# 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**).
- 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: 44.9; 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 ADSAS LDA in approximately half the patients**

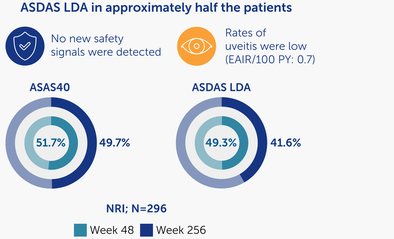


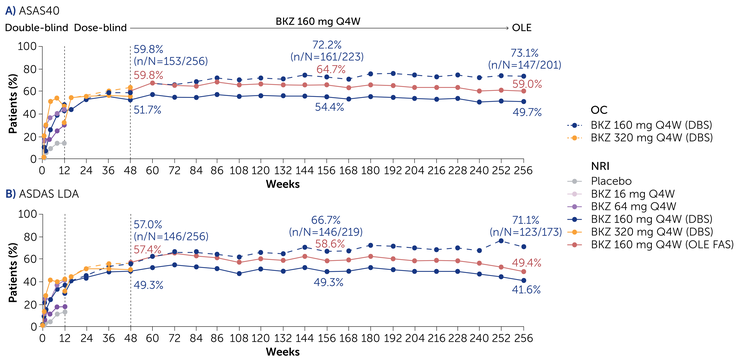


**Table 1** Safety to Week 256 for exposure to BKZ

| 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 (NRI, 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) for Weeks 48–256.

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

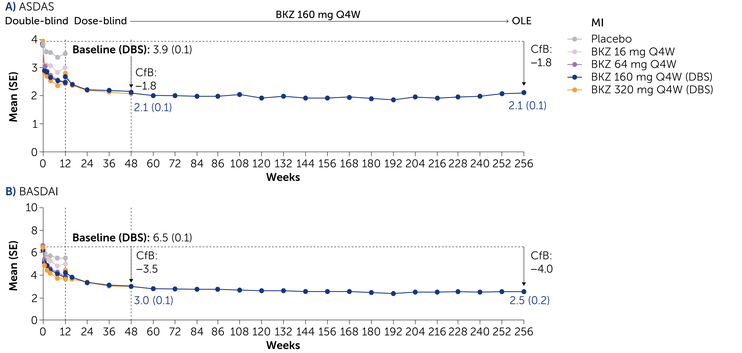



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**Figure 3** (A) BASFI and (B) total spinal pain scores to Week 256 (MI)

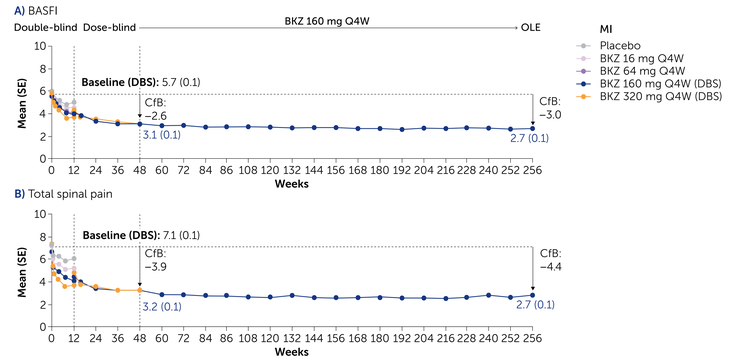


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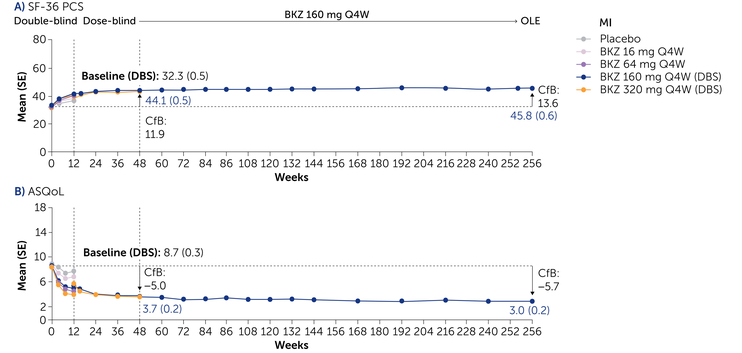
**Figure 4** (A) SF-36 PCS and (B) ASQoL scores to Week 256 (MI)




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:** Ivan der Heijde D. Ann Rheum Dis 2020;79:595–604; [2]Baraliakos X. Arthritis Rheumatol 2022;74:1943–58; [3]Rudwaleit M. Ann Rheum Dis 2009;68:1545–9. **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**.

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