Bimekizumab Impact on Dichotomous IHS4 Response Levels in Patients with Moderate to Severe Hidradenitis Suppurativa: Results up to Week 48 from BE HEARD I & II

Thrasyvoulos Tzellos,[1,2] Afsaneh Alavi,[2,3] Athanassios Kyrgidis,[2,4] Kelsey R. van Straalen,[2,5] Koremasa Hayama,[6] Robert Rolleri,[7] Paulatsya Joshi,[8] Leah Davis,[7] Ingrid Pansar,[9] Christos C. Zouboulis[2,10]

Objective

To report the proportion of patients achieving a 55%, 75% or 90% improvement in the International Hidradenitis Suppurativa Severity Score System (IHS4-55/75/90) at Week 16 and Week 48, from the phase 3 BE HEARD I & II trials of bimekizumab (BKZ) in patients with moderate to severe hidradenitis suppurativa (HS).

Background

- HS severity can be dynamically assessed using the IHS4, a validated clinician-rated tool that includes the number of inflammatory nodules, abscesses and draining tunnels.[1]
- The need for additional outcomes in clinical trial reporting led to the development of IHS4-55, enabling dynamic assessment of HS severity based on a 55% improvement in total score.[2]
- Bimekizumab (BKZ), a humanised IgG1 monoclonal antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated clinical improvements in IHS4.[3–5]

Materials and Methods

- Data from the randomised, double-blind, PBO-controlled, multicentre BE HEARD I & II trials included an initial (Weeks 0–16) and maintenance (Weeks 16–48) treatment period (**Figure 1**).[4,5]
  - Adult patients were randomised 2:2:2:1 (initial/maintenance) to receive BKZ 320 mg every 2 weeks (Q2W)/Q2W, BKZ Q2W/Q4W, BKZ Q4W/Q4W or PBO/BKZ Q2W.
- IHS4-55, -75, or -90 was achieved if a patient's IHS4 score improved by 55%, 75%, 90% or more, respectively, from baseline.
- Data are reported at Week 16 (study-level) and over time to Week 48 (pooled) using observed cases (OC) and modified non-responder imputation (mNRI).

Results

- At baseline, 1,014 patients were randomised to PBO/BKZ Q2W (N=146), BKZ Q4W/Q4W (N=288), BKZ Q2W/Q4W (N=292) or BKZ Q2W/Q2W (N=288; **Figure 1**).
- Demographics and disease characteristics at baseline were generally balanced across treatment regimens (**Table 1**).
- At Week 16, greater proportions of BKZ-treated patients achieved IHS4-55, -75 and -90 versus placebo, across BE HEARD I & II (**Figure 2**):
  - IHS4-55 was achieved by 51.1–62.9% of BKZ-treated patients (mNRI: 47.7–59.4%), versus 25.7–30.8% with PBO (mNRI: 23.9–28.6%).
- IHS4-55 response rates were sustained or improved over time to Week 48 for those who received BKZ from baseline (OC: 71.0–77.4%; mNRI: 56.7–60.6%; **Figures 3A–B**).
- Similar trends were observed for IHS4-75 and IHS4-90; responses improved over time to Week 48 with BKZ treatment (**Figures 3C–F**).
- Following switch to BKZ, patients who initially received PBO saw improved IHS4-55, -75 and -90 response rates by Week 48 comparable to those who received BKZ from baseline (**Figure 3**).

Conclusions

IHS4-55 and the more stringent IHS4-75 and IHS4-90 thresholds were achieved in greater proportions of patients treated with BKZ vs PBO at Week 16. These responses were sustained or increased by Week 48. PBO to BKZ switchers achieved comparable improvements at Week 48 to patients receiving continuous BKZ treatment.

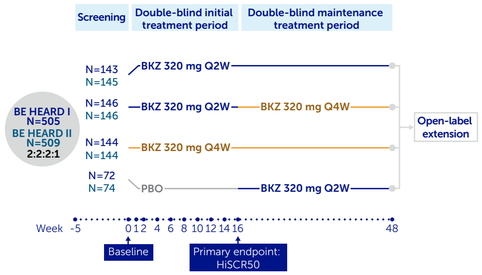
These findings demonstrate the utility of dichotomous IHS4 response levels to assess HS improvement in clinical trials.

Table 1 Baseline characteristics

	BKZ 320 mg Q2W/Q2W N=288	BKZ 320 mg Q2W/Q4W N=292	BKZ 320 mg Q4W/Q4W N=288	PBO/BKZ 320 mg Q2W N=146
Age, years, mean ± SD	36.8 ± 12.4	37.0 ± 12.4	35.8 ± 11.6	37.3 ± 12.8
Sex, female, n (%)	152 (52.8)	174 (59.6)	175 (60.8)	75 (51.4)
Racial group, white, n (%)	232 (80.6)	233 (79.8)	224 (77.8)	119 (81.5)
Smoking status, current, n (%)	127 (44.1)	134 (45.9)	126 (43.8)	75 (51.4)
BMI, kg/m², mean ± SD	32.7 ± 8.6	32.7 ± 7.9	33.8 ± 7.9	33.1 ± 8.3
Duration of disease, years, mean ± SD	7.6 ± 7.4	8.3 ± 7.7	7.3 ± 7.3	9.8 ± 9.4
AN count, mean ± SD	14.7 ± 11.6	17.2 ± 16.8	17.7 ± 20.9	14.4 ± 10.0
AB count	3.4 ± 4.6	3.6 ± 7.1	4.0 ± 6.9	2.7 ± 5.0
IN count	11.4 ± 10.0	13.6 ± 13.4	13.7 ± 18.4	11.8 ± 8.4
DT count, mean ± SD	3.8 ± 4.4	3.8 ± 4.4	3.3 ± 4.1	3.4 ± 3.8
IHS4 score, mean ± SD	33.4 ± 25.4	36.0 ± 34.0	35.0 ± 34.0	30.6 ± 21.8
IHS4 category, n (%)				
Severe	241 (83.7)	258 (88.4)	245 (85.1)	125 (85.6)
Moderate	47 (16.3)	34 (11.6)	42 (14.6)	21 (14.4)
Mild	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Prior biologic use,[a] n (%)	59 (20.5)	56 (19.2)	47 (16.3)	29 (19.9)
Baseline antibiotic use, n (%)	29 (10.1)	28 (9.6)	18 (6.3)	11 (7.5)

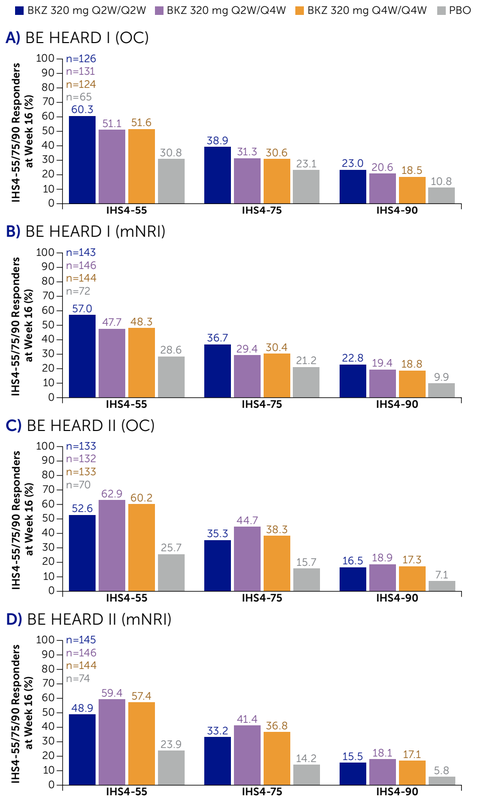
Randomised set (N=1,014). [a] Patients received prior biologic therapy for any indication.

Figure 1 BE HEARD I & II study design



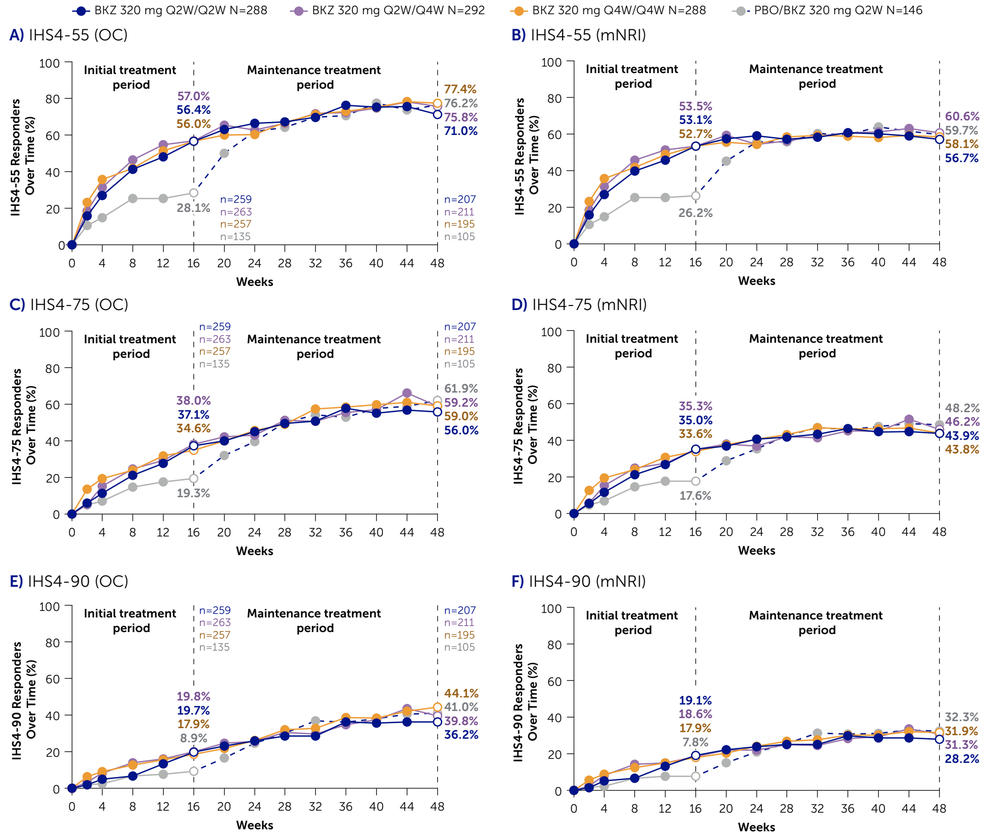
At baseline, patients with moderate to severe HS were randomised 2:2:2:1 to BKZ 320 mg Q2W to Week 48, BKZ 320 mg Q4W to Week 48, BKZ 320 mg Q2W to Week 16 then BKZ 320 mg Q4W to Week 48, or PBO to Week 16 then BKZ 320 mg Q2W to Week 48.

Figure 2 BE HEARD I & BE HEARD II IHS4-55/75/90 responses at Week 16 (OC, mNRI)



Randomised set (BE HEARD I: N=505; BE HEARD II: N=509). 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. OC: all available data after an intercurrent event were summarised as recorded in the database, and all missing data were left missing.

Figure 3 Pooled IHS4-55/75/90 responses over time to Week 48



Randomised set (pooled: N=1,014). 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. OC: all available data after an intercurrent event were summarised as recorded in the database, and all missing data were left missing. Treatment switch after the initial treatment period for the PBO/BKZ 320mg Q2W and BKZ 320mg Q2W/Q4W groups started at Week 16.

AB: abscess; **AN:** abscess and inflammatory nodule; **BKZ:** bimekizumab; **BMI:** body mass index; **DT:** draining tunnel; **HiSCR:** Hidradenitis Suppurativa Clinical Response; **HiSCR50:** ≥50% reduction from baseline in the total AN count with no increase from baseline in abscess or DT count; **HS:** hidradenitis suppurativa; **IHS4:** International Hidradenitis Suppurativa Severity Score System; **IHS4-55/75/90:** International Hidradenitis Suppurativa Severity Score System 55/75/90% reduction from baseline (i.e., improvement); **IgG:** immunoglobin; **IL:** interleukin; **IN:** inflammatory nodule; **mNRI:** modified non-responder imputation; **OC:** observed case; **PBO:** placebo; **Q2W:** every two weeks; **Q4W:** every four weeks.

Institutions: 1. Department of Dermatology, Nordland Hospital Trust, Bodø, Norway; 2. European Hidradenitis Suppurativa Foundation e.V., Dessau, Germany; 3. Mayo Clinic, Rochester, Minnesota, USA; 4. Department of Maxillofacial Surgery, Papanikolaou General Hospital of Thessaloniki, Aristotle University of Thessaloniki, Thessaloniki, Greece; 5. Department of Dermatology, Erasmus University Medical Center, Rotterdam, The Netherlands; 6. Department of Dermatology, Nihon University School of Medicine, Toyko, Japan; 7. UCB Pharma, Morrisville, North Carolina, USA; 8. UCB Pharma, Slough, UK; 9. UCB Pharma, Brussels, Belgium; 10. Departments of Dermatology, Venereology, Allergology and Immunology, Staedtisches Klinikum Dessau, Brandenburg Medical School Theodor Fontane and Faculty of Health Sciences Brandenburg, Dessau, Germany.

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