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

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Objective

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

Background

- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- An analysis of pooled safety data from the 16-week placebo-controlled periods of four phase 3 studies in patients with axSpA and PsA demonstrated that BKZ had a similar safety profile as reported in previous phase 2 trials.[1]

Methods

- Here, 1-year safety analyses are reported from six pooled phase 2b/3 studies and their open-label extensions, in patients with active axSpA (non-radiographic and radiographic axSpA) and active PsA (**Figure 1**).[2–6]
- Treatment-emergent adverse events (TEAEs) are reported as n (%) and exposure-adjusted incidence rate per 100 patient-years (EAIR/100 PY) according to MedDRA v19.0, for all patients who received ≥1 dose of BKZ (160 mg every four weeks, Q4W).
- Data are reported from the most recent data-cut (July 2022; after Week 52 completion of the pivotal phase 3 trials) across all treatment periods.

Results

Baseline Characteristics

- The axSpA and PsA safety pools included 848 patients (total BKZ exposure: 2,034.4 PY) and 1,407 patients (2,590.8 PY), respectively (**Figure 1**).
- Baseline characteristics are shown by indication in **Table 1**.

Overview of TEAEs

- TEAEs led to study withdrawal in 54 (6.4%) of patients with axSpA (EAIR/100 PY: 2.7) and 79 (5.6%) of patients with PsA (EAIR/100 PY: 3.1) (**Figure 2**).
  - 3 deaths (EAIR/100 PY: 0.1) occurred in each indication, none of which were considered drug-related by the study investigator (**Figure 2**).
- The most frequently reported TEAEs in patients with axSpA and PsA were nasopharyngitis, SARS-CoV-2 (COVID-19) infection, upper respiratory tract infection, oral candidiasis, headache, and diarrhea (**Figure 3**).

Safety Topics of Interest

- Safety topics of interest for BKZ are presented in **Figure 4**.
- Serious infections and infestations occurred in 29 (3.4%) patients with axSpA (EAIR/100 PY: 1.5) and 30 (2.1%) with PsA (EAIR/100 PY: 1.2).
- Adjudicated definite/probable IBD was reported in 16 (1.9%) patients with axSpA (EAIR/100 PY: 0.8) and 7 (0.5%) patients with PsA (EAIR/100 PY: 0.3), consistent with the higher background comorbidity of IBD often seen in axSpA compared with PsA.[7]
- Uveitis occurred in 25 (2.9%) patients with axSpA (EAIR/100 PY: 1.2); of these patients, 14/25 (56.0%) had prior history of uveitis. No uveitis cases were reported in patients with PsA.
- No cases of active tuberculosis or suicide were reported in any study; rates of suicidal ideation/behaviour and major adverse cardiac events are shown in **Figure 4**.

Fungal Infection TEAEs

- Fungal infections were reported in 161 (19.0%) patients with axSpA (EAIR/100 PY: 9.2) and 214 (15.2%) with PsA (EAIR/100 PY: 9.2) (**Figure 4**).
- No fungal infections were systemic; the majority of fungal infections were oral (MedDRA v19.0 preferred terms oral fungal infection, oral candidiasis, or oropharyngeal candidiasis), and the vast majority of oral cases were mild to moderate in severity (axSpA: 162/163 [99.4%]; PsA: 231/232 [99.6%]).
  - One patient in each indication experienced one severe oral fungal infection (oral candidiasis); both resolved with treatment.
- The number of patients who discontinued the study due to oral candidiasis TEAEs was 5 (0.6%) in axSpA and 7 (0.5%) in PsA.
  - Occurrence of oral candidiasis TEAEs within individual patients is reported in **Figure 5**.
- One serious case of oropharyngeal candidiasis was reported; the infection resolved with routine antifungal therapy and BKZ was resumed ~1 month later.

Conclusions

The overall safety profile of bimekizumab was consistent with previously reported data from phase 2b/3 trials in axSpA and PsA,[1–6] with a low rate of discontinuation. As expected, due to inhibition of IL-17,[8] oral candidiasis TEAEs were reported in both indications (EAIR/100 PY: ~4).

Summary

	axSpA	PsA
Population	N=848	N=1,407
Exposure	2,034.4 PY	2,590.8 PY
Trials included		
Phase 2	• BE AGILE (AS) • BE AGILE 2 (OLE of BE AGILE)	• BE ACTIVE (PsA) • BE ACTIVE 2 (OLE of BE ACTIVE)
Phase 3	• BE MOBILE 1 (nr-axSpA) • BE MOBILE 2 (r-axSpA) • BE MOVING (OLE of BE MOBILE 1 and 2)	• BE OPTIMAL (bDMARD-naïve) • BE COMPLETE (TNFi-IR) • BE VITAL (OLE of BE OPTIMAL and BE COMPLETE)

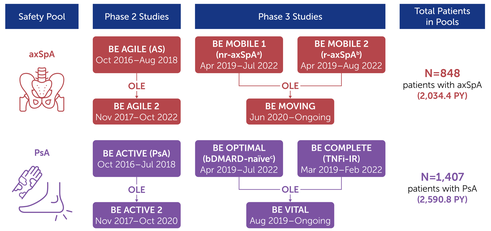
The most common TEAEs were nasopharyngitis, SARS-CoV-2 (COVID-19) infection, upper respiratory tract infection, oral candidiasis, headache, and diarrhea

Across all studies, rates of discontinuation due to TEAEs were low

No fungal infections were systemic; the majority were oral and mild to moderate in severity

Data from the most recent data-cut (July 2022) shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W in BE AGILE, BE MOBILE 1, BE MOBILE 2, and the OLEs BE AGILE 2 and BE MOVING (axSpA), or in BE ACTIVE, BE OPTIMAL, BE COMPLETE, and the OLEs BE ACTIVE 2 and BE VITAL (PsA).

Figure 1 Two safety pools (axSpA, PsA) of patients treated with BKZ 160 mg Q4W from six phase 2b/3 studies and their open-label extensions



Data from the most recent data-cut (July 2022) shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W. Actual study start dates and completion dates provided. [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, therefore the terms r-axSpA and AS may be used interchangeably.[9] [c] BE OPTIMAL also included an adalimumab treatment arm. Data from patients treated with adalimumab are not included in the PsA safety pool.

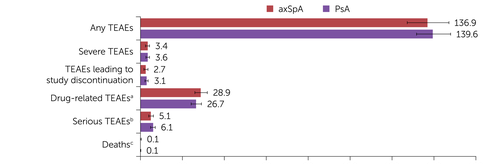
BE AGILE: NCT02963506; BE AGILE 2: NCT03355573; BE MOBILE 1: NCT03928704; BE MOBILE 2: NCT03928743; BE MOVING: NCT04436640;
BE ACTIVE: NCT02969525; BE ACTIVE 2: NCT03347110; BE OPTIMAL: NCT03895203; BE COMPLETE: NCT03895581; BE VITAL: NCT04009499.

Table 1 Baseline characteristics

	axSpA BKZ 160 mg Q4W (N=848)	PsA BKZ 160 mg Q4W (N=1,407)
Age, years, mean ± SD	40.3 ± 11.9	49.3 ± 12.4
Male, n (%)	606 (71.5)	671 (47.7)
Weight, kg, mean ± SD	80.7 ± 17.9	85.1 ± 19.4
BMI, kg/m^2, mean ± SD	27.0 ± 5.5	29.4 ± 6.3
Time since first diagnosis,[a] years, mean ± SD	6.1 ± 7.8	7.0 ± 8.0[b]
Time since first symptoms of axSpA, years, mean ± SD	12.4 ± 9.9	N/A
History of IBD, n (%)	15 (1.8)	13 (0.9)
History of uveitis, n (%)	130 (15.3)	21 (1.5)
Prior TNFi therapy, n (%)	108 (12.7)	425 (30.2)

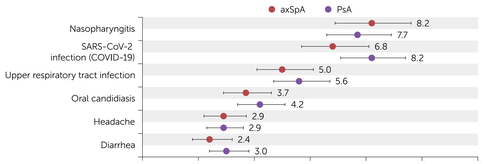
Data from the most recent data-cut (July 2022) shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W. [a] Diagnosis of axSpA or PsA; [b] n=1,394.

Figure 2 Summary of TEAEs



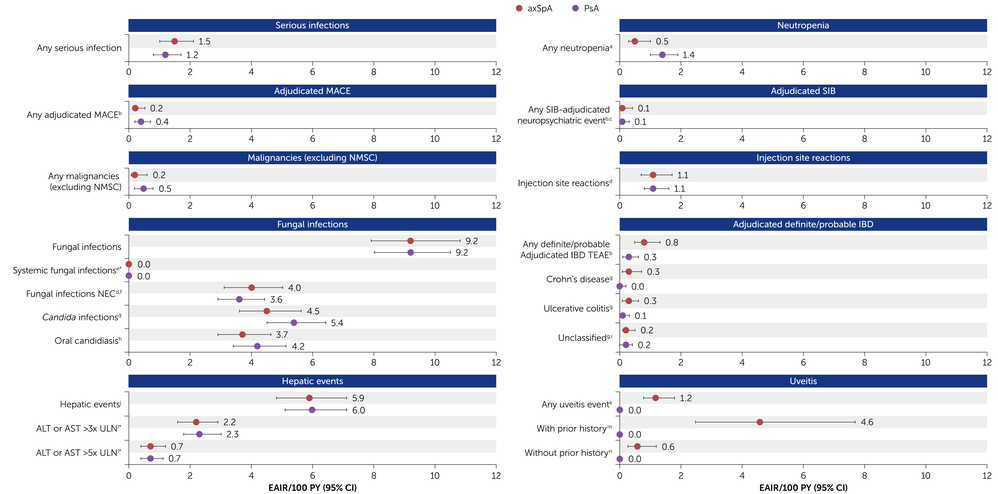
Data from the most recent data-cut (July 2022) shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W (axSpA, N=848; PsA, N=1,407).
[a] Per investigator assessment; [b] Serious TEAEs met one or more of the following criteria: death, life-threatening, significant or persistent disability/incapacity; congenital anomaly/birth defect, important medical event that may jeopardize the patient and may require medical/surgical intervention to prevent one of the previous mentioned outcomes, or initial inpatient hospitalization/prolongation of hospitalization; [c] 3 deaths occurred in each indication (by MedDRA v19.0 preferred term; axSpA: cardiac arrest, cardio-respiratory arrest, and road traffic accident; PsA: acute myocardial infarction, sudden death, and traumatic shock (from a motorcycle accident)). No deaths were considered drug-related by the investigator in any study.

Figure 3 Most common TEAEs



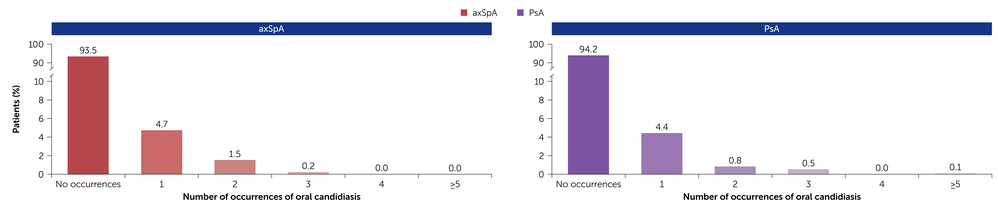
Data from the most recent data-cut (July 2022) shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W (axSpA, N=848; PsA, N=1,407). TEAEs defined by MedDRA v19.0 preferred term (except SARS-CoV-2 infection), occurring in ≥5% of patients in both the axSpA and PsA patient pools.

Figure 4 Safety topics of interest



Data from the most recent data-cut (July 2022) shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W (axSpA, N=848; PsA, N=1,407). TEAEs defined according to MedDRA v19.0 unless indicated with an asterisk (*). [a] No cases of neutropenia were associated with serious infection; [b] As determined by the appropriate independent Adjudication Committee; [c] No cases of suicide reported; [d] High Level Term; [e] Defined by omission, non-systemic infections were reported; [f] Not elsewhere classifiable; [g] Event type classification according to the adjudication committee; [h] Preferred term; [i] Unclassified/Microscopic Colitis/no further differentiation possible; [j] Includes events described as drug-related hepatic disorders, excluding liver neoplasms; [k] Includes the preferred terms uveitis, iridocyclitis and iritis; [l] Values for ULN were provided by the analyzing laboratory; [m] axSpA: n=130; PsA: n=21; [n] axSpA: n=718; PsA: n=1,386.

Figure 5 Low recurrence of oral candidiasis within individual patients with axSpA and PsA, during first year of treatment with bimekizumab



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 in Week 0–52 of treatment with BKZ.

ALT: alanine transaminase; **AS:** ankylosing spondylitis; **ASAS:** Assessment of SpondyloArthritis international Society; **AST:** aspartate aminotransferase; **axSpA:** axial spondyloarthritis; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **BMI:** body mass index; **CI:** confidence interval; **COVID-19:** coronavirus disease 2019; **EAIR:** exposure-adjusted incidence rate; **IBD:** inflammatory bowel disease; **IL:** interleukin; **MACE:** major adverse cardiovascular event; **N/A:** not applicable; **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 four weeks; **r-axSpA:** radiographic axSpA; **SARS-CoV-2:** severe acute respiratory syndrome coronavirus-2; **SD:** standard deviation; **SIB:** suicidal ideation or behavior; **TEAE:** treatment-emergent adverse event; **TNFi:** tumor necrosis factor inhibitor; **TNFi-IR:** inadequate response or intolerance to TNFi; **ULN:** upper limit of normal.

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