Reporting mental health and associated disorders from trials of bimekizumab in patients with active axial spondyloarthritis and psoriatic arthritis

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Objective

To report mental health data, including suicidal ideation and behavior (SIB), in patients with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) from phase 3 studies of bimekizumab (BKZ).

Introduction

- BKZ is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
- Anxiety and depression are highly prevalent in patients with axSpA and PsA.[1–4]
- All phase 3 BKZ in axSpA and PsA trials coincided at least partially with the COVID-19 pandemic, with local lockdown measures and health issues having varying impacts on mental health.

Materials and Methods

- Treatment-emergent adverse events (TEAEs) are reported for pooled axSpA and PsA populations from phase 2/3 trials. An independent Neuropsychiatric Adjudication Committee evaluated all potential SIB TEAEs, including abnormal electronic Columbia-Suicide Severity Rating Scale (eC-SSRS) and Patient Health Questionnaire (PHQ)-9 scores.
- eC-SSRS and PHQ-9 are patient-reported instruments used to assess mental health in the phase 3 studies of BKZ in patients with axSpA (BE MOBILE 1 & 2) and PsA (BE OPTIMAL and BE COMPLETE).
  - All studies were double-blind and placebo (PBO)-controlled through Week 16. Patients completing Week 16 of BE COMPLETE were eligible to enter the BE VITAL open-label extension.
  - BE OPTIMAL included an active reference arm (adalimumab 40 mg Q2W) to provide a reference for the benefit/risk profile of BKZ to Week 52.
  - Patients with active suicidal ideation, a recent suicide attempt, or moderately severe to severe depression were excluded at screening.
- The eC-SSRS questionnaire assesses SIB. eC-SSRS responses were pooled within phase 3 axSpA and PsA trials to Week 16 (PBO-controlled period); reported to Week 52 for BE OPTIMAL (active treatment-blind period with reference arm).
- We report depression severity scores to 1 year from phase 3 trials using PHQ-9. Data are reported as observed case (OC) or using multiple imputation (MI).

Results

- In pooled analyses of phase 2/3 trials including 2,804.0 patient-years (PY) of BKZ exposure in axSpA (N=928) and 3,949.0 PY in PsA (N=1,415), the exposure-adjusted incidence rate (EAIR)/100 PY (95% CI) of adjudicated SIB TEAEs was 0.11 (0.02, 0.31) for axSpA; 0.05 (0.01, 0.18) for PsA.
- EAIRs were low for anxiety and depressive disorders, and there were no completed suicides across trials (**Table 1**). Two events, reported as intentional self-injury and suicidal behavior, were adjudicated as suicide attempts.
- To Week 16, the proportion of BKZ-treated patients with overall and new-onset positive eC-SSRS responses (to any question 1–9) were low and generally similar to PBO in axSpA and PsA trials (**Table 2**). Most new onset responses were to eC-SSRS Q1, representing passive suicidal ideation.
- Mean PHQ-9 scores were low at baseline. To Week 16, mean PHQ-9 scores on BKZ remained low and were generally lower than PBO. Low mean PHQ-9 scores were sustained to 1 year on BKZ and were similar to the reference arm in BE OPTIMAL (**Figure 1**).
- Most patients had no/minimal depression (PHQ-9 score 0–4) at baseline, Week 16 and Week 52 (**Figure 2**).
- Trends were generally consistent across patients with axSpA and PsA; however, in this integrated analysis, direct comparison between patient populations and treatment arms was challenging.

Conclusions

Across trials of bimekizumab in patients with axSpA and PsA, eC-SSRS and PHQ-9 scores were low and similar to PBO to Week 16. Adjudicated SIB, anxiety and depression rates remained low to 1 year, despite impacts of the COVID-19 pandemic.

Summary

Mental health data, including suicidal ideation and behavior, anxiety and depression, are reported in **patients with axSpA or PsA from phase 3 studies of bimekizumab.**

Tools used to assess mental health:

TEAEs across phase 2/3 trials:
- **Adjudicated suicidal ideation and behavior**
- **Anxiety** disorders
- **Depressive** disorders

eC-SSRS
- Assesses suicidal ideation and behavior
- 9 questions of increasing severity

1 2 3 4 5 — Q1–5 assess suicidal ideation

6 7 8 9 — Q6–9 assess suicidal behavior

PHQ-9
- Assesses depression severity

0 No/minimal depression 5 Mild depression 10 Moderate depression 15 Moderately severe depression 20 Severe depression 27

Across trials of BKZ in patients with axSpA and PsA, eC-SSRS and PHQ-9 scores were **low and similar to PBO to Week 16.** Adjudicated SIB, anxiety and depression rates remained **low to 1 year on BKZ treatment** across trials.

Table 1 TEAEs from the integrated safety summary of phase 2/3 studies

	BKZ Total	
	axSpA (N=928)	PsA (N=1,415)
Total exposure, PY	2,804.0	3,949.0
EAIR/100 PY (95% CI)		
Any adjudicated SIB neuropsychiatric event[a]	0.11 (0.02, 0.31)	0.05 (0.01, 0.18)
Completed suicide	0	0
Suicide attempt	0.04 (0.00, 0.20)[b]	0.03 (0.00, 0.14)[c]
Preparatory action toward imminent suicidal behavior	0.04 (0.00, 0.20)	0
Suicidal ideation	0.04 (0.00, 0.20)	0.03 (0.00, 0.14)
Anxiety disorders	0.04 (0.00, 0.20)	0.03 (0.00, 0.14)
Anxiety disorder	0	0.03 (0.00, 0.14)
Generalized anxiety disorder	0.04 (0.00, 0.20)	0
Anxiety symptoms	0.36 (0.17, 0.66)	0.46 (0.27, 0.73)
Anxiety	0.36 (0.17, 0.66)	0.41 (0.23, 0.66)
Stress	0	0.05 (0.01, 0.18)
Depressive disorders	0.32 (0.15, 0.61)	0.41 (0.23, 0.66)
Depression	0.32 (0.15, 0.61)	0.41 (0.23, 0.66)

Events reported by preferred term, unless elsewhere specified. Data pooled from phase 2/3 trials for axSpA (BE AGILE 1 & 2, BE MOBILE 1 & 2, BE MOVING, AS0013) and PsA (BE ACTIVE 1 & 2, BE OPTIMAL, BE COMPLETE, BE VITAL). Data cut-off: 06 November 2023; some patients may have exposure beyond 1 year at the time of the data cut-off. [a] Reported by adjudication category event type; [b] One intentional self-injury TEAE in a patient with axSpA was adjudicated as suicidal attempt; patient had a history of anxiety, depression and alcohol use, and a family history of suicidal attempt; [c] One suicidal behavior TEAE in a patient with PsA was adjudicated as suicidal attempt; patient had a prior history of depression and anxiety, and was reported as being non-compliant with medication for these conditions.

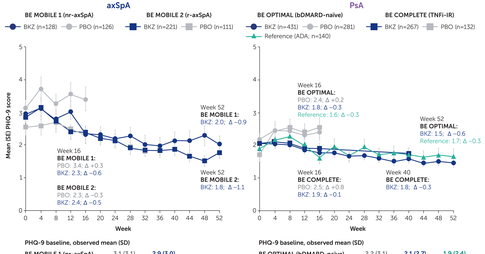
ADA: adalimumab; **axSpA:** axial spondyloarthritis; **bDMARD:** biologic disease-modifying antirheumatic drug; **BKZ:** bimekizumab; **eC-SSRS:** electronic Columbia-Suicide Severity Rating Scale questionnaire; **MI:** multiple imputation; **nr-axSpA:** non-radiographic axSpA; **OC:** observed case; **PBO:** placebo; **PHQ-9:** Patient Health Questionnaire-9; **PsA:** psoriatic arthritis; **Q:** question; **Q2W:** every 2 weeks; **Q4W:** every 4 weeks; **r-axSpA:** radiographic axSpA; **SD:** standard deviation; **SE:** standard error; **SIB:** suicidal ideation and behavior; **TEAE:** treatment-emergent adverse event; **TNFi-IR:** tumor necrosis factor inhibitor inadequate response or intolerance.

Table 2 Overall positive and new-onset positive responses to eC-SSRS, eC-SSRS Q1 and PHQ-9 Q9

	axSpA Pooled Phase 3 (Week 0–16)		PsA Pooled Phase 3 (Week 0–16)		PsA BE OPTIMAL (bDMARD-naïve) (Week 0–52)	
n (%)	PBO (n=237)	BKZ 160 mg Q4W (n=349)	PBO (n=413)	BKZ 160 mg Q4W (n=698)	BKZ 160 mg Q4W (n=431)	Ref (ADA) 40 mg Q2W (n=140)
Positive eC-SSRS response[a]	0	0	3 (0.7)	2 (0.3)	2 (0.5)	2 (1.4)
New-onset positive eC-SSRS response[b]	0	0	3 (0.7)	2 (0.3)	2 (0.5)[c]	0
New-onset positive eC-SSRS Q1 response,[b] "Wish to be dead"	0	0	3 (0.7)	2 (0.3)	1 (0.2)	0
New-onset positive PHQ-9 Q9 response,[b] "Thoughts that you would be better off dead or of hurting yourself"	10 (4.2)	8 (2.3)	8 (1.9)	4 (0.6)	7 (1.6)	2 (1.4)
New-onset positive response to both eC-SSRS Q1 and PHQ-9 Q9[b,d]	0	0	0	0	0	0

Pooled data from axSpA phase 3 trials includes BE MOBILE 1 (NCT03928704), BE MOBILE 2 (NCT03928743); pooled data from PsA phase 3 trials includes BE OPTIMAL (NCT03895203), BE COMPLETE (NCT03896581) and the open-label extension BE VITAL (NCT04009499). Patients completing Week 16 of BE COMPLETE or Week 52 of BE OPTIMAL were eligible to enter BE VITAL. [a] Positive eC-SSRS response defined as positive response to any question (Q1–9); [b] New-onset responses were defined as a positive post-baseline result with no positive results during screening or at baseline; [c] One positive response to Q1 ("Wish to be dead") and one positive response to Q2 ("Non-specific active suicidal thoughts"); [d] Positive responses are reported for each questionnaire at any visit during the placebo-controlled or active treatment-blind periods independently (positive response to each questionnaire may not have occurred at the same clinic visit).

Figure 1 PHQ-9 absolute values and change from baseline (MI)



PHQ-9 baseline, observed mean (SD)

BE MOBILE 1 (nr-axSpA)	3.5 (3.1)	**2.9 (3.0)**
BE MOBILE 2 (r-axSpA)	2.6 (2.7)	**2.8 (3.2)**

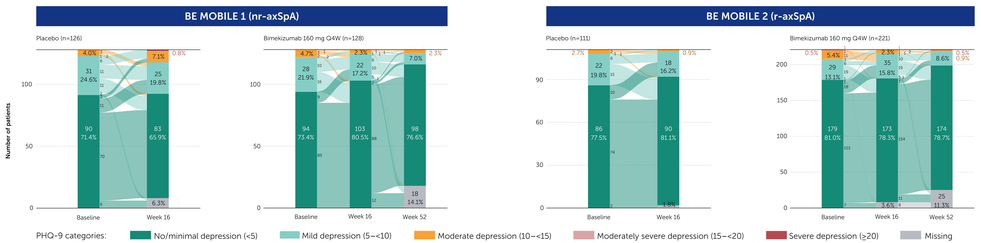
PHQ-9 baseline, observed mean (SD)

BE OPTIMAL (bDMARD-naïve)	2.2 (3.1)	**2.1 (2.7)**
BE COMPLETE (TNFi-IR)	2.0 (2.6)	**1.7 (2.4)**

PHQ-9 is scored 0 to 27, with higher scores indicating worse depression. Labels report PHQ-9 absolute scores and change from baseline (Δ). At Week 16, PBO patients switched to receive BKZ 160 mg Q4W; data not shown following PBO/BKZ switch. Patients completing Week 16 of BE COMPLETE or Week 52 of BE OPTIMAL were eligible to enter BE VITAL; patient populations referred to by the name of their starting study. BE OPTIMAL included a reference arm (ADA); not powered for comparison with BKZ or PBO.

Figure 2 Sankey plots showing PHQ-9 depression severity score changes from baseline to Week 52

A) axSpA trials



PHQ-9 depression severity scores (OC)

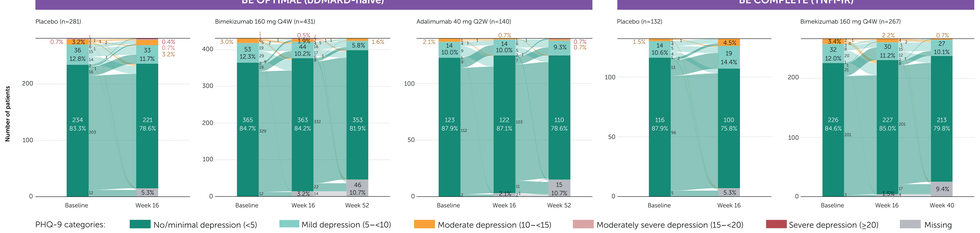
	PBO (n=126)	
n (%)	Baseline	Week 16
0–4	89/123 (72.4)	83/118 (70.3)
5–9	30/123 (24.4)	25/118 (21.2)
10–14	4/123 (3.3)	9/118 (7.6)
15–19	0	0
≥20	0	1/118 (0.8)

	BKZ 160 mg Q4W (n=128)		
	Baseline	Week 16	Week 52
0–4	94/128 (73.4)	103/128 (80.5)	96/108 (88.9)
5–9	28/128 (21.9)	22/128 (17.2)	9/108 (8.3)
10–14	6/128 (4.7)	3/128 (2.3)	3/108 (2.8)
15–19	0	0	0
≥20	0	0	0

	PBO (n=111)	
n (%)	Baseline	Week 16
0–4	83/107 (77.6)	90/109 (82.6)
5–9	21/107 (19.6)	18/109 (16.5)
10–14	3/107 (2.8)	1/109 (0.9)
15–19	0	0
≥20	0	0

	BKZ 160 mg Q4W (n=221)		
	Baseline	Week 16	Week 52
0–4	177/217 (81.6)	173/213 (81.2)	174/196 (88.8)
5–9	27/217 (12.4)	35/213 (16.4)	19/196 (9.7)
10–14	12/217 (5.5)	5/213 (2.3)	2/196 (1.0)
15–19	1/217 (0.5)	0	1/196 (0.5)
≥20	0	0	0

B) PsA trials



PHQ-9 depression severity scores (OC)

	PBO (n=281)	
n (%)	Baseline	Week 16
0–4	234/281 (83.3)	221/266 (83.1)
5–9	36/281 (12.8)	33/266 (12.4)
10–14	9/281 (3.2)	9/266 (3.4)
15–19	2/281 (0.7)	2/266 (0.8)
≥20	0	1/266 (0.4)

	BKZ 160 mg Q4W (n=431)		
	Baseline	Week 16	Week 52
0–4	365/431 (84.7)	363/417 (87.1)	353/385 (91.7)
5–9	53/431 (12.3)	44/417 (10.6)	25/385 (6.5)
10–14	13/431 (3.0)	8/417 (1.9)	7/385 (1.8)
15–19	0	2/417 (0.5)	0
≥20	0	0	0

	Reference (ADA 40 mg Q2W; n=140)		
	Baseline	Week 16	Week 52
0–4	123/140 (87.9)	122/137 (89.1)	110/125 (88.0)
5–9	14/140 (10.0)	14/137 (10.2)	13/125 (10.4)
10–14	3/140 (2.1)	1/137 (0.7)	1/125 (0.8)
15–19	0	0	1/125 (0.8)
≥20	0	0	0

	PBO (n=132)	
n (%)	Baseline	Week 16
0–4	116/132 (87.9)	100/125 (80.0)
5–9	14/132 (10.6)	19/125 (15.2)
10–14	2/132 (1.5)	6/125 (4.8)
15–19	0	0
≥20	0	0

	BKZ 160 mg Q4W (n=267)		
	Baseline	Week 16	Week 40
0–4	226/267 (84.6)	227/263 (86.3)	213/242 (88.0)
5–9	32/267 (12.0)	30/263 (11.4)	27/242 (11.2)
10–14	9/267 (3.4)	6/263 (2.3)	2/242 (0.8)
15–19	0	0	0
≥20	0	0	0

Sankey plots show the movement of patients through PHQ-9 depression severity score categories at baseline, Week 16 and Week 52. Sankey plots include patients with missing data; tables report data as observed. At Week 16, PBO patients switched to receive BKZ 160 mg Q4W; data not shown following PBO/BKZ switch. Patients completing Week 16 of BE COMPLETE or Week 52 of BE OPTIMAL were eligible to enter BE VITAL; patient populations referred to by the name of their starting study. BE OPTIMAL included a reference arm (ADA); not powered for comparison with BKZ or PBO. [a] PHQ-9 was not collected at Week 52 in BE COMPLETE; collected only to Week 40. PHQ-9 is scored 0 to 27, with higher scores indicating worse depression; scores ≥10 represent clinical depression.

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References: [1]Parkinson JT. Ther Adv Musculoskelet Dis 2020;12:1759720X20970028. [2]Wu JJ. J Eur Acad Dermatol 2017;31:1168–75. [3]Zhao SS. Clin Rheumatol 2020;39:217–25. [4]Reddy KN. Eur J Rheumatol 2021;9:8–13. [5]Baraliakos X. Ann Rheum Dis 2023;82(2):199–213 (NCT03928704; NCT03928743). [6]Ritchlin CT. Ann Rheum Dis 2023;82(11):1404–14 (NCT03895203). [7]Coates LC. RMD Open 2024;10(1):e003855 (NCT03896581). [8]BE VITAL: https://clinicaltrials.gov/study/NCT04009499. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **MM, DP, ML, RB, DdC, AM, LP, JLS, JFM.** Drafting of the publication; or reviewing it critically for important intellectual content: **MM, DP, ML, RB, DdC, AM, LP, JLS, JFM.** Final approval of the publication: **MM, DP, ML, RB, DdC, AM, LP, JLS, JFM.** **Author Disclosures: MM:** Consultancy fees from AbbVie, BMS, Eli Lilly, Novartis, Pfizer and UCB Pharma, and research grants from AbbVie, BMS and UCB Pharma. **DP:** Speaker for AbbVie, BMS, Eli Lilly, MSD, Novartis, Pfizer and UCB Pharma; consultant for AbbVie, Biocad, Eli Lilly, Gilead, GSK, MSD, Moonlake, Novartis, Pfizer, Samsung Bioepis and UCB Pharma; grant/research support from: AbbVie, Lilly, MSD, Novartis and Pfizer. **ML:** Employee of Mount Sinai and receives research funds from: Abbvie, Amgen, AnaDerm, Aveites, Boehringer Ingelheim, Cara Therapeutics, Dermavant Sciences, Eli Lilly and Company, Incyte, Inozyme, Janssen Research & Development, LLC, Ortho Dermatologics, Pfizer, Sanofi–Regeneron and UCB Pharma; consultant for Almirall, Aktrulbio Inc., AnaptysBio, Apogee, Arcutis Inc., AstraZeneca, Atomwise, Aveites Therapeutics, BMS, Boehringer Ingelheim, Brickell Biotech, Castle Biosciences, Celltrion, CorEvitas, Dermavant Sciences, EPI, Exommune 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, Sanofi–Regeneron, Seanergy, Strata, Takeda, Trevi and Verrica; **RB, DdC, LP, JLS:** Employees and shareholders of UCB Pharma; **AM:** Employee of UCB Pharma; **JFM:** Consultant and/or investigator for Abbvie, Amgen, Biogen, BMS, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen, LEO Pharma, MoonLake, Novartis, Pfizer, Sanofi–Regeneron, Sun Pharma and UCB Pharma. **Acknowledgements:** We would like to thank the patients and their caregivers in addition to all the investigators and their teams who contributed to this study. The authors acknowledge Celia Menckeberg, PhD, UCB Pharma, The Netherlands, and Heather Edens, PhD, UCB Pharma, USA for publication coordination, Sona Popat, BA, Costello Medical, London, UK for medical writing and editorial assistance, and the Costello Medical Creative team for design support. These studies were funded by UCB Pharma. All costs associated with development of this presentation were funded by UCB Pharma.