Reporting Mental Health and Associated Disorders from Trials of Bimekizumab in Patients with Active Axial Spondyloarthritis and Psoriatic Arthritis

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).

Background

- 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.

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



Preparatory action suicidal behavior Suicidal ideation

Anxiety disorders

Anxiety disorder

Generalized anxiety

Anxiety symptoms Anxiety

Stress

Depressive disorders

Depression

Events reported by preferred term, unless elsewhere specified. Data pooled from phase 2/3 trials for axSpA (BE AGILE 1 & 2, BE MOVING, ASO013) 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 suicidated as suicid 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 Ps was adjudicated as suicidal attempt; patient had a prior history of anxiety and depression, and was reported as being non-compliant with medication for these conditions.

treatment-emergent adverse event; TNFi-IR: tumor necrosis factor inhibitor inadequate response or intolerance.

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References: ¹Parkinson JT. Ther Adv Musculoskelet Dis 2020;12 1. Ei Lilly, ASD, And UCB, and U Ei Lilly, MSD, Novartis, and Pfizer, MSD, Novartis, and receives research funds from: AbbVie, Eli Lilly and Company, Incyte, Inozyme, Janssen, LLC, Ortho Dermatologics, Pfizer, Sanofi-Regeneron, and UCB; consultant for Almirall, AltruBio Inc., AstraZeneca, EPI, Evommune Inc., Facilitation of International Dermatologics, Pfizer, Sanofi-Regeneron, and UCB; consultant for Almirall, AltruBio Inc., AstraZeneca, Atomwise, Avotres Therapeutics, BMS, Boehringer Ingelheim, Cara Therapeutics, BMS, Boehringer Ingelheim, Brickell Biotech, Castle Biosciences, EPI, Evommune Inc., AstraZeneca, Atomwise, Avotres Therapeutics, BMS, Boehringer Ingelheim, Brickell Biotech, Castle Biosciences, EPI, Evommune Inc., Facilitation of International Dermatologics, Pfizer, Sanofi-Regeneron, and UCB; consultant for Almirall, AltruBio Inc., AstraZeneca, Atomwise, Avotres Therapeutics, BMS, Boehringer Ingelheim, Cara Therapeutics, BMS, Boehringer Ingelheim, Brickell Biotech, Cara Therapeutics, BMS, Boehringer Ingelheim, Brickell Biotech, Boehringer Ingelheim, Biotech, Boehringer Ingelheim, Biotech, Boehringer Ingelheim, Biotech, Boehringer trace biogen, BMS, Boehringer Ingelheim, Dermatology, Strata, Takeda, Trevi, and UCB. **Acknowledgments:** We would like to thank the patients and their and lor investigator for AbbVie, Amgen, AstraZeneca Biogen, BMS, Boehringer Ingelheim, Dermatology, Strata, Takeda, Trevi, and UCB. **Acknowledgments:** We would like to thank the patients and their and lor investigator for AbbVie, Amgen, AstraZeneca Biogen, BMS, Boehringer Ingelheim, Dermatology, Strata, Takeda, Trevi, and UCB. **Acknowledgments:** We would like to thank the patients and their and lor investigator for AbbVie, Amgen, AstraZeneca Biogen, BMS, Boehringer Ingelheim, Dermatology, Strata, Takeda, Trevi, and UCB. **Acknowledgments:** We would like to thank the patients and their and lor investigator for AbbVie, Amgen, AstraZeneca Biogen, BMS, Boehringer Ingelheim, Dermatology, Strata, Takeda, Trevi, and UCB. **Acknowledgments:** We would like to thank the patients and their and lor investigator for AbbVie, Amgen, AstraZeneca Biogen, BMS, Boehringer Ingelheim, Dermatology, Strata, Takeda, Trevi, and UCB. **Acknowledgments:** We would like to thank the patients and their and lor investigator for AbbVie, Amgen, AstraZeneca Biogen, BMS, Boehringer Ingelheim, Dermatology, Strata, Takeda, Trevi, and UCB. **Acknowledgments:** We would like to thank the patients and their and lor investigator for AbbVie, Amgen, AstraZeneca Biogen, BMS, Boehringer Ingelheim, Berna, Berna

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were low and similar to PBO to Week 16. Adjudicated suicidal ideation and behavior, anxiety and depression rates remained low to 1 year on bimekizumab treatment across trials.

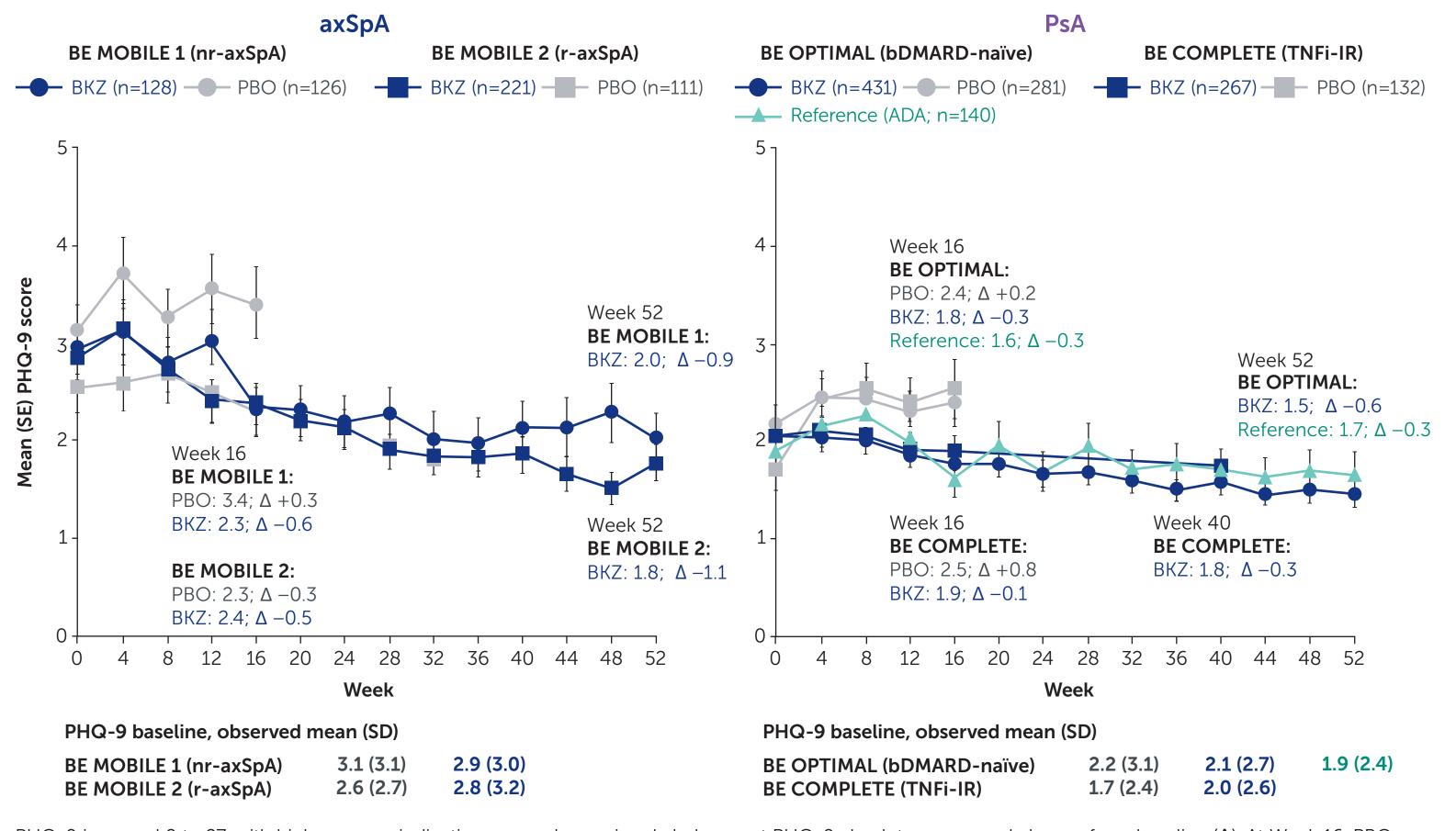
Table 1TEAEs from the integrated safety summary of phase 2/3 studies

	BKZ Total				
	axSpA N=928	PsA N=1,415			
	2,804.0	3,949.0			
B vent ^a	0.11 (0.02, 0.31)	0.05 (0.01, 0.18)			
9	0	0			
	0.04 (0.00, 0.20) ^b	0.03 (0.00, 0.14) ^c			
n toward imminent	0.04 (0.00, 0.20)	0			
	0.04 (0.00, 0.20)	0.03 (0.00, 0.14)			
	0.04 (0.00, 0.20)	0.03 (0.00, 0.14)			
	0	0.03 (0.00, 0.14)			
ty disorder	0.04 (0.00, 0.20)	0			
	0.36 (0.17, 0.66)	0.46 (0.27, 0.73)			
	0.36 (0.17, 0.66)	0.41 (0.23, 0.66)			
	0	0.05 (0.01, 0.18)			
rs	0.32 (0.15, 0.61)	0.41 (0.23, 0.66)			
	0.32 (0.15, 0.61)	0.41 (0.23, 0.66)			
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	Pooled	SpA Phase 3 (0–16	Pooled	PsA Phase 3 < 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).

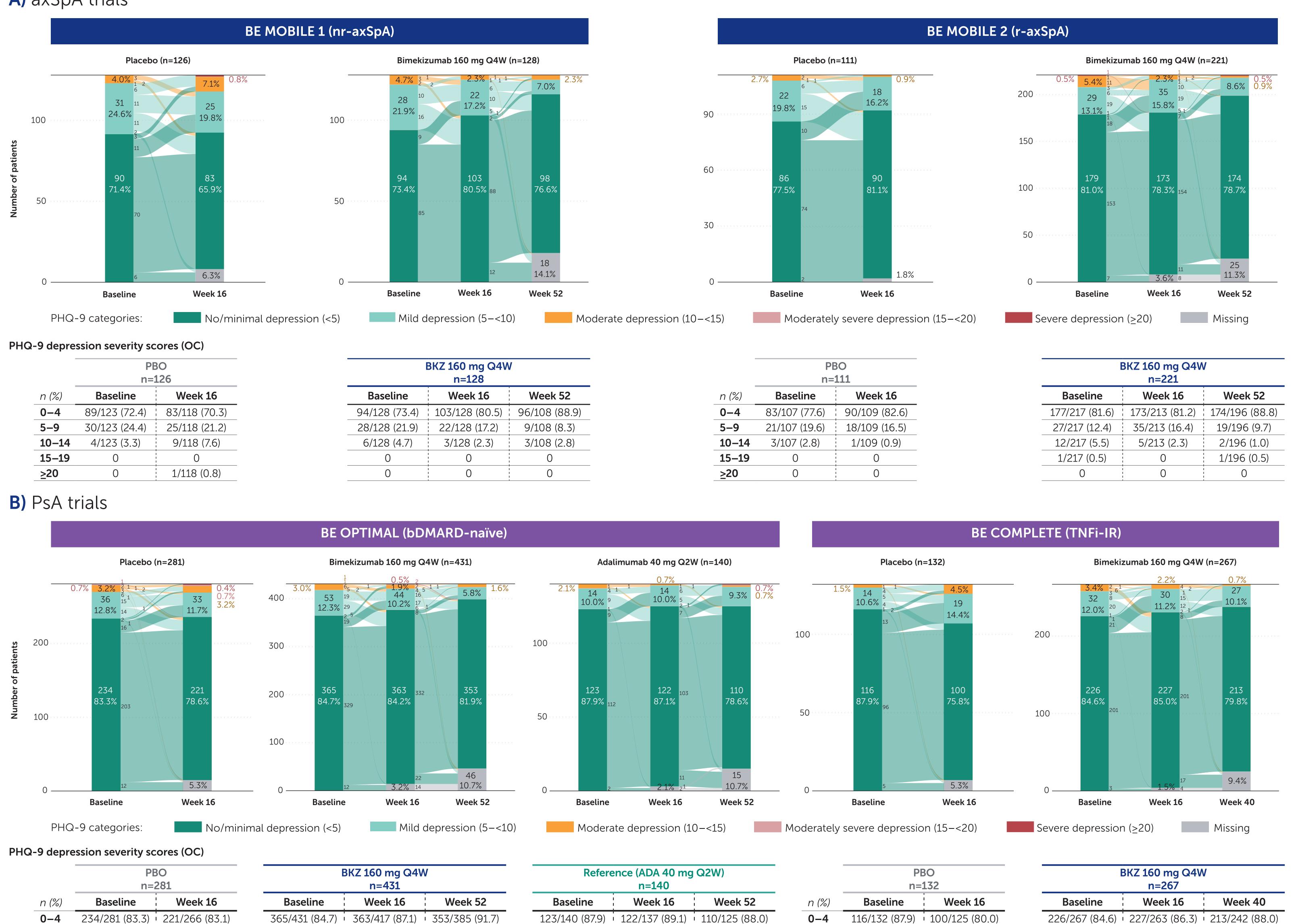
Figure 1 PHQ-9 absolute values and change from baseline (MI)



PHQ-9 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 are referred to by the name of their starting study. BE OPTIMAL included a reference arm (ADA); not powered for comparison with BKZ or PBO.

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

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



14/140 (10.0) · 14/137 (10.2) · 13/125 (10.4)

3/140 (2.1) 1/137 (0.7) 1/125 (0.8)

0 1/125 (0.8)

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		30 126		BKZ 160 mg Q n=128		
n (%)	Baseline	Week 16	Baseline	Week 16		
0-4	89/123 (72.4)	83/118 (70.3)	94/128 (73.4)	103/128 (80.5		
5–9	30/123 (24.4)	25/118 (21.2)	28/128 (21.9)	22/128 (17.2)		
10–14	4/123 (3.3)	9/118 (7.6)	6/128 (4.7)	3/128 (2.3)		
15–19	0	0	0	0		
≥20	0	1/118 (0.8)	0	0		

	PBO n=281		BKZ 160 mg Q4W n=431			
n (%)	Baseline	Week 16	Baseline	Week 16	Week 52	
0-4	234/281 (83.3)	221/266 (83.1)	365/431 (84.7)	363/417 (87.1)	353/385 (91.7)	
5–9	36/281 (12.8)	33/266 (12.4)	53/431 (12.3)	44/417 (10.6)	25/385 (6.5)	
10–14	9/281 (3.2)	9/266 (3.4)	13/431 (3.0)	8/417 (1.9)	7/385 (1.8)	
15–19	2/281 (0.7)	2/266 (0.8)	0	2/417 (0.5)	0	
<u>≥</u> 20	0	1/266 (0.4)	0	0	0	

Sankey plots show the movement of patients through PHQ-9 depression severity score categories at baseline, Week 16 and Week 4 completing Week 16 of BE COMPLETE or Week 52 of BE OPTIMAL were eligible to enter BE VITAL; patient populations are referred 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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k 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
ed 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

5–9 14/132 (10.6) 19/125 (15.2)

2/132 (1.5) · 6/125 (4.8)

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32/267 (12.0) 30/263 (11.4) 27/242 (11.2,



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