Long-Term Safety and Tolerability of Bimekizumab Treatment Across Phase 2b and Phase 3 Studies in Patients with Axial Spondyloarthritis or Psoriatic Arthritis: 3-Year Update from the Phase 3 Studies

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Objective

To report the overall safety profile for bimekizumab (BKZ) across patients with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) with long-term exposure in clinical trials.

Background

- Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- Previous analyses of phase 2b/3 safety data demonstrated that BKZ was generally well tolerated by patients with axSpA and PsA,[1] including up to 2 years of treatment in the phase 3 studies (data cut-off: July 2023; axSpA exposure: 2,513.8 patient-years [PY]; PsA exposure: 3,655.9 PY).[2]
- Continually evaluating the safety of treatments over a longer duration is essential to inform disease management for chronic conditions like axSpA and PsA.
- Here, we present updated safety analyses for an additional year of BKZ exposure in the ongoing phase 3 open-label extension (OLE) studies, BE MOVING and BE VITAL.

Methods

- Safety data are reported for two pools, each comprising one phase 2b and two phase 3 studies and their open-label extensions (OLEs), in patients with axSpA (non-radiographic and radiographic) and PsA, respectively (**Figure 1**).
- Exposure-adjusted incidence rates (EAIR)/100 PY and n (%) are reported for treatment-emergent adverse events (TEAEs; classified using MedDRA v19.0) among patients who received ≥1 dose of subcutaneous BKZ 160 mg every four weeks (Q4W) in any treatment period. For patients initially randomized to placebo or other treatment regimens, only TEAEs occurring during treatment with BKZ 160 mg Q4W were included.
- Data are reported to the data-cuts of September 2024 (axSpA) or August 2024 (PsA) in the ongoing BE MOVING and BE VITAL OLEs, which correspond with at least 156 weeks of total phase 3 study participation.

Results

Safety overview

- The axSpA and PsA safety pools included 848 patients (total BKZ exposure: 2,748.9 PY) and 1,409 patients (4,264.7 PY), respectively (**Figure 1**).
- Study discontinuations due to TEAEs were infrequent (EAIRs 2.2/100 PY in axSpA; 2.7/100 PY in PsA). No additional deaths occurred since the previous data-cut (July 2023; **Table**).
- Consistent with previous analyses,[1,2] the three most frequently reported TEAEs (by preferred term) in patients with axSpA and PsA were corona virus infection, nasopharyngitis, and upper respiratory tract infection (**Figure 2**).

Safety topics of interest

- Safety topics of interest across phase 2b/3 studies are reported in **Table**.
- With an additional year of BKZ treatment in the phase 2b/3 pools for axSpA and PsA, the EAIR/100 PY of safety topics of interest remained low, including serious infections, opportunistic infections, hepatic events, adjudicated major adverse cardiovascular events (MACE), adjudicated suicidal ideation/behavior (SIB), adjudicated probable/definite IBD, and uveitis (**Table**). No new safety signals or concerns were identified.
  - No patients reported active tuberculosis, histoplasmosis, coccidioidomycosis or blastomycosis in any study
  - Most hepatic events were transient liver enzyme abnormalities and there were no confirmed cases of Hy's law.
- In the phase 3 studies, the EAIR/100 PY of safety topics of interest generally remained stable or decreased in the third year of BKZ treatment (**Figure 3**).
  - One patient had adjudicated SIB (event type: suicidal ideation) and 3 patients had adjudicated MACE during Year 3 of exposure, all in the PsA cohort.

Fungal infections

- Fungal infections had an EAIR/100 PY of 8.1 in axSpA and 7.1 in PsA across phase 2b/3 studies (**Table**).
  - No patients reported systemic fungal infections, and most fungal infections were mucocutaneous and mild or moderate in severity.
- Oral candidiasis was the most frequently reported fungal infection in patients with axSpA and PsA.
  - The majority of oral candidiasis cases resolved with standard antifungal treatment, and BKZ discontinuation due to oral candidiasis was infrequent across the studies.
- In the phase 3 studies, the EAIR/100 PY of fungal infections was lower in Year 3 of BKZ treatment compared with Year 2 (axSpA: 7.6 versus 11.7; PsA: 6.9 versus 7.6).
  - The same was observed for oral candidiasis TEAEs (**Figure 3**). Occurrences of oral candidiasis TEAEs in individual patients are reported in **Figure 4**.

Conclusions

With an additional year of exposure in the phase 3 studies, the long-term safety profile of bimekizumab in patients with axSpA and PsA remained consistent with prior analyses; no new safety signals were identified or reported.[1-7]

These observations support the favorable benefit-risk profile of bimekizumab for the long-term treatment of axSpA and PsA.

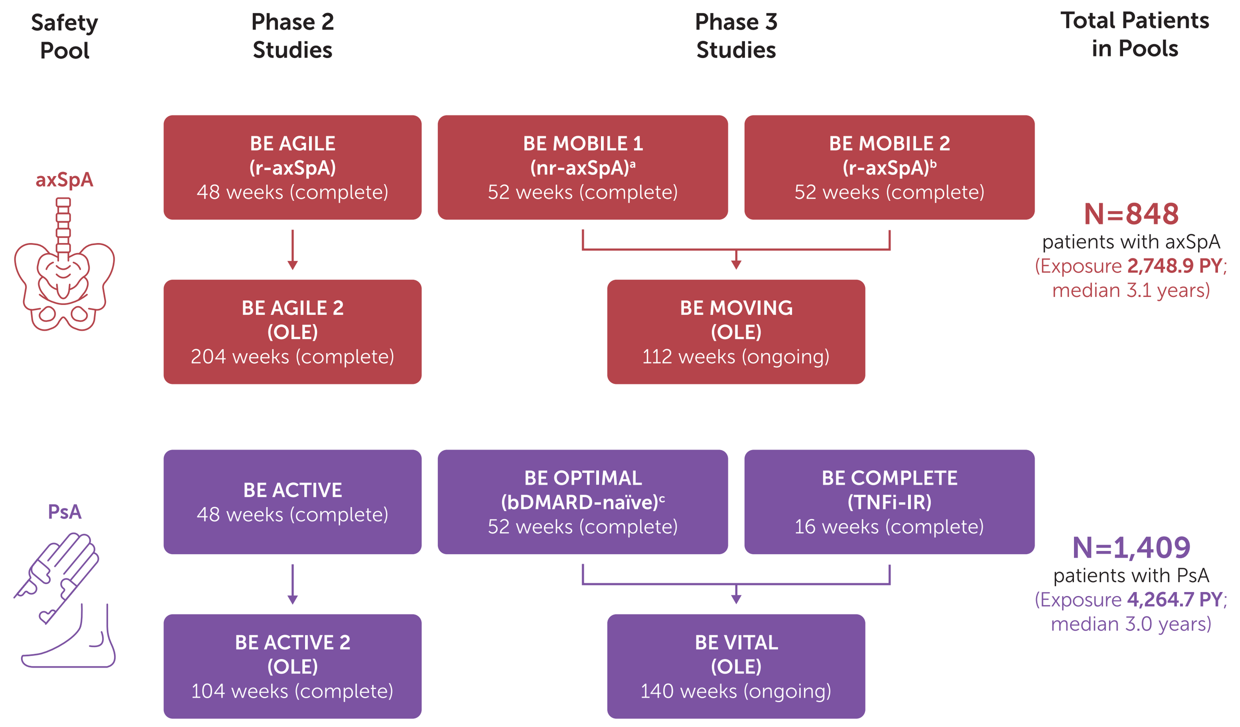
Summary

Following ~3 years of treatment with bimekizumab in the ongoing phase 3 studies, **no increased risk** (EAIR/100 PY) in the following outcomes was observed in **axSpA** or **PsA**:

EAIR/100 PY shown for TEAEs occurring in Year 3 of bimekizumab exposure in the phase 3 studies

Oral candidiasis	Hepatic events	Major adverse cardiovascular events	Suicidal ideation/behavior
3.2 / 3.7	2.9 / 4.1	0.0 / 0.3	0.0 / 0.1
Incidence rates remained low. Recurrence and treatment discontinuations due to **oral candidiasis** were infrequent.	Incidence rates of **elevated ALT or AST (>3 x ULN)** were low.	No patients with axSpA and three patients with PsA had **adjudicated MACE** in Year 3 of exposure.	No patients with axSpA and one patient with PsA had **adjudicated SIB** in Year 3 of exposure.

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



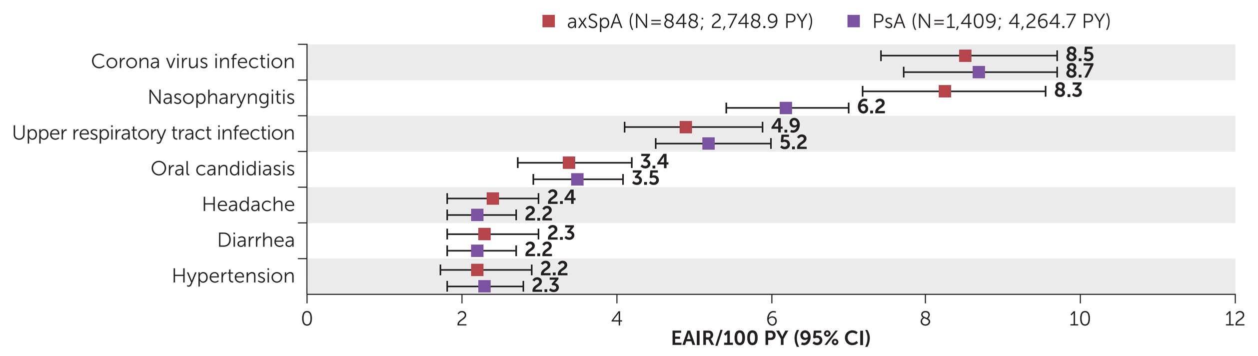
Data from the September 2024 (axSpA) and August 2024 (PsA) data-cuts shown; including all patients who received ≥1 dose of BKZ 160 mg Q4W in the phase 2b/3 studies. Duration of overall treatment period shown; BKZ treatment duration by data-cut varied between patients, depending on study duration and 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. 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.

Table Summary of TEAEs from phase 2b/3 studies, reported up to the phase 3 data cut (axSpA: September 2024; PsA: August 2024)

TEAEs (MedDRA v19.0), n (%) [EAIR/100 PY]	axSpA BKZ 160 mg Q4W (N=848; exposure 2,748.9 PY; median 3.1 years)	PsA BKZ 160 mg Q4W (N=1,409; exposure 4,264.7 PY; median 3.0 years)
Any TEAE	777 (91.6) [128.0]	1,256 (89.1) [122.5]
Severe TEAEs	79 (9.3) [3.0]	132 (9.4) [3.2]
Study discontinuations due to TEAEs	61 (7.2) [2.2]	114 (8.1) [2.7]
BKZ discontinuation due to oral candidiasis	6 (0.7) [0.2]	12 (0.9) [0.3]
Drug-related TEAEs[a]	417 (49.2) [24.3]	590 (41.9) [20.3]
Serious TEAEs[b]	127 (15.0) [5.0]	216 (15.3) [5.5]
Deaths	3 (0.4) [0.1][c]	5 (0.4) [0.1][c]
Safety topics of interest		
Fungal infections	188 (22.2) [8.1]	266 (18.9) [7.1]
Candida infections	104 (12.3) [4.1]	171 (12.1) [4.3]
Oral candidiasis	86 (10.1) [3.4]	138 (9.8) [3.5]
Fungal infections NEC	85 (10.0) [3.3]	118 (8.4) [2.9]
Tinea infections	25 (2.9) [0.9]	22 (1.6) [0.5]
Systemic fungal infections	0	0
Serious infections	37 (4.4) [1.4]	51 (3.6) [1.2]
Opportunistic infections[d]	16 (1.9) [0.6]	29 (2.1) [0.7]
Active tuberculosis	0	0
Hepatic events[e]	121 (14.3) [4.9]	177 (12.6) [4.6]
Elevated liver enzymes[f]	93 (11.0) [3.7]	145 (10.3) [3.7]
ALT or AST >3x ULN[g]	49 (5.8) [1.9]	73 (5.2) [1.8]
ALT or AST >5x ULN[g]	21 (2.5) [0.8]	23 (1.6) [0.5]
MACE, adjudicated	4 (0.5) [0.1]	13 (0.9) [0.3]
Malignancies (excluding NMSC)	10 (1.2) [0.4]	24 (1.7) [0.6]
Neutropenia[h]	14 (1.7) [0.5]	45 (3.2) [1.1]
SIB, adjudicated[i]	3 (0.4) [0.1]	2 (0.1) [0.0]
Administration/injection site reaction	28 (3.3) [1.0]	36 (2.6) [0.9]
IBD, probable/definite, adjudicated	19 (2.2) [0.7][j]	9 (0.6) [0.2][j]
With prior history[k]	3 (20.0) [6.0]	1 (7.7) [2.6]
Without prior history[l]	16 (1.9) [0.6]	8 (0.6) [0.2]
Uveitis[m]	33 (3.9) [1.2]	4 (0.3) [0.1]
With prior history[n]	20 (15.4) [5.0]	2 (9.5) [4.0]
Without prior history[o]	13 (1.8) [0.6]	2 (0.1) [0.0]

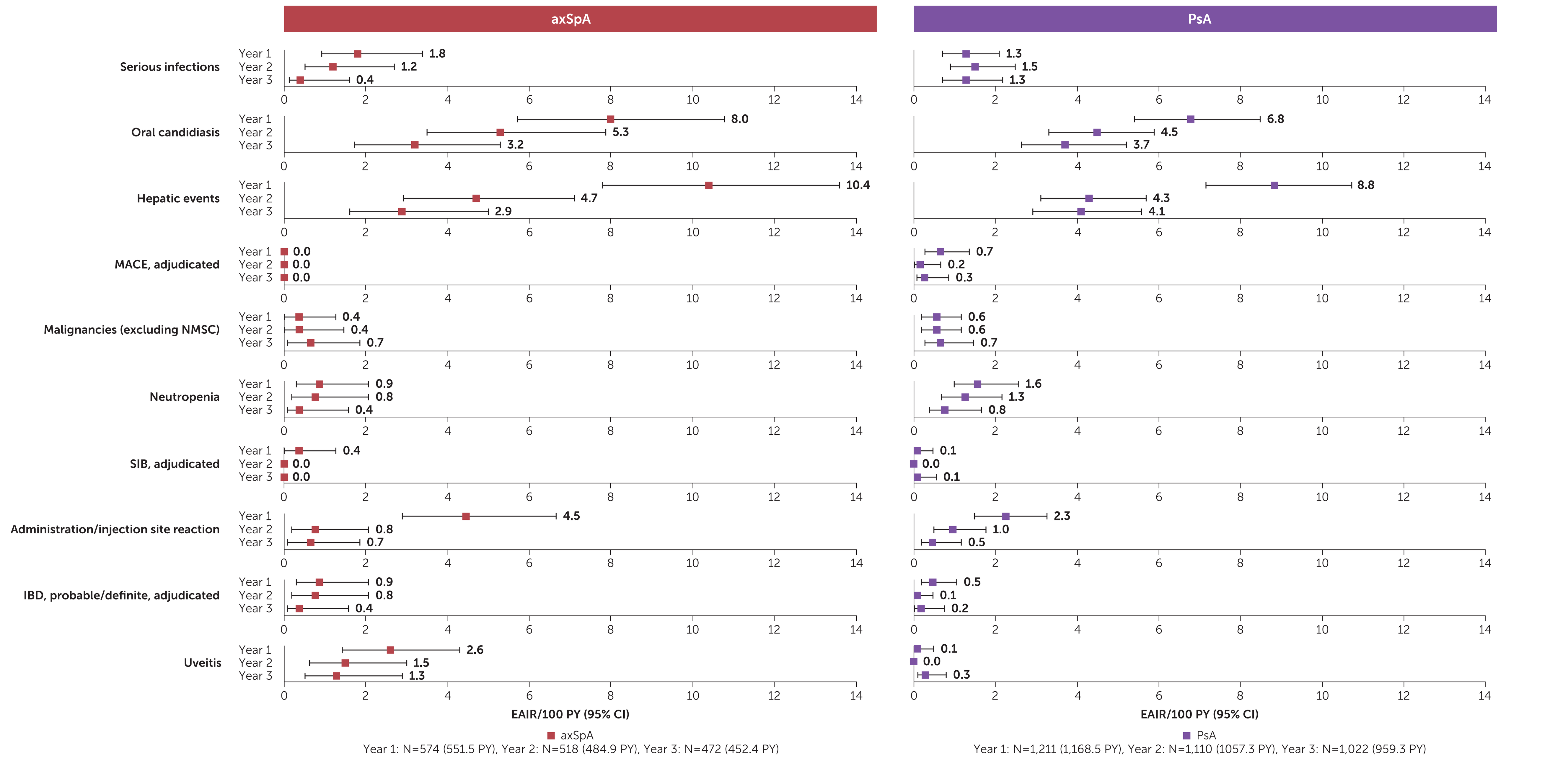
Data from the September 2024 (axSpA) and August 2024 (PsA) data-cuts shown; including all patients who received ≥1 dose of BKZ 160 mg Q4W. Data shows the number of patients experiencing a TEAE during the treatment period. Some events may have occurred before the previous data-cut (July 2023), but fall within Year 3 based on the definitions used in this analysis. **[a]** Per investigator assessment; **[b]** Serious TEAEs met one or more of the following criteria: death, life-threatening event, 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]** No deaths were considered drug-related by the investigator in any study; **[d]** Opportunistic infections (by high-level term) included *Candida* infections, Fungal infections NEC, and Herpes viral infections, in both patients with axSpA and PsA; **[e]** Includes events described as drug-related hepatic disorders, excluding liver neoplasms; **[f]** 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; **[g]** Based on laboratory data (axSpA: n=847; PsA: n=1,407); **[h]** Neutropenia includes additional preferred terms identified based on UCB-defined search criteria; **[i]** All patients had a history of psychiatric disorders or ongoing traumatic and stressful circumstances, and no cases of completed suicide were reported. One adjudicated SIB event (suicidal ideation) in a patient with axSpA was considered by the investigator to be indirectly related to BKZ; **[j]** Crohn's disease: axSpA, n=10 (1.2%); PsA, n=2 (0.1%); ulcerative colitis: axSpA, n=6 (0.7%); PsA, n=2 (0.1%); unclassified: axSpA, n=5 (0.6%); PsA, n=5 (0.4%); **[k]** axSpA, n=15; PsA, n=13; **[l]** axSpA, n=833; PsA, n=1,396; **[m]** Includes the preferred terms autoimmune uveitis, iridocyclitis, iritis, and uveitis; **[n]** axSpA, n=130; PsA, n=21; **[o]** axSpA, n=718; PsA, n=1,388.

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



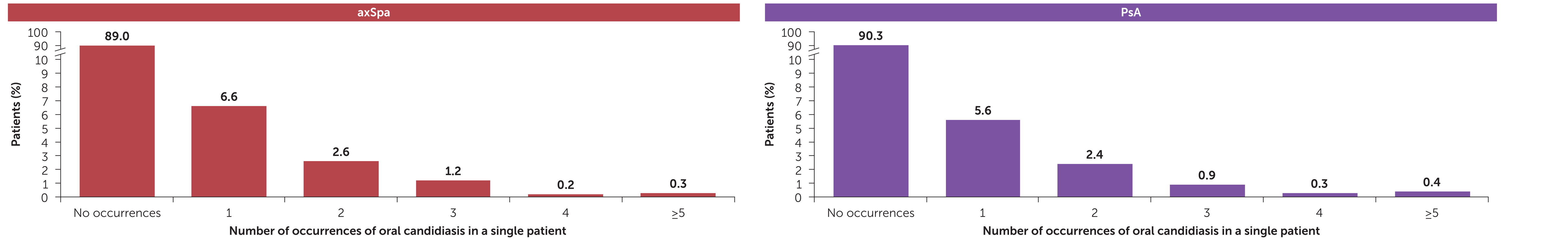
Data from the September 2024 (axSpA) and August 2024 (PsA) data-cuts shown, including all patients who received ≥1 dose of BKZ 160 mg Q4W. TEAEs defined by MedDRA v19.0 preferred term, occurring in ≥6% of patients in both the axSpA and PsA patient pools.

Figure 3 Safety topics of interest by year of bimekizumab treatment in the phase 3 studies (EAIR/100 PY [95% CI])



Data from the September 2024 (axSpA) and August 2024 (PsA) data-cuts shown, including all at-risk patients who received ≥1 dose of BKZ 160 mg Q4W in Weeks 0–52 (Year 1), Weeks >52–104 (Year 2), or Weeks >104–156 (Year 3) in the phase 3 studies. Patients were considered at-risk for up to 140 days after the last dose of BKZ.

Figure 4 Recurrence of oral candidiasis within individual patients during first 3 years of treatment with bimekizumab in the phase 3 studies



Data from the September 2024 (axSpA) and August 2024 (PsA) data-cuts 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 0–156 of treatment with BKZ.

ACR: American College of Rheumatology; **ALT:** alanine aminotransferase; **ASAS:** Assessment in SpondyloArthritis international Society; **AST:** aspartate aminotransferase; **axSpA:** axial spondyloarthritis; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **CI:** confidence interval; **EAIR:** exposure-adjusted incident rate; **IBD:** inflammatory bowel disease; **IgG:** immunoglobulin G; **IL:** interleukin; **MACE:** major adverse cardiovascular event; **MedDRA:** Medical Dictionary for Regulatory Activities; **NEC:** not elsewhere classified; **NMSC:** non-melanomic skin cancers; **nr-axSpA:** non-radiographic axial spondyloarthritis; **OLE:** open-label extension; **PsA:** psoriatic arthritis; **PY:** patient-years; **Q4W:** every 4 weeks; **r-axSpA:** radiographic axial spondyloarthritis; **SIB:** suicidal ideation and behavior; **TEAE:** treatment-emergent adverse event; **TNFi-IR:** prior inadequate response or intolerance to tumor necrosis factor-α inhibitors; **ULN:** upper limit of normal.

References: [1]Mease PJ. RMD Open 2025;11:e005026; [2]Mease PJ. Arthritis Rheumatol 2024;76(suppl 9). Abstract 2367; [3]Baraliakos X. Arthritis Rheumatol 2022;74:1943–58; [4]Baraliakos X. Ann Rheum Dis 2024;83:199–213; [5]Coates LC. Arthritis Rheumatol 2022;74:1959–70; [6]McInnes IB. Lancet 2023;401:25–37; [7]Merola JF. Lancet 2023;401:38–48.

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