Bimekizumab Long-Term Efficacy and Safety Over 96 Weeks in Patients with Ankylosing Spondylitis: Interim Results from a Phase 2b Open-Label Extension Study

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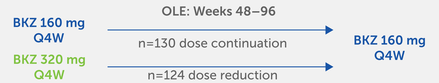
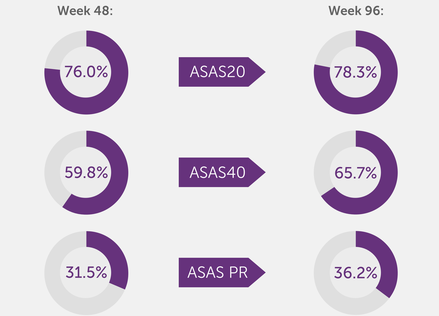
Summary

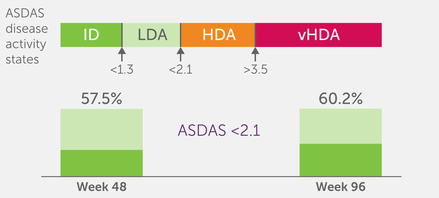
Patients with ankylosing spondylitis who completed 48 weeks' bimekizumab (BKZ) treatment (160 or 320 mg very 4 weeks [Q4W]) in BE AGILE entered the open-label extension (OLE)



Improvements in ASAS response rates and ASDAS were made in BE AGILE and maintained throughout the OLE to Week 96:

Data are for all BKZ (N=254; non-responder imputation)





Dose reduction from 320 mg to 160 mg Q4W was not followed by loss of response.

Long-term BKZ exposure was well tolerated.

Objective

To report 2-year interim efficacy and safety of bimekizumab (BKZ) in patients with active ankylosing spondylitis (AS) from a phase 2b dose-ranging study (BE AGILE; NCT02963506) and ongoing open-label extension (OLE; NCT03355573).

Background

- BKZ, a humanized IgG1 monoclonal antibody that selectively inhibits interleukin (IL)-17A and IL-17F, has demonstrated clinical efficacy in patients with AS treated over 48 weeks.[1]

Methods

Study Design and Patients

- Patients who completed 48 weeks of treatment in BE AGILE were eligible for entry into the OLE **(Figure 1)**.
- Patients were ≥18 years with active AS (BASDAI ≥4 and spinal pain ≥4), radiographic sacroiliitis meeting modified New York criteria, and inadequate response, contraindication or intolerance to NSAIDs.[1]

Study Assessments

- Efficacy outcomes are presented during Weeks 48 to 96; improvements from BE AGILE baseline (Week 0) are reported.
- Efficacy outcomes are reported for the OLE Full Analysis Set (patients who had ≥1 dose of BKZ and ≥1 valid efficacy variable measurement since entry into the OLE). Missing data were imputed using non-responder imputation (binary variables) or multiple imputation (continuous variables).
- Treatment-emergent adverse events (TEAEs) to Week 96 are reported separately for the BE AGILE Safety Set and OLE Safety Set (patients who received ≥1 dose of BKZ on study entry).

Results

Patients

- Baseline characteristics were comparable across treatment arms **(Table 1)**.
- Of 303 patients at BE AGILE baseline, 262 (87%) completed Week 48; 254 of 262 (97%) were included in the OLE Full Analysis Set, including 130 who continued on BKZ 160 mg Q4W and 124 who dose-reduced from BKZ 320 mg Q4W to BKZ 160 mg Q4W. 238 (94%) had an efficacy assessment at Week 96.

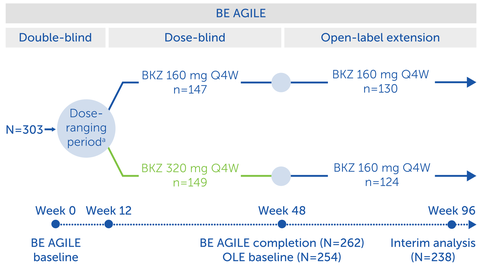
Efficacy Outcomes

- In BE AGILE, rapid improvements in efficacy outcomes were observed in BKZ-treated patients at Week 12;[1] these further increased to Week 48 and were maintained during the OLE from Weeks 48–96 **(Figure 2 and Table 2)**.
- Responses were similar for patients on BKZ 160 mg and 320 mg at Week 48; and remained similar between patients continuing on BKZ 160 mg and those dose-reduced from BKZ 320 mg to 160 mg up to Week 96 **(Figure 2)**.

Safety

- The exposure-adjusted incidence rate (EAIR) per 100 patient-years (PY) of TEAEs was 186.2 in BE AGILE (Weeks 0–48) and 111.7 in the OLE (Week 48 onwards); for serious TEAEs the EAIR/100 PY was 5.1 and 6.1, respectively **(Table 3)**.
- The EAIR/100 PY for the TEAEs uveitis and inflammatory bowel disease were 0.8 and 1.5 in BE AGILE, and 0.6 and 0.9 in the OLE.

Figure 1 Study design



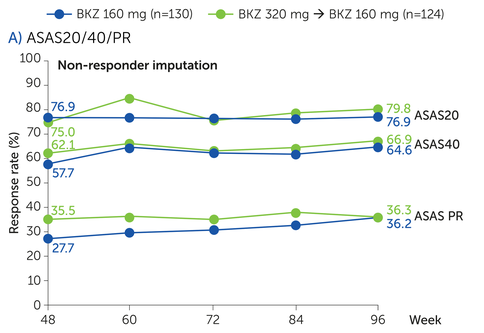
[a]Doses received in the dose-ranging period: BKZ 16 mg, 64 mg, 160 mg and 320 mg.

Table 1 BE AGILE patient characteristics and baseline demographics

	BKZ 160 mg → 160 mg (n=129)	BKZ 320 mg → 160 mg (n=126)	All BKZ (N=255)
Age, years, mean (SD)	41.2 (11.9)	42.4 (10.9)	41.8 (11.4)
Male, n (%)	111 (86)	106 (84)	217 (85)
HLA-B27 positive, n (%)	117 (91)	115 (91)	232 (91)
Time since first AS symptoms, years, mean (SD)	13.6 (9.0)	14.5 (9.9)	14.0 (9.4)
Prior TNFi therapy, n (%)	17 (13)	12 (10)	29 (11)
ASDAS-CRP, mean (SD)	3.9 (0.8)	3.9 (0.8)	3.9 (0.8)
BASDAI, mean (SD)	6.3 (1.3)	6.5 (1.4)	6.4 (1.4)
BASFI, mean (SD)	5.7 (1.8)	5.7 (2.0)	5.7 (1.9)
BASMI, mean (SD)[a]	4.6 (1.7)[b]	4.8 (1.7)[c]	4.7 (1.7)[d]
Total spine pain score, mean (SD)	6.8 (1.8)	7.2 (1.7)	7.0 (1.8)
PGADA, mean (SD)	6.8 (1.7)	7.0 (1.7)	6.9 (1.7)
CRP, mg/L, median (min, max)	13.1 (0.6, 130.1)	11.0 (0.3, 114.6)	12.1 (0.3, 130.1)

[a]Data are for Full Analysis Set. [b]n=130. [c]n=123. [d]n=253. OLE Safety Set (N=255): patients who received ≥1 dose of BKZ on study entry. Data are reported for BE AGILE baseline by treatment group at completion of BE AGILE; all patients received BKZ 160 mg in the OLE.

Figure 2 Efficacy responses to Week 96 (OLE Week 48)



Response rate at Week 96 (observed cases), %

ASAS20		ASAS40		ASAS PR	
82.6	84.6	69.4	70.9	38.8	38.5

ASDAS <2.1		ASDAS-ID	
66.1	62.9	29.8	31.0

Full Analysis Set (N=254).

Table 2 Continuous efficacy outcomes to Week 96 (OLE Week 48; multiple imputation)

Mean (SD)	BKZ 160 mg → 160 mg (n=130)			BKZ 320 mg → 160 mg (n=124)			All BKZ (N=254)		
	BL	Wk48	Wk96	BL	Wk48	Wk96	BL	Wk48	Wk96
ASDAS-CRP	3.9 (0.8)	2.1 (0.9)	1.9 (0.9)	3.9 (0.8)	2.0 (0.9)	1.9 (0.9)	3.9 (0.8)	2.0 (0.9)	1.9 (0.9)
BASDAI	6.3 (1.3)	2.8 (1.8)	2.5 (1.8)	6.5 (1.4)	2.8 (2.1)	2.7 (2.1)	6.4 (1.4)	2.8 (2.0)	2.6 (2.0)
BASFI	5.6 (1.9)	3.0 (2.0)	2.7 (2.1)	5.8 (2.0)	3.0 (2.4)	2.8 (2.4)	5.7 (1.9)	3.0 (2.2)	2.8 (2.2)
BASMI	4.6 (1.7)	4.0 (1.8)	3.9 (1.7)	4.8[a] (1.7)	3.9[a] (1.8)	3.9[a] (1.9)	4.7[b] (1.7)	4.0[b] (1.8)	3.9[b] (1.8)

[a]n=123; [b]n=253. Full Analysis Set (N=254). BL corresponds to Week 0 of the BE AGILE study.

Table 3 Safety in BE AGILE (Weeks 0–48) and OLE (Week 48 onwards)

n (%) [EAIR per 100 PY]	BE AGILE Weeks 0–48			OLE Week 48 onwards
	BKZ 160 mg (n=149 114.2 PY)	BKZ 320 mg (n=150 119.6 PY)	All BKZ (N=303 261.3 PY)	All BKZ (N=255 689.1 PY)
Any TEAE	103 (69.1) [168.7]	122 (81.3) [221.1]	235 (77.6) [186.2]	203 (79.6) [111.7]
Serious TEAEs	5 (3.4) [4.4]	6 (4.0) [5.1]	13 (4.3) [5.1]	27 (10.6) [6.1]
Study discontinuations due to TEAEs	7 (4.7)	10 (6.7)	20 (6.6)	12 (4.7)
Drug-related TEAEs	48 (32.2)	54 (36.0)	110 (36.3)	86 (33.7)
Deaths	1 (0.7)	0	1 (0.3)	1 (0.4)

TEAEs are reported for BE AGILE Safety Set (N=303) and OLE Safety Set (N=255); OLE safety data include TEAEs that occurred during Weeks 48–96 and beyond. There was one death in BE AGILE (cardiac arrest) and one in the OLE (road traffic accident), neither of which were considered treatment-related.

Conclusions

In patients with active AS who completed the first 48 weeks of BKZ treatment in BE AGILE, BKZ provides further sustained long-term improvements in key efficacy outcome measures over 96 weeks of treatment.

Dose reduction from 320 mg to 160 mg Q4W was not followed by loss of response.

There were no unexpected safety findings versus previous studies.[1]

AS: ankylosing spondylitis; ASAS20/40: Assessment of SpondyloArthritis international Society 20%/40% response; ASAS PR: ASAS partial remission; ASDAS: Ankylosing Spondylitis Disease Activity Score: ASDAS–ID: ASDAS inactive disease (ASDAS<1.3); ASDAS LDA: ASDAS low disease activity (ASDAS ≥1.3–<2.1); BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BKZ: bimekizumab; BL: baseline; CRP: C-reactive protein; EAIR: exposure-adjusted incidence rate; HDA: high disease activity; HLA-B27: human leukocyte antigen-B27; NSAID: non-steroidal anti-inflammatory drug; OLE: open-label extension; PGADA: Patient Global Assessment of Disease Activity; PY: patient-years; Q4W: every 4 weeks; SD: standard deviation; TEAE: treatment-emergent adverse event; TNFi: tumor necrosis factor inhibitor; vHDA: very high disease activity; Wk: week.

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References: [1]van der Heijde D. Ann Rheum Dis 2020;79:595–604. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **XB**, **AD**, **MD**, **MO**, **NdP**, **MB**, **TV**, **CF**, **DvdH**; Drafting of the publication, or revising it critically for important intellectual content: **XB**, **AD**, **MD**, **MO**, **NdP**, **MB**, **TV**, **CF**, **DvdH**; Final approval of the publication: **XB**, **AD**, **MD**, **MO**, **NdP**, **MB**, **TV**, **CF**, **DvdH**. **Author Disclosures: XB:** Personal fees from AbbVie, Bristol-Myers Squibb, Celgene, Chugai, Janssen, MSD, Novartis, Pfizer and UCB Pharma; grant/research support from Abbvie, MSD and Novartis. **AD:** Grant/research support and/or consulting fees from AbbVie, Amgen, BMS, Boehringer Ingelheim, Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB Pharma. **MD:** Grant/research support and/or consulting fees from AbbVie, Eli Lilly, Merck, Novartis, Pfizer, UCB Pharma. **MO, NdP, MB, TV, CF:** Employees of UCB Pharma. **DvdH:** Grant/research support and/or consulting fees from AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eli Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; director of Imaging Rheumatology BV. **Acknowledgments:** This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. The authors acknowledge Simone E. Auteri, MSc EMS PhD, UCB Pharma, Brussels, Belgium, for publication coordination, Abbie Rogers, BSc, Costello Medical, Manchester, UK, for medical writing and editorial assistance and the Costello Medical Design Team for design support. All costs associated with development of this poster were funded by UCB Pharma.

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