Bimekizumab in patients with moderate to severe plaque psoriasis: Analysis of mental health and associated disorders

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Synopsis

- Patients with psoriasis have a greater risk of mental health disorders, such as anxiety, depression, and suicidality, than the general population.[1]

Objective

To report anxiety, depression, and suicidal ideation and behavior (SIB) data over 16 weeks and longer-term in bimekizumab (BKZ)-treated patients with moderate to severe plaque psoriasis.

Methods

- The BKZ in psoriasis clinical development program exhaustively monitored and collected patient data related to depression and suicidality.
  - This program includes nine global phase 2/3 trials: BE ABLE 1, BE ABLE 2, PS0016, PS0018 (phase 2); BE VIVID, BE READY, BE SURE, their ongoing open-label extension (OLE), BE BRIGHT, and the ongoing BE RADIANT trial (phase 3).[2–10]
  - Full study designs have been published previously.[2–4,6–10]

PHQ-9

- The Patient Health Questionnaire (PHQ)-9 measured depression severity monthly to Week 16 (regular, longer intervals during the BE BRIGHT OLE) and was scored 0–27; higher scores indicate worse depression.[11]
- Mean PHQ-9 scores are reported through:
  - Week 0–16 of BE VIVID and BE READY pooled together (BKZ 320 mg every 4 weeks [Q4W] vs placebo [PBO]).
  - Comparator-controlled periods of BE VIVID (BKZ vs ustekinumab [UST]), BE SURE (BKZ vs adalimumab [ADA]), and BE RADIANT (BKZ vs secukinumab [SEC]).
  - 3 years of the BE BRIGHT OLE following the feeder studies.
- Depression categories defined according to PHQ-9 scores are also reported from Week 0–16 of BE VIVID/BE READY.

Anxiety, Depression, and Adjudicated SIB TEAEs

- An independent Neuropsychiatric Adjudication Committee evaluated potential neuropsychiatric events and determined whether abnormal PHQ-9 and electronic Columbia-Suicide Severity Rating Scale scores, and treatment-emergent adverse events (TEAEs), met criteria for SIB.
- Incidence rates/100 patient-years (PY) of anxiety disorders and symptoms, depressive disorders, and adjudicated SIB TEAEs were reported using data pooled from all nine phase 2/3 trials (BKZ Total), including up to 5 years of BKZ exposure (4 years of BE BRIGHT).

PHQ-9

- At baseline and through PBO- and comparator-controlled periods, mean PHQ-9 scores with BKZ were low, numerically lower than PBO, and similar to active comparators (**Figure 1**).
  - Low mean PHQ-9 scores were maintained with BKZ over 3 years of the BE BRIGHT OLE (mean PHQ-9 after 144 weeks of BE BRIGHT: 1.2).
- At Week 16 of BE VIVID/BE READY, 92.9% of BKZ patients scored 0–4 in PHQ-9 (no/minimal depression) vs 81.1% of PBO patients (**Figure 2**); 1.2% vs 6.3% scored ≥10 (moderate–severe depression).
  - 0.7% of BKZ-treated patients scored ≥15 in PHQ-9 (moderately severe–severe depression) at any post-baseline visit during Weeks 0–16, vs 4.1% in the PBO group.

Anxiety, Depression, and Adjudicated SIB TEAEs

- Over 7,166 PY of BKZ exposure, the rates of anxiety disorders (0.1/100 PY) and symptoms (0.5/100 PY), depressive disorders (0.5/100 PY), and adjudicated SIB (0.1/100 PY) TEAEs were low (**Table 1**).
- The rates of adjudicated SIB (0.13/100 PY), suicidal behavior (0.06/100 PY), and completed suicides (0.01/100 PY) with BKZ were comparable to rates with anti-interleukin (IL)-17A and anti-IL-23 therapies in psoriasis (**Table 2**);[12–16] inclusion and exclusion criteria, and definitions and monitoring of suicidal ideation, differed between studies, with extensive monitoring in the BKZ studies; therefore, caution should be taken when making comparisons across studies.
  - The adjudicated SIB rate with BKZ was lower than reported for brodalumab (0.38).[15]
  - The adjudicated SIB rate was also similar to rates seen in the general psoriasis population (0.09–0.54/100 PY).[1,17,18]

Conclusions

The vast majority of BKZ patients had no/minimal depression at Week 16. Low PHQ-9 scores were observed with BKZ treatment, which were numerically lower than PBO and similar to those seen with active comparators; low scores were maintained through an additional 3 years of BKZ treatment following phase 3 feeder studies.

The long-term incidence rates of anxiety, depression, and adjudicated SIB were low with BKZ; adjudicated SIB rates were comparable with rates seen in the general psoriasis population and in patients receiving anti-IL-17A and anti-IL-23 therapies.

Summary

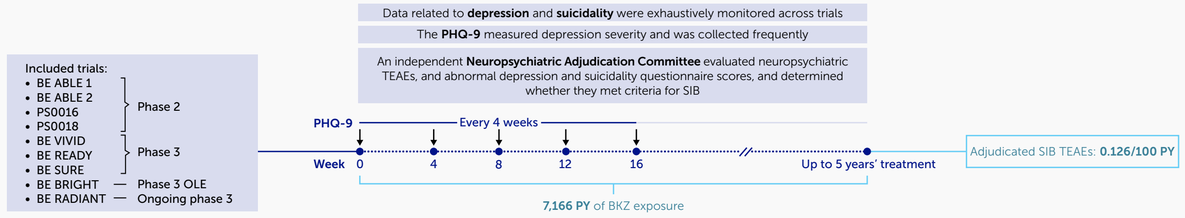
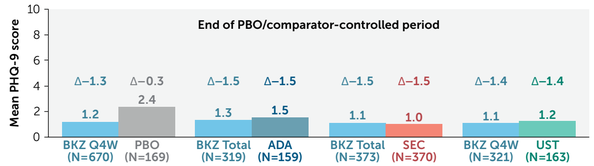
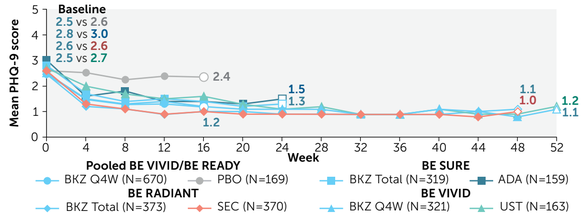


Figure 1 Mean PHQ-9 scores through PBO- and comparator-controlled periods (MI)

A) At end of PBO/comparator-controlled period

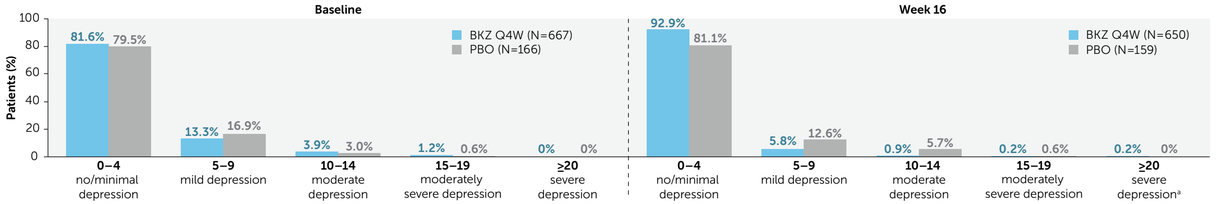


B) Over time



All baseline, Week 16, and change from baseline values are rounded to 1 decimal place. Delta values indicate change from baseline in mean PHQ-9 scores at the end of PBO- and comparator-controlled periods. BKZ Total includes data from all doses of BKZ pooled together. The PBO-controlled period in BE VIVID and BE READY lasted for 16 weeks. The active comparator-controlled periods lasted for 24 weeks (BKZ vs ADA; BE SURE), 48 weeks (BKZ vs SEC; BE RADIANT), and 52 weeks (BKZ vs UST; BE VIVID). Using multiple imputation methodology, intermittent missing data were imputed based on the Markov Chain Monte Carlo method, and monotone missing data were imputed using monotone regression.

Figure 2 Incidence of PHQ-9 scores by depression category at baseline and Week 16 in BE VIVID/BE READY pooled (OC)



Data are presented for patients with available data only (observed case). [a]One patient receiving BKZ 320 mg Q4W was categorized as having severe depression at Week 16; this patient had a medical history of bipolar disorder, anxiety, and depression.

ADA: adalimumab; **BKZ:** bimekizumab; **BRO:** brodalumab; **CI:** confidence interval; **DLQI:** Dermatology Life Quality Index; **EAIR:** exposure-adjusted incidence rate; **GUS:** guselkumab; **HRQoL:** health-related quality of life; **IL:** interleukin; **IXE:** ixekizumab; **MedDRA:** Medical Dictionary for Regulatory Activities; **MI:** multiple imputation; **N/R:** not reported; **OLE:** open-label extension; **PASI:** Psoriasis Area and Severity Index; **PBO:** placebo; **PHQ-9:** Patient Health Questionnaire-9; **PY:** patient-years; **Q4W:** every 4 weeks; **RZB:** risankizumab; **SEC:** secukinumab; **SIB:** suicidal ideation and behavior; **TEAE:** treatment-emergent adverse event; **TIL:** tildrakizumab; **UST:** ustekinumab.

Table 1 Anxiety disorders and symptoms, depressive disorders, and adjudicated SIB TEAEs

A) Anxiety disorders and symptoms and depressive disorders TEAEs

	BKZ Total (N=2,480)
Total exposure, PY	7,166
TEAEs, EAIR/100 PY (95% CI)	
Anxiety disorders[a]	0.1 (0.1, 0.2)
Anxiety disorder	<0.1 (0.0, 0.1)
Generalized anxiety disorder	<0.1 (0.0, 0.1)
Neurosis	<0.1 (0.0, 0.1)
Anxiety symptoms[a]	0.5 (0.4, 0.7)
Anxiety	0.5 (0.3, 0.7)
Stress	0.1 (0.0, 0.2)
Depressive disorders[a]	0.5 (0.4, 0.7)
Depression	0.5 (0.3, 0.7)
Persistent depressive disorder	<0.1 (0.0, 0.1)

B) Adjudicated SIB TEAEs

	BKZ Total (N=2,480)
Total exposure, PY	7,166
TEAEs, EAIR/100 PY (95% CI)	
Adjudicated SIB[b]	0.126 (0.058, 0.239)
Adjudicated suicidal ideation[b,c]	0.084 (0.031, 0.182)
Adjudicated suicidal behavior[b]	0.056[d]
Suicide attempt	0.042 (0.009, 0.122)
Completed suicide	0.014 (0.000, 0.078)

BKZ Total includes data pooled from all nine phase 2/3 BKZ in psoriasis trials, including up to 5 years of BKZ exposure. [a]Includes all TEAEs which code to the equivalent MedDRA high-level terms; [b]Adjudicated via an independent Neuropsychiatric Adjudication Committee; [c]Includes events adjudicated as 'suicidal ideation', rather than events coded to this preferred term; [d]The EAIR of suicidal behavior is the sum of the EAIRs for suicide attempt and completed suicide; the CI has not been calculated.

Table 2 Comparison of SIB TEAEs across anti-IL-17 and anti-IL-23 clinical development programs in psoriasis

Anti-IL-17A/F | Anti-IL-17A | Anti-IL-17A receptor | Anti-IL-23

	BKZ Total (N=2,480)	SEC[12] (N=5,181)	IXE[15] (N=4,209)	BRO[15] (N=4,464)	RZB[13] (N=3,072)	GUS[14] (N=2,891)	TIL[16] (N=1,994)
Total exposure, PY	7,166	10,417	6,480	9,162	7,927	8,662	4,130
TEAEs, EAIR/100 PY (n)							
SIB[a]	0.13 (9)	0.08[b] (8)	0.14 (9)	0.38 (35)	0.09[b] (7)	0.10 (9)	0.19 (8)
Suicidal behavior	0.06 (4)	0.05[b] (5)	0.14 (9)	0.21 (19)	N/R	0.02[b] (2)	0.07[b] (3)
Suicide attempt	0.04 (3)	0.04[b] (4)	0.14 (9)	0.16 (15)	N/R	0.01[b] (1)	0.02 (1)
Completed suicide	0.01 (1)	0.01[b] (1)	0	0.04 (4)	0	0.01[b] (1)	0.05 (2)

[a]SIB events were adjudicated in the BKZ in psoriasis clinical development program via an independent Neuropsychiatric Adjudication Committee; in the psoriasis development programs for the other treatments shown, SIB events were defined using Standardized MedDRA Query. Inclusion and exclusion criteria, and definitions and monitoring of suicidal ideation, differed between studies, with extensive monitoring in the BKZ studies; therefore, caution should be taken when making comparisons across studies; †EAIRs were not reported in the original reference; rates were estimated based on the PY of exposure and number of cases reported in the reference.

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Final approval of the publication: **AB**, **AA**, **JFM**, **BS**, **DdC**, **LP**, **OD**, **JLS**, **ML**. **Author Disclosures: AB:** Served as a speaker (received honoraria) for AbbVie, Bristol Myers Squibb, Eli Lilly, Pfizer, Regeneron, and Sanofi; served as a scientific adviser (received honoraria) for AbbVie, Abcentra, Aclaris, Affibody, Aligos, Almirall, Alumis, Amgen, AnaptysBio, Apogee, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, CTI BioPharma, Dermavant, EcoR1, Eli Lilly, Escient, Evelo, Evommune, Forte, Galderma, HighlightII Pharma, Incyte, InnoventBio, Janssen, Landos, LEO Pharma, Merck, Novartis, Pfizer, Rani, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, Takeda, TLL Pharmaceutical, TrialSpark, UCB Pharma, Union, Ventyx, Vibliome, and Xencor; clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Alaunos, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Concert, Dermavant, Eli Lilly, Evelo, Evommune, Galderma, Incyte, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, Sun Pharma, UCB Pharma, and Ventyx. **AA:** Served as a research investigator and/or scientific advisor to AbbVie, Almirall, Amgen, Arcutis, ASLAN, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly, EPI, Incyte, Janssen, LEO Pharma, Nimbus, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sun Pharma, Sanofi, and UCB Pharma. **JFM:** Consultant and/or investigator for AbbVie, Amgen, Biogen, Bristol Myers Squibb, Dermavant, Eli Lilly, Janssen, LEO Pharma, Pfizer, Novartis, Regeneron, Sanofi, Sun Pharma, and UCB Pharma. **BS:** Consultant (honoraria) for AbbVie, Alumis, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Immunic Therapeutics, Bristol Myers Squibb, Connect Biopharma, Dermavant, Eli Lilly, Evelo Biosciences, Janssen, LEO Pharma, Maruho, Meiji Seika Pharma, Mindera Health, Novartis, Pfizer, Regeneron, Sanofi-Genzyme, Sun Pharma, UCB Pharma, Union Therapeutics, Ventyxbio, and vTv Therapeutics; stock options from Connect Biopharma and Mindera Health; speaker for AbbVie, Arcutis, Dermavant, Eli Lilly, Incyte, Janssen, Regeneron, and Sanofi-Genzyme; scientific co-director (consulting fee) for CorEvitas (formerly Corrona) Psoriasis Registry; investigator for AbbVie, Cara, CorEvitas Psoriasis Registry, Dermavant, Dermira, and Novartis; editor-in-chief (honorarium) for Journal of Psoriasis and Psoriatic Arthritis. **DdC**, **LP**, **OD**, **JLS:** Employees and shareholders of UCB Pharma. **ML:** Employee of Mount Sinai and receives research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Dermavant, Eli Lilly, Incyte, Inozyme, Janssen, Ortho Dermatologics, Sanofi-Regeneron, and UCB Pharma; consultant for Almirall, AltruBio Inc., AnaptysBio, Arcutis Inc., AstraZeneca, Avotres Therapeutics, Brickell Biotech, Boehringer Ingelheim, Bristol Myers Squibb, Castle Biosciences, Celltrion, CorEvitas, Dermavant, EPI, Evommune Inc., Facilitation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Galderma, Genentech, Incyte, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Seanergy, Strata, Trevi, and Verrica. **Acknowledgments:** This study was funded by UCB Pharma. 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