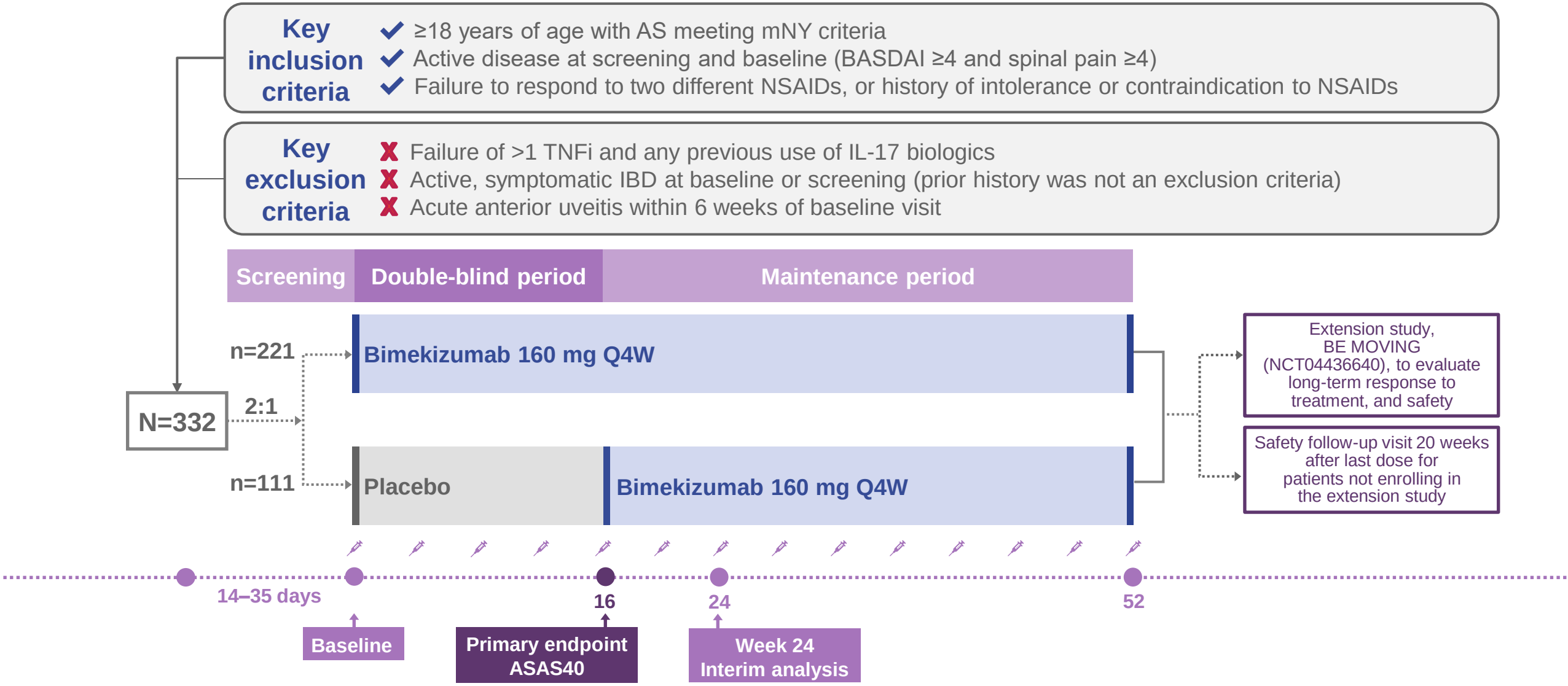
IL-17A and IL-17F[3]



OBJECTIVE: To assess efficacy and safety of subcutaneous bimekizumab vs placebo (PBO) in patients with active AS up to Week 24 in the ongoing pivotal phase 3 study, BE MOBILE 2.

1. van der Heijde D. Ann Rheum Dis 2020;79:595–604; 2. Gensler L. Arthritis Rheumatol 2021;73(suppl 10):0491; 3. Yang XO. J Exp Med. 2008;1063–1075; 4. Goepfert A. Immunity. 2020;52(3):499–512.e5; 5. Glatt S. Ann Rheum Dis. 2018;77:523–532. AS: ankylosing spondylitis; Ig: immunoglobulin; IL: interleukin; RA: receptor A; RC: receptor C.

Study Design



Patients eligible to receive non-biologic rescue therapy from Week 20 at the discretion of the investigator while continuing to receive BKZ. AS: ankylosing spondylitis; ASAS40: Assessment of Spondyloarthritis international Society 40% response; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; IBD: inflammatory bowel disease; IL-17i: interleukin 17 inhibitor; mNY: modified New York; NSAID: non-steroidal anti-inflammatory drug; Q4W: every 4 weeks; TNFi: tumour necrosis factor inhibitor.

Patient Demographics and Baseline Disease Characteristics

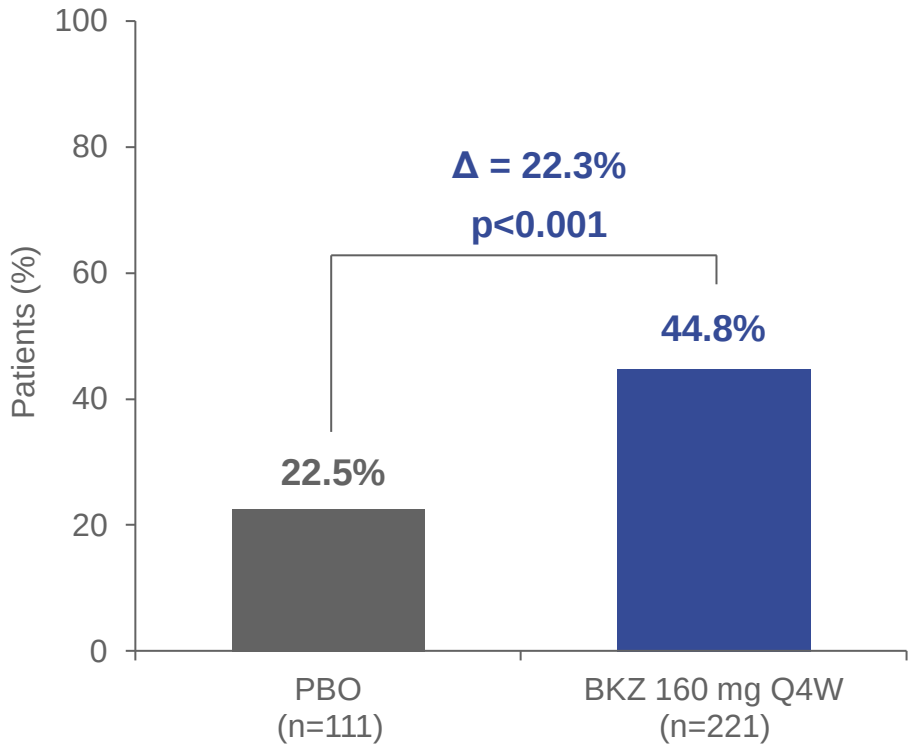
	PBO n=111	BKZ 160 mg Q4W n=221
Age, years, mean (SD)	39.2 (12.6)	41.0 (12.1)
Sex, male, n (%)	80 (72.1%)	160 (72.4%)
HLA-B27 positive, n (%)	93 (83.8%)	191 (86.4%)
Symptom duration, years, mean (SD)	11.9 (8.6)	14.2 (11.0)
ASDAS-CRP, mean (SD)	3.7 (0.8)	3.7 (0.8)
BASDAI, mean (SD)	6.5 (1.3)	6.5 (1.3)
hs-CRP, mg/L, median (min, max)	6.3 (0.3, 104.3)	8.2 (0.1, 105.4)
hs-CRP >ULN,[a] n (%)	67 (60.4%)	137 (62.0%)
Total spinal pain, mean (SD)	7.2 (1.2)	7.1 (1.6)
Current enthesitis (MASES >0), n (%)	67 (60.4%)	132 (59.7%)
MRI spine Berlin score, mean (SD) [Nsub][b]	3.3 (4.9) [45]	3.8 (5.3) [82]
SPARCC MRI SIJ score, mean (SD) [Nsub][b]	5.8 (7.7) [45]	7.4 (10.7) [83]
Prior TNFi exposure, n (%)	17 (15.3%)	37 (16.7%)

Randomised set. [a] ULN value for hs-CRP is 5 mg/L; [b] Only patients enrolled in the SIJ and spine MRI sub-study are included in this analysis. ASDAS: Ankylosing Spondylitis Disease Activity Score; BKZ: bimekizumab; BMI: body mass index; CRP: C-reactive protein; csDMARD: conventional synthetic disease-modifying antirheumatic drug; HLA-B27: human leukocyte antigen-B27; hs-CRP: high-sensitivity C-reactive protein; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; MRI: magnetic resonance imaging; NSAID: non-steroidal anti-inflammatory drug; Nsub: number of patients in subgroup; PBO: placebo; Q4W: every 4 weeks; SD: standard deviation; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada; TNFi: tumour necrosis factor inhibitor; ULN: upper limit of normal.

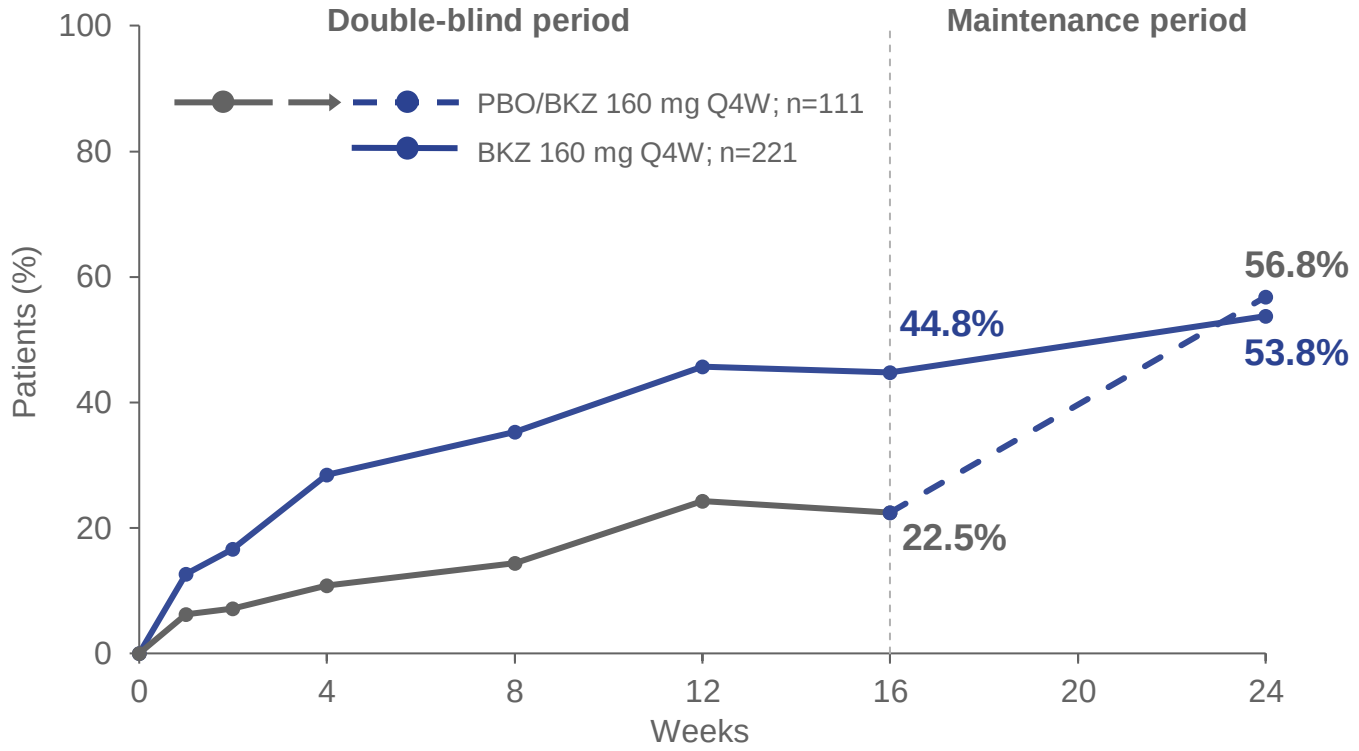
Significantly Greater ASAS40 Response Rate with BKZ vs PBO

Primary endpoint: ASAS40 response with BKZ compared to PBO at Week 16

ASAS40 response at Week 16 (NRI)



ASAS40 kinetics of response to Week 24 (NRI)



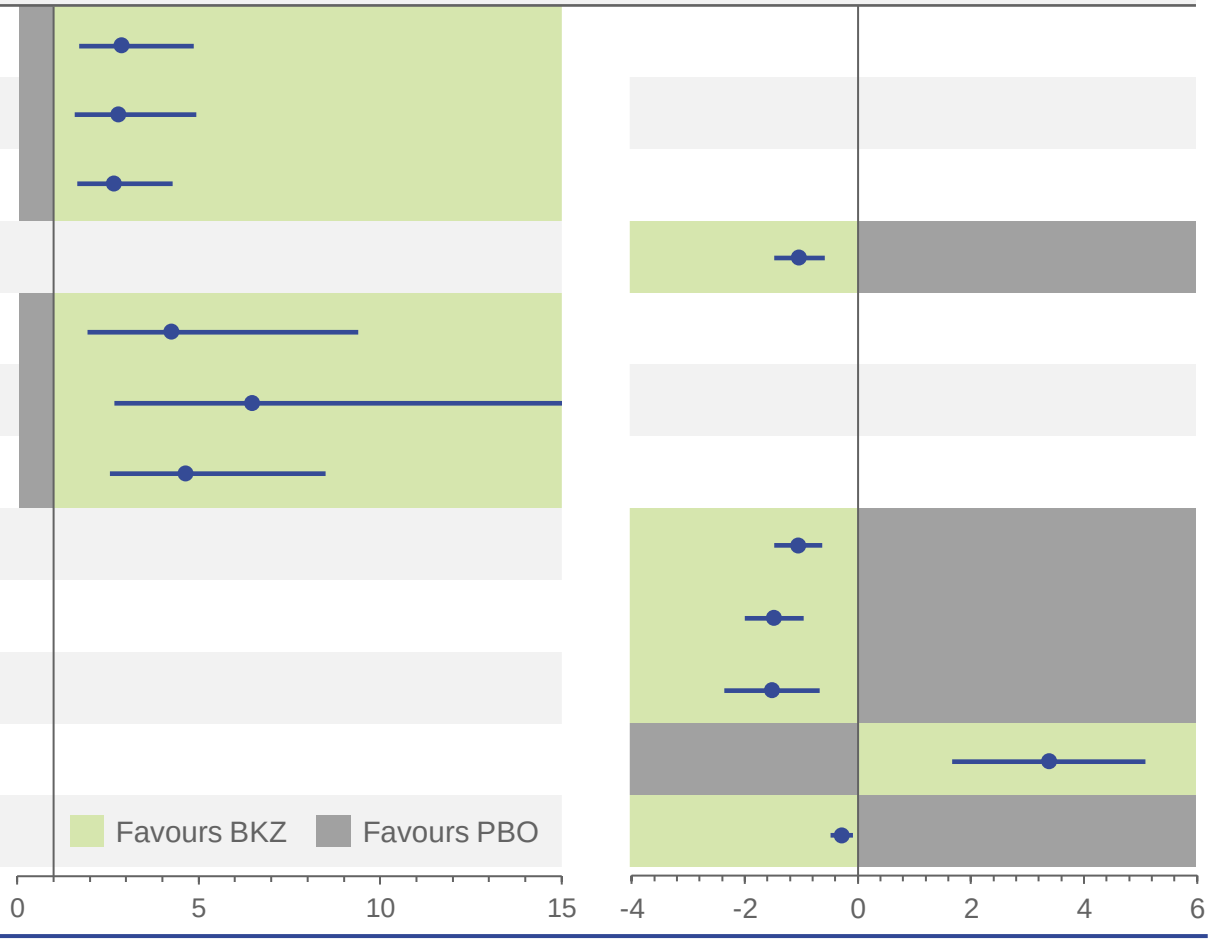
Study completion to Week 16/24, n (%)

PBO	111 (100%)	109 (98.2%)	108 (97.3%)
BKZ	221 (100%)	213 (96.4%)	205 (92.8%)

Randomised set. p value was calculated using logistic regression with treatment, prior TNFi exposure and region as factors. ASAS40: Assessment of Spondyloarthritis international Society 40% response; BKZ: bimekizumab; NRI: non-responder imputation; PBO: placebo; Q4W: every 4 weeks; TNFi: tumour necrosis factor inhibitor.

Primary and All Ranked Secondary Endpoints Were Met at Week 16

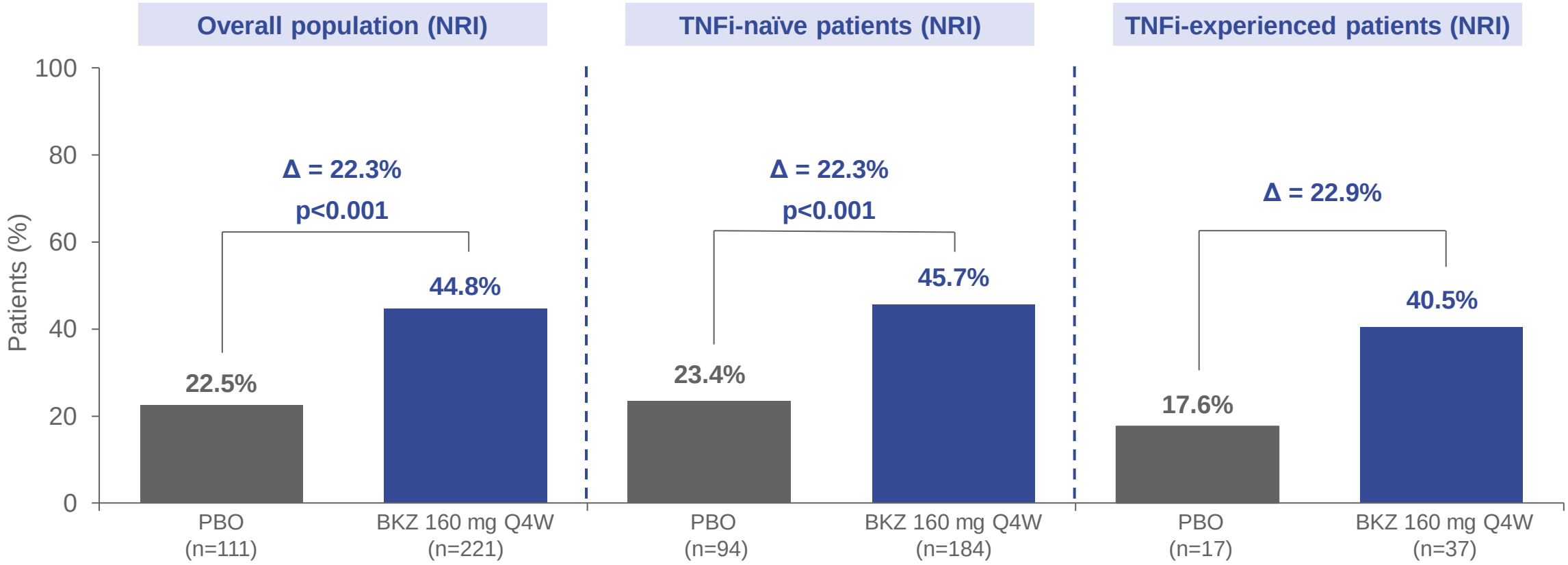
	Efficacy endpoint	PBO n=111	BKZ 160 mg Q4W n=221	p value[a]
1	**ASAS40**,* n (%)	25 (22.5)	99 (44.8)	<0.001
2	**ASAS40 (TNFi-naïve patients)**,† n (%)	22 (23.4)[b]	84 (45.7)[c]	<0.001
3	**ASAS20**,† n (%)	48 (43.2)	146 (66.1)	<0.001
4	**BASDAI** CfB,† mean (SE)	–1.9 (0.2)	–2.9 (0.1)	<0.001
5	**ASAS partial remission**,† n (%)	8 (7.2)	53 (24.0)	<0.001
6	**ASDAS-MI**,† n (%)	6 (5.4)	57 (25.8)	<0.001
7	**ASAS 5/6**,† n (%)	16 (14.4)	94 (42.5)	<0.001
8	**BASFI** CfB,† mean (SE)	–1.1 (0.2)	–2.2 (0.1)	<0.001
9	**Nocturnal spinal pain** CfB,† mean (SE)	–1.9 (0.2)	–3.3 (0.2)	<0.001
10	**ASQoL** CfB,† mean (SE)	–3.2 (0.3)	–4.9 (0.3)	<0.001
11	**SF-36 PCS** CfB,† mean (SE)	5.9 (0.8)	9.3 (0.6)	<0.001
12	**BASMI** CfB,† mean (SE)	–0.2 (0.1)	–0.5 (0.1)	0.005



Randomised set. *Primary endpoint; †Secondary endpoint. [a] All tests performed at a 2-sided alpha level of 0.05. For binary variables, p values were calculated by logistic regression with treatment, prior TNFi exposure and region as factors. For continuous variables, p values were obtained by ANCOVA with treatment, prior TNFi exposure and region as fixed effects, and baseline values as covariates; [b] n=94; [c] n=184. Missing data were imputed using non-responder imputation for binary endpoints and reference-based multiple imputation for continuous endpoints (based on data from the placebo group). ANCOVA: analysis of covariance; ASAS20/40: Assessment of Spondyloarthritis international Society 20%/40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; 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; CI: confidence interval; MI: major improvement; PBO: placebo; PCS: Physical Component Summary; Q4W: every 4 weeks; SE: standard error; SF-36: Short-Form 36-item Health Survey; TNFi: tumour necrosis factor inhibitor.

Consistent ASAS40 Response Rate with BKZ in TNFi-Naïve and TNFi-Experienced Patients

Ranked secondary endpoint: ASAS40 response at Week 16 in TNFi-naïve patients
Exploratory endpoint: ASAS40 response at Week 16 in TNFi-experienced patients

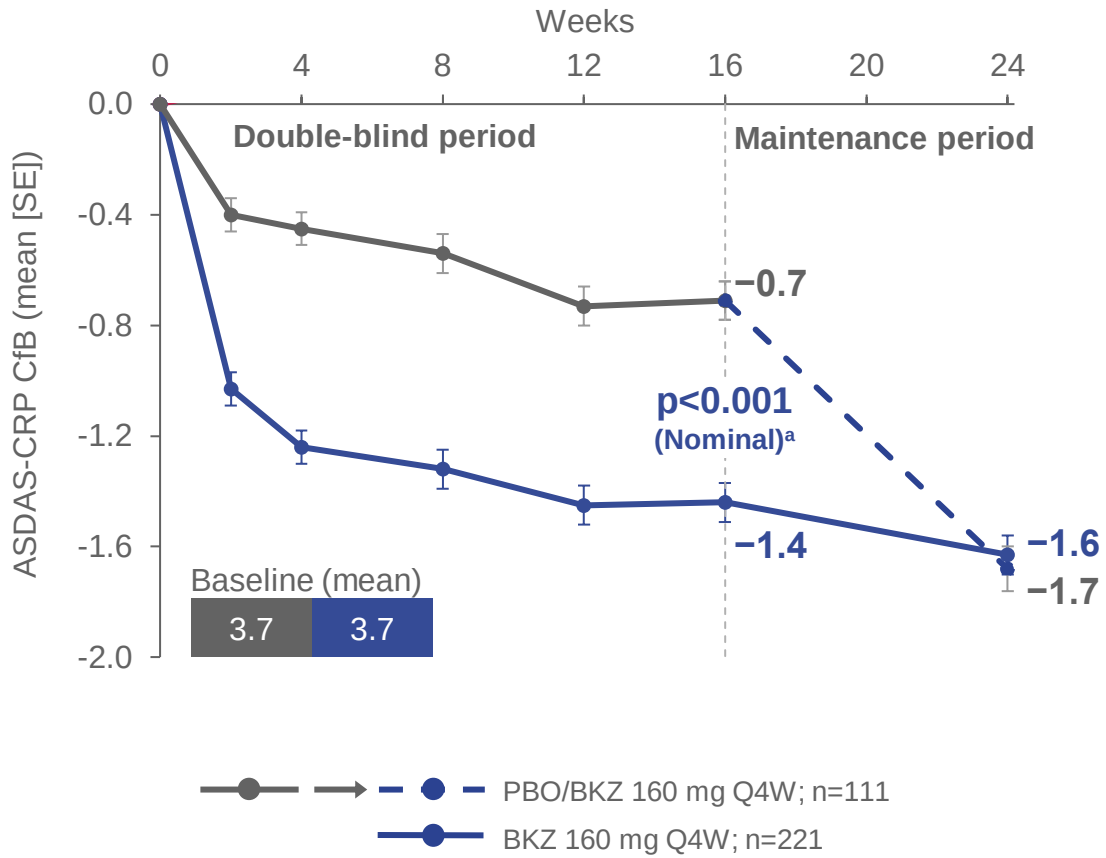


Randomised set. p values were calculated using logistic regression with treatment, prior TNFi exposure and region as factors (overall population) or treatment and region as factors (TNFi-naïve patients). ASAS40: Assessment of Spondyloarthritis international Society 40% response; BKZ: bimekizumab; CRP: C-reactive protein; NRI: non-responder imputation; PBO: placebo; Q4W: every 4 weeks; TNFi: tumour necrosis factor inhibitor.

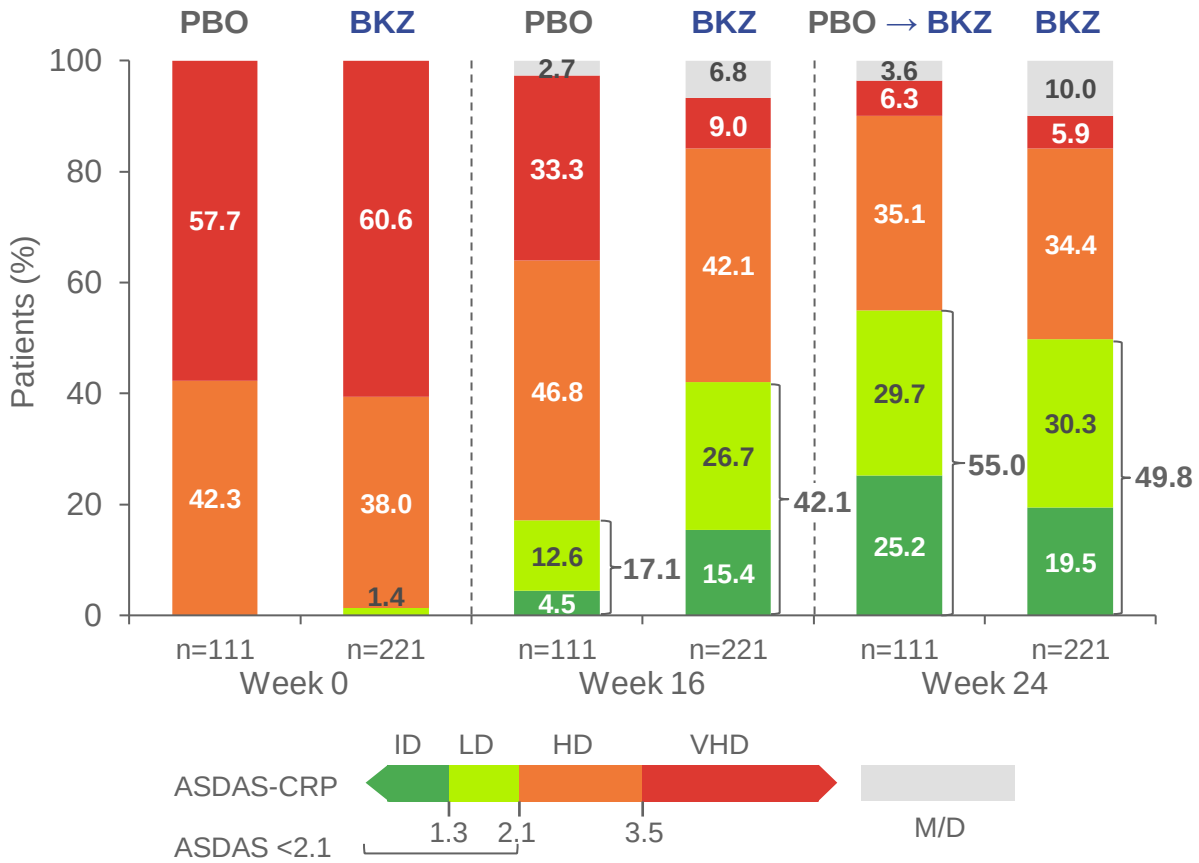
Improvement in ASDAS with BKZ

Exploratory endpoints: ASDAS disease states and change from baseline in ASDAS-CRP with BKZ compared to PBO

ASDAS-CRP CfB (MI)



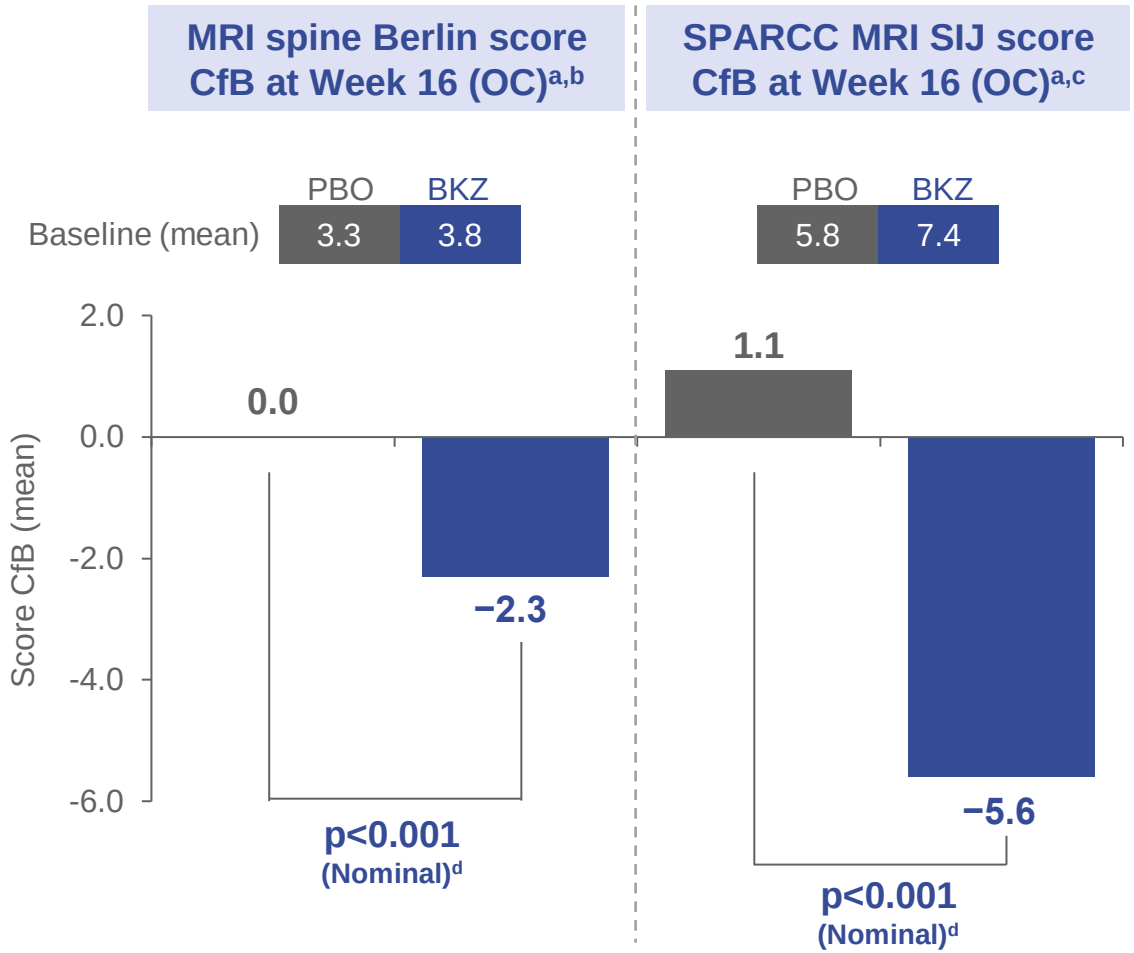
ASDAS Disease States (OC)

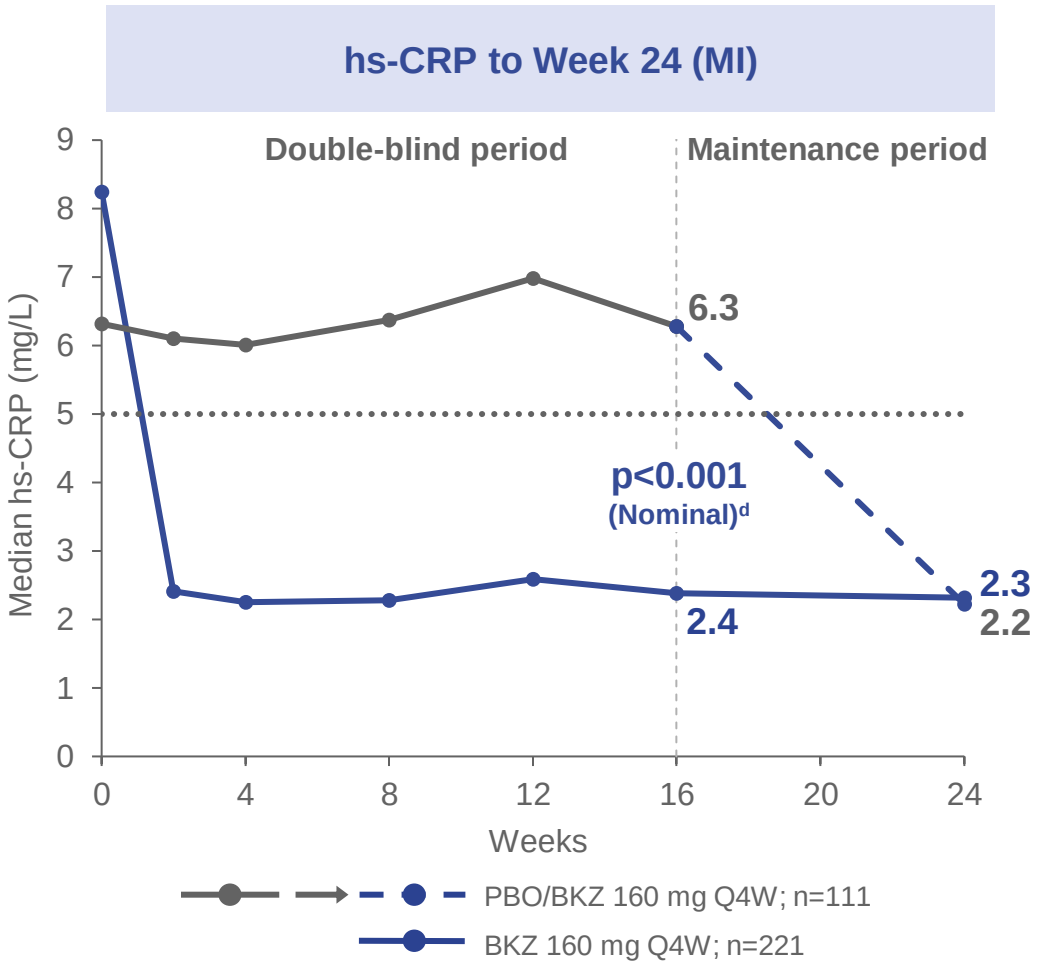


Randomised set. [a] Nominal p values were not controlled for multiplicity. p value was obtained by ANCOVA with treatment, prior TNFi exposure and region as fixed effects, and baseline values as covariates. For ASDAS-CRP CfB, MI was based on the missing at random assumption. VHD: ASDAS >3.5; HD: ASDAS ≥2.1–≤3.5; LD: ASDAS ≥1.3–<2.1; ID: ASDAS <1.3. ANCOVA: analysis of covariance; ASDAS: Ankylosing Spondylitis Disease Activity Score; BKZ: bimekizumab; CfB: change from baseline; CRP: C-reactive protein; HD: high disease; ID: inactive disease; LD: low disease; M/D: missing data; MI: multiple imputation; OC: observed case; PBO: placebo; Q4W: every four weeks; SE: standard error; VHD: very high disease.

Reduction in Objective Signs of Inflammation with BKZ

Exploratory endpoints: Change from baseline in MRI spine Berlin score and SPARCC MRI SIJ score, and median hs-CRP with BKZ compared to PBO





Randomised set. [a] Only patients enrolled in the SIJ and spine MRI sub-study are included in this analysis; [b] At baseline, n=45 (PBO) and n=82 (BKZ), at Week 16, n=43 (PBO) and n=79 (BKZ); [c] At baseline, n=45 (PBO) and n=83 (BKZ), at Week 16, n=43 (PBO) and n=79 (BKZ); [d] Nominal p values were not controlled for multiplicity. MRI spine Berlin score ranges from 0 to 69 with lower scores indicating less spinal inflammation, and a negative change representing improvement. SPARCC MRI SIJ score ranges from 0 to 72 with lower scores indicating less SIJ inflammation, and a negative change representing improvement. For hs-CRP, MI was based on the missing at random assumption. p values were obtained by ANCOVA with treatment, prior TNFi exposure and region as fixed effects, and baseline values as covariates. ANCOVA: analysis of covariance; BKZ: bimekizumab; CfB: change from baseline; hs-CRP: high-sensitivity C-reactive protein; MI: multiple imputation; MRI: magnetic resonance imaging; OC: observed case; PBO: placebo; Q4W: every 4 weeks; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada; TNFi: tumour necrosis factor inhibitor.

Safety Overview

n (%)	Double-blind period (Weeks 0–16)		Overall (Weeks 0–24)
	PBO n=111	BKZ 160 mg Q4W n=221	BKZ 160 mg Q4W Total[a] N=330
Any treatment-emergent adverse event (TEAE)	48 (43.2)	120 (54.3)	183 (55.5)
Most frequently reported TEAEs[b]			
Nasopharyngitis	4 (3.6)	17 (7.7)	21 (6.4)
Diarrhoea	1 (0.9)	7 (3.2)	13 (3.9)
Headache	5 (4.5)	9 (4.1)	12 (3.6)
Oral candidiasis[c]	0	9 (4.1)	10 (3.0)
Serious TEAEs	1 (0.9)	4 (1.8)	12 (3.6)
Study discontinuation due to TEAEs	0	6 (2.7)	11 (3.3)
Drug-related TEAEs	19 (17.1)	65 (29.4)	96 (29.1)
Severe TEAEs	0	3 (1.4)	9 (2.7)
Fungal infections	0	13 (5.9)	21 (6.4)
Systemic fungal infections	0	0	0
Adjudicated IBD[d]			
Definite Crohn's disease	0	1 (0.5)	1 (0.3)
Probable ulcerative colitis	0	1 (0.5)	1 (0.3)
Uveitis[e,f]	5 (4.5)	0	2 (0.6)

- All fungal infections were mild or moderate, localised, and mucocutaneous; few led to treatment discontinuation (2 patients: 1 oral and 1 oesophageal candidiasis)
- A case of herpes zoster occurred in 1 (0.9%) patient in the placebo group; no cases were reported with bimekizumab
- No active tuberculosis, adjudicated MACE or deaths were reported
- Overall, safety was consistent with prior studies[1,2]

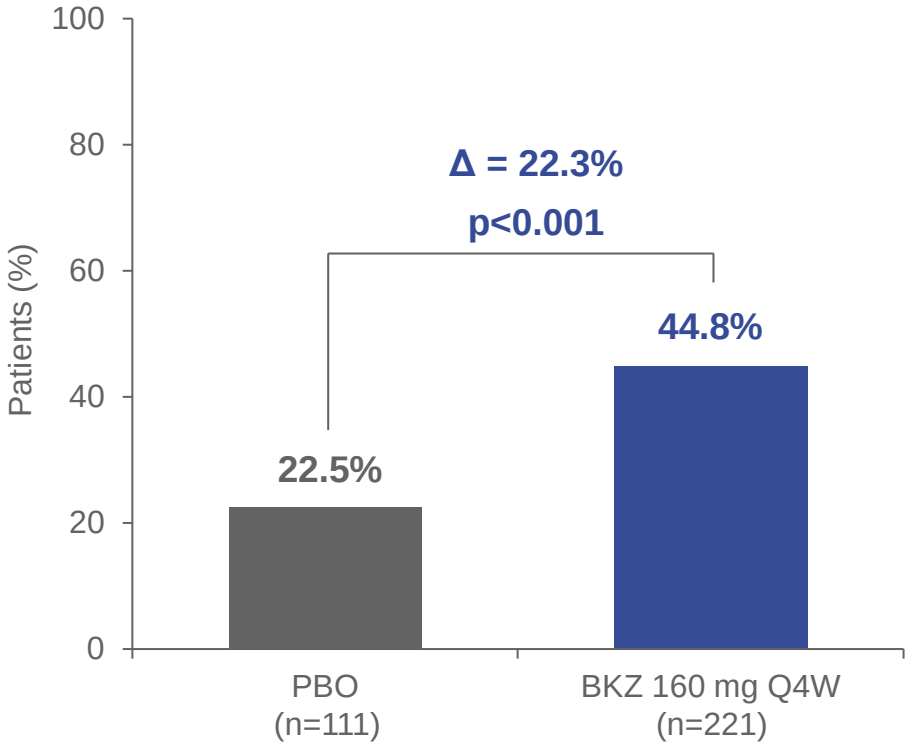
1. van der Heijde D. Ann Rheum Dis 2020;79:595–604; 2. Gensler L. Arthritis Rheumatol 2021;73(suppl 10):0491. Safety set. MedDRA (Version 19.0). [a] Includes patients who switched from PBO to BKZ (events after switch only); [b] TEAEs >3% in either BKZ are reported by preferred term; [c] All oral candidiasis cases were mild to moderate; [d] Neither patient had a medical history of IBD; [e] At baseline, 24/111 (21.6%) patients on PBO and 33/221 (14.9%) patients on BKZ had a medical history of uveitis; [f] Includes the preferred terms autoimmune uveitis, uveitis, iridocyclitis and iritis. BKZ: bimekizumab; IBD: inflammatory bowel disease; MACE: major adverse cardiovascular event; n: number of patients reporting at least one TEAE in that category; PBO: placebo; Q4W: every 4 weeks; TEAE: treatment-emergent adverse event.

Consistency of BKZ Across the Spectrum of Axial Spondyloarthritis

Results from the BE MOBILE 2 study in patients with AS (i.e. radiographic axial spondyloarthritis) were consistent with findings from the BE MOBILE 1 study in patients with non-radiographic axial spondyloarthritis (nr-axSpA).[1]

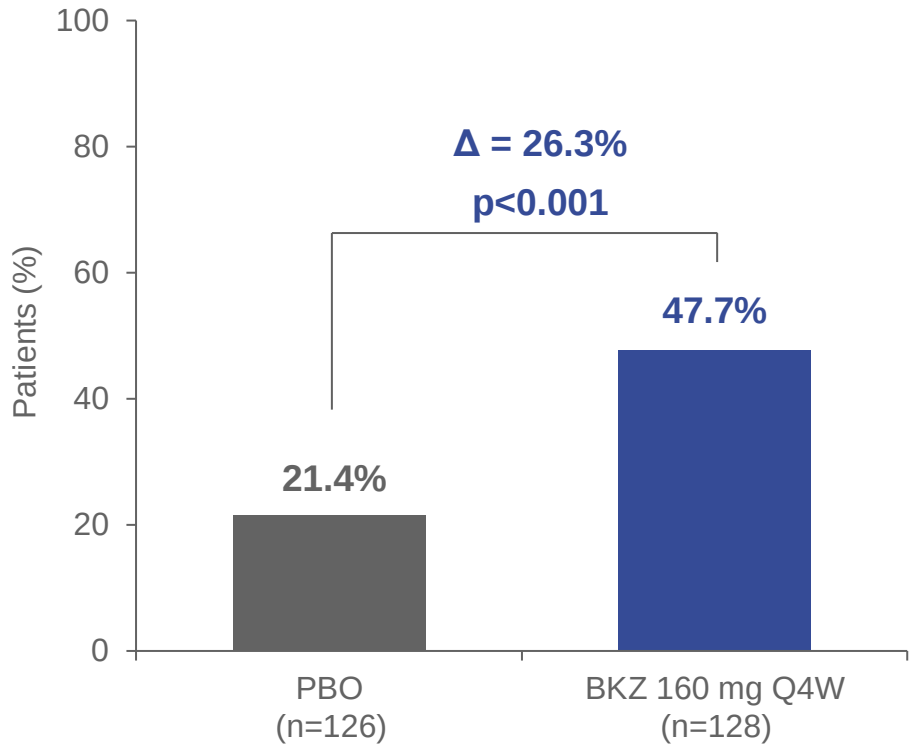
Patients with AS (BE MOBILE 2)

ASAS40 response at Week 16 (NRI)



Patients with nr-axSpA (BE MOBILE 1)

ASAS40 response at Week 16 (NRI)



1. Deodhar A. EULAR 2022;POS0939. Randomised set. In BE MOBILE 2, p value was calculated using logistic regression with treatment, prior TNFi exposure and region as factors. In BE MOBILE 1, p value was calculated using logistic regression with treatment, MRI/CRP classification and region as factors. AS: ankylosing spondylitis; ASAS40: Assessment of Spondyloarthritis international Society 40% response; BKZ: bimekizumab; CRP: C-reactive protein; MRI: magnetic resonance imaging; NRI: non-responder imputation; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; Q4W: every 4 weeks; TNFi: tumour necrosis factor inhibitor.

Conclusions

The BE MOBILE 2 phase 3 study, evaluating dual inhibition of IL-17A and IL-17F with bimekizumab in patients with AS, met all its primary and secondary endpoints.

Patients with active AS treated with bimekizumab showed rapid and clinically meaningful reductions in key signs and symptoms of disease, with ≥50% patients achieving ASDAS <2.1 by Week 24. Consistent ASAS40 response rates were observed between TNFi-naïve and TNFi-experienced patients.

Objective signs of inflammation were markedly reduced in bimekizumab-treated patients, as measured by CRP level and MRI inflammation of the sacroiliac joints and spine.

The results presented here from the BE MOBILE 2 study in patients with AS (i.e. radiographic axial spondyloarthritis) are consistent with findings from the BE MOBILE 1 study in patients with non-radiographic axial spondyloarthritis (nr-axSpA).[1]

The safety profile was consistent with prior studies, with no new safety signals observed.[2,3]

1. Deodhar A. EULAR 2022;POS0939; 2. van der Heijde D. Ann Rheum Dis 2020;79:595–604; 3. Gensler L. Arthritis Rheumatol 2021;73(suppl 10):0491. AS: ankylosing spondylitis; ASAS40: Assessment of Spondyloarthritis international Society 40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: C-reactive protein; IL: interleukin; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; TNFi: tumour necrosis factor inhibitor.