Bimekizumab efficacy by prior biologic treatment in patients with moderate to severe hidradenitis suppurativa: 48-week pooled data from the randomized, double-blind, placebo-controlled, multicenter BE HEARD I and II phase 3 trials

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Synopsis

- Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease that presents with painful nodules and abscesses, purulent drainage, and scars.[1]
- Prior biologic use may influence or be predictive of response to subsequent biologics in inflammatory conditions of skin,[2] but there is a lack of research investigating this influence in HS specifically.
- BKZ, a humanized IgG1 monoclonal antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated clinically meaningful improvements in patients with HS.[3,4]
- Here, we present efficacy of BKZ by prior biologic treatment in patients with moderate to severe HS.

Objective

To investigate the impact of prior biologic use on the efficacy of BKZ in patients with moderate to severe HS.

Methods

- BE HEARD I and II[5,6] were identically-designed, randomized, double-blind, placebo (PBO)-controlled phase 3 studies comprising initial (Weeks 0–16) and maintenance (Weeks 16–48) treatment periods (**Figure 1**).
- Here, we report proportions of patients achieving a 50/75/90% HS Clinical Response (HiSCR50/75/90) and Dermatology Life Quality Index Minimal Clinically Important Difference (DLQI MCID; ≥4-point reduction in those with a score of ≥4 at baseline) for individuals who received prior biologic treatment for any indication vs those who were biologic-naïve across initial randomization groups from baseline through Week 48.
- All prior biologic treatments received by patients were for HS; two patients initially included in the "prior biologic use" subgroup were switched to the "biologic-naïve" subgroup, as they had not received true biologic therapy.
- Data are reported using modified non-responder imputation (mNRI) and observed case (OC).

Results

Baseline Demographics

- Of the 1,014 patients randomized at baseline, 18.8% (n=191) of patients had previously received biologic therapy and 81.2% (n=823) were biologic-naïve.
- Sex, age and weight were similar across patients with prior biologic use and patients who were biologic-naïve (**Table 1**).
- More patients with prior biologic use had Hurley Stage III compared to biologic-naïve patients (62.8% vs 40.0%; **Table 1**).

Response by Prior Biologic Use

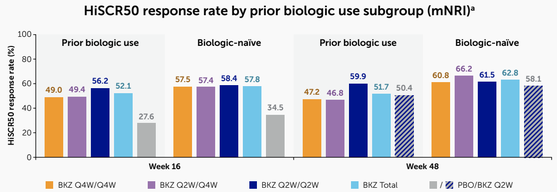
- Among patients with a history of prior biologic use in the BKZ Q4W/Q4W, BKZ Q2W/Q4W, BKZ Q2W/Q2W, and PBO/BKZ Q2W groups, 49.0%, 49.4%, 56.2%, and 27.6% achieved HiSCR50 at Week 16, respectively (**Figure 2A**).
  - In biologic-naïve patients, responses with BKZ (57.5%, 57.4%, and 58.4%) were higher vs. PBO (34.5%) at Week 16, respectively (**Figure 2B**).
- At Week 48, levels of HiSCR50 response were maintained or higher across treatment regimens vs. at Week 16 (**Figure 2A–B**).
- HiSCR75/90 responses were also maintained through Week 48 across treatment regimens for both patients who had received prior biologic use and biologic-naïve patients (**Tables 2** and **3**).
- High proportions of DLQI MCID responders at Week 16 were also observed in both subgroups across treatment regimens, with responses maintained to Week 48 (**Figure 2C–D**).

Conclusions

BKZ demonstrated consistent efficacy in the achievement and maintenance of HiSCR and DLQI MCID clinical responses to Week 48 regardless of prior biologic use in patients with moderate to severe HS.

Greater levels of HiSCR clinical responses were observed for BKZ-treated patients vs. PBO-treated patients across prior biologic subgroups at Week 16.

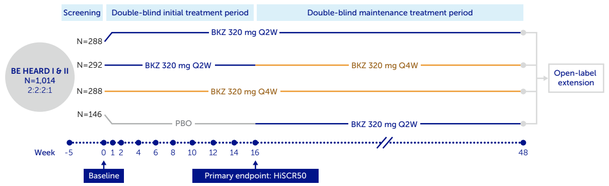
Summary



BKZ demonstrated high efficacy in the rapid achievement and maintenance of HiSCR50 response regardless of prior biologic use

[a]mNRI: Patients who took systemic antibiotics as rescue medication for HS, as defined by the PI or who discontinued due to AE or lack of efficacy, were treated as non-responders at all subsequent visits. Other missing data were imputed via multiple imputation.

Figure 1 Study design



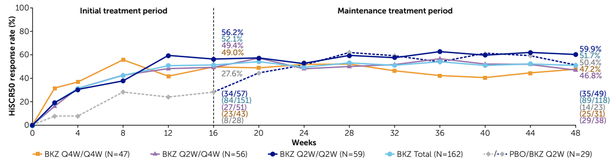
At baseline, 1,014 patients with moderate to severe HS were randomized 2:2:2:1 to BKZ 320 mg Q2W to Week 48, BKZ 320 mg Q4W to Week 48, BKZ 320 mg Q2W to Week 16 then BKZ 320 mg Q4W to Week 48, or PBO to Week 16 then BKZ 320 mg Q2W to Week 48. In this analysis, data from patients initially randomized to BKZ were pooled for the BKZ Total group.

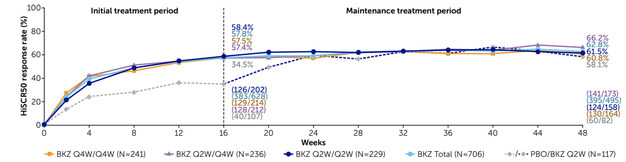
Table 1 Baseline characteristics

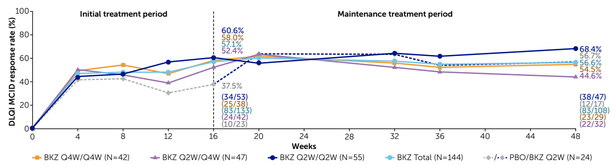
	Prior biologic use patients (N=191)	Biologic-naïve patients (N=823)
Age, years, mean (SD)	38.2 (12.4)	36.3 (12.1)
Sex, female, n (%)	106 (55.5)	470 (57.1)
Racial group, white, n (%)	158 (82.7)	650 (79.0)
Weight, kg, mean (SD)	97.9 (26.0)	97.1 (24.0)
BMI, kg/m^2, mean (SD)	33.0 (8.1)	33.1 (8.2)
Duration of HS, years, mean (SD)	9.3 (8.0)	7.7 (7.7)
Hurley stage, n (%)		
II	71 (37.2)	494 (60.0)
III	120 (62.8)	329 (40.0)
DLQI total score, mean (SD)	13.2 (7.2)	10.9 (6.8)
Baseline antibiotic use, n (%)	14 (7.3)	72 (8.7)

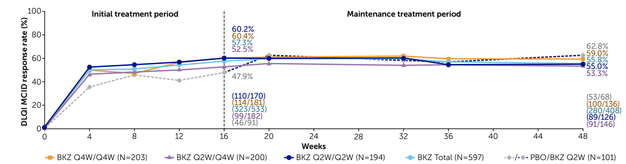
Randomized set.

Figure 2 Proportion of patients achieving HiSCR50 (A–B) and DLQI MCID (C–D) responses through Week 48 by prior biologic use across treatment arms (mNRI % [OC n/N])









In this analysis, data from patients initially randomized to BKZ are pooled for the BKZ Total group. mNRI: Patients who take systemic antibiotics as rescue medication for HS, as defined by the PI or who discontinue due to AE or lack of efficacy, were treated as non responders at all subsequent visits. Other missing data were imputed via multiple imputation. OC: N represents the number of patients with a non-missing lesion count assessment at the given week, and percentages should be calculated accordingly (i.e. where data recorded after an intercurrent event were included as recorded).

Table 2 Proportion of patients achieving HiSCR responses among prior biologic use subgroups at Week 16 (OC, mNRI)

		HiSCR50					HiSCR75					HiSCR90				
		BKZ Q4W/Q4W	BKZ Q2W/Q4W	BKZ Q2W/Q2W	BKZ Total	PBO/ BKZ Q2W	BKZ Q4W/Q4W	BKZ Q2W/Q4W	BKZ Q2W/Q2W	BKZ Total	PBO/ BKZ Q2W	BKZ Q4W/Q4W	BKZ Q2W/Q4W	BKZ Q2W/Q2W	BKZ Total	PBO/ BKZ Q2W
Prior biologic use (N=191)	OC, % (n/Nsub)	53.5 (23/43)	52.9 (27/51)	59.6 (34/57)	55.6 (84/151)	28.6 (8/28)	34.9 (15/43)	39.2 (20/51)	38.6 (22/57)	37.7 (57/151)	14.3 (4/28)	18.6 (8/43)	21.6 (11/51)	19.3 (11/57)	19.9 (30/151)	3.6 (1/28)
	mNRI, %	49.0 (n=47)	49.4 (n=56)	56.2 (n=59)	52.1 (n=162)	27.6 (n=29)	31.1 (n=47)	36.5 (n=56)	35.6 (n=59)	35.0 (n=162)	13.8 (n=29)	15.6 (n=47)	20.0 (n=56)	18.6 (n=59)	18.5 (n=162)	3.4 (n=29)
Biologic-naïve (N=823)	OC, % (n/Nsub)	60.3 (129/214)	60.4 (128/212)	62.4 (126/202)	61.0 (383/628)	37.4 (40/107)	36.4 (78/214)	42.0 (89/212)	43.6 (88/202)	40.6 (255/628)	19.6 (21/107)	22.0 (47/214)	23.1 (49/212)	22.3 (45/202)	22.5 (141/628)	11.2 (12/107)
	mNRI, %	57.5 (n=241)	57.4 (n=236)	58.4 (n=229)	57.8 (n=706)	34.5 (n=117)	34.5 (n=241)	39.6 (n=236)	40.4 (n=229)	38.6 (n=706)	17.8 (n=117)	21.5 (n=241)	22.3 (n=236)	21.6 (n=229)	21.8 (n=706)	9.7 (n=117)

In this analysis, data from patients initially randomized to BKZ are pooled for the BKZ Total group. OC: Nsub represents the number of patients with a non-missing lesion count assessment at the given week, and percentages are calculated accordingly (i.e. where data recorded after an intercurrent event are included as recorded); mNRI: Patients who take systemic antibiotics as rescue medication for HS as defined by the PI or who discontinue due to AE or lack of efficacy are treated as non-responders at all subsequent visits. Other missing data were imputed via multiple imputation.

Table 3 Proportion of patients achieving HiSCR responses among prior biologic use subgroups at Week 48 (OC, mNRI)

		HiSCR50					HiSCR75					HiSCR90				
		BKZ Q4W/Q4W	BKZ Q2W/Q4W	BKZ Q2W/Q2W	BKZ Total	PBO/ BKZ Q2W	BKZ Q4W/Q4W	BKZ Q2W/Q4W	BKZ Q2W/Q2W	BKZ Total	PBO/ BKZ Q2W	BKZ Q4W/Q4W	BKZ Q2W/Q4W	BKZ Q2W/Q2W	BKZ Total	PBO/ BKZ Q2W
Prior biologic use (N=191)	OC, % (n/Nsub)	80.6 (25/31)	76.3 (29/38)	71.4 (35/49)	75.4 (89/118)	60.9 (14/23)	64.5 (20/31)	50.0 (19/38)	51.0 (25/49)	54.2 (64/118)	52.2 (12/23)	45.2 (14/31)	26.3 (10/38)	28.6 (14/49)	32.2 (38/118)	34.8 (8/23)
	mNRI, %	47.2 (n=47)	46.8 (n=56)	59.9 (n=59)	51.7 (n=162)	50.4 (n=29)	37.9 (n=47)	30.7 (n=56)	43.2 (n=59)	37.3 (n=162)	46.2 (n=29)	27.6 (n=47)	17.6 (n=56)	23.4 (n=59)	22.6 (n=162)	31.2 (n=29)
Biologic-naïve (N=823)	OC, % (n/Nsub)	79.3 (130/164)	81.5 (141/173)	78.5 (124/158)	79.8 (395/495)	73.2 (60/82)	65.9 (108/164)	62.4 (108/173)	63.9 (101/158)	64.0 (317/495)	65.9 (54/82)	41.5 (68/164)	45.1 (78/173)	43.0 (68/158)	43.2 (214/495)	41.5 (34/82)
	mNRI, %	60.8 (n=241)	66.2 (n=236)	61.5 (n=229)	62.8 (n=706)	58.1 (n=117)	49.6 (n=241)	50.9 (n=236)	49.3 (n=229)	49.9 (n=706)	50.7 (n=117)	31.9 (n=241)	36.7 (n=236)	33.0 (n=229)	33.9 (n=706)	33.5 (n=117)

In this analysis, data from patients initially randomized to BKZ are pooled for the BKZ Total group. OC: Nsub represents the number of patients with a non-missing lesion count assessment at the given week, and percentages are calculated accordingly (i.e. where data recorded after an intercurrent event are included as recorded); mNRI: Patients who take systemic antibiotics as rescue medication for HS as defined by the PI or who discontinue due to AE or lack of efficacy are treated as non-responders at all subsequent visits. Other missing data were imputed via multiple imputation.

AE: adverse event; **BKZ:** bimekizumab; **DLQI:** Dermatology Life Quality Index; **HiSCR:** Hidradenitis Suppurativa Clinical Response; **HiSCR50/75/90:** ≥50/75/90% reduction in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; **HS:** hidradenitis suppurativa; **IL:** interleukin; **MCID:** Minimal Clinically Important Difference; **mNRI:** modified non-responder imputation; **OC:** observed case; **PI:** principal investigator; **PBO:** placebo; **Q2W:** every 2 weeks; **Q4W:** every 4 weeks; **SD:** standard deviation.

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