Updated Long-Term Safety and Tolerability of Bimekizumab in Patients with Axial Spondyloarthritis and Psoriatic Arthritis: Pooled Results from Phase 2b/3 Studies

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Objective

To report updated pooled safety data for bimekizumab (BKZ) across integrated phase 2b/3 studies in patients with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA).

Background

- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- A previous analysis of pooled safety data from phase 2b/3 studies demonstrated that BKZ was generally well tolerated by patients with axSpA and PsA.[1] Here, we report an updated pooled safety analysis with an additional 1 year of BKZ exposure from the ongoing phase 3 open-label extension (OLE) studies.

Methods

- Treatment-emergent adverse events (TEAEs) are reported as n (%) and exposure-adjusted incidence rate per 100 patient-years (EAIR/100 PY), coded using MedDRA v19.0, for all patients who received ≥1 dose of BKZ (160 mg every 4 weeks, Q4W) across all treatment periods.
- Data are reported up to the data-cut (July 2023), corresponding with at least 104 weeks of total study participation for ongoing patients in the BE MOVING and BE VITAL OLEs (**Figure 1**).[2–6]

Results

Safety Overview

- The axSpA and PsA safety pools included 848 patients (total BKZ exposure: 2,513.8 PY) and 1,409 patients (3,655.9 PY), respectively (**Figure 1**).
- Study discontinuations due to TEAEs were infrequent (EAIRs 2.4/100 PY in axSpA; 2.9/100 PY in PsA; **Table 1**).
  - During the studies, 3 deaths were reported among patients with axSpA and 5 deaths among patients with PsA, none of which were considered drug-related by the investigators (**Table 1**).
- The three most frequently reported TEAEs in patients with axSpA and PsA were SARS-CoV-2 (COVID-19) infection, nasopharyngitis, and upper respiratory tract infection (**Figure 2**).

Safety Topics of Interest

- Safety topics of interest are reported across the phase 2b/3 studies in **Table 1**.
- The EAIR of serious infections was 1.4/100 PY in patients with axSpA and 1.3/100 PY in patients with PsA.
- The EAIR of hepatic events was 5.3/100 PY in patients with axSpA and 5.0/100 PY in patients with PsA (**Table 1**). Most hepatic events were transient liver enzyme abnormalities and there were no confirmed cases of Hy's law.
- For adjudicated definite or probable IBD, the EAIR was 0.7/100 PY in axSpA and 0.2/100 PY in PsA, consistent with the higher background comorbidity of IBD often seen in axSpA compared with PsA.[7]
- Uveitis occurred at an EAIR/100 PY of 1.3 in axSpA and 0.1 in PsA.
- Rates of adjudicated suicidal ideation or behavior and major adverse cardiovascular events were low (**Table 1**).
- No cases of active tuberculosis or completed suicide were reported in any study.
- In the phase 3 studies, the EAIRs of safety topics of interest generally remained stable or decreased in the second year of BKZ treatment (**Figure 3**).

Fungal Infections

- The EAIR of fungal infections was 8.4/100 PY in patients with axSpA and 7.9/100 PY in patients with PsA (**Table 1**).
- No systemic fungal infections were reported and most were mild or moderate in severity.
  - The most common fungal infections were *Candida* infections, all of which were localized mucocutaneous (mostly oral).
- In the phase 3 studies, the EAIR of oral candidiasis decreased in the second year of bimekizumab treatment for both patients with axSpA and PsA (**Figure 3**).
  - The occurrences of oral candidiasis TEAEs in individual patients are reported in **Figure 4**.
- Across the phase 2b/3 studies, permanent discontinuation of BKZ due to oral candidiasis was infrequent (axSpA: 0.2/100 PY; PsA: 0.4/100 PY).

Conclusions

With an additional year of exposure, the long-term safety profile of bimekizumab in patients with axSpA and PsA remained consistent with prior analyses;[1–6] no new safety signals or concerns were raised in this analysis. The incidence rate of oral candidiasis decreased over time, and infrequently led to bimekizumab discontinuation. These observations support the favorable benefit-risk profile of bimekizumab for the treatment of axSpA and PsA.

Summary

Bimekizumab demonstrated a consistent safety profile in patients with axSpA and PsA over extended periods of exposure

axSpA
N=848
2,513.8 PY

PsA
N=1,409
3,655.9 PY

The three **most common TEAEs** were **SARS-CoV-2 (COVID-19) infection**, **nasopharyngitis**, and **upper respiratory tract infection**

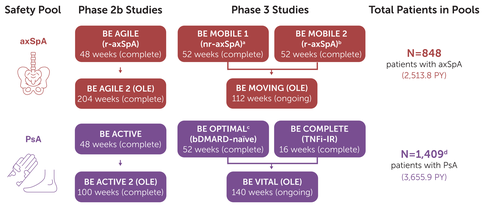
No systemic fungal infections

Incidence rates of oral candidiasis decreased over time; no systemic fungal infections were reported

Low discontinuation rates

Study discontinuations due to TEAEs were infrequent, supporting good tolerability of bimekizumab in axSpA and PsA

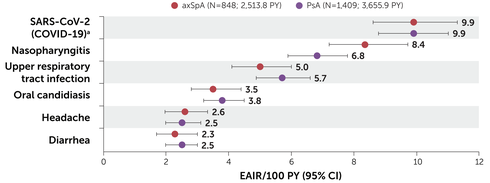
Figure 1 The two safety pools (axSpA, PsA) of patients treated with BKZ 160 mg Q4W across six phase 2b/3 studies and their OLEs



Data from the July 2023 data-cut shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W in the phase 2b/3 studies. Duration of overall treatment period shown; BKZ treatment duration by data-cut varied between patients, depending on study duration and initial randomization in the feeder studies. **[a]** Patients with nr-axSpA met Assessment of SpondyloArthritis international Society (ASAS) classification criteria. Patients with radiographic sacroiliitis were excluded; **[b]** Patients with r-axSpA met modified New York criteria and fulfilled ASAS classification criteria; **[c]** BE OPTIMAL also included an adalimumab treatment arm. Data from patients treated with adalimumab were not included in the PsA safety pool prior to switching to BKZ, but were included following the switch; **[d]** Since the previous data-cut (July 2022),[2] additional patients started receiving BKZ in BE VITAL (originally randomized to adalimumab).

BE AGILE: NCT02963506; BE AGILE 2: NCT03355573; BE MOBILE 1: NCT03928704; BE MOBILE 2: NCT03928743; BE MOVING: NCT04436640; BE ACTIVE: NCT02969525; BE ACTIVE 2: NCT03347110; BE OPTIMAL: NCT03895203; BE COMPLETE: NCT03896581; BE VITAL: NCT04009499.

Figure 2 Most common TEAEs in the phase 2b/3 studies



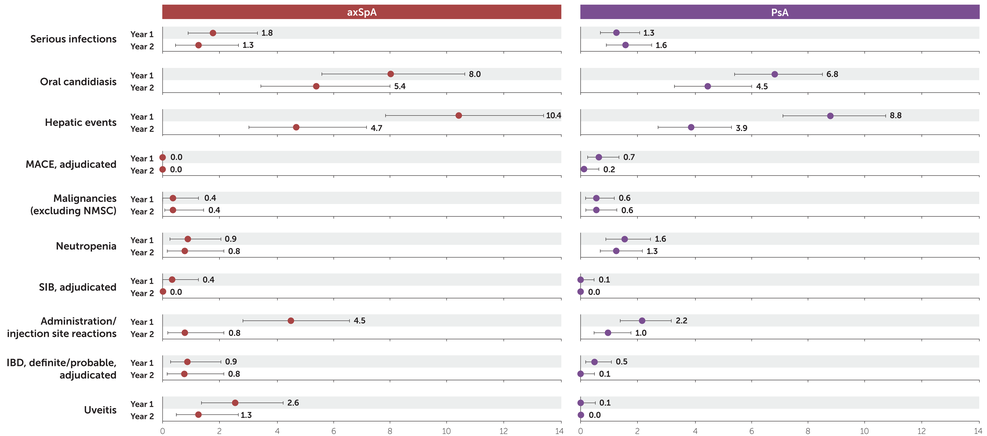
Data from the July 2023 data-cut shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W in the phase 2b/3 studies. TEAEs defined by MedDRA v19.0 preferred term (except SARS-CoV-2 infection), occurring in ≥5% of patients in both the axSpA and PsA patient pools. **[a]** Specific terms for SARS-CoV-2 (COVID-19) infection were not available in MedDRA v19.0. Therefore, symptomatic, confirmed or suspected COVID-19 was coded as the preferred term "Corona virus infection" (axSpA: 8.6/100 PY; PsA: 9.0/100 PY) and asymptomatic, confirmed COVID-19 was coded as the preferred term "Coronavirus test positive" (axSpA: 1.1/100 PY; PsA: 0.8/100 PY).

Table 1 Summary of TEAEs reported up to the phase 3 data-cut (July 2023)

TEAEs n (%) [EAIR/100 PY]	axSpA BKZ 160 mg Q4W (N=848; exposure 2,513.8 PY)	PsA BKZ 160 mg Q4W (N=1,409; exposure 3,655.9 PY)
Any TEAE	772 (91.0) [129.6]	1,239 (87.9) [126.9]
Severe TEAEs	78 (9.2) [3.2]	121 (8.6) [3.5]
Study discontinuations due to TEAEs	59 (7.0) [2.4]	104 (7.4) [2.9]
Drug related TEAEs[a]	410 (48.3) [25.2]	574 (40.7) [22.4]
Serious TEAEs	123 (14.5) [5.3]	197 (14.0) [5.8]
Deaths	3 (0.4) [0.1][b]	5 (0.4) [0.1][b]
Safety topics of interest		
Fungal infections	179 (21.1) [8.4]	253 (18.0) [7.9]
Candida infections	100 (11.8) [4.3]	161 (11.4) [4.7]
Oral candidiasis	83 (9.8) [3.5]	132 (9.4) [3.8]
Fungal infections NEC	82 (9.7) [3.5]	111 (7.9) [3.2]
Tinea infection	20 (2.4) [0.8]	21 (1.5) [0.6]
Serious infections	34 (4.0) [1.4]	46 (3.3) [1.3]
Hepatic events[c]	119 (14.0) [5.3]	167 (11.9) [5.0]
Elevated liver enzymes[d]	91 (10.7) [3.9]	133 (9.4) [3.9]
>3x ULN ALT or AST[b]	48 (5.7) [2.0]	68 (4.8) [1.9]
>5x ULN ALT or AST[b]	21 (2.5) [0.8]	22 (1.6) [0.6]
MACE, adjudicated	4 (0.5) [0.2]	12 (0.9) [0.3]
Malignancies (excluding NMSC)[e]	9 (1.1) [0.4]	19 (1.3) [0.5]
Neutropenia[g]	12 (1.4) [0.5]	42 (3.0) [1.2]
SIB, adjudicated[h]	3 (0.4) [0.1]	2 (0.1) [0.1]
Serious hypersensitivity reaction	0	0
Administration/injection site reaction	27 (3.2) [1.1]	33 (2.3) [0.9]
IBD, probable/definite, adjudicated	18 (2.1) [0.7][i]	8 (0.6) [0.2][j]
With prior history[k]	3 (20.0) [6.6]	1 (7.7) [2.9]
Without prior history[l]	15 (1.8) [0.6]	7 (0.5) [0.2]
Uveitis[m]	31 (3.7) [1.3]	3 (0.2) [0.1]
With prior history[n]	18 (13.8) [4.8]	1 (4.8) [2.4]
Without prior history[o]	13 (1.8) [0.6]	2 (0.1) [0.1]

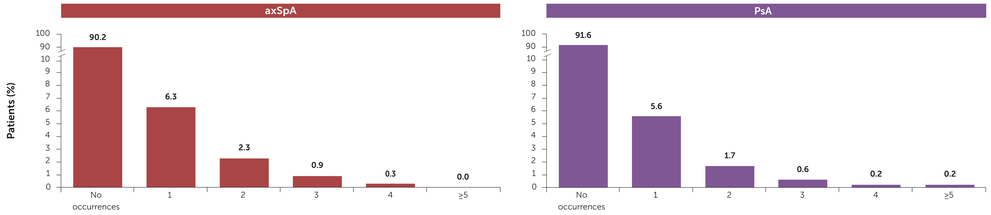
Data to the July 2023 data-cut shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W in the phase 2b/3 studies. **[a]** Per investigator assessment; **[b]** By MedDRA v19.0 preferred term, axSpA: Cardiac arrest, Cardio-respiratory arrest, and Road traffic accident; PsA: Acute myocardial infarction, Cardiac arrest, Hepatobiliary neoplasm, Sudden death, and Traumatic shock (from a motorcycle accident). No deaths were considered drug-related by the investigator in any study; **[c]** Includes events described as drug-related hepatic disorders, excluding liver neoplasms; **[d]** Elevated liver enzymes include the following preferred terms reported as adverse events: increased/abnormal levels of ALT, AST, Blood bilirubin, Gamma-glutamyltransferase, Hepatic enzyme, Liver function test, Total bile acids, or Transaminases; **[e]** axSpA: n=847; PsA: n=1,407; **[f]** Includes all TEAEs identified using the SMQs "Malignant tumours (SMQ)"; **[g]** Neutropenia includes additional preferred terms identified based on UCB-defined search criteria; **[h]** All patients with adjudicated SIB had a history of psychiatric disorders or ongoing traumatic and stressful circumstances; **[i]** 9 (1.1%) patients with Crohn's disease, 6 (0.7%) Ulcerative colitis, 4 (0.5%) Unclassified; **[j]** 2 (0.1%) patients with Crohn's disease, 2 (0.1%) Ulcerative colitis, 4 (0.1%) Unclassified; **[k]** axSpA, n=15; PsA, n=13; **[l]** axSpA, n=833; PsA, n=1,396; **[m]** Includes the preferred terms Autoimmune uveitis, Uveitis, Iridocyclitis, and Iritis; **[n]** axSpA, n=130; PsA, n=21; **[o]** axSpA, n=718; PsA, n=1,388.

Figure 3 Safety topics of interest by year of BKZ treatment in the phase 3 studies



Data from the July 2023 data-cut shown, including all at-risk patients who received ≥1 dose of BKZ 160 mg Q4W in Weeks 0–52 (axSpA, N=574; PsA, N=1,211) or Weeks >52–104 (axSpA, N=518; PsA, N=1,110) of the phase 3 studies. Patients were considered at-risk for up to 140 days after the last dose of BKZ.

Figure 4 Low recurrence of oral candidiasis in individual patients with axSpA and PsA during the first 2 years of treatment with BKZ in the phase 3 studies



Data from the July 2023 data-cut shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W in the phase 3 studies (axSpA, N=574; PsA, N=1,211). Data labels indicate percentage of patients reporting the respective number of occurrences of Oral candidiasis TEAEs (preferred term according to MedDRA v19.0) with relative day of onset during Weeks 0–104 of treatment with BKZ.

ALT: alanine transaminase; **AS:** ankylosing spondylitis; **AST:** aspartate aminotransferase; **ASAS:** Assessment of SpondyloArthritis international Society; **axSpA:** axial spondyloarthritis; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **CI:** confidence interval; **EAIR:** exposure-adjusted incidence rate; **IBD:** inflammatory bowel disease; **IL:** interleukin; **MACE**: major adverse cardiovascular event; **MedDRA:** Medical Dictionary for Regulatory Activities; **NEC:** not elsewhere classifiable; **NMSC:** non-melanoma skin cancer; **nr-axSpA:** non-radiographic axSpA; **OLE:** open-label extension; **PsA:** psoriatic arthritis; **PY:** patient-years; **Q4W:** every 4 weeks; **r-axSpA:** radiographic axSpA; **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2; **SIB:** suicidal ideation or behavior; **SMQ:** Standardized MedDRA Query; **TEAE:** treatment-emergent adverse event; **TNFi-IR:** tumor necrosis factor inhibitor inadequate response; **ULN:** upper limit of normal.

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