SIUU Communications: Bimekizumab in HS

For proactive use by medical affairs personnel

Inspired by **patients.**
Driven by **science.**

Intended for healthcare professionals

Disclaimer

This slide deck is for proactive use by medical affairs personnel as part of the US Food and Drug Administration (FDA) guidance for Scientific Information on Unapproved Use (SIUU) of Approved Medical Products.

BIMZELX® (bimekizumab-bkzx) has not been approved by the FDA for use in hidradenitis suppurativa, and the safety and effectiveness of BIMZELX for the treatment of hidradenitis suppurativa has not been established.

BIMZELX is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. BIMZELX may increase the risk of suicidal ideation and behavior. Advise patients and caregivers to monitor and seek medical attention for the emergence or worsening of depression, suicidal ideation, or other mood changes. BIMZELX may increase the risk of infection. Instruct patients to report signs and symptoms of clinically important infection during treatment. Should such an infection occur, discontinue BIMZELX until infection resolves. Evaluate patients for tuberculosis infection prior to initiating treatment with BIMZELX. Test liver enzymes, alkaline phosphatase, and bilirubin at baseline and periodically during treatment with BIMZELX. Avoid use in patients with acute liver disease or cirrhosis, and in patients with active IBD. Avoid use of live vaccines in BIMZELX patients.

Scan for BIMZELX Prescribing Information

US-BK-2400964 | Date of preparation: June 2024

BIMZELX® [prescribing information]. Smyrna, GA: UCB, Inc.

Publications of BKZ Phase 3 Trials in HS

Kimball AB, et al. (**2024**)
Efficacy and safety of bimekizumab in patients with moderate-to-severe hidradenitis suppurativa (**BE HEARD I** and **BE HEARD II**): two 48-week, randomized, double-blind, placebo-controlled, multicenter Phase 3 trials

US-BK-2401105

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BKZ: bimekizumab; HS: hidradenitis suppurativa.

Inclusion and Exclusion Criteria

Inclusion Criteria

Adults (aged **≥18 years**) with **moderate-to-severe HS**

- Moderate-to-severe disease was defined as presence of **≥5 inflammatory lesions** (abscesses, inflammatory nodules, or both) affecting **≥2 distinct anatomical areas**, one of which was at least **Hurley Stage II or III** (at both screening and baseline visits), evidenced by clinical history and physical examination, and **diagnosed ≥6 months before the baseline** visit

Documented history of **inadequate response**, as assessed by a physician, to **systemic antibiotics for the treatment of HS** (e.g., tetracyclines, clindamycin, and rifampicin) at screening

Patients using a stable dose (pro re nata use not accepted) of **doxycycline**, **minocycline**, or an equivalent **systemic tetracycline** for **28 days before baseline** were allowed to continue antibiotics and enroll in the studies alongside patients who were not receiving antibiotics

Exclusion Criteria

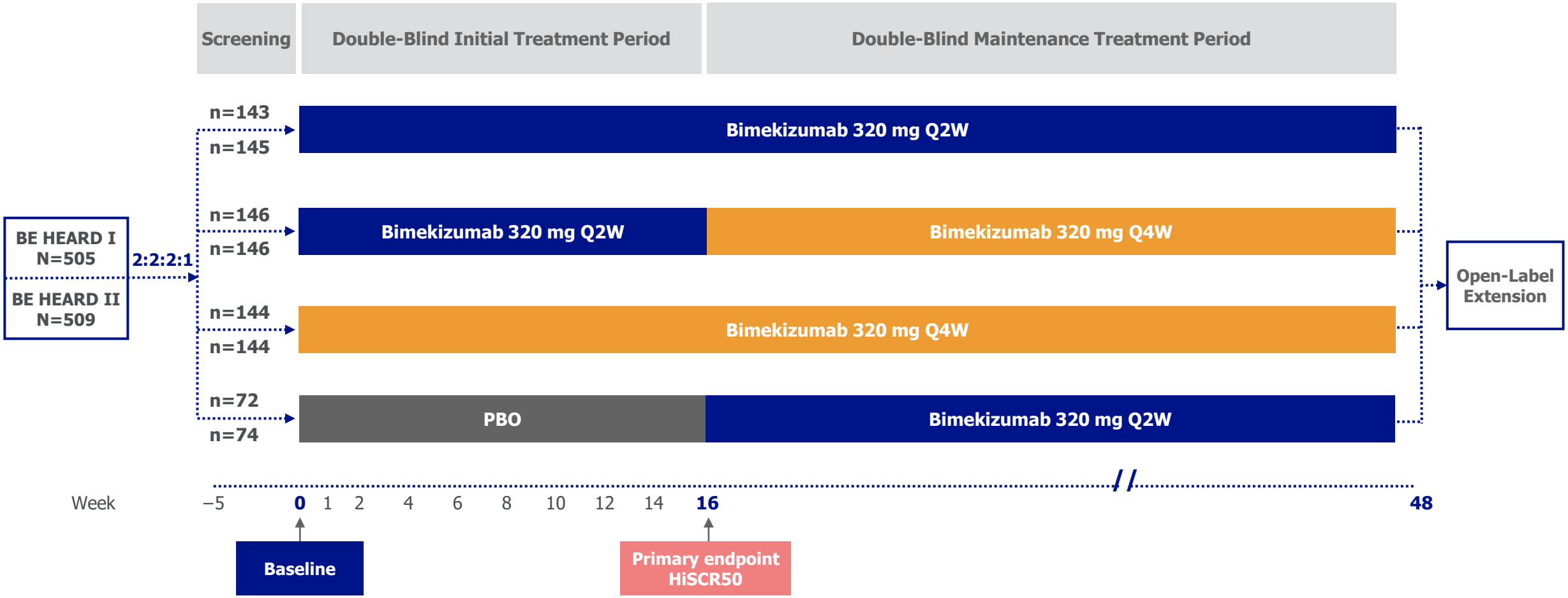
Patients were **excluded** if they had **>20 DTs** at baseline, had another **active skin disease** or condition that could interfere with HS assessment, had received **TNF-α inhibitors within 12 weeks,** or **IL-17 biological response modifier therapy within 6 months** of baseline, or **topical therapy within 14 days** of baseline, or had received **systemic therapy for the treatment of HS**

Patients with **active IBD** were **excluded**. Patients with **Crohn's disease** or **ulcerative colitis with no active symptomatic disease** at screening or baseline were **allowed**

DTs: draining tunnels; HS: hidradenitis suppurativa; IL-17: interleukin 17; TNF-α: tumor necrosis factor-alpha.

Kimball AB, et al. *Lancet*. Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6

BE HEARD I & II Study Design[1]

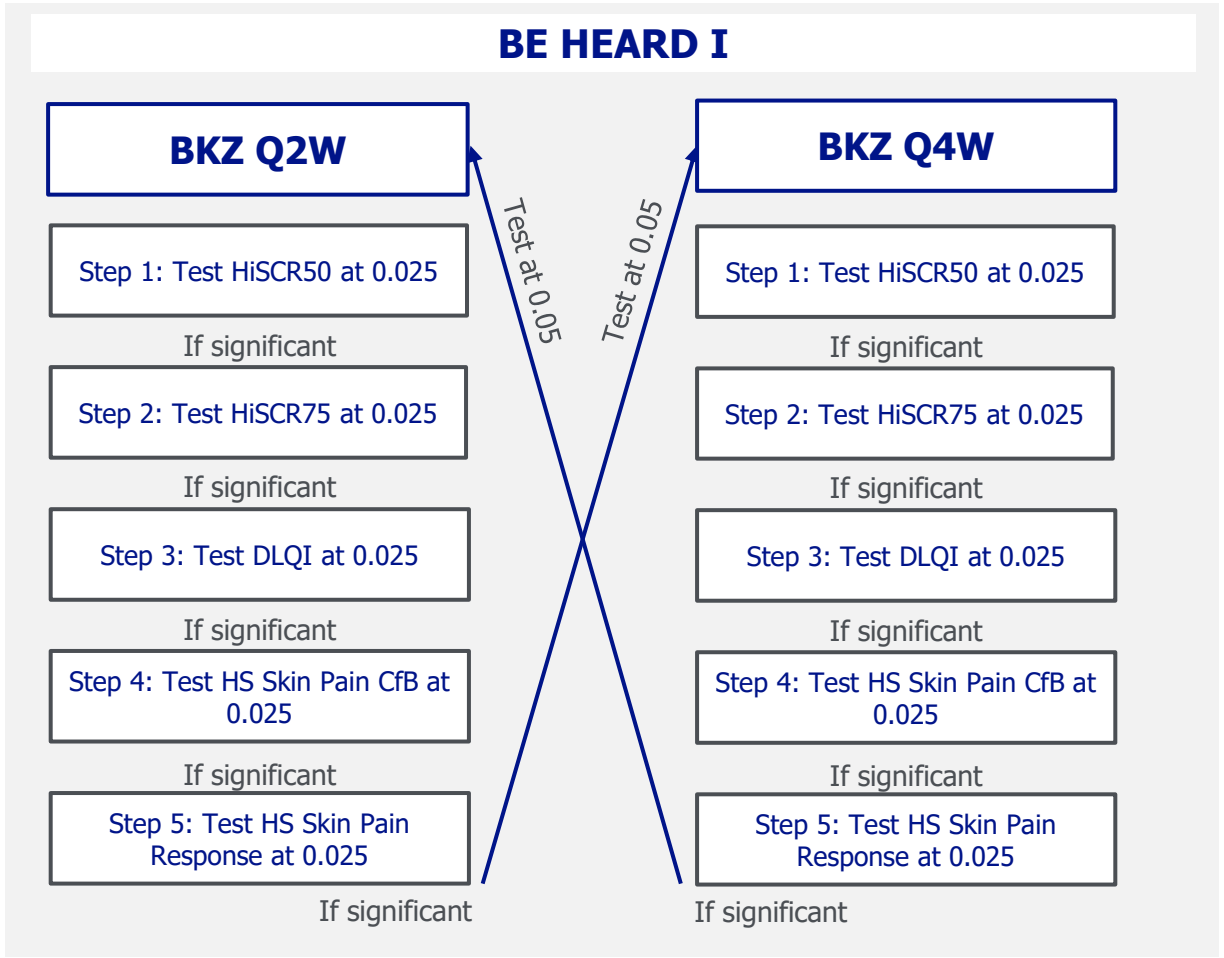


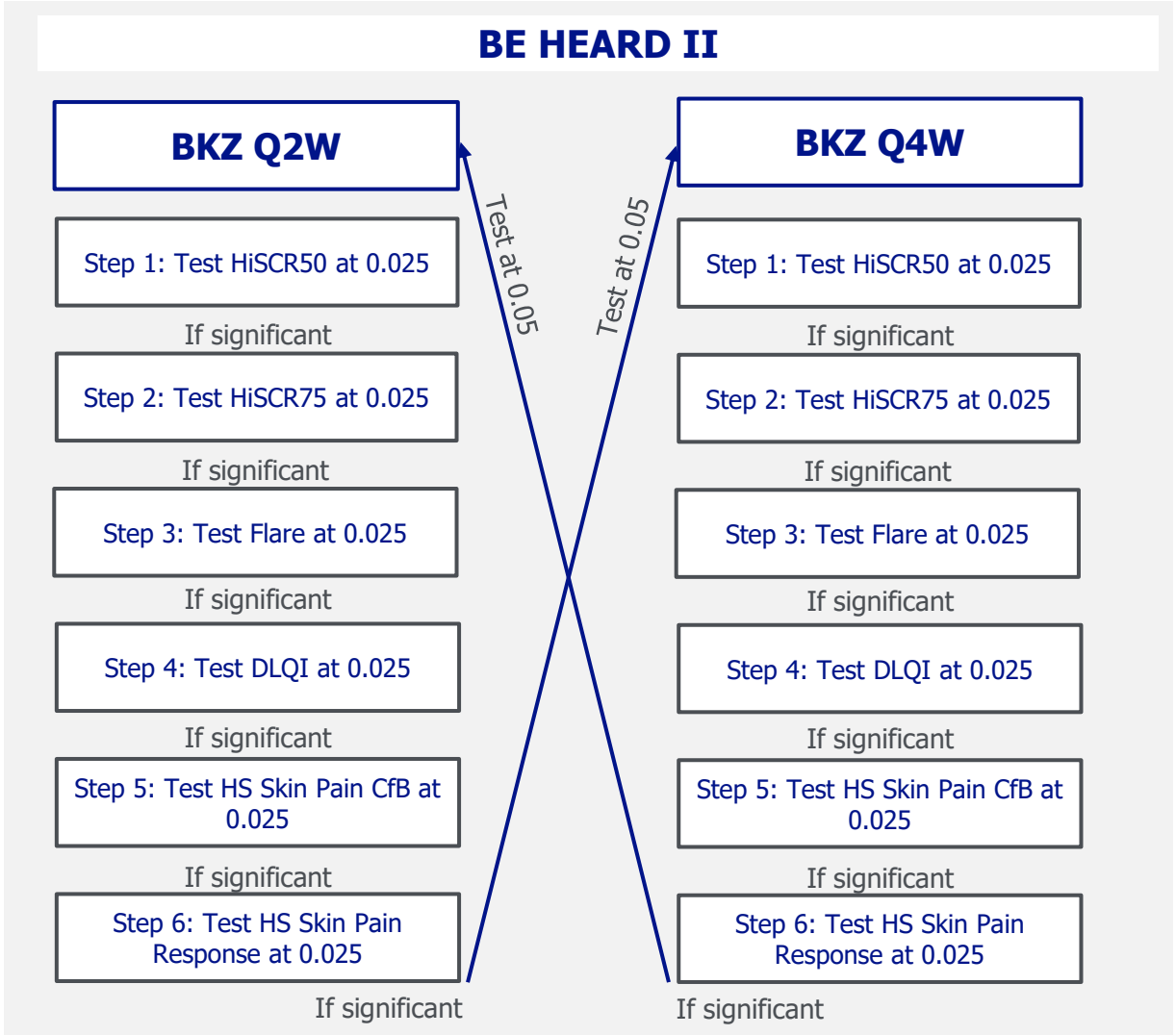
HiSCR50: ≥50% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count[2]

HiSCR50: Hidradenitis Suppurativa Clinical Response of ≥50% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

1. Kimball AB, et al. *Lancet.* Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6 2. Kimball AB, et al. *J Eur Acad Dermatol Venereol.* 2016;30(6):989-94. doi: 10.1111/jdv.13216

Statistical Testing Hierarchy





US-BK-2400964 | Date of preparation: June 2024

HS skin pain response was tested among study patients with a score of ≥3 at baseline. BKZ: bimekizumab; CfB: change from baseline; DLQI: Dermatology Life Quality Index; HiSCR50/75: Hidradenitis Suppurativa Clinical Response of ≥50%/ ≥75% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; Q2W: every 2 weeks; Q4W: every 4 weeks.

Kimball AB, et al. *Lancet*. Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6

Explanation of Statistical Methods

Non-responder imputation (mNRI)

mNRI [ALL-ABX]

Patients who took any systemic antibiotics* or who discontinued due to adverse events or lack of efficacy were treated as non-responders at all subsequent visits

mNRI [HS-ABX]

Patients who took systemic antibiotics identified as rescue medication for HS by the principal investigator or who discontinued due to adverse events or lack of efficacy were treated as non-responders at all subsequent visits

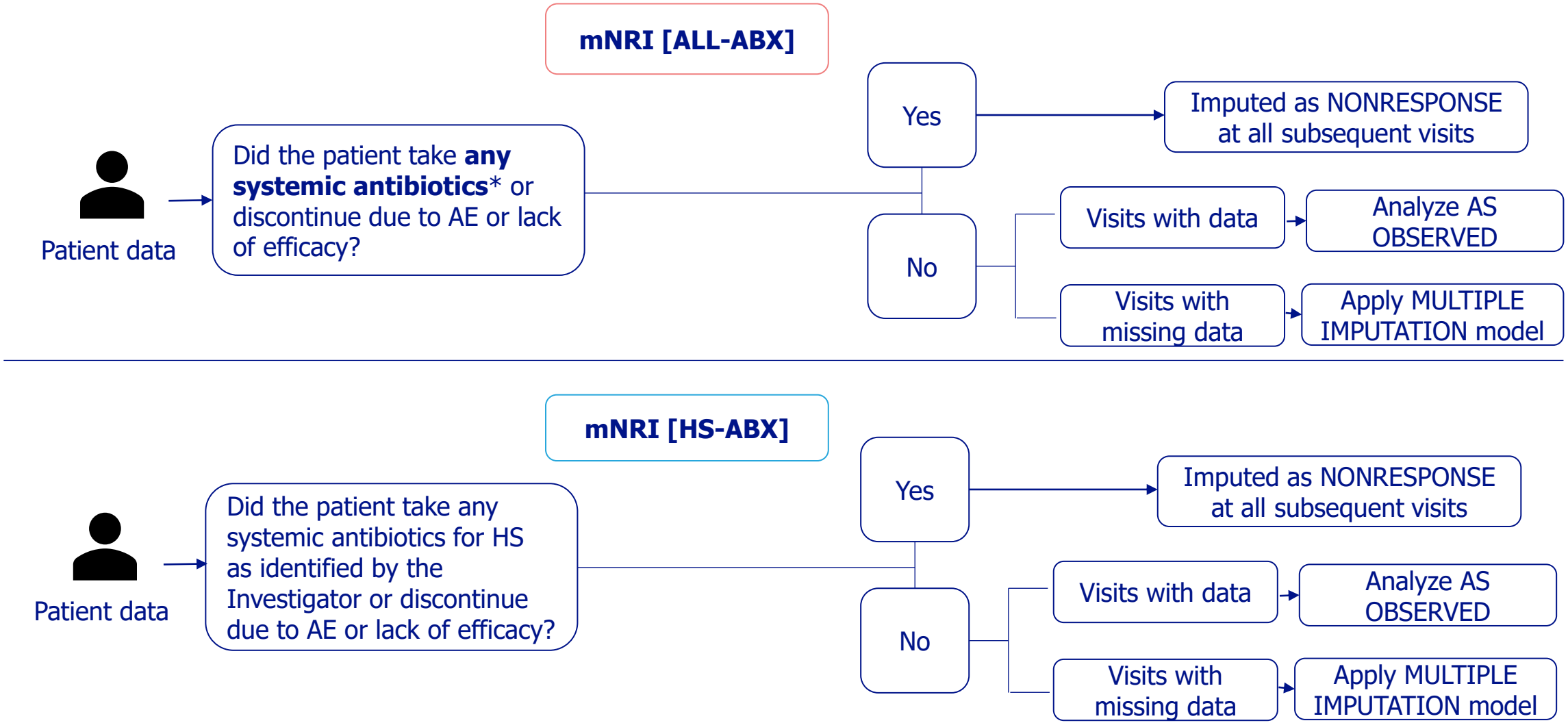
Observed Case (OC)

All available data after an intercurrent event were summarized as recorded in the database, and all missing data were left missing

US-BK-2400964 | Date of preparation: June 2024

*This refers to any new systemic antibiotic for those who were not on systemic antibiotics at baseline and any change in dose for those who were on systemic antibiotics at baseline.
ABX: antibiotics; HS: hidradenitis suppurativa.
Kimball AB, et al. *Lancet.* Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6

Missing Data Handling



*This refers to any new systemic antibiotic for those who were not on systemic antibiotics at baseline and any change in dose for those who were on systemic antibiotics at baseline.
ABX: antibiotics; AE: adverse event; HS: hidradenitis suppurativa; mNRI: modified nonresponder imputation.
Kimball AB, et al. *Lancet.* Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6

Baseline Patient Demographics

	BE HEARD I			BE HEARD II		
	BKZ 320 mg Q2W (n=289)*	**BKZ 320 mg Q4W (n=144)**	**PBO (n=72)**	**BKZ 320 mg Q2W (n=291)***	**BKZ 320 mg Q4W (n=144)**	**PBO (n=74)**
Age, median (IQR), y	36.0 (26.0-46.0)	35.0 (27.0-45.0)	33.5 (26.0-46.0)	35.0 (27.0-45.0)	33.0 (26.0-42.5)	37.0 (28.0-47.0)
Age group, n (%)						
<40 years	174 (60)	93 (65)	45 (63)	180 (62)	97 (67)	46 (62)
40 years to <65 years	109 (38)	50 (35)	26 (36)	107 (37)	45 (31)	24 (32)
≥65 years	6 (2)	1 (<1)	1 (1)	4 (1)	2 (1)	4 (5)
Sex, n (%)						
Female	176 (61)	98 (68)	44 (61)	150 (52)	77 (54)	31 (42)
Male	113 (39)	46 (32)	28 (39)	141 (48)	67 (46)	43 (58)
Body weight, mean (SD), kg	97.2 (25.4)	102.7 (24.7)	94.6 (24.8)	95.4 (24.2)	95.3 (22.0)	100.3 (23.7)
BMI, mean (SD)	33.4 (8.3)	35.4 (8.1)	32.4 (7.8)	32.0 (8.0)	32.2 (7.5)	33.8 (8.7)
Smoking status, n (%)						
Current	127 (44)	53 (37)	37 (51)	134 (46)	73 (51)	38 (51)
Former†	43 (15)	28 (19)	7 (10)	49 (17)	14 (10)	10 (14)
Race, n (%)						
White	233 (81)	105 (73)	55 (76)	232 (80)	119 (83)	64 (86)
Black	41 (14)	21 (15)	8 (11)	22 (8)	13 (9)	5 (7)
Asian	2 (<1)	3 (2)	3 (4)	22 (8)	7 (5)	5 (7)
Previous use of biological therapy,‡ n (%)	76 (26)	31 (22)	19 (26)	41 (14)	16 (11)	10 (14)

Percentages might not add up to 100% due to rounding. *Data were pooled for all patients randomly assigned to BKZ 320 mg Q2W for the first 16 weeks. †Patients were included in the former smoker category if they had been a smoker at any previous point. ‡A full list of excluded prior biological agents is provided in appendix 2 (pp 43–45, pp 167–169). BKZ: bimekizumab; BMI: body mass index; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

Kimball AB, et al. *Lancet.* Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6

Baseline Disease Characteristics

	BE HEARD I			BE HEARD II		
	BKZ 320 mg Q2W (n=289)*	**BKZ 320 mg Q4W (n=144)**	**PBO (n=72)**	**BKZ 320 mg Q2W (n=291)***	**BKZ 320 mg Q4W (n=144)**	**PBO (n=74)**
Disease duration, median (IQR), y	5.7 (3.1-12.0)	5.6 (2.6-11.9)	8.7 (4.5-15.4)	4.9 (2.1-10.4)	4.2 (1.9-7.8)	4.8 (1.3-12.3)
Abscess and inflammatory nodule count, mean (SD)	15.3 (13.5)	17.8 (25.3)	15.0 (11.9)	16.7 (15.5)	17.6 (15.4)	13.9 (7.8)
Abscess count	3.7 (6.1)	4.5 (8.4)	2.9 (6.6)	3.3 (5.9)	3.5 (5.0)	2.4 (2.8)
Inflammatory nodule count	11.6 (11.4)	13.3 (22.4)	12.2 (10.0)	13.4 (12.2)	14.1 (13.3)	11.4 (6.7)
DT count, mean (SD)	4.0 (4.9)	3.8 (4.9)	3.2 (4.0)	3.6 (4.0)	2.8 (3.1)	3.5 (3.7)
Hurley stage, n (%)						
II	149 (52)	71 (49)	34 (47)	177 (61)	89 (62)	45 (61)
III	140 (48)	73 (51)	38 (53)	114 (39)	55 (38)	29 (39)
DLQI total score, mean (SD)	11.5 (6.6)	12.8 (7.6)	12.4 (8.0)	10.6 (6.5)	10.5 (7.0)	11.9 (6.1)
Concomitant antibiotic use, n (%)	27 (9)	8 (6)	5 (7)	30 (10)	10 (7)	6 (8)
HSSDD worst skin pain score, mean (SD)	5.5 (2.5)	5.9 (2.6)	6.0 (2.5)	5.3 (2.4)	5.3 (2.5)	5.0 (2.4)

Percentages might not add up to 100% due to rounding. *Data were pooled for all patients randomly assigned to BKZ 320 mg Q2W for the first 16 weeks. BKZ: bimekizumab; DLQI: Dermatology Life Quality Index; DT: draining tunnel; HSSDD: Hidradenitis Suppurativa Symptom Daily Diary; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

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Primary and Key Ranked Secondary Efficacy Endpoints at Week 16

n (%), unless otherwise specified for the randomized set	BE HEARD I			BE HEARD II		
	BKZ 320 mg Q2W* (n=289)	**BKZ 320 mg Q4W (n=144)**	**PBO (n=72)**	**BKZ 320 mg Q2W* (n=291)**	**BKZ 320 mg Q4W (n=144)**	**PBO (n=74)**
Primary efficacy endpoint						
HiSCR50†,‡	138 (48%)	65 (45%)	21 (29%)	151 (52%)	77 (54%)	24 (32%)
BKZ Q2W vs PBO, OR (97.5% CI); *P*-value	2.23 (1.16 - 4.31) *P*=0.0060§	..	..	2.29 (1.22 - 4.29) *P*=0.0032§	..	..
BKZ Q4W vs PBO, OR (97.5% CI); *P*-value	..	2.00 (0.98 - 4.09) *P*=0.030‖ (not significant)	..	..	2.42 (1.22 - 4.80) *P*=0.0038§	..
Ranked secondary endpoints						
HiSCR75†,‡	97 (33%)	36 (25%)	13 (18%)	104 (36%)	49 (34%)	12 (16%)
BKZ Q2W vs PBO, OR (97.5% CI); *P*-value	2.18 (1.02 - 4.64) *P*=0.021§	..	..	3.01 (1.37 - 6.58) *P*=0.0016§	..	..
BKZ Q4W vs PBO, OR (97.5% CI); *P*-value	..	1.42 (0.62 - 3.26) *P*=0.35‖ (not significant)	..	..	2.72 (1.18 - 6.27) *P*=0.0071§	..
Flare†,‡,¶	NA	NA	NA	84 (29%)	34 (24%)	21 (28%)
BKZ Q2W vs PBO, OR (97.5% CI); *P*-value	NA	NA	NA	1.05 (0.54 - 2.04) *P*=0.87‖ (not significant)	..	..
BKZ Q4W vs PBO, OR (97.5% CI); *P*-value	NA	NA	NA	..	0.80 (0.38 - 1.68) *P*=0.50‖ (not significant)	..

Randomized set. ORs are presented for binary variables and least-squares mean difference presented for continuous variables. For multiply imputed binary variables, the rounded average number of patients with response based on 100 imputations is reported. *Data were pooled for all patients randomly assigned to BKZ 320 mg Q2W for the first 16 weeks. †Data were imputed by means of an mNRI (ALL-ABX): patients who received any systemic antibiotic (new or increased dose) or who discontinued due to an adverse event or absence of efficacy were treated as nonresponders (or treated as experiencing flare for the flare endpoint) at all subsequent visits. Other missing data were imputed via MI (primary, prespecified analysis method). ‡*P*-values (from Wald tests) for adjusted responder rates obtained from logistic regression with treatment, Hurley stage at baseline, and baseline antibiotic use (and analgesic use for pain response only) as factors. §Statistically significant per the statistical hierarchy. ‖*P*-value calculated based on statistical testing methodology, had the given BKZ regimen succeeded at hierarchical testing. ¶Flare by Week 16 was defined as at least 1 occurrence of flare between baseline and up to Week 16, in which flare was defined as at least a 25% increase in AN count with an increase of at least 2 ANs relative to baseline. Flare was not a secondary endpoint in BE HEARD I, so these cells have been marked with NA. ABX: antibiotics; AN: abscess and inflammatory nodule; BKZ: bimekizumab; HiSCR50/75: Hidradenitis Suppurativa Clinical Response of ≥50%/ ≥75% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; MI: multiple imputation; mNRI: modified nonresponder imputation; NA: not applicable; OR: odds ratio; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

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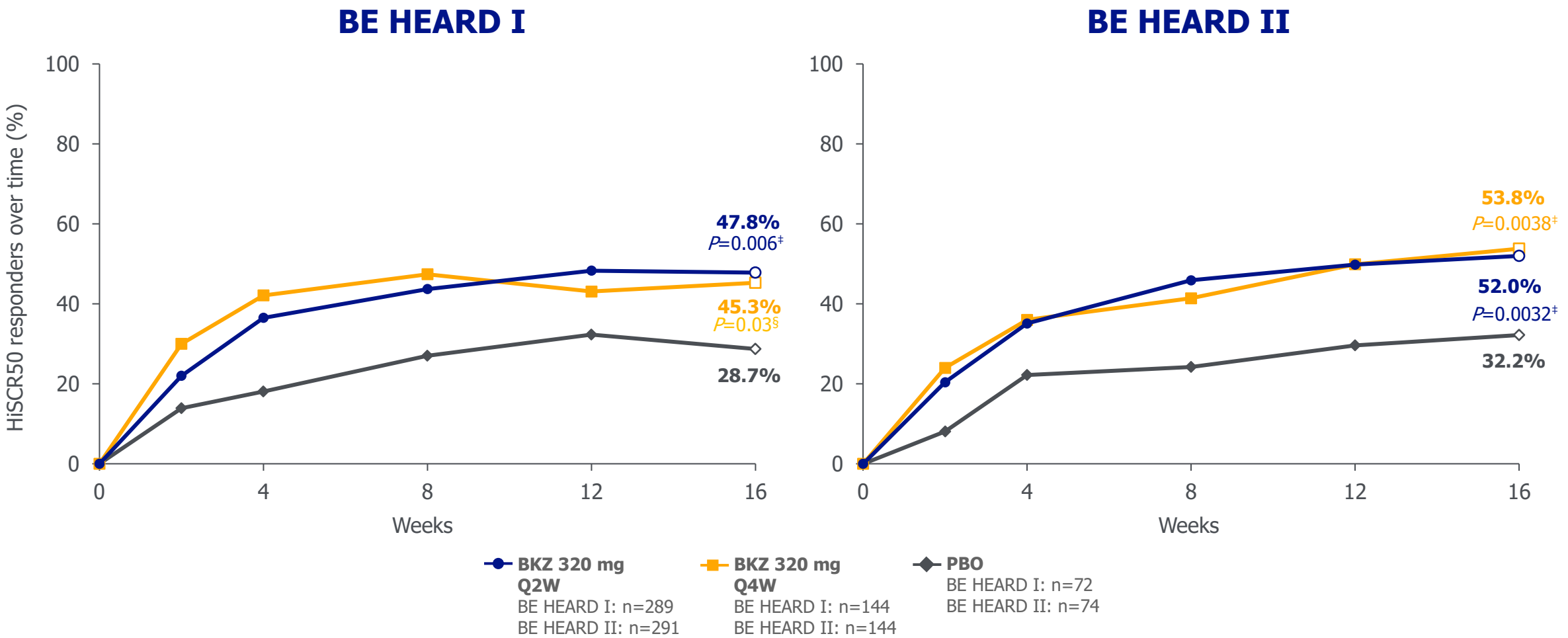
Key Ranked Secondary Efficacy Endpoints at Week 16

n (%), unless otherwise specified for the randomized set	BE HEARD I			BE HEARD II		
	BKZ 320 mg Q2W* (n=289)	**BKZ 320 mg Q4W (n=144)**	**PBO (n=72)**	**BKZ 320 mg Q2W* (n=291)**	**BKZ 320 mg Q4W (n=144)**	**PBO (n=74)**
Ranked secondary endpoints (continued)						
DLQI total score change from baseline, mean (SE)[†,‡]	-5.0 (0.4)	-5.5 (0.5)	-2.7 (0.7)	-4.5 (0.3)	-4.1 (0.4)	-3.1 (0.6)
BKZ Q2W vs PBO, LS mean difference (97.5% CI); *P*-value	-2.68 (-4.39 to -0.97) *P*=0.0005[§]	..	..	-2.31 (-3.71 to -0.91) *P*=0.0002[‖] (not significant)	..	..
BKZ Q4W vs PBO, LS mean difference (97.5% CI); *P*-value	..	-2.57 (-4.47 to -0.68) *P*=0.0024[‖] (not significant)	..	..	-2.39 (-3.92 to -0.87) *P*=0.0004[‖] (not significant)	..
HSSDD worst skin pain score change from baseline, mean (SE)[†,¶]	-1.9 (0.2)	-1.7 (0.2)	-1.1 (0.2)	-1.9 (0.1)	-1.7 (0.2)	-0.4 (0.3)
BKZ Q2W vs PBO, LS mean difference (97.5% CI); *P*-value	-1.19 (-2.05 to -0.32) *P*=0.0022[§]	..	..	-1.27 (-1.98 to -0.55) *P*<0.0001[‖] (not significant)	..	..
BKZ Q4W vs PBO, LS mean difference (97.5% CI); *P*-value	..	-0.55 (-1.52 to 0.42) *P*=0.20[‖] (not significant)	..	..	-0.90 (-1.68 to -0.11) *P*=0.010[‖] (not significant)	..
HSSDD worst skin pain response[**,††,‡‡]	61 (32%)	23 (22%)	7 (1%)	66 (32%)	31 (29%)	5 (11%)
BKZ Q2W vs PBO, OR (97.5% CI); *P*-value	2.76 (0.91 - 8.36) *P*=0.041[‖] (not significant)	..	..	3.76 (1.19 - 11.87) *P*=0.010[‖] (not significant)	..	..
BKZ Q4W vs PBO, OR (97.5% CI); *P*-value	..	1.62 (0.49 - 5.35) *P*=0.37[‖] (not significant)	..	..	3.27 (0.97 - 11.00) *P*=0.028[‖] (not significant)	..

Randomized set. ORs are presented for binary variables and least-squares mean difference presented for continuous variables. For multiply imputed binary variables, the rounded average number of patients with response based on 100 imputations is reported. *Data were pooled for all patients randomly assigned to BKZ 320 mg Q2W for the first 16 weeks. †Data were imputed by means of MI (ALL-ABX): patients who received any systemic antibiotic (new or increased dose) or who discontinued due to an adverse event or absence of efficacy were treated as nonresponders (or treated as experiencing flare for the flare endpoint) at all subsequent visits. Other missing data were imputed via MI (primary, prespecified analysis method). ‡*P*-values based on an ANCOVA with fixed effects of treatment, Hurley stage at baseline, baseline antibiotic use, and baseline DLQI total score as covariates. §Statistically significant per the statistical hierarchy. ‖*P*-value calculated based on statistical testing methodology, had the given BKZ regimen succeeded at hierarchical testing. ¶*P*-values based on an ANCOVA with fixed effects of treatment, Hurley stage at baseline, baseline antibiotic use, analgesic use, and baseline HSSDD worst skin pain score as covariates. **Data were imputed using mNRI (All-ABX): patients who discontinued study treatment due to absence of efficacy or adverse events, or who received any systemic antibiotics during the study (new or increased dose), were set to missing and subsequently imputed using MI. ††*P*-values (from Wald tests) for adjusted responder rates obtained from logistic regression with treatment, Hurley stage at baseline, and baseline antibiotic use (and analgesic use for pain response only) as factors. ‡‡Pain response was defined as an improvement from baseline in HSSDD weekly worst skin pain score of at least 3 points among patients with a baseline score of 3 or higher. ABX: antibiotics; ANCOVA: analysis of covariance; BKZ: bimekizumab; DLQI: Dermatology Life Quality Index; HS: hidradenitis suppurativa; HSSDD: HS Symptom Daily Diary; LS: least squares; MI: multiple imputation; mNRI: modified nonresponder imputation; OR: odds ratio; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks. Kimball AB, et al. *Lancet*. Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6

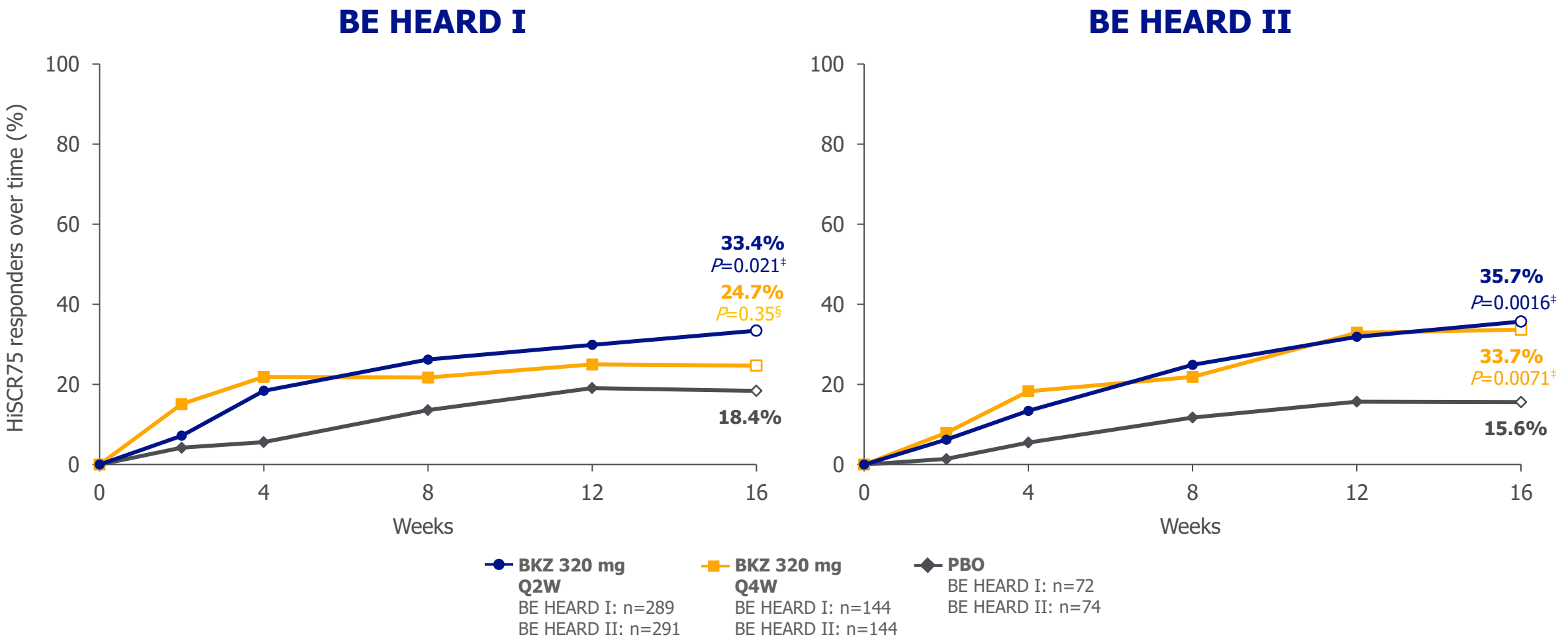
Primary Endpoint: HiSCR50 Responses at Week 16 in Patients Treated With BKZ versus PBO (mNRI [ALL-ABX])*,†



*The rates of HiSCR50 r from randomization to Week 16 in BE HEARD I and BE HEARD II mNRI (ALL-ABX): patients who received any systemic antibiotic (new or increased dose) or who discontinued due to an adverse event or absence of efficacy were treated as nonresponders at all subsequent visits. Other missing data were imputed via MI (primary, prespecified analysis method). †The primary endpoint of HiSCR50 at Week 16 was met for BKZ 320 mg Q2W vs placebo in BE HEARD I and for both BKZ dosing regimens in BE HEARD II. ‡Statistically significant per the statistical hierarchy. §*P*-value calculated based on statistical testing methodology had the given BKZ regimen succeeded at hierarchical testing. ABX: antibiotics; BKZ: bimekizumab; DT: draining tunnel; HiSCR: Hidradenitis Suppurativa Clinical Response; HiSCR50: ≥50% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; MI: multiple imputation; mNRI: modified nonresponder imputation; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

Kimball AB, et al. *Lancet*. Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6

Key Ranked Secondary Endpoint: HiSCR75 Responses at Week 16 in Patients Treated With BKZ versus PBO (mNRI [ALL-ABX])*,†



*The rates of HiSCR75 from randomization to Week 16 in BE HEARD I and BE HEARD II mNRI (ALL-ABX): patients who received any systemic antibiotic (new or increased dose) or who discontinued due to an adverse event or absence of efficacy were treated as nonresponders at all subsequent visits. Other missing data were imputed via MI (primary, prespecified analysis method). †The secondary endpoint of HiSCR75 at Week 16 was met for BKZ 320 mg Q2W vs placebo in BE HEARD I and for both BKZ dosing regimens in BE HEARD II. ‡Statistically significant per the statistical hierarchy. §*P*-value calculated based on statistical testing methodology had the given BKZ regimen succeeded at hierarchical testing. ABX: antibiotics; AN: abscess and inflammatory nodule; BKZ: bimekizumab; HiSCR75: Hidradenitis Suppurativa Clinical Response of ≥ 75% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; MI: multiple imputation; mNRI: modified nonresponder imputation; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

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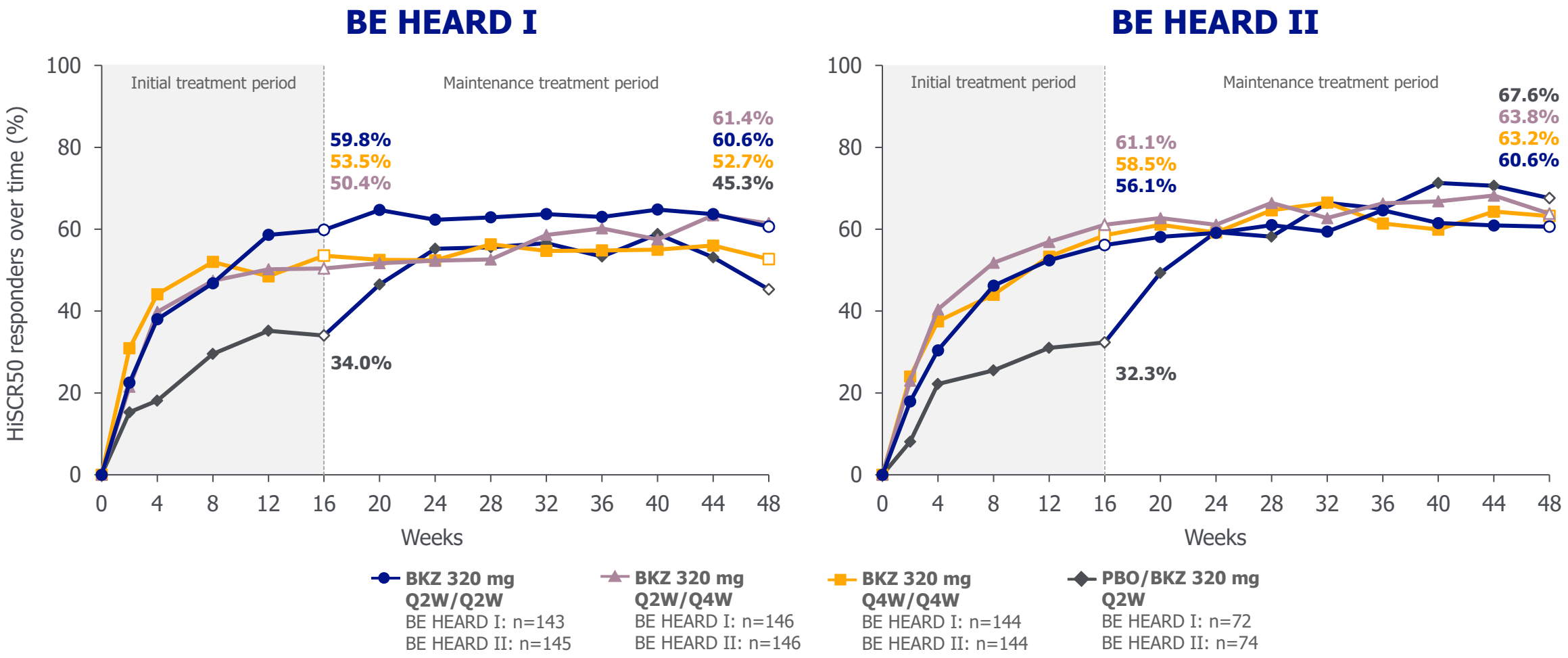
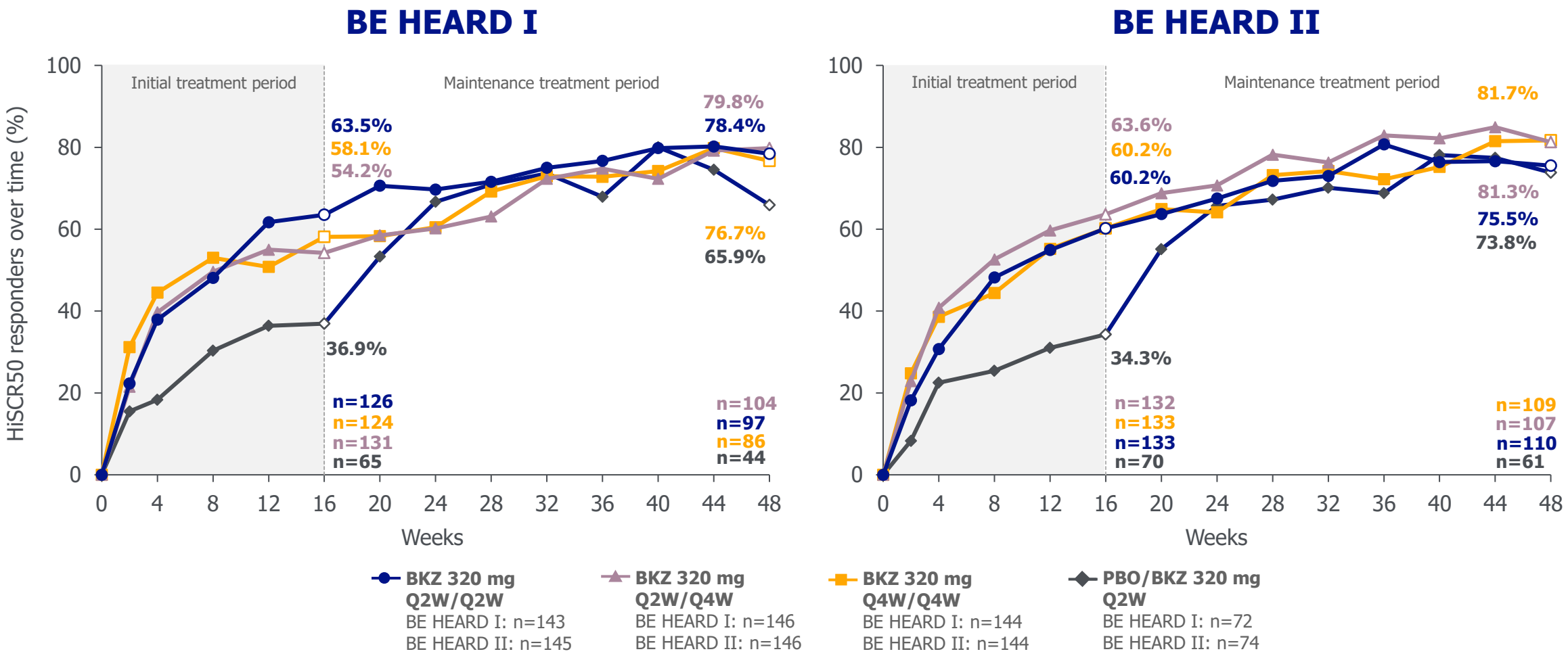
HiSCR50 Responses Over 48 Weeks With BKZ versus PBO (mNRI [HS-ABX])*



*mNRI (HS-ABX): patients who took systemic antibiotics defined as rescue medication for HS by the principal investigator or who discontinued due to adverse events or lack of efficacy were treated as nonresponders at all subsequent visits. Other missing data were imputed via MI. ABX: antibiotics; AN: abscess and inflammatory nodule; BKZ: bimekizumab; DT: draining tunnel; HiSCR50: Hidradenitis Suppurativa Clinical Response of ≥50% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; MI: multiple imputation; mNRI: modified non-responder imputation; Q2W: every 2 weeks; Q4W: every 4 weeks. Kimball AB, et al. *Lancet*. Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6.

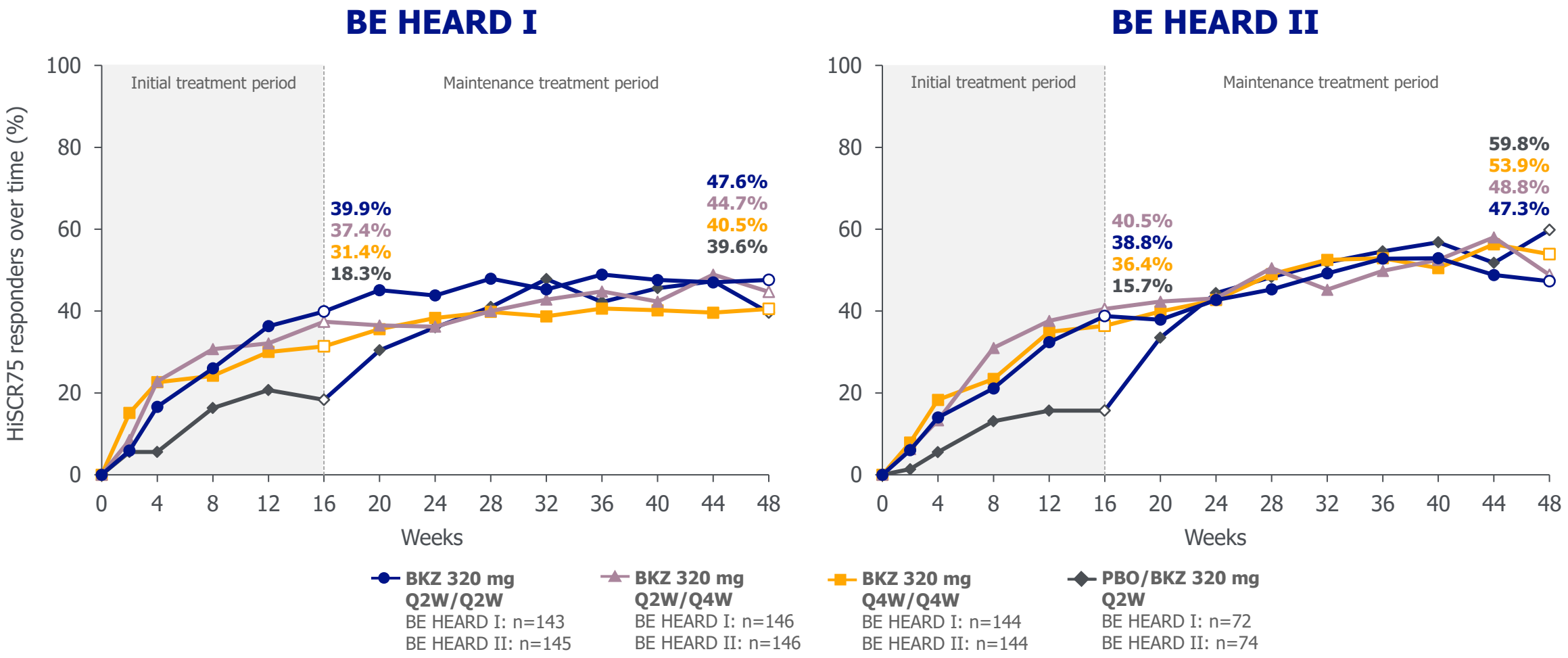
HiSCR50 Responses Over 48 Weeks With BKZ versus PBO (OC)*



*The rates of HiSCR50 from randomization to Week 48 in BE HEARD I and BE HEARD II. Data are shown for OC (i.e., all available data after an intercurrent event were summarized as recorded in the database, and all missing data were left missing). AN: abscess and inflammatory nodule; BKZ: bimekizumab; HiSCR50: Hidradenitis Suppurativa Clinical Response of ≥50% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; OC: observed case; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

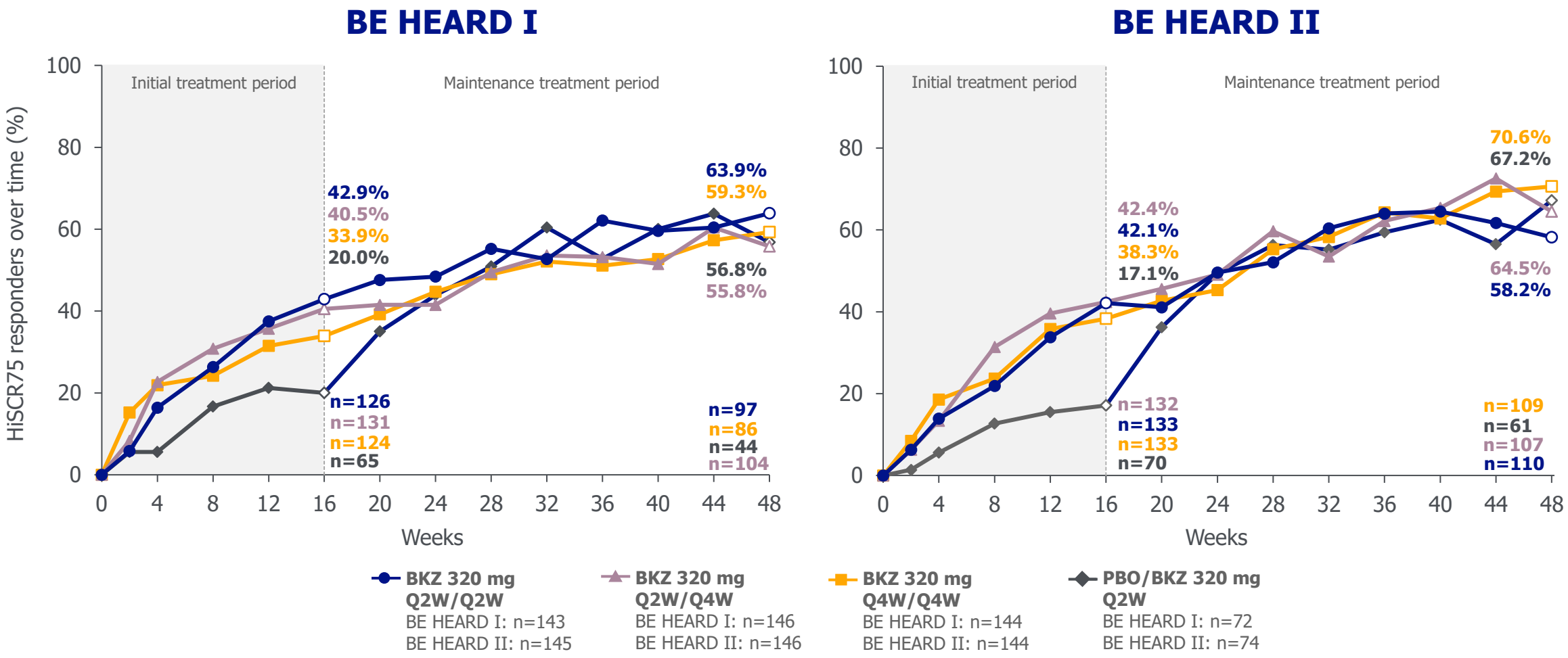
Kimball AB, et al. *Lancet.* Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6

HiSCR75 Responses Over 48 Weeks With BKZ versus PBO (mNRI [HS-ABX])*



*mNRI (HS-ABX): patients who took systemic antibiotics defined as rescue medication for HS by the principal investigator or who discontinued due to adverse events or lack of efficacy were treated as nonresponders at all subsequent visits. Other missing data were imputed via MI. ABX: antibiotics; AN: abscess and inflammatory nodule; BKZ: bimekizumab; DT: draining tunnel; HiSCR75: Hidradenitis Suppurativa Clinical Response of ≥75% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; MI: multiple imputation; mNRI: modified non-responder imputation; Q2W: every 2 weeks; Q4W: every 4 weeks. Kimball AB, et al. *Lancet*. Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6.

HiSCR75 Responses Over 48 Weeks With BKZ versus PBO (OC)*



*The rates of HiSCR75 from randomization to Week 48 in BE HEARD I and BE HEARD II. Data are shown for OC (i.e., all available data after an intercurrent event were summarized as recorded in the database, and all missing data were left missing). AN: abscess and inflammatory nodule; BKZ: bimekizumab; HiSCR75: Hidradenitis Suppurativa Clinical Response of ≥75% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; OC: observed case; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

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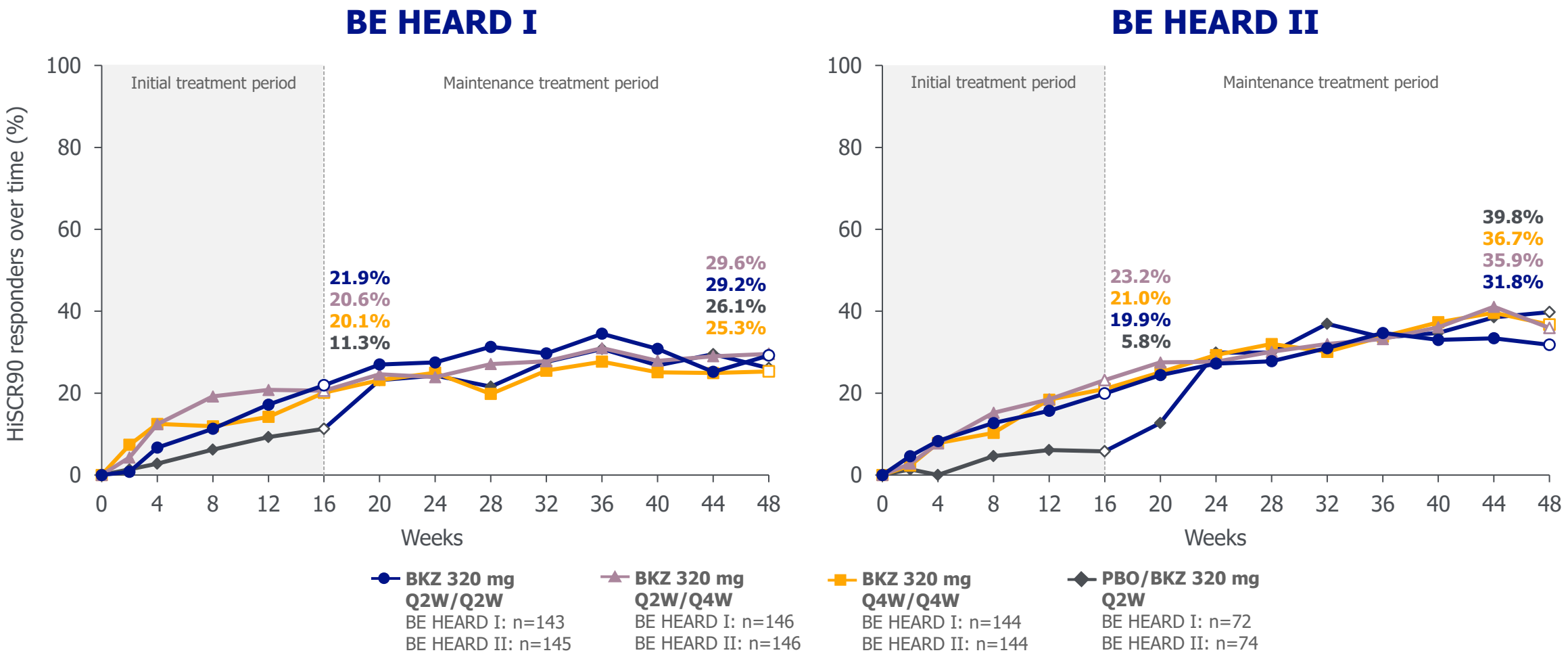
HiSCR90 Responses Over 48 Weeks With BKZ versus PBO (mNRI [HS-ABX])*



*mNRI (HS-ABX): patients who took systemic antibiotics defined as rescue medication for HS by the principal investigator or who discontinued due to adverse events or lack of efficacy were treated as nonresponders at all subsequent visits. Other missing data were imputed via MI.

ABX: antibiotics; AN: abscess and inflammatory nodule; BKZ: bimekizumab; HiSCR90: Hidradenitis Suppurativa Clinical Response of ≥ 90% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; MI: multiple imputation; mNRI: modified non-responder imputation; Q2W: every 2 weeks; Q4W: every 4 weeks.

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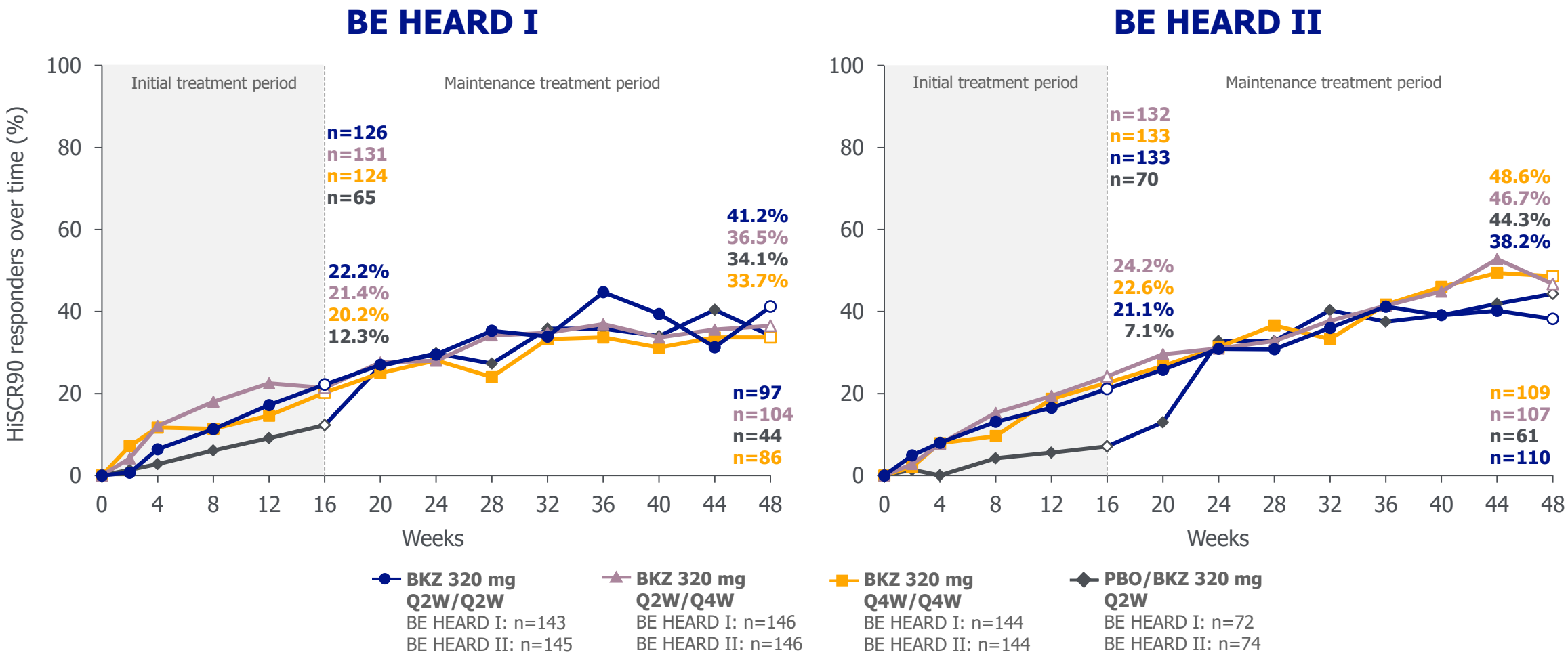
HiSCR90 Responses Over 48 Weeks With BKZ versus PBO (OC)*



*OC: all available data after an intercurrent event were summarized as recorded in the database, and all missing data were left missing.
AN: abscess and inflammatory nodule; BKZ: bimekizumab; HiSCR90: Hidradenitis Suppurativa Clinical Response of ≥90% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; OC: observed case; Q2W: every 2 weeks; Q4W: every 4 weeks.
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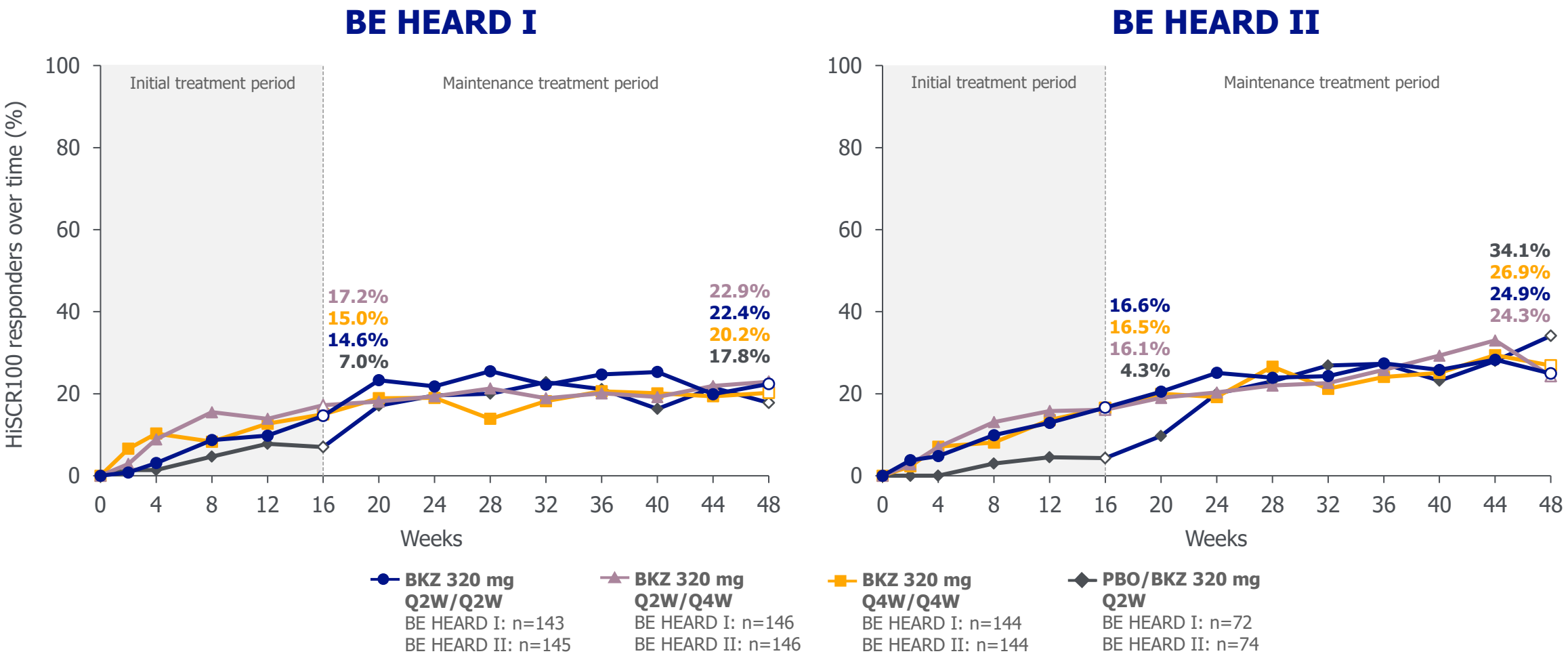
HiSCR100 Responses Over 48 Weeks With BKZ versus PBO (mNRI [HS-ABX])*



*mNRI (HS-ABX): patients who took systemic antibiotics defined as rescue medication for HS by the principal investigator or who discontinued due to adverse events or lack of efficacy were treated as nonresponders at all subsequent visits. Other missing data were imputed via MI.

ABX: antibiotics; AN: abscess and inflammatory nodule; BKZ: bimekizumab; DT: draining tunnel; HiSCR100: Hidradenitis Suppurativa Clinical Response of 100% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; MI: multiple imputation; mNRI: modified non-responder imputation; Q2W: every 2 weeks; Q4W: every 4 weeks.

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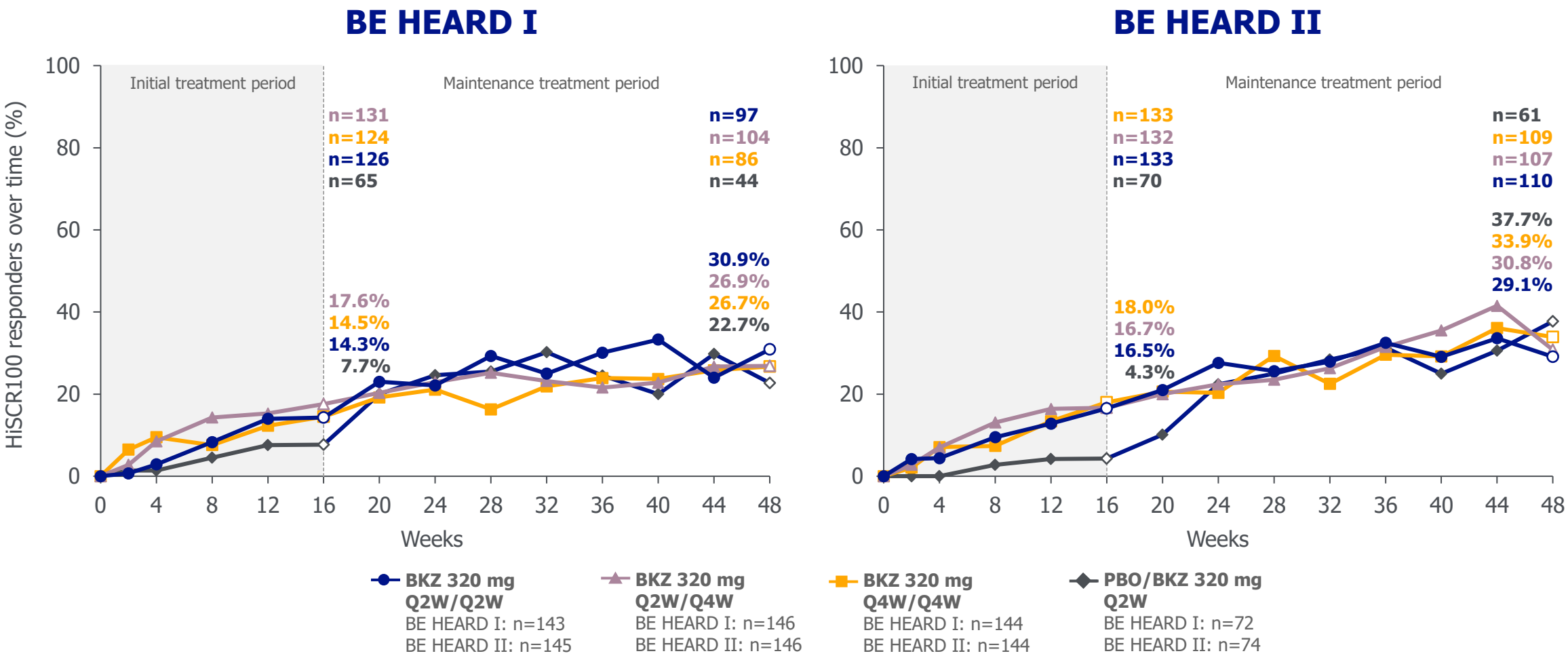
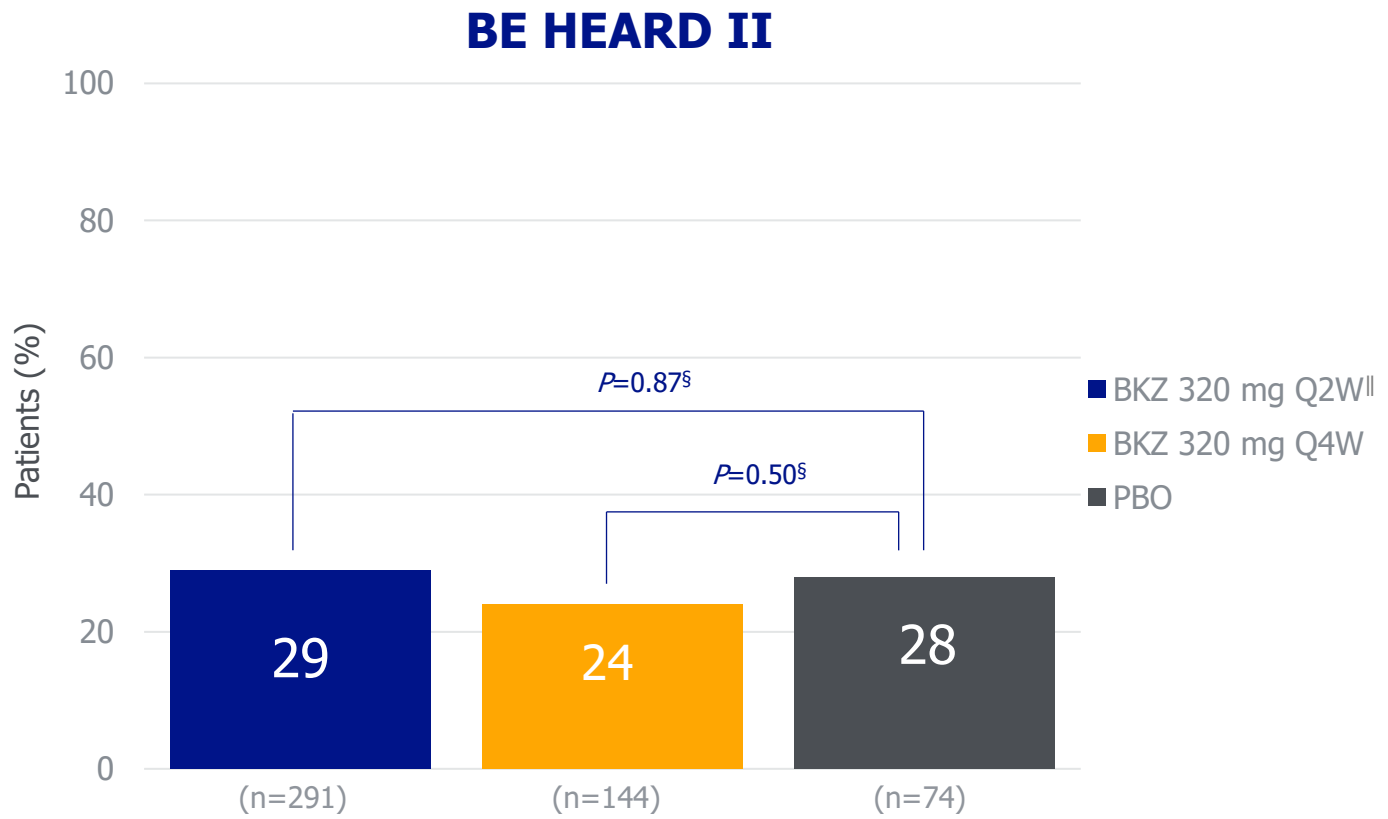
HiSCR100 Responses Over 48 Weeks With BKZ versus PBO (OC)*



*OC: all available data after an intercurrent event were summarized as recorded in the database, and all missing data were left missing.
AN: abscess and inflammatory nodule; BKZ: bimekizumab; DT: draining tunnel; HiSCR100: Hidradenitis Suppurativa Clinical Response of 100% reduction from baseline in the total abscess and inflammatory nodule count with no increase from baseline in abscess or draining tunnel count; OC: observed case; Q2W: every 2 weeks; Q4W: every 4 weeks.

Kimball AB, et al. *Lancet.* Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6.

Proportion of Patients Experiencing Flare Across Treatment Groups by Week 16 (mNRI [ALL-ABX])*,†,‡



*Data were imputed by means of an mNRI (ALL-ABX): patients who received any systemic antibiotic (new or increased dose) or who discontinued due to an adverse event or absence of efficacy were treated as nonresponders (or treated as experiencing flare for the flare endpoint) at all subsequent visits. Other missing data were imputed via multiple imputation (primary, prespecified analysis method). †*P*-values (from Wald tests) for adjusted responder rates obtained from logistic regression with treatment, Hurley stage at baseline, and baseline antibiotic use (and analgesic use for pain response only) as factors. ‡Flare by Week 16 was defined as at least 1 occurrence of flare between baseline and up to Week 16, in which flare was defined as at least a 25% increase in abscess and inflammatory nodule count with an increase of at least 2 abscessess and inflammatory nodules relative to baseline. Flare was not a secondary endpoint in BE HEARD I. §*P*-value calculated based on statistical testing methodology, had the given BKZ regimen succeeded at hierarchical testing. ‖Data were pooled for all patients randomly assigned to BKZ 320 mg Q2W for the first 16 weeks.
ABX: antibiotics; BKZ: bimekizumab; mNRI: modified nonresponder imputation; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.
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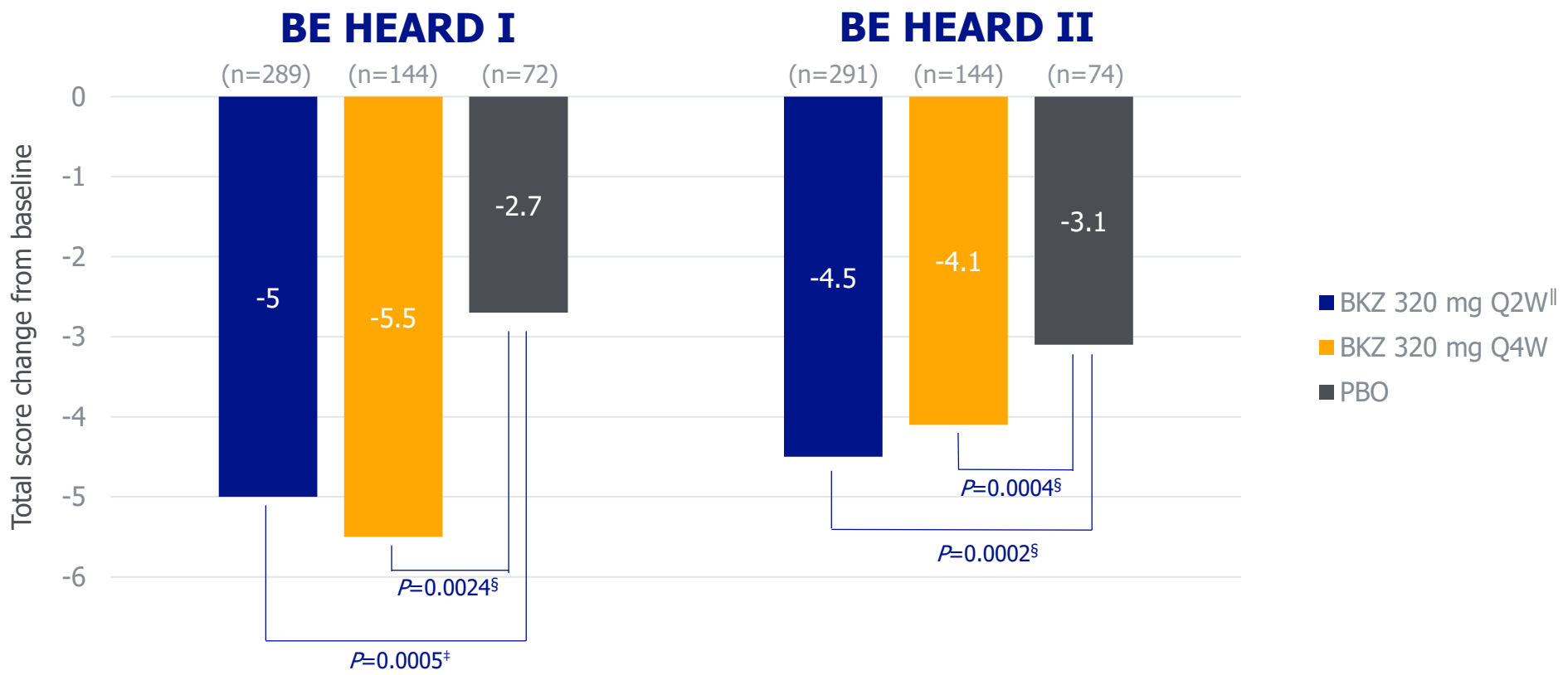
CfB in DLQI Total Score at Week 16—BKZ versus PBO (MI [ALL-ABX])*,†



*Data were imputed using multiple imputation (ALL-ABX): patients who discontinued study treatment due to absence of efficacy or adverse events, or who received any systemic antibiotics during the study (new or increased dose), were set to missing and subsequently imputed using multiple imputation. All other missing data were also imputed using multiple imputation. †*P*-values based on an ANCOVA with fixed effects of treatment, Hurley stage at baseline, baseline antibiotic use, and baseline DLQI total score as covariates. ‡Statistically significant per the statistical hierarchy. §*P*-value calculated based on statistical testing methodology, had the given BKZ regimen succeeded at hierarchical testing. ‖Data were pooled for all patients randomly assigned to BKZ 320 mg Q2W for the first 16 weeks. ABX: antibiotics; ANCOVA: analysis of covariance; BKZ: bimekizumab; CfB: change from baseline; DLQI: Dermatology Life Quality Index; MI: multiple imputation; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

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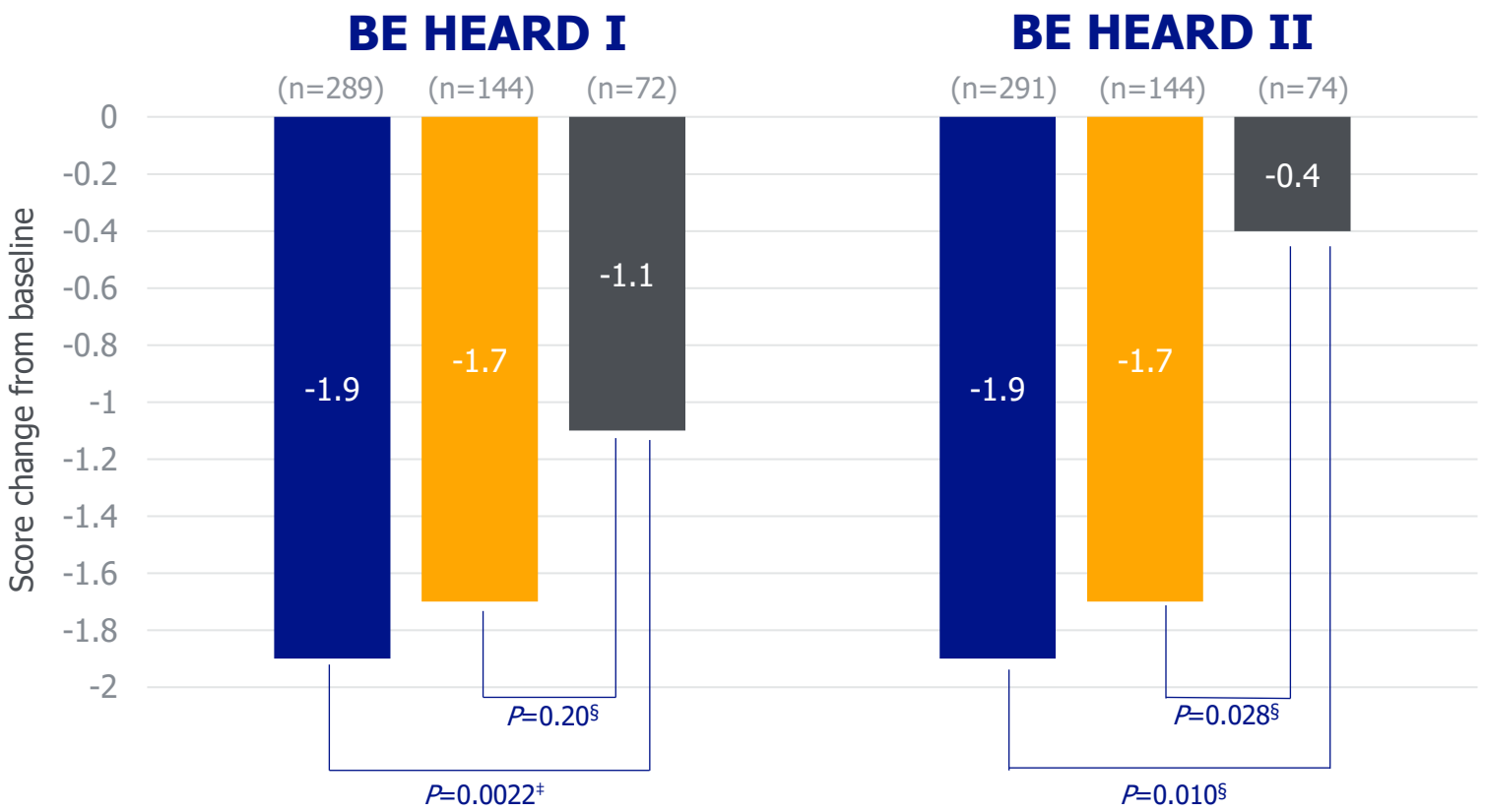
CfB in HSSDD Worst Skin Pain Score at Week 16—BKZ versus PBO (MI [ALL-ABX])*,†



HSSDD
5 item HS-specific, patient-reported outcome tool

Worst skin pain, average skin pain, itch at its worst, smell or odor, and drainage or oozing

- Patients select a number that best describes the intensity of their HS symptoms in the past 24 hours on a 0–10 scale
- For each item, the HSSDD score is derived from the weekly averages of the daily scores from a given week

- BKZ 320 mg Q2W‖
- BKZ 320 mg Q4W
- PBO

*Data were imputed using multiple imputation (ALL-ABX): patients who discontinued study treatment due to absence of efficacy or adverse events, or who received any systemic antibiotics during the study (new or increased dose), were set to missing and subsequently imputed using multiple imputation. All other missing data were also imputed using multiple imputation. †*P*-values based on an ANCOVA with fixed effects of treatment, Hurley stage at baseline, baseline antibiotic use, analgesic use, and baseline HSSDD worst skin pain score as covariates. ‡Statistically significant per the statistical hierarchy. §*P*-value calculated based on statistical testing methodology had the given bimekizumab regimen succeeded at hierarchical testing. ‖Data were pooled for all patients randomly assigned to BKZ 320 mg Q2W for the first 16 weeks. ABX: antibiotics; ANCOVA: analysis of covariance; BKZ: bimekizumab; CfB: change from baseline; HSSDD: Hidradenitis Suppurativa Symptom Daily Diary; MI: multiple imputation; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

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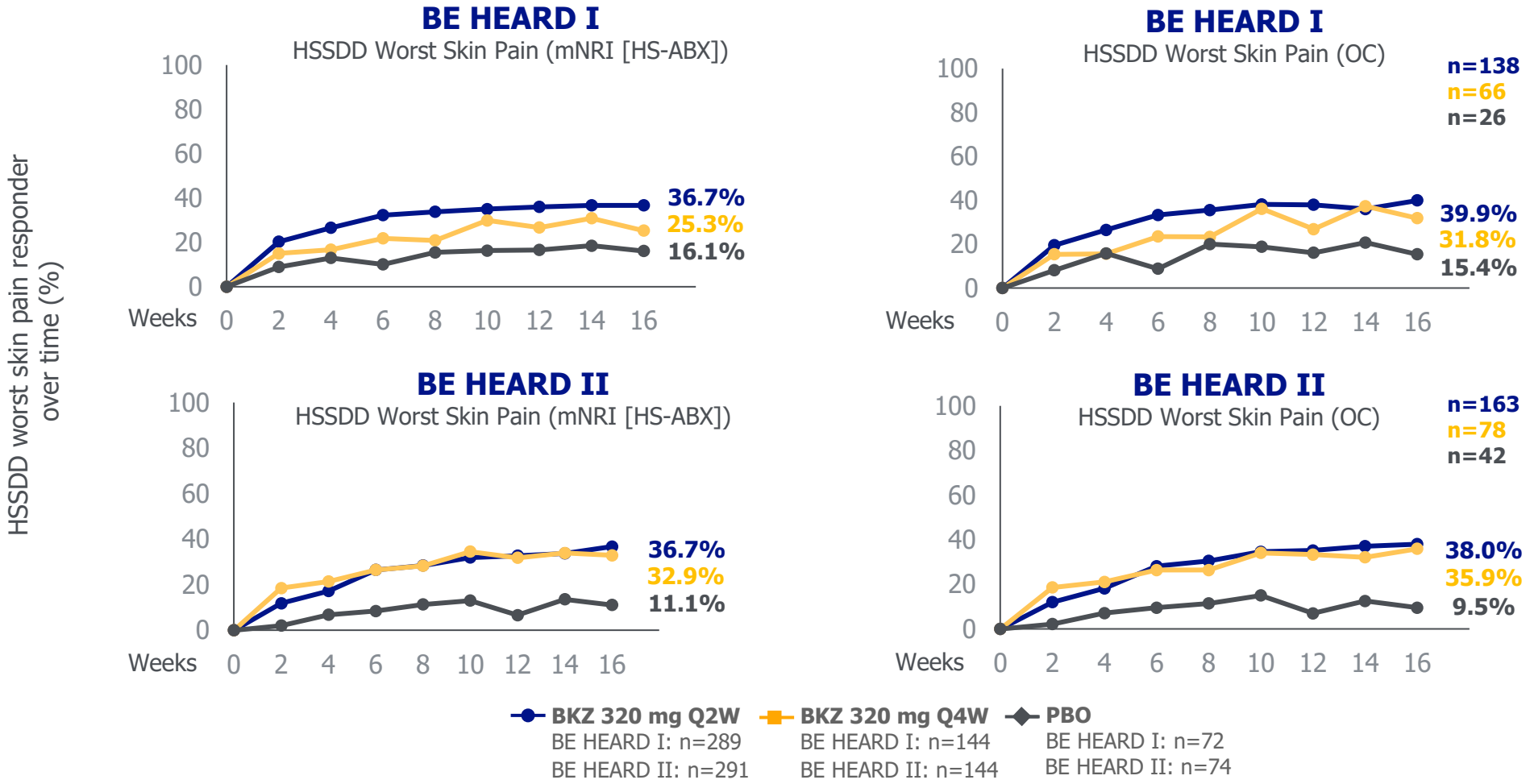
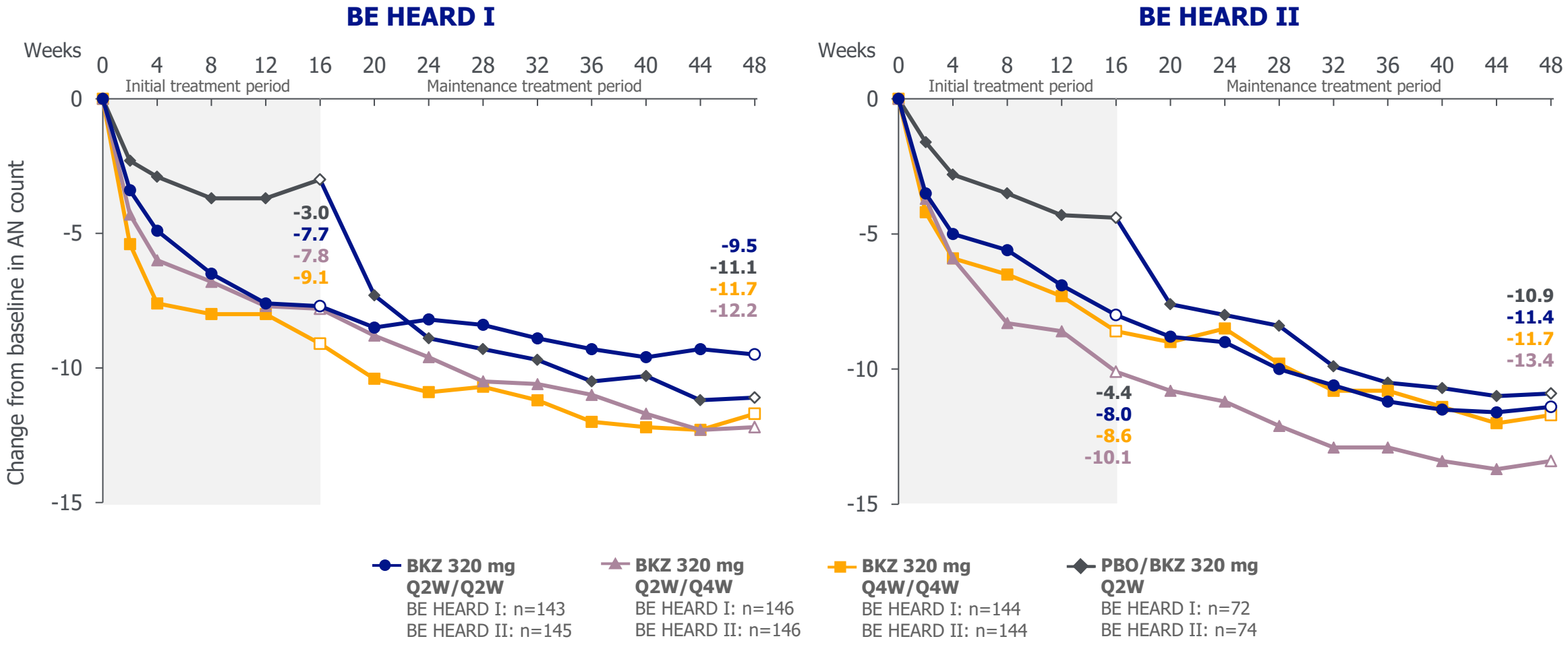
Change in HSSDD Worst Skin Pain Over 16 Weeks With BKZ versus PBO (mNRI [HS-ABX]/OC)*,†,‡



*mNRI (HS-ABX): patients who received systemic antibiotics defined as rescue medication for HS by the principal investigator or who discontinued due to adverse events or lack of efficacy were treated as non-responders at all subsequent visits. Other missing data were imputed via MI. †OC: all available data after an intercurrent event were summarized as recorded in the database, and all missing data were left missing. ‡Pain response was defined as an improvement from baseline in HSSDD weekly worst skin pain score of at least 3 points among patients with a baseline score of 3 or higher.
ABX: antibiotics; BHI: BE HEARD I; BHII: BE HEARD II; BKZ: bimekizumab; HS: hidradenitis suppurativa; HSSDD: HS Symptom Daily Diary; MI: multiple imputation; mNRI: modified non-responder imputation; OC: observed case; Q2W: every 2 weeks; Q4W: every 4 weeks.

Kimball AB, et al. *Lancet.* Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6

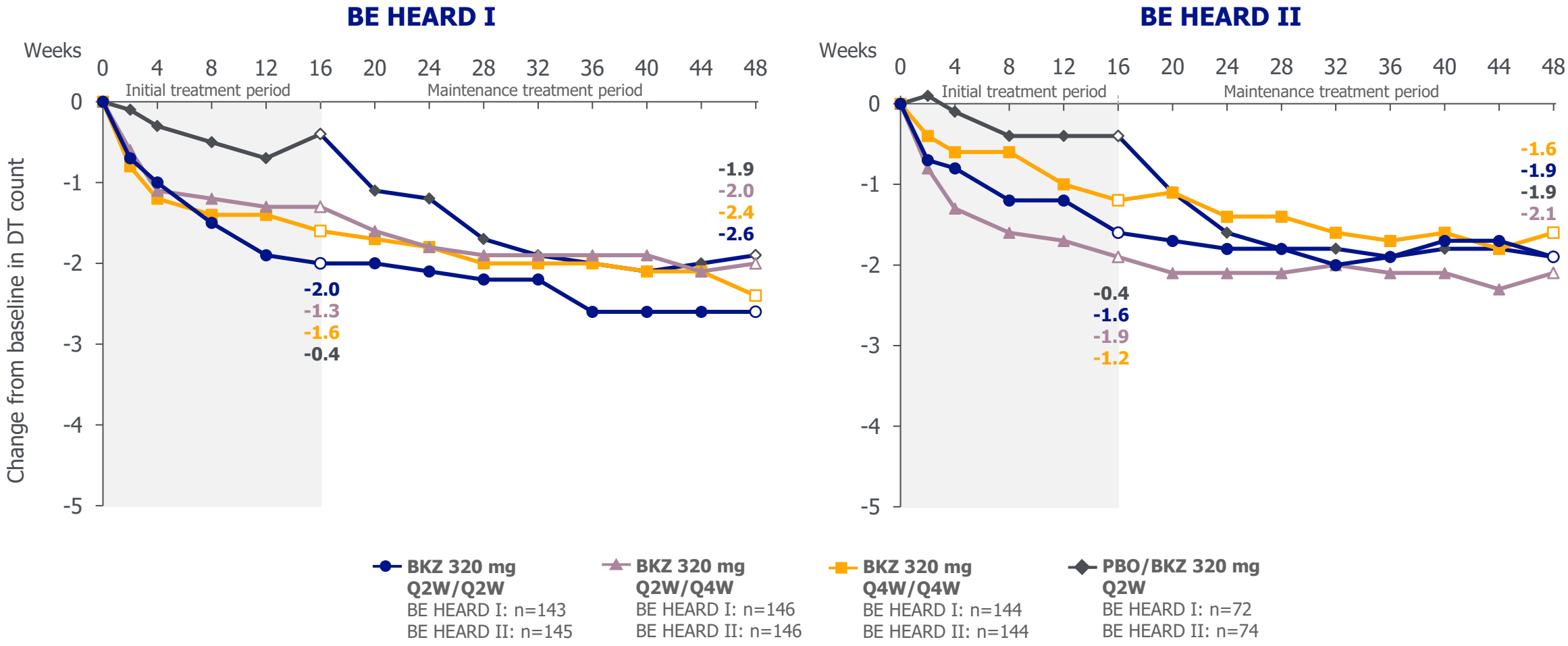
Change in Abscess and Inflammatory Nodule Counts Over 48 Weeks (MI [HS-ABX])*



*Data were imputed using MI (HS-ABX): patients who discontinued study treatment due to lack of efficacy or adverse events, or who took systemic antibiotics as rescue medication for HS as defined by the principal investigator, were set to missing and subsequently imputed using MI. ABX: antibiotics; AN: abscess and inflammatory nodule; BKZ: bimekizumab; HS: hidradenitis suppurativa; MI: multiple imputation; Q2W: every 2 weeks; Q4W: every 4 weeks.

Kimball AB et al. *Lancet.* Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6.

Change in Draining Tunnel Count Over 48 Weeks (MI [HS-ABX])*



*Data were imputed using MI (HS-ABX): patients who discontinued study treatment due to lack of efficacy or adverse events, or who took systemic antibiotics as rescue medication for HS as defined by the principal investigator, were set to missing and subsequently imputed using MI. ABX: antibiotics; BKZ: bimekizumab; DT: draining tunnel; HS: hidradenitis suppurativa; MI: multiple imputation; Q2W: every 2 weeks; Q4W: every 4 weeks.

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BKZ Adverse Event Summary (1 of 2)

n (%)	Initial treatment period only (Weeks 0–16)						Initial and maintenance treatment period (Weeks 0–48)	
	BE HEARD I			BE HEARD II			BE HEARD I	BE HEARD II
	BKZ 320 mg Q2W* (n=286) 100 PY=0.87	BKZ 320 mg Q4W (n=143) 100 PY=0.43	PBO (n=72) 100 PY=0.22	BKZ 320 mg Q2W* (n=290) 100 PY=0.88	BKZ 320 mg Q4W (n=142) 100 PY=0.44	PBO (n=74) 100 PY=0.23	BKZ Total (n=494) 100 PY=3.99	BKZ Total (n=501) 100 PY=4.14
Any TEAE	192 (67)	94 (66)	48 (67)	187 (64)	73 (51)	42 (57)	425 (86)	412 (82)
Serious TEAE	6 (2)	4 (3)	0	9 (3)	3 (2)	0	40 (8)	24 (5)
Discontinuation due to TEAE	10 (3)	6 (4)	1 (1)	12 (4)	3 (2)	0	40 (8)	27 (5)
Drug-related TEAE	84 (29)	37 (26)	12 (17)	105 (36)	38 (27)	8 (11)	227 (46)	217 (43)
Severe TEAE	8 (3)	3 (2)	0	12 (4)	5 (4)	2 (3)	42 (9)	39 (8)
Deaths	0	0	0	0	0	0	1 (<1)	0
Most common TEAEs								
Hidradenitis	19 (7)	12 (8)	10 (14)	25 (9)	13 (9)	5 (7)	96 (19)	90 (18)
Coronavirus infection	9 (3)	2 (1)	2 (3)	11 (4)	3 (2)	0	71 (14)	36 (7)
Oral candidiasis	17 (6)	2 (1)	0	24 (8)	5 (4)	0	47 (10)	64 (13)
Diarrhea	18 (6)	12 (8)	1 (1)	18 (6)	5 (4)	6 (8)	49 (10)	36 (7)
Headache	22 (8)	8 (6)	3 (4)	18 (6)	7 (5)	7 (9)	43 (9)	43 (9)
TEAEs of interest								
Infections and infestations	98 (34)	52 (36)	18 (25)	95 (33)	39 (27)	12 (16)	301 (61)	277 (55)
Serious infections	1 (<1)	0	0	0	0	0	11 (2)	5 (1)
Opportunistic infections†	1 (<1)	1 (<1)	0	0	1 (<1)	0	8 (2)	4 (<1)

Safety set (Weeks 0–16) and active medication set (Weeks 0–48), as per MedDRA (version 19.0). *Data were pooled for all patients randomly assigned to BKZ 320 mg Q2W for the first 16 weeks. †Opportunistic infections were localized mucocutaneous events, as defined by internal company conventions. BKZ: bimekizumab; MedDRA: Medical Dictionary for Regulatory Activities; PBO: placebo; PY: patient-year; Q2W: every 2 weeks; Q4W: every 4 weeks; TEAE: treatment-emergent adverse event.

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BKZ Adverse Event Summary (2 of 2)

n (%)	Initial treatment period only (Weeks 0–16)						Initial and maintenance treatment period (Weeks 0–48)	
	BE HEARD I			BE HEARD II			BE HEARD I	BE HEARD II
	BKZ 320 mg Q2W* (n=286) 100 PY=0.87	BKZ 320 mg Q4W (n=143) 100 PY=0.43	PBO (n=72) 100 PY=0.22	BKZ 320 mg Q2W* (n=290) 100 PY=0.88	BKZ 320 mg Q4W (n=142) 100 PY=0.44	PBO (n=74) 100 PY=0.23	BKZ Total (n=494) 100 PY=3.99	BKZ Total (n=501) 100 PY=4.14
TEAEs of interest (continued)								
Fungal infections	34 (12)	17 (12)	1 (1)	41 (14)	18 (13)	0	112 (23)	124 (25)
Candida infections	22 (8)	7 (5)	0	26 (9)	15 (11)	0	67 (14)	86 (17)
Oral candidiasis	17 (6)	2 (1)	0	24 (8)	5 (4)	0	47 (10)	64 (13)
Neutropenia	0	0	0	0	0	0	1 (<1)	0
Hypersensitivity reaction (SMQ, narrow)†	30 (10)	12 (8)	4 (6)	32 (11)	9 (6)	1 (1)	105 (21)	84 (17)
Dermatitis and eczema	14 (5)	6 (4)	3 (4)	21 (7)	8 (6)	1 (1)	62 (13)	60 (12)
Serious hypersensitivity reaction	0	0	0	0	0	0	0	1 (<1)
Adjudicated SIB	0	2 (1)	0	1 (<1)	0	0	5 (1)	1 (<1)
Adjudicated MACE	0	0	0	0	0	0	3 (<1)	0
Hepatic events‡	8 (3)	2 (1)	4 (6)	6 (2)	3 (2)	0	25 (5)	19 (4)
>5× ULN elevation of AST/ALT§	3/284 (1)	0/140	0/71	0/288	0	0/73	4/489 (<1)	4/499 (<1)
Malignancies	0	0	0	1 (<1)	0	0	1 (<1)	3 (<1)
Definite or probable adjudicated IBD	0	1 (<1)	0	1 (<1)	2 (1)	0	3 (<1)	4 (<1)

Safety set (Weeks 0–16) and active medication set (Weeks 0–48), as per MedDRA (version 19.0). *Data were pooled for all patients randomly assigned to BKZ 320 mg Q2W for the first 16 weeks. †Using the narrow SMQ definition of hypersensitivity reaction events. ‡The hepatic events category includes events in the SMQ drug-related hepatic disorders comprehensive search SMQ, excluding the 2 sub-SMQs of benign liver neoplasms (including cysts and polyps) SMQ and malignant and unspecified liver neoplasms SMQ. §No elevations of greater than 5 times the ULN were adjudicated to be highly likely or definitely related to BKZ. ALT: alanine aminotransferase; AST: aspartate aminotransferase; BKZ: bimekizumab; IBD: inflammatory bowel disease; MACE: major adverse cardiovascular events; MedDRA: Medical Dictionary for Regulatory Activities; PBO: placebo; PY: patient-year; Q2W: every 2 weeks; Q4W: every 4 weeks; SIB: suicidal ideation and behavior; SMQ: Standardized MedDRA Query; TEAEs: treatment-emergent adverse events; ULN: upper limit of normal.

Kimball AB, et al. *Lancet.* Published online May 22, 2024. doi:10.1016/S0140-6736(24)00101-6

Limitations

Kimball AB, et al. (**2024**)
Efficacy and safety of bimekizumab in patients with moderate-to-severe hidradenitis suppurativa (**BE HEARD I** and **BE HEARD II**): two 48-week, randomised, double-blind, placebo-controlled, multicentre phase 3 trials

- The relatively short initial 16-week placebo-controlled period might affect the interpretability of later efficacy results
- A lack of an active comparator across 48 weeks of treatment
- Evaluating the efficacy of a treatment for HS in the presence of rescue systemic antibiotic is challenging. The methods used to calculate efficacy rates under these conditions have not yet been standardized across trials in hidradenitis suppurativa
- In clinical trials of patients with hidradenitis suppurativa, a patient's underlying disease severity or multifactorial etiology of underlying disease could lead to variability in observed efficacy and subsequent interpretation of results
- Hidradenitis suppurativa head-to-head comparator studies are scarce. Although numerically greater proportions of patients met HiSCR50 by week 48 in BE HEARD I and II than in other long-term phase 3 trials of hidradenitis suppurativa (using observed case analysis), further research is needed to formally compare these outcomes between biologic therapies because of the inevitable heterogeneity in trial populations and differing analysis methods used across studies

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Efficacy and safety of bimekizumab in patients with moderate-to-severe hidradenitis suppurativa (**BE HEARD I** and **BE HEARD II**): two 48-week, randomised, double-blind, placebo-controlled, multicentre phase 3 trials

Alexa B. Kimball, Gregor B.E. Jemec, Christopher J. Sayed, Joslyn S. Kirby, Errol Prens, John R. Ingram, Amit Garg, Alice B. Gottlieb, Jacek C. Szepietowski, Falk G. Bechara, Evangelos J. Giamarellos-Bourboulis, Hideki Fujita, Robert Rolleri, Paulatsya Joshi, Pratiksha Dokhe, Edward Muller, Luke Peterson, Cynthia Madden, Muhammad Bari, Christo C. Zouboulis

Author Contributions: Substantial contributions to study conception and design, analysis and interpretation of the data, drafting the article or revising it critically for important intellectual content, final approval of the version of the article to be published: **ABK, GBEJ, CJS, JSK, EP, JRI, AG, ABG, JCS, FGB, EJGB, HJ, RR, PJ, PD, EM, LP, CM, MB, CCZ**

Disclosures:
ABK: Grants/research support from **UCB Pharma**, consulting fees from **UCB Pharma**.
GBEJ: Honoraria from **UCB Pharma.**
CJS: Investigator for **UCB Pharma**, consulting fees from **UCB Pharma**.
JSK: Personal fees from **UCB Pharma**, consultancy fees from **UCB Pharma**.
EP: Honoraria from **UCB Pharma**, his department received investigator-initiated grant support from **UCB Pharma**.
JRI: Consultant for **UCB Pharma**.
AG: Consulting fees from **UCB Pharma**.
ABG: Honoraria as advisory board member, and consultant from **UCB Pharma**, research/educational grants from **UCB Pharma**.
JCS: Speaker and investigator for **UCB Pharma**.
FGB: Honoraria as an advisory board member, clinical trials contribution, and speaker from **UCB Pharma**.
HF: Honoraria or fees for serving on advisory boards as a speaker, and as a consultant, and grants as an investigator from **UCB Pharma**.
RR, PJ, PD, EM, LP: Employees and shareholders of **UCB Pharma**.
CM: Former employee and shareholder of **UCB Pharma**.
MB: **Employee of UCB Pharma**.
CCZ: Grants paid to institution from **UCB Pharma** for participation as a clinical and research investigator, consulting fees from **UCB Pharma**.

UCB Pharma contributed to study design, participated in data collection, completed the data analysis, and participated in data interpretation. UCB Pharma also participated in writing, review, and approval of the manuscript. All authors had full access to the data, reviewed and approved the final version, and were responsible for the decision to submit for publication. A medical writing agency, employed by UCB Pharma, assisted with manuscript preparation under the authors' direction.

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