Bimekizumab: Network meta-analysis to establish comparative efficacy in moderate-to-severe hidradenitis suppurativa patients

P0193

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Objective

This network meta-analysis (NMA) assesses the efficacy of bimekizumab (BKZ) 320 mg every 2 weeks (Q2W) in moderate-to-severe hidradenitis suppurativa (HS) compared with approved biologic therapies at Week 12–16.

Background

- BKZ is a selective inhibitor of interleukin (IL)-17F in addition to IL-17A, that has recently demonstrated significant and rapid improvement in efficacy outcomes vs placebo for the treatment of moderate-to-severe HS.[1,2]
- A systematic literature review (SLR) and NMA have been conducted to establish the short-term efficacy of BKZ 320 mg Q2W compared with other approved biologic therapies for HS at Week 12–16.

Methods

Systematic literature review

- A SLR was conducted to identify randomised controlled trial (RCT) evidence on the efficacy of biologic therapies (BKZ, secukinumab [SEC], adalimumab, [ADA]) for the treatment of adult patients with HS, up to October 2023, in accordance with PRISMA.[1]

Network meta-analysis

- Efficacy outcomes of interest at Week 12–16 included improvement in HS Clinical Response with ≥50/≥75/≥90/100% reduction from baseline in abscesses and inflammatory nodule count, with no increase of abscesses or draining tunnel count (HiSCR50/75/90/100), and improvement from baseline in International Hidradenitis Suppurativa Severity Score System of ≥55% (IHS4-55).
- BKZ trial data were re-analysed to match intercurrent event handling and imputation strategies in the SEC trials, based on mNRI with rescue antibiotics for HS, and discontinuation due to adverse events or lack of efficacy as intercurrent events (HS-ABX) for the base case HiSCR outcomes. Data were only reported using NRI in ADA RCTs. IHS4-55 (base case) and HiSCR50 (sensitivity analysis) were also evaluated using NRI calculated from observed data from the BKZ and SEC trials.
- Bayesian binomial models with a logit link were used to analyse binary outcomes; fixed- and random-effect models were explored and included placebo baseline risk adjustment for HiSCR outcomes; models were selected based on best model fit.
- Overall ranking is expressed as a surface under the cumulative ranking curve (SUCRA) value ranging from 0–100%, with higher values indicating higher ranked treatment.

Results

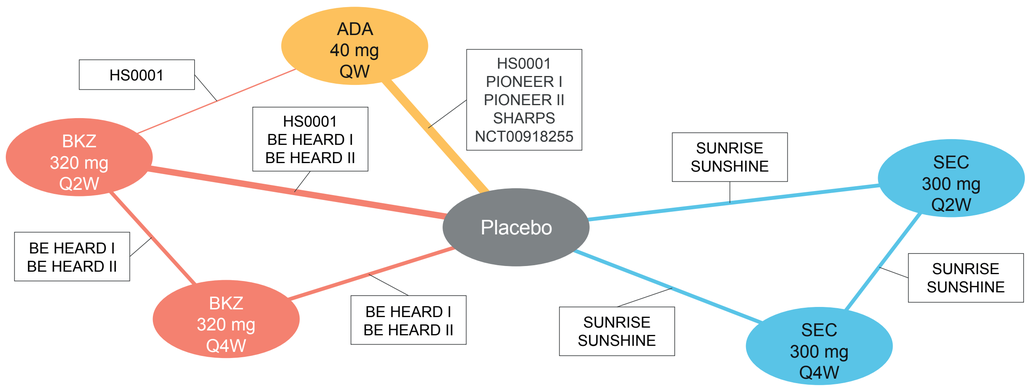
- Of the 11 trials identified by the SLR, nine RCTs reported outcomes of interest for the NMA for BKZ (320 mg Q2W)[2-4] and approved doses of SEC (300 mg Q2W or Q4W)[5] and of ADA (40 mg QW)[6-9] (**Figure 1**).
- The most comprehensive network was a global network population, which comprised all studies and patients with relevant outcome data, regardless of previous biologic therapy exposure status and consisting of predominantly biologic-naïve patients (**Table 1**).
- BKZ Q2W ranked first across all outcomes based on the SUCRA (**Figure 2**).
  - Patients treated with BKZ showed significantly better odds of achieving HiSCR50, HiSCR100, and IHS4-55 compared with SEC, and numerically higher odds compared with ADA.
  - Patients treated with BKZ had statistically significantly higher odds of achieving HiSCR75 and HiSCR90 compared with SEC and ADA.
- Consistent with the base case analysis, sensitivity analysis of HiSCR50 (NRI) showed that patients treated with BKZ Q2W had higher odds of achieving HiSCR50 compared with all other treatments; the comparisons vs both SEC Q4W and Q2W were statistically significant.

Conclusion

BKZ 320 mg Q2W achieved significantly higher response rates at Week 12–16 for all HiSCR outcomes and IHS4-55 compared with approved doses of SEC (300 mg Q2W and Q4W), and significantly higher response rates for HiSCR75/90 compared with ADA (40 mg QW). BKZ 320 mg Q2W ranked first for all efficacy outcomes analysed.

This NMA assessed up-to-date efficacy data for BKZ, SEC, and ADA for the treatment of moderate-to-severe HS, and is the first to standardise imputation methods and account for intercurrent events.

Figure 1 Evidence networks for predominantly biologic-naïve patients with HS



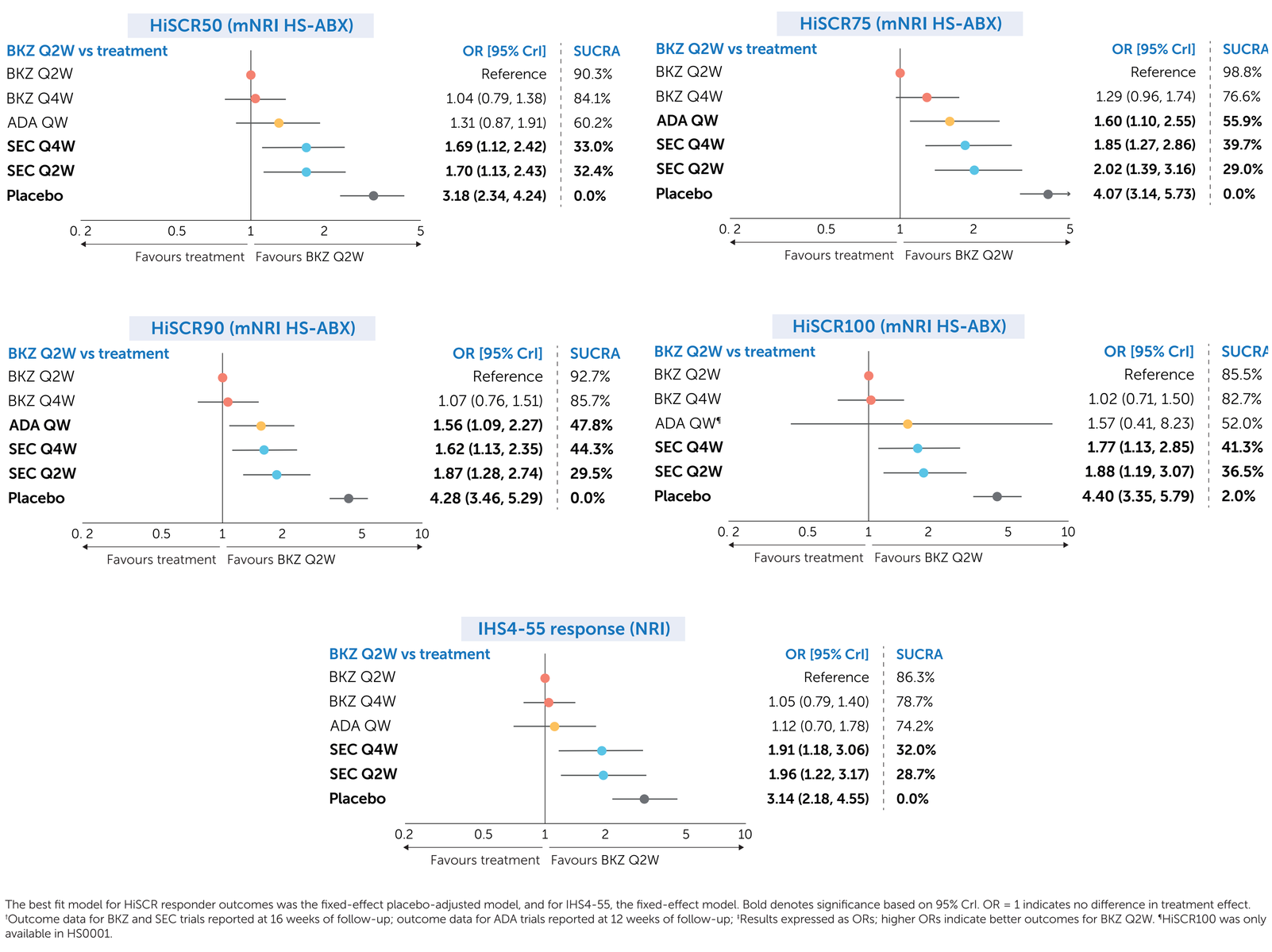
Note: SEC Q2W dose recommended if a patient does not adequately respond to SEC Q4W.

Table 1 Baseline background, demographic, and disease characteristics of patients included in the NMA (N=9)

Characteristics	HS0001	BE HEARD I	BE HEARD II	PIONEER I	PIONEER II	NCT00918255†	SHARPS	SUNRISE	SUNSHINE
Intervention	BKZ vs ADA vs PBO	BKZ vs PBO	BKZ vs PBO	ADA vs PBO	ADA vs PBO	ADA vs PBO	ADA vs PBO	SEC vs PBO	SEC vs PBO
N	90	505	509	307	326	102	206	543	541
Age, mean (SD) years	36.7 (12.0)	36.7 (12.0)	36.6 (12.4)	37.0 (11.1)	35.5 (11.2)	36.5 (11.4)	37.6 (11.3)	36.3 (11.4)	36.1 (11.7)
BMI, mean (SD)	34.8 (8.4)	33.8 (8.2)	32.3 (8.0)	33.8 (7.8)	32.1 (7.7)	NR (NR)	32.1 (7.1)	31.8 (7.6)	32.5 (7.6)
AN count, mean (SD)	17.7 (14.8)	16.0 (17.5)	16.5 (14.6)	14.4 (13.4)	11.3 (9.7)	NR (NR)	10.8 (10.3)	13.3 (9.1)	12.8 (8.8)
Abscesses, mean (SD)	4.8 (5.1)	3.8 (6.9)	3.2 (5.3)	2.7 (3.6)	2.2 (3.0)	1.7 (NR)	2.6 (5.1)	3.3 (4.9)	2.8 (4.0)
DT count, mean (SD)	5.1 (4.9)	3.8 (4.8)	3.4 (3.7)	4.2 (4.8)	3.4 (4.7)	4.5 (NR)	3.8 (4.7)	2.7 (3.4)	2.6 (3.4)
HS duration, years, mean (SD)	9.0 (8.0)	9.0 (8.3)	7.0 (7.1)	9.1 (NR)‡	9.5 (NR)‡	12.4 (9.8)	10.9 (9.8)	7.4 (7.4)	7.2 (7.3)
Male, %	31.0	37.0	49.3	36.2	32.2	29.4	49.0	43.6	43.8
White, %	67.8	77.8	81.5	76.2	83.7	72.5	94	76.4	79.5
Current smokers, %	NR	43.0	48.1	56.4	65.6	57.8	68	54.0	54.0
Hurley III, %	51	49.7	38.9	47.6	46.3	29.4	48	40.5	34.0
Prior systemic biologic therapy, %	0.0§	25.1	13.0	0.0††	0.0††	0.0††	NR	23.2	23.8

†Unlicensed ADA arm is excluded from summaries for NCT00918255; ‡Median reported rather than mean; ¶From clinicaltrials.gov record; §Patients were eligible if they had not received prior IL-17 or TNFα inhibitor; ††Patients were eligible if they had not received prior TNFα inhibitor treatment

Figure 2 BKZ vs comparators for HiSCR50/75/90/100 (mNRI HS-ABX), IHS4-55 (NRI) at Week 12–16† (ORs [95% CrI]‡ and SUCRA values)



The best fit model for HiSCR responder outcomes was the fixed-effect placebo-adjusted model, and for IHS4-55, the fixed-effect model. Bold denotes significance based on 95% CrI. OR = 1 indicates no difference in treatment effect. †Outcome data for BKZ and SEC trials reported at 16 weeks of follow-up; outcome data for ADA trials reported at 12 weeks of follow-up; ‡Results expressed as ORs; higher ORs indicate better outcomes for BKZ Q2W. ¶HiSCR100 was only available in HS0001.

Limitations

- Heterogeneity observed within the study design and trial patient populations, such as prior systemic biologic therapy (**Table 1**).
- Short-term efficacy analyses (12–16 weeks).
- ADA trials were older and conducted in a different treatment landscape compared with the more recent BKZ and SEC trials.
- Quantitative analyses of safety and tolerability were not performed due to small event numbers and resulting instability in treatment effects.
- Methods were aligned between BKZ and SEC trials, but not with ADA due to data being reported using NRI in ADA RCTs. Despite this, the HiSCR50 sensitivity analysis supported the base case findings.

Abbreviations: ABX, antibiotics; ADA, adalimumab; BKZ, bimekizumab; BMI, body mass index; CrI, credible interval; DT, draining tunnel; HiSCR, Hidradenitis Suppurativa Clinical Response; HiSCR50/75/90/100, HS Clinical Response of ≥50%/≥75%/≥90%/100%; HS, hidradenitis suppurativa; IHS4-55, International Hidradenitis Suppurativa Severity Score System improvement of ≥55%; IL, interleukin; mNRI, modified non-responder imputation; NMA, network-meta analyses; NRI, non-responder imputation; OR, odds ratio; PBO, placebo; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; QW, once every week; Q2W, once every 2 weeks; Q4W, once every 4 weeks; RCT, randomised controlled trial; SD, standard deviation; SEC, secukinumab; SLR, systematic literature review; SUCRA, surface under the cumulative ranking curve; TNF, tumour necrosis factor; vs, versus.

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