Bimekizumab safety in patients with moderate to severe plaque psoriasis: Pooled data from up to three years of treatment in randomized phase 3 trials

Running head: BE BRIGHT 3-Year Safety


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Data availability: Underlying data from this manuscript may be requested by qualified researchers six months after product approval in the US and/or Europe, or global development is discontinued, and 18 months after trial completion. Investigators may request access to anonymized individual patient-level data and redacted trial documents, which may include: analysis-ready datasets, study protocol, annotated case report form, statistical analysis plan, dataset specifications, and clinical study report. Prior to use of the data, proposals need to be approved by an independent review panel at www.Vivli.org and a signed data sharing agreement will need to be executed. All documents are available in English only, for a pre-specified time, typically 12 months, on a password protected portal.

Ethics statement: All studies were conducted in accordance with the principles of the Declaration of Helsinki and approved by an Independent Review Board and Independent Ethics Committee. All participants provided informed written consent.

What is already known about this topic?

• Individuals with moderate to severe plaque psoriasis require long-term management; therefore, the long-term safety of biologics must be determined.

• Previously, 2-year data pooled from phase 2 and 3 trials have demonstrated that bimekizumab is well-tolerated.

What does this study add?

• Here, we report the first 3-year safety data for bimekizumab in patients with moderate to severe plaque psoriasis, pooled from three phase 3 trials and their open-label extension.

• No new safety signals were observed through 3 years of bimekizumab treatment. The risk of adverse events either remained consistent or decreased with longer bimekizumab exposure, and was lower with bimekizumab every 8 weeks versus every 4 weeks.
Abstract

Background: Patients with psoriasis require long-term management; therefore, understanding the long-term safety of new treatments, such as bimekizumab, is crucial.

Objectives: To evaluate bimekizumab’s 3-year safety profile in patients with moderate to severe plaque psoriasis.

Methods: Three years of safety data were pooled from three phase 3 trials (BE VIVID, BE READY, BE SURE) and their ongoing open-label extension (BE BRIGHT). Treatment-emergent adverse events (TEAEs) are reported using exposure-adjusted incidence rates (EAIRs) per 100 patient-years (PY).

Results: 1,495 patients received ≥1 bimekizumab dose; total bimekizumab exposure was 3,876.4 PY. The overall EAIR of TEAEs was 175.5/100 PY and decreased with longer exposure to bimekizumab. The most commonly reported TEAEs were nasopharyngitis, oral candidiasis, and upper respiratory tract infection (EAIRs of 15.0/100 PY, 10.1/100 PY, and 6.5/100 PY, respectively); 99.3% of oral candidiasis events were mild or moderate in severity, none were serious, and few led to discontinuation. EAIRs of other TEAEs of interest were low, including serious infections (1.2/100 PY), adjudicated inflammatory bowel disease (0.2/100 PY), and laboratory elevations in aspartate aminotransferase or alanine aminotransferase (>5x upper limit of normal: 0.6/100 PY).

Conclusions: In these analyses pooled across 3 years, no new safety signals were observed with longer exposure to bimekizumab. The vast majority of oral candidiasis events were mild or moderate in severity, as reported previously.

A video summarising this manuscript is available below.

Clinicaltrials.gov identifiers: NCT03412747, NCT03370133, NCT03410992, NCT03598790

Introduction

Psoriasis is a chronic inflammatory systemic disease placing significant burden on patients’ health and quality of life.\textsuperscript{1-4} Patients with psoriasis have higher risk of type 2 diabetes, hypertension, obesity, inflammatory bowel disease (IBD), anxiety, and...
depression than the general population. Therefore, assessing long-term safety of psoriasis treatments is essential.

Current moderate to severe psoriasis treatment focuses on advanced biologic therapies, such as tumor necrosis factor alpha (TNF-alpha) and interleukin (IL)-23 and IL-17A inhibitors, which target key cytokines in psoriasis pathogenesis and have well-established safety profiles. Bimekizumab is a monoclonal IgG1 antibody that selectively inhibits IL-17A and IL-17F. Dual inhibition with bimekizumab in patients with psoriasis has resulted in superior efficacy compared with placebo, adalimumab (anti-TNF-alpha), ustekinumab (anti-IL-12/23), and secukinumab (anti-IL-17A). Further investigations have reported long-term maintenance of efficacy with bimekizumab over 2 years, as indicated by complete/near-complete skin clearance.

Previously, 2-year data pooled from phase 2 and 3 trials demonstrated that bimekizumab is well-tolerated. Here, we report the first 3-year safety data for bimekizumab in patients with moderate to severe plaque psoriasis, pooled from three phase 3 trials and their open-label extension (OLE).

Methods

Patients

Safety data were pooled from three completed phase 3 trials: BE VIVID (NCT03370133), BE READY (NCT03410992), BE SURE (NCT03412747), and their ongoing OLE BE BRIGHT (NCT03598790). The BE BRIGHT data cut-off was October 23, 2021, the date when the last ongoing patient reached 3 years of study treatment.

Full inclusion/exclusion criteria have been published. Eligible patients for all trials were adults with moderate to severe plaque psoriasis, with baseline Psoriasis Area and Severity Index (PASI) $\geq 12$, $\geq 10\%$ body surface area affected by psoriasis, and Investigator’s Global Assessment $\geq 3$ on a 5-point scale, who were eligible for systemic psoriasis therapy and/or phototherapy.
Patients were excluded if they had active symptomatic IBD, recent (<6 months before screening) myocardial infarction/stroke, high risk of acquiring a tuberculosis (TB) infection (or active TB infection), or active suicidal ideation <1 month or suicide attempt <5 years before screening.

**Study designs**

All studies were conducted in accordance with the principles of the Declaration of Helsinki and approved by an Independent Review Board and Independent Ethics Committee. All participants provided informed written consent.

Study designs for the 52-week BE VIVID trial comparing bimekizumab versus placebo and ustekinumab, 56-week BE READY trial comparing bimekizumab versus placebo, and 56-week BE SURE trial comparing bimekizumab versus adalimumab, have been published (overview: Table S1). 24-26

Upon completion of each trial, patients were eligible to enroll in BE BRIGHT: an ongoing, multicenter, OLE study in which patients received bimekizumab 320 mg every 4 weeks (Q4W) or every 8 weeks (Q8W), depending on treatment, dose, and PASI response at feeder study end (Figure 1). Following protocol amendment, at OLE Week 48 (end of second year of treatment) or the next scheduled clinic visit, all patients receiving bimekizumab Q4W switched to Q8W dosing.

**Safety evaluations**

Treatment-emergent adverse events (TEAEs), serious and severe TEAEs, and TEAEs leading to discontinuation are reported. TEAEs were defined as AEs that occurred during exposure to treatment, including up to 140 days (six half-lives of bimekizumab) after the last dose was received. Serious TEAEs were TEAEs that led to ≥1 of the following: death, life-threatening event, substantial/persistent disability or incapacity, congenital anomaly or birth defect, important medical event, and initial/prolongation of hospitalization. TEAEs were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) version 19.0. AE intensity was assessed by investigators as mild, moderate, or severe, independently from seriousness.

TEAEs of interest were infections (serious, opportunistic, TB, and fungal), malignancies, major adverse cardiac events (MACE), neutropenia, suicidal ideation...
and behavior (SIB), IBD, injection site and hypersensitivity reactions, and laboratory elevations in aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >3x and >5x the upper limit of normal (ULN).

Predefined cardiovascular, gastrointestinal, and neuropsychiatric TEAEs were reviewed and adjudicated by independent Cardiovascular, IBD, and Neuropsychiatric Adjudication Committees, respectively. SIB was assessed using the electronic Columbia-Suicide Severity Rating Scale (eC-SSRS). Opportunistic infections were predefined using company conventions. Patients were screened to evaluate TB signs, symptoms, and possible exposure. If a patient had a positive TB test, study treatment was stopped immediately and patients were referred to a TB specialist for further evaluation.

**Statistical analysis**

Pooled safety data were analyzed, using SAS v9.4, for all patients who received ≥1 bimekizumab dose in the phase 3 trials (bimekizumab total). Safety data were also analyzed separately for bimekizumab Q4W and Q8W treatment groups. TEAEs were attributed to the treatment and dose most recently received before the onset date.

Exposure-adjusted incidence rates (EAIRs) were used to evaluate TEAEs; EAIRs represent the number of patients with a particular AE adjusted for duration of exposure. EAIRs are reported per 100 patient-years (PY) with associated 95% confidence intervals (CIs). Psoriasis Longitudinal Assessment and Registry (PSOLAR) ranges are reported for TEAEs of interest where available.

Data are presented for the full pooled trial period for the bimekizumab total group and Q4W and Q8W dosing groups, and separately for Years 1 (Week 0–52), 2 (Week >52–104), and 3 (Week >104–156) of bimekizumab exposure for the bimekizumab total group. Safety data are also reported through Weeks 0–16 for patients who received bimekizumab during the initial placebo- or active-controlled trial periods.
Results

Patients

In total, 1,495 patients received \( \geq 1 \) bimekizumab dose across the phase 3 trials (Figure S1); baseline characteristics were similar between dosing groups and were representative of plaque psoriasis patients eligible for biologic therapy (Table S2). Total bimekizumab exposure was 3,876.4 PY (Q4W: 1,965.6 PY; Q8W: 1,914.5 PY) and median exposure duration was 1,058.0 days (range: 23–1,326; Table 1).

Overall safety

The EAIR of TEAEs over 3 years was 175.5/100 PY (Table 1), and decreased with each year of bimekizumab exposure (Figure 2). EAIRs of TEAEs during Weeks 0–16 are also reported in Table 1. EAIRs of TEAEs were numerically lower in patients receiving bimekizumab Q8W versus Q4W (Table 1). Serious TEAEs and TEAEs leading to discontinuation occurred at rates of 5.5 and 3.2/100 PY, respectively (Table 1), and did not increase with longer exposure to bimekizumab (Figure 2). The vast majority of TEAEs were mild or moderate; the EAIR of severe TEAEs was 4.5/100 PY.

The most commonly reported TEAEs across the phase 3 trials by MedDRA preferred term were nasopharyngitis, oral candidiasis, and upper respiratory tract infection, with EAIRs of 15.0, 10.1, and 6.5/100 PY, respectively (Table S3).

Deaths

Over 3 years, 16 deaths (0.4/100 PY) were reported (Table 1). None were reported as treatment-related by the investigators. Causes of death were reported under the following preferred terms, each for one patient unless otherwise specified (patients could have multiple preferred terms identified as leading to death): aortic aneurysm rupture, brain neoplasm, cardiac arrest (four patients), cardiopulmonary failure, chronic obstructive pulmonary disease, circulatory collapse, completed suicide, coronavirus infection (three patients), death (two patients, each of unknown cause approximately 3 months after last bimekizumab dose), hemorrhagic anemia, hypovolemic shock, and myocardial infarction.
Infections

Over 3 years, the EAIRs of infections and serious infections (Table 2) were 81.8 and 1.2/100 PY, respectively; serious infection rates were within the PSOLAR range (0.93–2.91/100 PY). The most common serious infection was coronavirus (nine events; 0.2/100 PY). Three coronavirus events were fatal (patients had relevant comorbidities and no completed vaccination scheme); no other coronavirus events led to discontinuation. Though 17 patients had concurrent/history of latent TB and received prophylactic treatment, no patients developed active TB (Table 2).

Opportunistic infections had an EAIR of 0.9/100 PY. All were localized mucocutaneous fungal infections predefined as opportunistic, except for one serious case of ophthalmic herpes zoster that resolved with treatment and did not lead to discontinuation.

Fungal infections had an EAIR of 16.7/100 PY. Most were Candida infections (11.5/100 PY); EAIRs for other fungal infections were low (Table 2).

Candidiasis

The majority of Candida infections were reported as oral candidiasis (10.1/100 PY; Table 2). Oral candidiasis EAIRs decreased with longer bimekizumab exposure (Figure 3), and rates were numerically lower with bimekizumab Q8W versus Q4W (Table 2). The vast majority of oral candidiasis events were mild or moderate in severity (99.3%); five were severe, none were serious. One patient receiving bimekizumab Q4W reported a serious, severe case of esophageal candidiasis, as previously reported. Rates of vulvovaginal candidiasis did not increase with longer bimekizumab exposure (Table 2). Seven patients discontinued bimekizumab due to Candida infections; five of these discontinued due to oral candidiasis (three in Year 1; three/two whilst receiving Q4W/Q8W dosing, respectively).

Over the 3-year period, 154 patients (10.3%) reported one occurrence of oral candidiasis, 78 (5.2%) reported two, 38 (2.5%) reported three, 22 (1.5%) reported four, and 32 (2.1%) reported five or more. Investigators determined treatment for oral candidiasis. Most cases were treated with nystatin and/or fluconazole; median (interquartile range) duration of antifungal therapy was 12.0 (7.0–23.0) days.
Adjudicated IBD

The 3-year EAIR for adjudicated definite or probable IBD was low (0.2/100 PY; Table 2). EAIRs did not increase with longer exposure to bimekizumab (Figure 3). In total, seven cases were adjudicated as definite (two Crohn’s disease, one ulcerative colitis, one unclassified) or probable IBD (one ulcerative colitis, two undifferentiated). Three patients had a medical history of IBD; one experienced an IBD TEAE. Five cases led to treatment discontinuation and were considered treatment-related by investigators.

Malignancies

EAIRs of malignancies excluding non-melanoma skin cancer (NMSC) were low (0.5/100 PY; including NMSC, 0.8/100 PY; Table 2) and were within the PSOLAR range. Excluding NMSC, 21 occurrences of malignancies were reported in 21 patients (including NMSC, 37 occurrences in 31 patients). Malignancy EAIRs remained low with longer bimekizumab exposure (Figure 3). Two malignancies (one breast, one prostate) were assessed as treatment-related by investigators.

Liver function analyses

EAIRs of laboratory elevations in either AST or ALT >3x and >5x ULN were 2.1 and 0.6/100 PY, respectively, and did not increase with longer bimekizumab exposure (Table 2); most elevations were transient and few led to discontinuation. EAIRs of elevations >3x ULN were 2.7, 2.7, and 2.6/100 PY in Years 1, 2, and 3, respectively; EAIRs of elevations >5x ULN were 1.0, 0.4, and 0.5/100 PY.

Other TEAEs of interest

The EAIR of adjudicated MACE was low (0.6/100 PY) and remained low with longer bimekizumab exposure (Figure 3). The EAIR for adjudicated SIB was 0.1/100 PY (Table 2) and remained low with longer bimekizumab exposure (Figure 3). No SIB events were reported in the third year of treatment. One suicidal ideation event and one completed suicide from the first 2 years of treatment were previously reported; neither were treatment-related. Since the previously reported 2-year safety analyses, one further patient with a history of anxiety and depression, and concurrent substance abuse, experienced adjustment disorder with depressed mood and abnormal eC-SSRS score in the second year of BKZ exposure, and was adjudicated as having suicidal ideation. The EAIR of the high-level term ‘depressive
disorders’ was low (0.4/100 PY). Neutropenia rates were low (0.4/100 PY); none were temporally associated with serious infections. Rates of injection site reactions (1.8/100 PY) and serious hypersensitivity reactions (0.1/100 PY) were low (Table 2); no anaphylactic reactions were reported.

Discussion

These analyses reported 3-year safety data for patients with moderate to severe plaque psoriasis who received bimekizumab, pooled to include three phase 3 trials and their OLE. Over 3 years of treatment, EAIRs of TEAEs decreased with longer exposure to bimekizumab (Year 1: 221.6/100 PY; Year 2: 150.6/100 PY; Year 3: 103.7/100 PY) and were lower in patients who received bimekizumab Q8W versus Q4W. Discontinuations due to TEAEs were low throughout. A video summarizing the main findings of this analysis is available above and online at [placeholder for link].

The most common TEAEs reported with bimekizumab were nasopharyngitis, oral candidiasis, and upper respiratory tract infection, consistent with previous reports.24-26,30 Individuals with psoriasis have a higher risk of infection than the general population and the use of biologics and systemic treatments may increase this risk, as well as the risk of serious infections.4,34-36 However, the EAIR of serious infections in this analysis was low (1.2/100 PY), did not increase with longer bimekizumab exposure, and was within the PSOLAR range (0.9–2.9/100 PY).33 Serious infection rates were also comparable to studies investigating other IL-17 inhibitors, such as brodalumab (1.0–1.3/100 PY),20 secukinumab (1.4–1.5/100 PY),18,37 and ixekizumab (1.3–2.3/100 PY).15,19,38 The most common serious infection was coronavirus infection, due to the third year of treatment taking place during the COVID-19 pandemic. No patients developed active TB, despite 17 patients having concurrent/history of latent TB and receiving prophylactic treatment.

Treatment with IL-17 inhibitors can increase risk of oral candidiasis, due to IL-17’s defensive role against fungal infections at the oral mucosa.39-43 Furthermore, some individuals have a predisposed greater risk of oral candidiasis, including those who are elderly, smoke, or have endocrine disorders or nutritional deficiencies.44 Although oral candidiasis rates with bimekizumab remain higher than with other IL-17 inhibitors,19,37,38 EAIRs decreased with longer bimekizumab exposure, and were
numerically lower in patients receiving bimekizumab Q8W versus Q4W. Over the
3-year period, the vast majority of oral candidiasis events were mild or moderate
(99.3%); few patients who experienced oral candidiasis discontinued as a result
(1.5%).

Occurrences of AST and ALT elevations in this analysis did not increase with longer
exposure to bimekizumab; most elevations were transient and few led to
discontinuation. These observations were as expected for the study populations as
psoriasis is linked to non-alcoholic fatty liver disease, obesity, diabetes, and
excessive alcohol consumption,45,46 all of which are known to affect liver function.

Other TEAEs of interest had low EAIRs over the 3-year period, such as MACE
(0.6/100 PY) and malignancies (excluding NMSC; 0.5/100 PY). On rare occasion, new
onset or exacerbation of IBD has been reported with other IL-17 inhibitors,47,48 but
IBD rates were low with bimekizumab (0.2/100 PY), and were similar to those
reported in previous studies of individuals with psoriasis.18,19,37,49 Those with psoriasis
are also at increased risk of depression and SIB;50-52 however, EAIRs of depression
and adjudicated SIB were low with bimekizumab throughout (0.4 and 0.1/100 PY).

This analysis is strengthened by its long-term nature and large sample size.
Furthermore, these long-term safety data show lower TEAE rates with the
bimekizumab Q8W dosing regimen, the recommended maintenance dose for most
patients following initial Q4W dosing for 16 weeks,53 supporting its use in clinical
practice. However, as Q8W dosing has been associated with lower rates of certain
TEAEs versus Q4W,24 and Year 3 data include a greater proportion of patients
receiving Q8W dosing than Years 1 and 2, this may have contributed to the lower
TEAE rates seen through Year 3. Due to the OLE’s nature, patients were not blinded
during this period, so Year 2 and 3 data are subject to reporting bias. Moreover,
these findings may be limited in their generalizability to real-world populations, due
to minimal racial diversity in the patient populations and stringent patient exclusion
criteria. OLE data may also have been affected by the COVID-19 pandemic coinciding
with its second year (third year of treatment overall). Potential confounding factors,
such as social isolation, mask wearing, and lockdowns may have affected TEAE
rates, in particular respiratory infections such as nasopharyngitis.
In these analyses pooled across 3 years of treatment from three phase 3 clinical trials and their OLE, bimekizumab demonstrated a favorable safety profile, with no new safety signals observed. The risk of AEs either remained consistent or decreased with longer bimekizumab exposure, and was lower with bimekizumab Q8W versus Q4W.

References


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**Figure legends**

**Figure 1. BE BRIGHT Study Design**

All patients who did not achieve PASI 90 at end of feeder study received bimekizumab 320 mg Q4W upon OLE entry. Patients who were receiving bimekizumab 320 mg Q8W and achieved PASI 90 remained on Q8W dosing. Patients who were receiving bimekizumab 320 mg Q4W and achieved PASI 90 were randomized 4:1 to receive bimekizumab 320 mg Q4W or Q8W. Patients who were receiving ustekinumab at the end of BE VIVID and achieved PASI 90 were randomized 1:1 to receive bimekizumab 320 mg Q4W or Q8W. Patients who received bimekizumab 320 mg Q4W during the initial 16-week treatment period of BE READY and were re-randomized to placebo for the randomized withdrawal period received bimekizumab 320 mg Q4W upon OLE entry. *Patients who completed the BE VIVID, BE READY, or BE SURE phase 3 trials were eligible to enroll in the BE BRIGHT OLE; **BE SURE and BE READY had a duration of 56 weeks and BE VIVID had a duration of 52 weeks; †At Week 24 of the BE BRIGHT OLE, patients receiving bimekizumab 320 mg Q4W who had achieved PASI 90 could be switched to receive bimekizumab 320 mg Q8W at the discretion of the investigator; ‡At Week 48 of the OLE, or at the next scheduled clinic visit, all patients who had remained on bimekizumab 320 mg Q4W
were re-assigned to bimekizumab 320 mg Q8W, via protocol amendment. OLE: open-label extension; PASI: Psoriasis Area and Severity Index; PASI 90: ≥90% reduction from baseline in PASI; Q4W: every 4 weeks; Q8W: every 8 weeks; Q12W: every 12 weeks.

Figure 2. Incidence Rates of Overall TEAEs, Serious TEAEs, TEAEs Leading to Discontinuation, and Severe TEAEs

Data are reported as EAIRs; error bars represent 95% CIs. Data are presented separately for Years 1 (Week 0–52), 2 (Week >52–104), and 3 (Week >104–156) of bimekizumab exposure for the bimekizumab total group. BKZ: bimekizumab; CI: confidence interval; EAIR: exposure-adjusted incidence rate; PY: patient-years; TEAE: treatment-emergent adverse event.

Figure 3. Incidence Rates of TEAEs of Interest

Data are reported as EAIRs; error bars represent 95% CIs. Data are presented separately for Years 1 (Week 0–52), 2 (Week >52–104), and 3 (Week >104–156) of bimekizumab exposure for the bimekizumab total group. PSOLAR ranges are shown for TEAEs of interest for which ranges are available (serious infections, malignancies [excluding NMSC], and adjudicated MACE). ALT: alanine transaminase; AST: aspartate aminotransferase; BKZ: bimekizumab; CI: confidence interval; EAIR: exposure-adjusted incidence rate; IBD: inflammatory bowel disease; MACE: major adverse cardiac event; NMSC: non-melanoma skin cancer; PSOLAR: Psoriasis Longitudinal Assessment and Registry; PY: patient-years; SIB: suicidal ideation and behavior; TEAE: treatment-emergent adverse event; ULN: upper limit of normal.
Table 1. Summary of Treatment Exposure and TEAEs in Bimekizumab-Treated Patients in the Phase 3 Trials

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<thead>
<tr>
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<th>By Time Period</th>
<th>Over 3 Years</th>
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<tr>
<td></td>
<td>Week 0–16 (N=989)</td>
<td>Year 1 (N=1,495)</td>
</tr>
<tr>
<td>Total exposure, PY</td>
<td>306.0</td>
<td>1,435.7</td>
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<tr>
<td>Mean exposure (SD), days</td>
<td>110.3 (9.3)</td>
<td>932.4 (317.7)</td>
</tr>
<tr>
<td>Median exposure (range), days</td>
<td>112.0 (23–122)</td>
<td>1,058.0 (23–1,326)</td>
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Summary of TEAEs, EAIR/100 PY (95% CI)

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<tr>
<td>Any TEAE</td>
<td>315.7 (290.8, 342.1)</td>
<td>221.6 (209.3, 234.4)</td>
<td>150.6 (140.8, 160.9)</td>
<td>103.7 (95.7, 112.2)</td>
<td>217.9 (205.8, 230.5)</td>
<td>115.6 (108.2, 123.3)</td>
</tr>
<tr>
<td>Serious TEAEs</td>
<td>4.9 (2.8, 8.1)</td>
<td>6.3 (5.0, 7.8)</td>
<td>5.6 (4.4, 7.2)</td>
<td>5.5 (4.1, 7.2)</td>
<td>6.2 (5.1, 7.4)</td>
<td>5.4 (4.4, 6.5)</td>
</tr>
<tr>
<td>TEAEs leading to</td>
<td>5.6 (3.5, 8.9)</td>
<td>4.6 (3.5, 5.8)</td>
<td>2.5 (1.7, 3.6)</td>
<td>1.9 (1.1, 3.0)</td>
<td>3.8 (2.9, 4.7)</td>
<td>2.5 (1.9, 3.3)</td>
</tr>
<tr>
<td>discontinuation</td>
<td>3.9 (2.0, 6.9)</td>
<td>5.3 (4.1, 6.6)</td>
<td>5.0 (3.8, 6.5)</td>
<td>4.4 (3.2, 6.0)</td>
<td>5.3 (4.3, 6.4)</td>
<td>4.2 (3.3, 5.2)</td>
</tr>
<tr>
<td>Severe TEAEs</td>
<td>0.3 (0.0, 1.8)</td>
<td>0.2 (0.0, 0.6)</td>
<td>0.4 (0.1, 1.0)</td>
<td>0.6 (0.2, 1.4)</td>
<td>0.4 (0.2, 0.8)</td>
<td>0.4 (0.2, 0.8)</td>
</tr>
</tbody>
</table>

Data are shown as of the data cut-off (October 23, 2021). Data are pooled from the phase 3 BE VIVID, BE READY, and BE SURE phase 3 trials and their open-label extension BE BRIGHT. Data are presented for the bimekizumab Q4W dosing group for the initial 16-week treatment period, bimekizumab total and Q4W and Q8W dosing groups for the full pooled trial period, and separately for Years 1 (Week 0–52), 2 (Week >52–104), and 3 (Week >104–156) of bimekizumab exposure for the bimekizumab total group. aBKZ Total includes all patients who received ≥1 BKZ dose in the included studies; bPatients who received both BKZ 320 mg Q4W and Q8W are included in the population count of
both dosing groups, but only once in each BKZ Total group; Total BKZ exposure over 3 years is greater than the sum of BKZ exposure in individual years, as data beyond Week 156 are included due to the use of a cut-off date. BKZ: bimekizumab; CI: confidence interval; EAIR: exposure-adjusted incidence rate; PY: patient-years; Q4W: every 4 weeks; Q8W: every 8 weeks; SD: standard deviation; TEAE: treatment-emergent adverse event.
Table 2. Incidence Rates of TEAEs of Interest

<table>
<thead>
<tr>
<th>TEAEs of interest, EAIR/100 PY (95% CI)</th>
<th>By Time Period</th>
<th>Over 3 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BKZ 320 mg Q4W</td>
<td>BKZ Totala</td>
</tr>
<tr>
<td></td>
<td>Week 0–16 (N=989)</td>
<td>Year 1 (N=1,456)</td>
</tr>
<tr>
<td>Serious infections</td>
<td>1.0 (0.2, 2.9)</td>
<td>1.5 (0.9, 2.3)</td>
</tr>
<tr>
<td>Active tuberculosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fungal infections</td>
<td>43.7 (36.4, 52.0)</td>
<td>28.2 (25.3, 31.3)</td>
</tr>
<tr>
<td><em>Candida</em> infections</td>
<td>30.6 (24.6, 37.6)</td>
<td>20.5 (18.1, 23.2)</td>
</tr>
<tr>
<td>Oral candidiasis</td>
<td>25.3 (19.9, 31.8)</td>
<td>17.6 (15.4, 20.0)</td>
</tr>
<tr>
<td>Oral pharyngeal candidiasis</td>
<td>3.6 (1.8, 6.5)</td>
<td>1.4 (0.9, 2.2)</td>
</tr>
<tr>
<td>Oral skin candidiasis</td>
<td>0.7 (0.1, 2.4)</td>
<td>0.6 (0.2, 1.1)</td>
</tr>
<tr>
<td>Vulvovaginal candidiasis</td>
<td>1.3 (0.4, 3.3)</td>
<td>0.9 (0.5, 1.6)</td>
</tr>
<tr>
<td>Esophageal candidiasis</td>
<td>0</td>
<td>0.3 (0.1, 0.8)</td>
</tr>
<tr>
<td><em>Tinea</em> infections</td>
<td>7.3 (4.6, 11.0)</td>
<td>3.6 (2.7, 4.8)</td>
</tr>
<tr>
<td>Fungal infections NEC</td>
<td>5.6 (3.3, 8.9)</td>
<td>3.9 (2.9, 5.1)</td>
</tr>
<tr>
<td>Adjudicated IBD</td>
<td>1.0 (0.2, 2.9)</td>
<td>0.3 (0.1, 0.8)</td>
</tr>
<tr>
<td>Adjudicated MACE</td>
<td>0.3 (0.0, 1.8)</td>
<td>0.6 (0.3, 1.2)</td>
</tr>
<tr>
<td>Malignancies</td>
<td>1.3 (0.4, 3.4)</td>
<td>0.8 (0.4, 1.4)</td>
</tr>
<tr>
<td>Excluding NMSC</td>
<td>0.3 (0.0, 1.8)</td>
<td>0.3 (0.1, 0.8)</td>
</tr>
<tr>
<td>Adjudicated SIB</td>
<td>0</td>
<td>0.1 (0.0, 0.4)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>2.3 (0.9, 4.7)</td>
<td>0.9 (0.5, 1.6)</td>
</tr>
<tr>
<td>AST or ALT elevations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3x ULN</td>
<td>4.3 (2.3, 7.3)</td>
<td>2.7 (1.9, 3.7)</td>
</tr>
<tr>
<td>&gt;5x ULN</td>
<td>1.0 (0.2, 2.9)</td>
<td>1.0 (0.5, 1.7)</td>
</tr>
<tr>
<td>Serious hypersensitivity reactionsd</td>
<td>0</td>
<td>0.1 (0.0, 0.4)</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>9.0 (5.9, 13.1)</td>
<td>2.9 (2.1, 4.0)</td>
</tr>
</tbody>
</table>

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Figure 1

246x139 mm (x DPI)
Figure 2

246x139 mm (x DPI)
Figure 3

246x70 mm (x DPI)