Bimekizumab in patients with moderate to severe plaque psoriasis by bodyweight: Pooled results from phase 3 trials

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Objective

To evaluate the effect of bodyweight on response to bimekizumab (BKZ) when dosed 320 mg every 4 weeks (Q4W) or every 8 weeks (Q8W) during maintenance treatment, following an initial 16 weeks of treatment with 320 mg Q4W.

Introduction

- Increased bodyweight may affect response to biologic treatments in patients with moderate to severe plaque psoriasis.[1]
- Here, we report the efficacy and safety of BKZ dosing regimens over 48 weeks using data pooled from four phase 3/3b studies in patients with moderate to severe plaque psoriasis categorised by bodyweight at baseline.

Materials and Methods

- Data were pooled from three BKZ in plaque psoriasis phase 3/3b trials: BE SURE (NCT03412747), BE VIVID (NCT03370133) and BE RADIANT (NCT03536884).[2–4] For safety analyses, and efficacy analyses over the initial 16-week period, the phase 3 randomized withdrawal trial BE READY (NCT03410992) was also included.[5]
- Analyses included patients who were randomized to BKZ 320 mg Q4W for 16 weeks. At Week 16, patients could either continue on BKZ 320 mg Q4W (Q4W/Q4W) or switch to BKZ 320 mg Q8W (Q4W/Q8W) for maintenance treatment to Week 48.
- Patients were categorised by baseline bodyweight: <120 kg and ≥120 kg. 120 kg was identified as a potential weight threshold above which efficacy may differ between dosing regimens based on PK-PD modelling.
- Missing efficacy data were imputed as non-response (NRI).
- Safety analyses were conducted during the maintenance period (Weeks 16–48) by maintenance dosing regimen (Q4W versus Q8W).
- Treatment-emergent adverse events (TEAEs) were coded using MedDRA v19.0.

Results

- Baseline characteristics for patients categorised by bodyweight are presented in **Table 1**.
- 116/1,362 (8.5%) patients included in efficacy analyses to Week 16 had bodyweight ≥120 kg (**Figure 1**).
- At Week 16, PASI 90, PASI 100 and IGA 0 responses for all patients randomized to BKZ 320 mg Q4W were higher in patients <120 kg vs ≥120 kg (**Table 2**).
- 88/975 (9.0%) patients included in the maintenance period efficacy analyses had bodyweight ≥120 kg.
- For patients <120 kg, Week 16 PASI 90, PASI 100 and IGA 0 response rates were maintained to Week 48 for both dose regimens (**Table 2**; **Figure 2A**).
- For patients ≥120 kg, greater increases in the proportions of patients achieving PASI 100 and IGA 0 were observed in those receiving BKZ Q4W/Q4W vs BKZ Q4W/Q8W between Week 16 and Week 48 (**Table 2**; **Figure 2B**).
- Among patients ≥120 kg who did not achieve PASI 100 at Week 16 (n=51), a greater proportion of those who continued on BKZ 320 mg Q4W achieved PASI 100 at Week 48 compared with those who switched to BKZ 320 mg Q8W (**Figure 3**).
- The three most common TEAEs across both bodyweight categories and dosing regimens were nasopharyngitis, oral candidiasis and upper respiratory tract infection. No safety concerns were identified that would preclude BKZ 320 mg Q4W/Q4W maintenance dosing in patients ≥120 kg who may benefit from more frequent dosing (**Table 3**).

Summary

Data were pooled from four BKZ in plaque psoriasis phase 3/3b trials

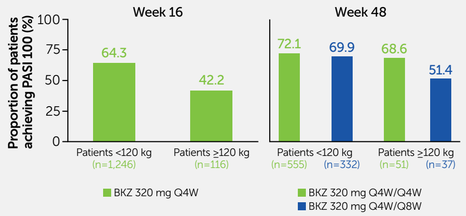
BE SURE (NCT03412747)

BE VIVID (NCT03370133)

BE RADIANT (NCT03536884)

BE READY (NCT03410992)

PASI 100 response in patients at Week 16 and Week 48 by baseline bodyweight categories[a]



At Week 16, a greater proportion of patients <120 kg achieved PASI 100 vs those ≥120 kg. At Week 48, higher PASI 100 responses were observed in patients ≥120 kg receiving BKZ Q4W vs Q8W, supporting use of Q4W maintenance dosing in patients ≥120 kg who do not achieve complete skin clearance at Week 16.

Table 1 Baseline characteristics

	Bodyweight <120 kg	Bodyweight ≥120 kg
	BKZ Q4W (N=1,246)	BKZ Q4W (N=116)
Age (years), mean ± SD	45.1 ± 13.8	45.3 ± 11.7
Male, n (%)	858 (68.9)	91 (78.4)
Caucasian, n (%)	1079 (86.6)	109 (94.0)
Weight (kg), mean ± SD	85.5 ± 17.1	135.0 ± 17.0
Disease duration (years), mean ± SD	18.2 ± 12.7	19.3 ± 11.8
PASI, mean ± SD	20.6 ± 7.5	21.8 ± 8.7
BSA (%), mean ± SD	25.7 ± 15.4	28.6 ± 17.3
IGA score, n (%)		
2: mild	3 (0.2)	0
3: moderate	831 (66.7)	65 (56.0)
4: severe	412 (33.1)	51 (44.0)
DLQI total score, mean ± SD	10.6 ± 6.5	9.6 ± 5.9
Prior systemic therapy, n (%)	961 (77.1)	77 (66.4)
Prior biologic therapy, n (%)	464 (37.2)	41 (35.3)
Anti-TNF	192 (15.4)	16 (13.8)
Anti-IL-17	248 (19.9)	22 (19.0)
Anti-IL-23	133 (10.7)	16 (13.8)

Baseline characteristics are reported using data for the initial treatment period from BE SURE, BE VIVID, BE RADIANT and BE READY. Following an initial 16 weeks of treatment with BKZ 320 mg Q4W, patients could either continue on BKZ 320 mg Q4W (Q4W/Q4W) or switch to BKZ 320 mg Q8W (Q4W/Q8W).

Table 2 Overview of efficacy outcomes by baseline bodyweight category (NRI)

	Bodyweight <120 kg		Bodyweight ≥120 kg	
	BKZ Q4W (N=1,246), %		BKZ Q4W (N=116), %	
Week 16[a]				
PASI 90	87.7		78.4	
PASI 100	64.3		42.2	
IGA 0	65.4		42.2	
	BKZ Q4W/Q4W (N=555), %	BKZ Q4W/Q8W (N=332), %	BKZ Q4W/Q4W (N=51), %	BKZ Q4W/Q8W (N=37), %
Week 16[b]				
PASI 90	88.6	90.4	84.3	83.8
PASI 100	62.5	68.4	39.2	45.9
IGA 0	63.4	69.9	37.3	45.9
Week 48[b]				
PASI 90	87.4	86.7	76.5	83.8
PASI 100	72.1	69.9	68.6	51.4
IGA 0	72.4	70.8	68.6	51.4

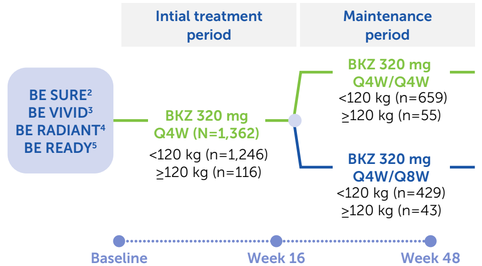
Analyses include patients who were randomized to BKZ 320 mg Q4W for 16 weeks. At Week 16, patients could either continue on BKZ 320 mg Q4W (Q4W/Q4W) or switch to BKZ 320 mg Q8W (Q4W/Q8W) for maintenance treatment to Week 48. [a] Data reported include data pooled from BE SURE, BE VIVID, BE RADIANT and BE READY; [b] Data reported are for the maintenance efficacy set, including data pooled from BE SURE, BE VIVID and BE RADIANT.

Table 3 Summary of TEAEs during the maintenance period (Weeks 16–48)

	Bodyweight <120 kg		Bodyweight ≥120 kg	
	BKZ Q4W/Q4W (N=659) n (%)	BKZ Q4W/Q8W (N=429) n (%)	BKZ Q4W/Q4W (N=55) n (%)	BKZ Q4W/Q8W (N=43) n (%)
Any TEAE	492 (74.7)	328 (76.5)	42 (76.4)	31 (72.1)
Serious TEAEs	21 (3.2)	18 (4.2)	4 (7.3)	2 (4.7)
Discontinuations due to TEAEs	17 (2.6)	7 (1.6)	2 (3.6)	1 (2.3)
Drug-related TEAEs	196 (29.7)	131 (30.5)	16 (29.1)	10 (23.3)
Severe TEAEs	18 (2.7)	20 (4.7)	5 (9.1)	2 (4.7)
Deaths	0	1 (0.2)	1 (1.8)	0
Three most common TEAEs				
Nasopharyngitis	101 (15.3)	79 (18.4)	11 (20.0)	5 (11.6)
Oral candidiasis	82 (12.4)	57 (13.3)	4 (7.3)	5 (11.6)
Upper respiratory tract infection	44 (6.7)	38 (8.9)	7 (12.7)	4 (9.3)
TEAEs of interest				
Serious infections	5 (0.8)	8 (1.9)	1 (1.8)	0
IBD	0	0	0	0
Adjudicated SIB	1 (0.2)	0	0	0
Malignancies	2 (0.3)	4 (0.9)	0	1 (2.3)
Serious hypersensitivity reactions	0	0	0	0
Adjudicated MACE	3 (0.5)	1 (0.2)	0	0
Hepatic events	14 (2.1)	14 (3.3)	1 (1.8)	1 (2.3)

Safety data from the randomized withdrawal trial BE READY are included. Data collected after the point of escape in BE READY are excluded.

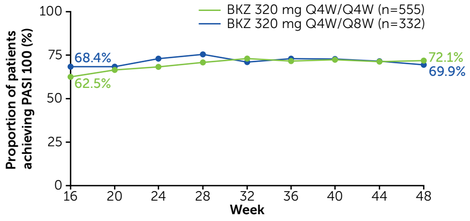
Figure 1 Cumulative EAIRs for TEAEs over three years in the phase 2 and 3 trials



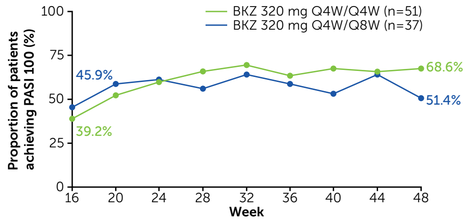
Data were pooled from BE SURE, BE VIVID, BE RADIANT and BE READY. Patient numbers presented during the maintenance period are those for the maintenance period safety set. For the maintenance period efficacy analysis set, of patients <120 kg, 555 received BKZ Q4W/Q4W and 332 recieved BKZ Q4W/Q8W and of patients ≥120 kg, 51 received BKZ Q4W/Q4W and 37 received BKZ Q4W/Q8W.

Figure 2 PASI 100 responses through Weeks 16–48 by baseline bodyweight category (NRI)

A) PASI 100 in patients <120 kg

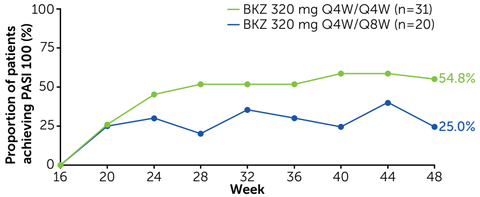


B) PASI 100 in patients ≥120 kg



Data reported are for the maintenance efficacy set, including data pooled from BE SURE, BE VIVID and BE RADIANT.

Figure 3 PASI 100 responses through Weeks 16–48 in Week 16 PASI 100 non-responder patients ≥120 kg (NRI)



Data reported are for the maintenance efficacy set, including data pooled from BE SURE, BE VIVID and BE RADIANT.

BKZ: bimekizumab; **BSA**: body surface area; **DLQI**: Dermatology Life Quality Index; **IBD:** inflammatory bowel disease; **IGA 0:** score of 0 (clear) with ≥2-category improvement relative to baseline in Investigator's Global Assessment; **IL**: interleukin; **MACE:** major cardiovascular event; **NRI:** non-responder imputation; **PASI 90/100:** ≥90/100% improvement from baseline in Psoriasis Area and Severity Index; **PK-PD:** pharmacokinetic-pharmacodynamic; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SD:** standard deviation; **SIB:** suicidal ideation and behavior; **TEAE:** treatment-emergent adverse event; **TNF:** tumour necrosis factor.

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References: [1]Puig L. J Eur Acad Dermatol 2011;25:1,007–011; [2]Warren RB. N Engl J Med 2021;385:130–41; [3]Reich K. Lancet 2021;397:487–98; [4]Reich K. N Engl J Med 2021;385:142–52; [5]Gordon KB. Lancet 2021;397:475–86. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **AP, BS, DR, PG, VV, LP, CM, DDC, RBW**; Drafting of the publication, or revising it critically for important intellectual content: **AP, BS, DR, PG, VV, LP, CM, DDC, RBW**; Final approval of the publication: **AP, BS, DR, PG, VV, LP, CM, DDC, RBW**. **Author Disclosures: AP**: Investigator and/or speaker and/or advisor for AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, GSK, Hexal, Janssen, LEO Pharma, MC2, Medac, Merck Serono, Mitsubishi Pharma, MSD, Novartis, Pfizer, Regeneron, Roche, Sandoz, Schering-Plough, Tigercat Pharma, and UCB Pharma. **BS:** Consultant (honoraria) for AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Bristol Myers Squibb, Connect Biopharma, Dermavant, Eli Lilly, EPI Health, Evelo Biosciences, Immunic Therapeutics, Janssen, LEO Pharma, Maruho, Meiji Seika Pharma, Mindera Health, Novartis, Ono, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, UCB Pharma, Union Therapeutics, Ventyxbio, and vTv Therapeutics; Stock Options for Connect Biopharma and Mindera Health; Speaker for AbbVie, Eli Lilly, Janssen, Regeneron, and Sanofi Genzyme; Scientific Co-Director (consulting fee) for CorEvitas (formerly Corronal) Psoriasis Registry; Investigator for AbbVie, Cara, CorEvitas Psoriasis Registry, Dermavant, Dermira, and Novartis; Editor-in-Chief (honorarium) for the Journal of Psoriasis and Psoriatic Arthritis. **DR**: Received honoraria as a consultant for AbbVie, Abcuro, AltruBio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Concert, Dermavant, Dermira, Eli Lilly, Incyte, Janssen, Kyowa Kirin, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, UCB Pharma, and VielaBio; has received research support from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly, Galderma, Incyte, Janssen, Merck, Novartis, Pfizer, and Regeneron; and has served as a paid speaker for AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Regeneron, and Sanofi. **PG**: Consultant for AbbVie, Abiogen, Almirall, Celgene, Eli Lilly, Janssen, LEO Pharma, Merck, MSD, Novartis, Otsuka, Pfizer, Pierre Fabre, Sanofi, and UCB Pharma. **VV, LP, CM, DDC**: Employees and shareholders of UCB Pharma. **RBW**: Consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; research grants to his institution from AbbVie, Almirall, Janssen, LEO Pharma, Novartis, and UCB Pharma; honoraria from Astellas, DiCE, GSK, and Union. **Acknowledgements:** These studies were funded by UCB Pharma. RBW is supported by the NIHR Manchester Biomedical Centre. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to these studies. The authors acknowledge Susanne Wiegratz, MSc, UCB Pharma, Monheim, Germany for publication coordination, Natalie Nunez Gomez, MD, former employee of UCB Pharma, Monheim, Germany for critical review; Ruth Moulson, MPH, Costello Medical, for medical writing and the Design team at Costello Medical for graphic design assistance. All costs associated with development of this poster were funded by UCB Pharma.

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Conclusions

At Week 48, for patients <120 kg, PASI 100 and IGA 0 response rates were similar regardless of maintenance dosing regimen (Q4W vs Q8W). For patients ≥120 kg, higher responses were observed when BKZ was dosed Q4W vs Q8W.