Bimekizumab Efficacy by Disease Duration in Patients with Moderate to Severe Hidradenitis Suppurativa: Week 48 Results from BE HEARD I & II

Alexa B. Kimball,[1] Vivian Y. Shi,[2] Martina Porter,[3] Georgios Kokolakis,[4] Linnea Thorlacius,[5,6] Vincent Piguet,[7] Jérémy Lambert,[8] Robert Rolleri,[9] Edward Muller,[10] John R. Ingram[11]

Objective

To present post hoc analyses assessing the impact of disease duration since diagnosis on bimekizumab (BKZ) efficacy in patients with moderate to severe hidradenitis suppurativa (HS) in two phase 3 trials.

Introduction

- Patients with HS can face a long delay to diagnosis, with an average time after symptom onset of seven to ten years.[1,2] Due to the progressive nature of HS, by the time of diagnosis most patients present with severe disease, which makes symptom management more difficult.[3–5]
- Following diagnosis, patients may be treated with suboptimal therapies, allowing disease progression to continue.[3,4] Therefore, it is important that patients receive effective treatment early after diagnosis to improve outcomes.[1,2]
- BKZ is a humanised IgG1 monoclonal antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, which has demonstrated clinical efficacy in patients with moderate to severe HS in the phase 3 BE HEARD I & II trials.[6–8]

Methods

- Data from the randomised, double-blind, PBO-controlled, multicentre BE HEARD I & II trials included initial (Weeks 0–16) and maintenance (Weeks 16–48) treatment periods.[7,8] At baseline, patients were randomised 2:2:2:1 to BKZ 320 mg every 2 weeks (Q2W) to Week 48, BKZ 320 mg Q4W to Week 48, BKZ 320 mg Q2W to Week 16 then BKZ 320 mg Q4W to Week 48, or PBO to Week 16 then BKZ 320 mg Q2W to Week 48. In this analysis, BKZ-randomised patients are pooled across treatment arms for the BKZ Total group.
- The proportions of patients with a ≥50/75/90/100% HS Clinical Response (HiSCR50/75/90/100) are reported by lowest (<2.40 years) and highest (≥10.87 years) quartiles of disease duration from diagnosis date, over the 48-week trial period.
- Data are reported primarily using the observed case (OC), with modified non-responder imputation (mNRI) also shown.
  - For the mNRI analyses, patients who discontinued due to lack of efficacy/adverse events, or received systemic antibiotics identified as rescue medication for HS by the principal investigator, were considered non-responders; multiple imputation was used for all other missing data.

Results

- In BE HEARD I & II, 1,014 patients with moderate to severe HS were randomised; of these patients, 868 were randomised to BKZ and 146 to PBO. Of patients randomised to BKZ with disease duration <2.40 years, 62.7% and 37.3% had Hurley Stage II and III at baseline, respectively. Of patients randomised to BKZ with disease duration ≥10.87 years, 55.3% and 44.7% had Hurley Stage II and III at baseline, respectively (**Table 1**).
- At Week 16, a numerically higher proportion of BKZ and PBO-randomised patients achieved HiSCR50 and HiSCR75 responses in the group of patients with the lowest disease duration (<2.40 years) vs those with the highest disease duration (≥10.87 years) (**Figure 1A**, **1B** & **Table 2**).
- Higher HiSCR50 and HiSCR75 response rates were both achieved for BKZ-randomised patients compared to PBO-randomised patients at Week 16 (**Figure 1A**, **1B**).
- HiSCR responses were sustained or improved to Week 48, with patients in the lowest disease duration quartile of <2.40 years, again achieving markedly higher responses compared with patients in the upper quartile of ≥10.87 years.
- At Week 48, patients randomised to PBO at baseline who switched to BKZ Q2W at Week 16 achieved similar HiSCR50/HiSCR75 responses to those on continuous BKZ from baseline (**Figure 1A**, **1B** & **Table 2**).
- Similar trends were reported for the increasingly stringent HiSCR90 and HiSCR100 outcomes at both timepoints in the lowest vs highest duration quartiles (**Figure 1C**, **1D** & **Table 2**). Higher response rates were seen in patients in the <2.40-year quartile than in the ≥10.87-year quartile.

Conclusions

BKZ demonstrated clinical efficacy for patients in both the lowest and highest disease duration quartiles compared with PBO at Week 16. Results with BKZ were sustained across 48 weeks of treatment.

Treatment in patients with shorter disease duration resulted in higher response rates than for those with longer disease duration, even with these studies exclusively enrolling patients with moderate to severe disease, emphasising the importance of timely treatment with effective therapies following diagnosis of HS.

Table 1 Baseline characteristics

	Disease duration <2.40 years		Disease duration ≥10.87 years		Overall
	BKZ 320 mg Total N=220	PBO/BKZ 320 mg Q2W N=33	BKZ 320 mg Total N=206	PBO/BKZ 320 mg Q2W N=48	All patients N=1,014
Age, years, mean ± SD	34.9 ± 13.4	38.3 ± 15.4	41.2 ± 10.4	42.3 ± 10.4	36.6 ± 12.2
Sex, female, n (%)	112 (50.9)	12 (36.4)	133 (64.6)	31 (64.6)	576 (56.8)
Racial group, white, n (%)	179 (81.4)	28 (84.8)	165 (80.1)	39 (81.3)	808 (79.7)
BMI, kg/m², mean ± SD	32.0 ± 7.6	32.9 ± 7.7	33.7 ± 8.2	34.1 ± 8.5	33.1 ± 8.1
Smoking status, current, n (%)	85 (38.6)	18 (54.5)	96 (46.6)	26 (54.2)	462 (45.6)
Duration of HS, years, mean ± SD	1.3 ± 0.6	1.1 ± 0.6	18.6 ± 7.0	20.4 ± 8.9	8.0 ± 7.8
AN count, mean ± SD	15.3 ± 13.3	13.4 ± 9.4	17.3 ± 21.5	15.0 ± 12.0	16.3 ± 16.1
DT count, mean ± SD	3.0 ± 3.5	3.7 ± 3.1	3.9 ± 4.7	2.3 ± 2.8	3.6 ± 4.3
Hurley stage, n (%)					
II	138 (62.7)	19 (57.6)	114 (55.3)	29 (60.4)	565 (55.7)
III	82 (37.3)	14 (42.4)	92 (44.7)	19 (39.6)	449 (44.3)
DLQI total score, mean ± SD	9.7 ± 6.8	11.5 ± 7.0	12.9 ± 7.1	12.2 ± 7.0	11.4 ± 6.9
Prior biologic use,[a] n (%)	16 (7.3)	3 (9.1)	48 (23.3)	12 (25.0)	193 (19.0)
Baseline antibiotic use, n (%)	20 (9.1)	2 (6.1)	21 (10.2)	4 (8.3)	86 (8.5)

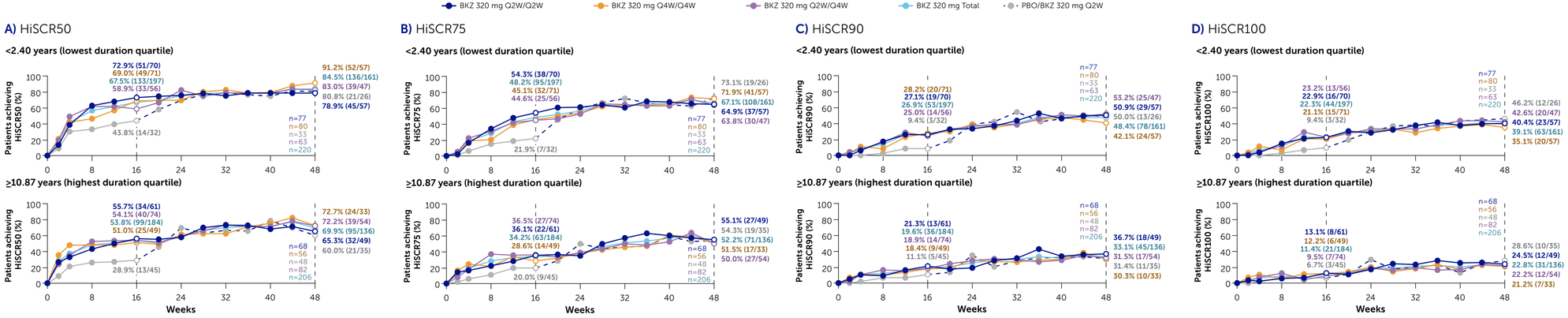
Randomised set (N=1,014). The BKZ Total group pools data from all patients randomised to BKZ at baseline. [a] Patients received prior biologic therapy for any indication.

Table 2 HiSCR response rates by lowest and highest disease duration quartiles (mNRI)

			HiSCR50		HiSCR75		HiSCR90		HiSCR100	
	Lowest duration, n	Highest duration, n	<2.40 years %	≥10.87 years %	<2.40 years %	≥10.87 years %	<2.40 years %	≥10.87 years %	<2.40 years %	≥10.87 years %
Week 16										
BKZ 320 mg Q2W/Q2W (N=288)	77	68	69.8	52.2	51.6	33.1	27.2	19.5	23.0	12.2
BKZ 320 mg Q2W/Q4W (N=292)	63	82	56.9	52.1	42.6	35.1	24.0	18.7	22.1	10.0
BKZ 320 mg Q4W/Q4W (N=288)	80	56	65.6	48.6	43.4	27.3	27.8	18.8	21.3	12.9
BKZ Total (N=868)	220	206	64.5	51.5	46.4	32.8	26.3	19.0	22.2	11.4
PBO (N=146)	33	48	42.5	26.2	21.2	17.1	9.1	8.6	9.1	6.3
Week 48										
BKZ 320 mg Q2W/Q2W (N=288)	77	68	64.0	57.1	51.2	46.7	41.3	30.7	34.3	20.9
BKZ 320 mg Q2W/Q4W (N=292)	63	82	69.2	53.4	54.7	38.1	44.2	25.3	35.2	18.0
BKZ 320 mg Q4W/Q4W (N=288)	80	56	72.2	49.9	57.1	38.2	35.3	23.1	29.3	18.2
BKZ Total (N=868)	220	206	68.5	53.7	54.3	41.0	40.0	26.5	32.7	19.0
PBO/BKZ 320 mg Q2W (N=146)	33	48	72.1	51.5	67.9	45.2	46.6	26.0	40.7	24.8

Randomised set (N=1,014). The BKZ Total group pools data from all patients randomised to BKZ at baseline. The duration of disease (years) was calculated using the date of randomisation and the date of HS diagnosis. mNRI: patients who discontinued due to lack of efficacy/adverse events, or received systemic antibiotics identified as rescue medication for HS by the principal investigator, were considered non-responders; multiple imputation was used for all other missing data.

Figure 1 HiSCR response rates by lowest and highest disease duration quartiles over time to Week 48 (OC)



The BKZ Total group pools data from all patients randomised to BKZ at baseline. The duration of disease (years) was calculated using the date of randomisation and the date of HS diagnosis. OC, n/N: N represents number of patients with a non-missing lesion count assessment in the given week, and percentages are calculated accordingly (i.e. where data recorded after an intercurrent event are included as recorded).

AN: abscess and inflammatory nodule; **BMI:** body mass index; **BKZ:** bimekizumab; **DLQI:** Dermatology Life Quality Index; **DT:** draining tunnel; **HiSCR:** HS Clinical Response; **HiSCR50/75/90/100:** ≥50%/≥75%/≥90%/100% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; **HS:** hidradenitis suppurativa; **IL:** interleukin; **mNRI:** modified non-responder imputation; **OC:** observed case; **PBO:** placebo; **Q2W:** every 2 weeks; **Q4W:** every 4 weeks; **SD:** standard deviation.

Institutions: 1. Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts, USA; 2. Department of Dermatology, University of Arkansas for Medical Sciences, Little Rock, Arizona, USA; 3. Beth Israel Deaconess Medical Center, Department of Dermatology, Harvard Medical School, Boston, Massachusetts, USA; 4. Psoriasis Research and Treatment Center, Clinic of Dermatology, Venereology and Allergology, Charité–Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; 5. Department of Dermatology, Zealand University Hospital, Roskilde; 6. Health Sciences Faculty, University of Copenhagen, Copenhagen, Denmark; 7. Division of Dermatology, Department of Medicine, Women's College Hospital, University of Toronto, Toronto, Ontario, Canada; 8. UCB Pharma, Colombes, France; 9. UCB Pharma, Morrisville, North Carolina, USA; 10. UCB Pharma, Slough, UK; 11. Department of Dermatology & Academic Wound Healing, Division of Infection and Immunity, Cardiff University, Cardiff, UK.

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