Long-term safety and efficacy of bimekizumab in patients with active ankylosing spondylitis: 5-year results from a phase 2b study and its open-label extension

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Objective

To report the long-term safety and efficacy of bimekizumab (BKZ) in patients with active ankylosing spondylitis (AS) up to 5 years of treatment in the phase 2b study BE AGILE and its open-label extension (OLE).

Introduction

- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.[1,2]
- BKZ has previously demonstrated clinical efficacy and safety up to 3 years in patients with active AS (i.e., radiographic axial spondyloarthritis)[3] in the phase 2b study BE AGILE and its OLE.[1,2]

Methods

- As previously reported,[1,2] the dose-ranging BE AGILE study (NCT02963506) consisted of a 12-week double-blind, placebo-controlled period, then a dose-blind period to Week 48 where patients received subcutaneous BKZ 160 or 320 mg every 4 weeks (Q4W). Patients completing Week 48 were eligible to enter the OLE (NCT03355573) where all patients received BKZ 160 mg Q4W to Week 256.
- Treatment-emergent adverse events (TEAEs; MedDRA v19.0) are reported for BKZ exposure from Week 0–256. Efficacy is reported from Week 0–256; unless stated otherwise, results are reported for the dose-blind set (DBS; patients who started the dose-blind period at Week 12 and received ≥1 dose of BKZ during the dose-blind period, including the dose at Week 12). Analyses used non-responder imputation (NRI; patients who did not enter the OLE were considered non-responders from Week 48), observed cases (OC), or multiple imputation (MI).

Results

Patients

- Of 255/303 (84.2%) patients who entered the OLE at Week 48, and received ≥1 BKZ dose, 202/255 (79.2%) completed to Week 256 (66.7% of patients initially randomized).

Safety

- From Week 0–256, exposure-adjusted incidence rates (EAIRs) per 100 patient-years (PY) were 134.6 for any TEAE and 5.2 for serious TEAEs (**Table 1**).
- The most frequent TEAEs by preferred term included nasopharyngitis (21.8%), upper respiratory tract infection (14.5%), bronchitis (13.2%), and pharyngitis (10.6%).
- The EAIR of *Candida* infections over 256 weeks was low (2.6). All *Candida* infections were mild or moderate and the majority were oral. One oral candidiasis event led to discontinuation. No systemic fungal infections were reported.
- Over 256 weeks, EAIRs of serious infections and infestations (1.4), injection site reactions (0.4), hepatic enzymes and function abnormalities (0.2) and serious hypersensitivity reactions (0) remained low.
- EAIRs of inflammatory bowel disease (IBD; 0.8) and uveitis (0.7) were also low.

Efficacy

- Using conservative NRI, 51.7% (153/296) of the DBS (N=296) achieved ASAS40, while 49.3% (146/296) achieved ASDAS low disease activity (LDA; <2.1) at Week 48. At Week 256, 49.7% (147/296) and 41.6% (123/296) of patients achieved these endpoints, respectively (NRI; **Figure 1**). Of the patients with an assessment at Week 256, 73.1% (147/201) and 71.1% (123/173) achieved these endpoints at Week 256, respectively (OC; **Figure 1**).
  - At Week 256, 66.0% of the OLE full analysis set (FAS) achieved ASDAS LDA (MI; **Figure 1**).
- Improvements in disease activity from baseline to Week 48 were sustained (**Figure 2A**) or further improved (**Figure 2B**) to Week 256 (MI), notably in mean ASDAS (baseline: 3.9; Week 48: 2.1; Week 256: 2.1) and BASDAI (baseline: 6.5; Week 48: 3.0; Week 256: 2.5) values.
- Mean BASFI (baseline: 5.7; Week 48: 3.1; Week 256: 2.7) and total spinal pain (baseline: 7.1; Week 48: 3.2; Week 256: 2.7) improvements from baseline to Week 48 were sustained to Week 256 (MI; **Figure 3**).
- A similar trend was also observed for SF-36 PCS (baseline: 32.3; Week 48: 44.1; Week 256: 45.8) and ASQoL (baseline: 8.7; Week 48: 3.7; Week 256: 3.0), respectively (MI; **Figure 4**).

Conclusions

The long-term safety profile of bimekizumab in patients with AS was consistent with previous observations, showing that it is well tolerated. No new safety signals were identified after 5 years of exposure and rates of uveitis remained low.

Clinical efficacy outcomes reported using NRI, MI, and OC, including improvements in signs and symptoms, disease activity, physical function, and health-related quality of life, were sustained up to 5 years of bimekizumab treatment.

Summary

In patients with active AS, treatment with bimekizumab over 5 years was well tolerated and resulted in maintenance of ASAS40 response and ASDAS LDA in approximately half the patients

No new safety signals were detected

Rates of uveitis were low (EAIR/100 PY: 0.7)

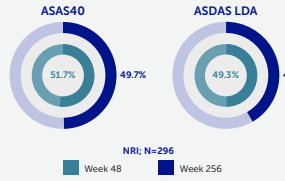


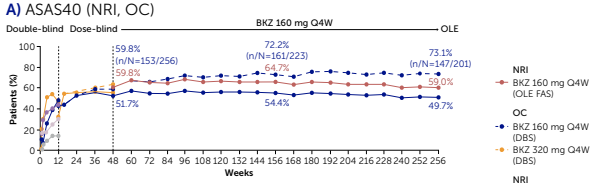
Table 1 Safety to Week 256 for exposure to BKZ

TEAEs[a] n (%) [EAIR/100 PY]	BE AGILE and OLE Weeks 0–256
	Total (N=303; exposure 1,231 PY)
Any TEAE	289 (95.4) [134.6]
Severe TEAEs	37 (12.2) [3.2]
Study discontinuations due to TEAEs	43 (14.2) [3.5]
Drug-related TEAEs	160 (52.8) [21.8]
Serious TEAEs	58 (19.1) [5.2]
Deaths	3 (1.0) [0.2][b]
Safety topics of interest	
Fungal infections[c]	74 (24.4) [7.4]
Candida infections by preferred term[d]	30 (9.9) [2.6]
Oral candidiasis	25 (8.3) [2.2]
Skin *Candida*	4 (1.3) [0.3]
Vulvovaginal candidiasis	2 (0.7) [0.2]
Candida infection	1 (0.3) [0.1]
Oropharyngeal candidiasis	1 (0.3) [0.1]
Serious infections and infestations	17 (5.6) [1.4]
Neutropenia	4 (1.3) [0.3]
Adjudicated SIB	1 (0.3) [0.1][e]
Injection site reactions	5 (1.7) [0.4]
Definite and probable IBD[f]	10 (3.3) [0.8][g]
With prior history	2 (0.7)[h]
Without prior history	8 (2.6)[h]
Uveitis[i,j]	9 (3.0) [0.7][k]
With prior history	3 (1.0)[h]
Without prior history	6 (2.0)[h]

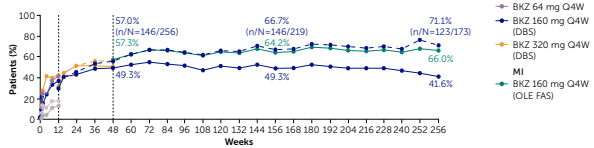
Safety set. TEAEs occurring on placebo treatment are not included. Drug-related TEAEs are reported as assessed by the investigator. Neutropenia is reported as TEAEs. [a]Defined according to MedDRA v19.0. [b]There was one death in BE AGILE (Week 0–48; cardiac arrest) and two in the OLE (Week 48–256; cardiac arrest, road traffic accident). None were considered treatment related. [c]Other than *Candida* infections, fungal infections included *Tinea* and not elsewhere classified infections, and were localized to the skin, scalp, ear, mouth, tongue, nails, vulva, and feet; none were systemic. [d]All *Candida* infections were mild or moderate, none were systemic. [e]No deaths resulted from adjudicated SIB. [f]Includes the preferred terms Crohn's disease, colitis ulcerative, and colitis. [g]In the safety set, four patients had IBD TEAEs in BE AGILE (Week 0–48). [h]Proportion calculated using total number of patients in safety set as the denominator (N=303). [i]Includes the preferred terms iritis, iridocyclitis, and uveitis. [j]Uveitis was not a safety topic of interest in this study and is included as an extra-musculoskeletal manifestation. [k]In the safety set, two uveitis cases occurred in BE AGILE (Week 0–48).

Figure 1 (A) ASAS40 and (B) ASDAS LDA responses to Week 256

A) ASAS40 (NRI, OC)



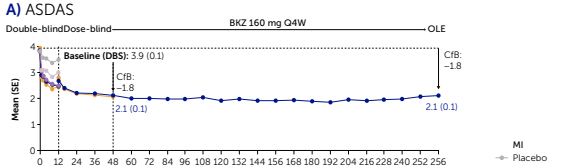
B) ASDAS LDA (NRI, MI, OC)



BE AGILE FAS (all randomized patients who received ≥1 dose of BKZ and had a valid measurement of the ASAS components at baseline; N=303) for Weeks 0–12; DBS (patients who started the dose-blind period at Week 12 and received ≥1 dose of BKZ during the dose-blind period, including the dose at Week 12; n=296) for Weeks 12–256; OLE FAS (patients who entered the OLE and had ≥1 scheduled efficacy assessment at OLE entry; n=249 [248 patients included in the MI model]) for Weeks 48–256.

Figure 2 (A) ASDAS and (B) BASDAI scores to Week 256 (MI)

A) ASDAS



B) BASDAI

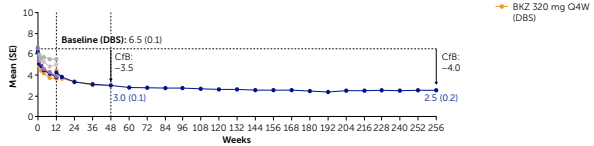


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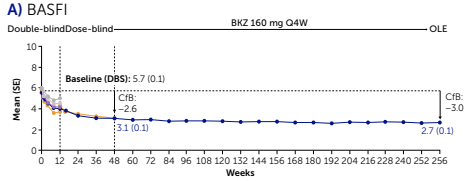
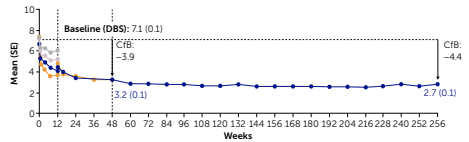
Figure 3 (A) BASFI and (B) total spinal pain scores to Week 256 (MI)

A) BASFI



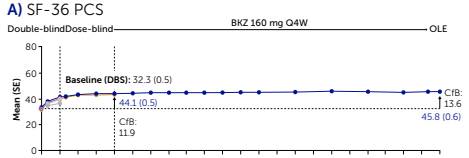
B) Total spinal pain



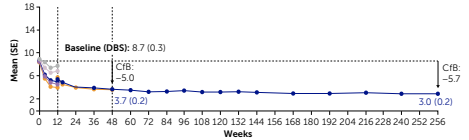
BE AGILE FAS (all randomized patients who received ≥1 dose of BKZ and had a valid measurement of the ASAS components at baseline; N=303) for Weeks 0–12; DBS (patients who started the dose-blind period at Week 12 and received ≥1 dose of BKZ during the dose-blind period, including the dose at Week 12; n=296) for Weeks 12–256. Baseline BASFI and total spinal pain are shown for the DBS.

Figure 4 (A) SF-36 PCS and (B) ASQoL scores to Week 256 (MI)

A) SF-36 PCS



B) ASQoL



BE AGILE FAS (all randomized patients who received ≥1 dose of BKZ and had a valid measurement of the ASAS components at baseline; N=303) for Weeks 0–12; DBS (patients who started the dose-blind period at Week 12 and received ≥1 dose of BKZ during the dose-blind period, including the dose at Week 12; n=296) for Weeks 12–256. Baseline SF-36 PCS and ASQoL are shown for the DBS.

AS: ankylosing spondylitis; **ASAS:** Assessment of SpondyloArthritis international Society; **ASAS40:** ASAS 40% response; **ASDAS:** Ankylosing Spondylitis Disease Activity Score; **ASDAS LDA:** ASDAS low disease activity (<2.1); **ASQoL:** Ankylosing Spondylitis Quality of Life; **BASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BASFI:** Bath Ankylosing Spondylitis Function Index; **BKZ:** bimekizumab; **BL:** baseline; **CfB:** change from baseline; **DBS:** dose-blind set; **EAIR:** exposure-adjusted incidence rate; **FAS:** full analysis set; **IBD:** inflammatory bowel disease; **IgG1:** immunoglobulin G1; **IL:** interleukin; **MI:** multiple imputation; **NRI:** non-responder imputation; **OC:** observed case; **OLE:** open-label extension; **PY:** patient-years; **Q4W:** every 4 weeks; **SE:** standard error; **SF-36 PCS:** Short Form 36 physical component summary; **SIB:** suicidal ideation and behavior; **TEAE:** treatment-emergent adverse event.

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References: [1]van der Heijde D. Ann Rheum Dis 2020;79:595–604; [2]Baraliakos X. Arthritis Rheumatol.2022;74:1943–58; [3]Boel A. Ann Rheum Dis 2019;78:1545–9. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **AD**, **VNC**, **DP**, **LSG**, **SR**, **TT**, **HMO**, **CF**, **TV**, **UM**, **DvdH**, **XB**; Drafting of the publication, or reviewing it critically for important intellectual content: **AD**, **VNC**, **DP**, **LSG**, **SR**, **TT**, **HMO**, **CF**, **TV**, **UM**, **DvdH**, **XB**; Final approval of the publication: **AD**, **VNC**, **DP**, **LSG**, **SR**, **TT**, **HMO**, **CF**, **TV**, **UM**, **DvdH**, **XB**. **Author Disclosures:** **AD:** Speaker for Eli Lilly and Company, Janssen, Novartis, Pfizer, and UCB Pharma; consultant for AbbVie, Bristol Myers Squibb, Eli Lilly and Company, Janssen, MoonLake, Novartis, Pfizer and UCB Pharma; grant/research support from Bristol Myers Squibb, Celgene, Eli Lilly and Company, Novartis, Pfizer, and UCB Pharma; **VNC:** Speakers bureau for AbbVie, Eli Lilly and Company, Fresenius Kabi, Janssen, MSD, Novartis, Pfizer, and UCB Pharma; consultant for AbbVie, Eli Lilly and Company, Galapagos, Moonlake, MSD, Novartis, Pfizer, and UCB Pharma; grant/research support from AbbVie and Novartis; **DP:** Speaker for AbbVie, Bristol Myers Squibb, Eli Lilly and Company, MSD, Novartis, Pfizer, and UCB Pharma; consultant for AbbVie, Biocad, Eli Lilly and Company, Gilead, GSK, MSD, Moonlake, Novartis, Pfizer, Samsung Bioepis, and UCB Pharma; grant/research support from: AbbVie, Eli Lilly and Company, MSD, Novartis, and Pfizer; **LSG:** Grants from Novartis and UCB Pharma paid to institution; consulting fees from AbbVie, Acelyrin, Eli Lilly and Company, Fresenius Kabi, Janssen, Novartis, Pfizer, and UCB Pharma; **SR:** Grants from AbbVie, Galapagos, MSD, Novartis, Pfizer, and UCB Pharma; consulting fees from AbbVie, Eli Lilly and Company, Novartis, Pfizer, Sanofi, and UCB Pharma; **TT:** Consulting fees from AbbVie, Eli Lilly and Company, Gilead, Novartis, and Pfizer; speaker fees from AbbVie, Astellas, Bristol Myers Squibb, Eisai, Eli Lilly and Company, Janssen, Kyowa Kirin, Mitsubishi-Tanabe, Novartis, and Pfizer; **HMO:** Speaking honoraria and/or consultancy fees from AbbVie, Amgen, Biogen, Eli Lilly and Company, Janssen, MoonLake, Novartis, Pfizer, Takeda, and UCB Pharma; research grants from Janssen, Novartis, Pfizer, and UCB Pharma; **CF, TV, UM:** Employees of UCB Pharma; **DvdH:** Consulting fees from AbbVie, Bayer, Bristol Myers Squibb, Galapagos, Gilead, GSK, Janssen, Eli Lilly and Company, Novartis, Pfizer, Takeda, and UCB Pharma, and is the director of Imaging Rheumatology BV; **XB:** Speakers bureau from AbbVie, Bristol Myers Squibb, Chugai, Eli Lilly and Company, Galapagos, MSD, Novartis, Pfizer, UCB Pharma; paid instructor for AbbVie, Bristol Myers Squibb, Chugai, Eli Lilly and Company, Galapagos, MSD, Novartis, Pfizer, and UCB Pharma; consultant for AbbVie, Bristol Myers Squibb, Chugai, Eli Lilly and Company, Galapagos, Gilead, Novartis, Pfizer, and UCB Pharma; grant/research support from: Novartis and UCB Pharma. **Acknowledgements:** We would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to this study. The authors acknowledge Celia Menckeberg, PhD, UCB Pharma, for publication coordination, Hugh Osborne, PhD, Costello Medical, Cambridge, UK for medical writing and editorial assistance, and the Costello Medical Creative team for design support. This study was funded by UCB Pharma. All costs associated with development of this presentation were funded by UCB Pharma.

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