A network meta-analysis of cumulative clinical benefit of anti-IL biologics for the treatment of moderate to severe psoriasis over 48–52 weeks

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Objectives

To perform a network meta-analysis (NMA) to assess cumulative benefits over one year of bimekizumab (BKZ) vs anti-interleukin (IL)-17A, anti-IL-23, and anti-IL-12/23 therapies, in the treatment of moderate to severe plaque psoriasis.

Introduction

- Although BKZ in plaque psoriasis phase 3/3b studies provide head-to-head comparisons to secukinumab (SEC), adalimumab (ADA), and ustekinumab (UST),[1–3] there are no assessments of BKZ vs other anti-ILs.
- Examining cumulative treatment benefit over time, rather than focusing on individual timepoints, can help assess a treatment's efficacy profile in a broader sense,[4] capturing elements of speed and durability of responses.

Materials and Methods

- A previously conducted systematic literature review (July 2020) was used to identify randomised controlled trials of comparator biologics of interest (**Table 1**).
- Cumulative clinical benefit was measured by area under the curve (AUC) analyses of published figures showing the proportions of patients achieving 100% improvement from baseline in Psoriasis Area and Severity Index (PASI 100) over 48–52 weeks of treatment (all normalised to 52 weeks).
- A fixed-effects Bayesian NMA model of continuous endpoints with normal likelihood and identity link was selected based on goodness of fit, to compare cumulative clinical benefit between treatments at Weeks 48–52. This was conducted using R V4.0.1 software with the BUGSnet package.
- Results are expressed as the number of cumulative days that patients achieved PASI 100 (with 95% credible intervals [CrI]), and as the differences in these values (with 95% CrIs) for all treatment comparisons.
- BE SURE, BE VIVID, and BE RADIANT data were included for BKZ; BKZ-treated patients were dosed 320 mg every 4 weeks throughout (Q4W/Q4W) or switched to every 8 week dosing from Week 16 onwards (Q4W/Q8W). On-label doses of comparators were included.
- Treatment ranks were based on surface under the cumulative ranking curves (SUCRA).

Results

- Ten head-to-head studies and six comparators alongside BKZ were included in the NMA, totalling 5,177 patients (**Figure 1**).
- NMA-adjusted cumulative number of days with PASI 100 over one year was calculated for each treatment, based on AUC data **(Figure 2)**.
- Among assessed treatments, BKZ Q4W/Q4W and Q4W/Q8W showed similar results, ranking first and second with 186 days and 184 days of PASI 100 achievement, respectively. Risankizumab (RZB: 175 days) and ixekizumab (IXE: 156 days) followed in third and fourth (**Figure 2**).
- Patients treated with BKZ achieved clear skin for significantly more days over one year vs brodalumab (BRO), guselkumab (GUS), SEC, and UST (**Table 2**); patients had 19%, 31%, 44% and 101% more days of clear skin with BKZ Q4W/Q8W, respectively.
- BKZ-treated patients also achieved clear skin for numerically more days than RZB and IXE (**Table 2**).

Defining the AUC

An NMA was conducted to compare cumulative clinical benefit, measured by AUC analyses.

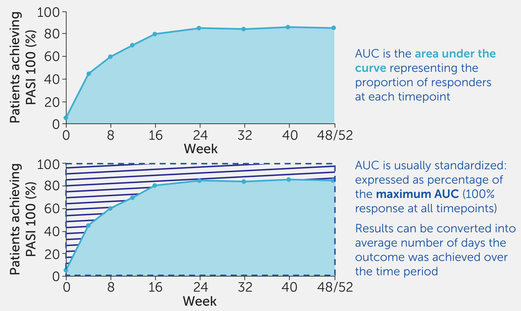
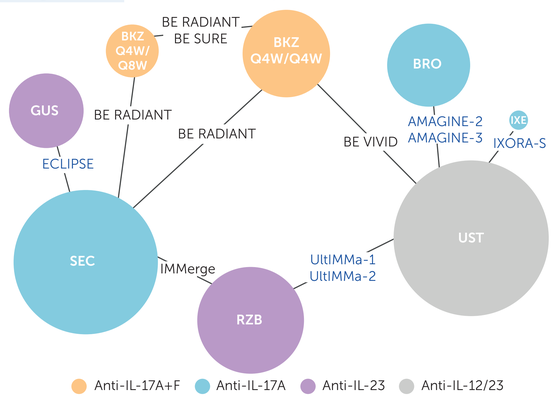


Figure 1 Network diagram



Node diameter is proportional to the number of patients treated with each biologic of interest in the trials included in this NMA: 6 involving UST; 3 BKZ; 3 RZB; 3 SEC; 2 BRO; 1 GUS; 1 IXE. Values were estimated from published figures for the UltiMMa-1, -2, AMAGINE 2, 3, IXORA-S, and ECLIPSE trials (blue text), in order to calculate the AUC. BKZ dosed 320 mg Q4W throughout (Q4W/Q4W), or switched to Q8W dosing from Week 16 (Q4W/Q8W). BRO dosed 210 mg at Weeks 0, 1, and 2, then 210 mg Q2W. GUS dosed 100 mg at Weeks 0 and 4, then Q8W. IXE dosed 160 mg at Week 0, 80 mg Q2W to Week 12, then Q4W. RZB dosed 150 mg at Weeks 0 and 4, then Q12W. SEC dosed 300 mg at Weeks 0, 1, 2, 3, and 4, then Q4W. UST dosed 45 mg or 90 mg (weight-based per label) at Weeks 0 and 4, then Q12W.

Table 1 Inclusion and exclusion criteria for the NMA

PICOS	Inclusion for Analysis	Exclusion Criteria
Population	• Adult (≥18 years) patients with moderate to severe chronic psoriasis with or without concomitant psoriatic arthritis (PsA) • Studies providing subgroup data for those with moderate to severe psoriasis	• Studies in patients primarily in PsA or with a treatment focus for PsA
Intervention/ Comparator	• Anti-IL-17A: BKZ, BRO, IXE, SEC • Anti-IL-23: GUS, RZB • Anti-IL-12/23: UST	• Studies in biosimilar compounds
Outcomes	• PASI 100[a] with non-responder imputation	• PASI 100 with other imputation methodology (e.g. observed cases or multiple imputation)
Study Design	• Randomised controlled trials without treatment switching after induction	• Observational/real-world evidence studies • Single-arm trials, open-label extensions or follow-up periods that are not randomised • Arms for which patients are re-randomised or have a planned treatment switch after induction
Timepoints	• Multiple assessments from baseline to Week 48–52	• Trials reporting a single timepoint at Week 48/52 • Total follow-up shorter than 48 weeks

When needed, values were estimated from published figures using the BormiSoft DigitizeIt software.
[a]PASI 100 is a clinically meaningful outcome for patients.[5]

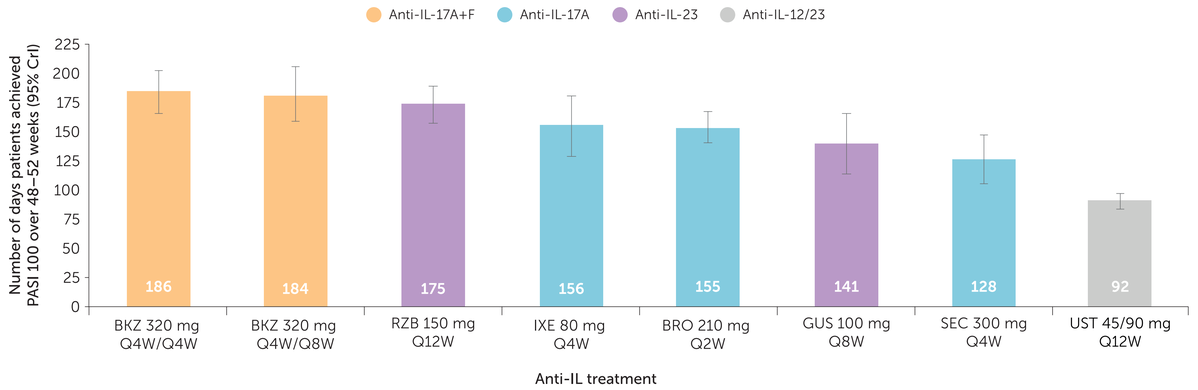
Table 2 Differences in average number of days patients achieved PASI 100 between biologic treatments

versus	BKZ Q4W/Q4W	BKZ Q4W/Q8W	RZB	IXE	BRO	GUS	SEC	UST
BKZ Q4W/Q4W	1.9 (-15.1, 18.8)							
BKZ Q4W/Q8W	11.0 (-10.4, 32.5) 7%	9.2 (-15.3, 33.6) 5%						
RZB	29.7 (-3.1, 62.0) 19%	27.9 (-7.7, 63.1) 18%	18.6 (-12.1, 49.3)					
IXE	**30.5 (7.2, 53.9) 20%**	**28.7 (1.2, 56.0) 19%**	19.5 (-1.4, 40.3)	0.8 (-28.5, 30.4)				
BRO	**45.4 (22.3, 68.4) 32%**	**43.6 (20.2, 66.7) 31%**	**34.3 (8.9, 59.8)**	15.6 (-21.6, 53.0)	14.8 (-14.7, 44.2)			
GUS	**58.5 (40.7, 76.3) 46%**	**56.7 (38.6, 74.6) 44%**	**47.5 (26.6, 68.3)**	28.8 (-5.4, 63.0)	**28.0 (2.2, 53.7)**	13.1 (-1.6, 28.0)		
SEC	**94.2 (75.1, 113.4) 103%**	**92.3 (68.7, 115.8) 101%**	**83.1 (67.3, 99.0)**	**64.4 (38.4, 90.6)**	**63.6 (50.2, 77.1)**	**48.8 (22.6, 75.1)**	**35.6 (13.9, 57.3)**	
UST								

Anti-IL-17A+F · Anti-IL-17A · Anti-IL-23 · Anti-IL-12/23

Values presented are the differences in number of days of clear skin (PASI 100) over a year of biologic treatment (95% CrI), with percentage increase in the number of days for each BKZ dose versus comparators. For example, on average, patients treated with BKZ Q4W/Q4W have 30.5 additional days of clear skin versus patients treated with BRO during the first year of treatment, an increase of 20%. Values in bold are statistically significant. Blue dashed arrows indicate how to read the table.

Figure 2 NMA-adjusted cumulative number of days patients achieved PASI 100 over one year of biologic treatment



Number of days patients achieved PASI 100 over 48–52 weeks (95% CrI). Only patients receiving the same compound for 48–52 weeks were included in these analyses.

ADA: adalimumab; **AUC:** area under the curve; **BKZ:** bimekizumab; **BRO:** brodalumab; **CrI:** credible interval; **GUS:** guselkumab; **IL:** interleukin; **IXE:** ixekizumab; **NMA:** network meta-analysis; **PASI 100:** 100% improvement from baseline in Psoriasis Area and Severity Index; **PICOS:** population, intervention, comparator, outcomes, and study design; **PsA:** psoriatic arthritis; **Q2W:** every 2 weeks; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **Q12W:** every 12 weeks; **RZB:** risankizumab; **SEC:** secukinumab; **SUCRA:** surface under the cumulative ranking curves; **UST:** ustekinumab.

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References: [1]Reich K et al. N Engl J Med 2021;385:142–52, NCT03536884; [2]Warren RB et al. N Engl J Med 2021;385:130–41, NCT03412747; [3]Reich K et al. Lancet 2021;397:487–98, NCT03370133; [4]Warren RB et al. J Am Acad Dermatol 2019;82:1138–49; [5]Strober B et al. J Am Acad Dermatol. 2016;75:77–82.e7; [6]Lebwohl M et al. Presented at EADV 2021, P1292; [7]Lebwohl M et al. Presented at IFPA, 35180. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **RBW, AA, ML, KG, CL, NNG, VT, SV, SK, AK;** Drafting of the publication, or revising it critically for important intellectual content: **RBW, AA, ML, KG, CL, NNG, VT, SV, SK, AK**; Final approval of the publication: **RBW, AA, ML, KG, CL, NNG, VT, SV, SK, AK**. **Author Disclosures: RBW:** Consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; research grants to his institution from AbbVie, Almirall, Janssen, LEO Pharma, Novartis, and UCB Pharma; honoraria from Astellas, DiCE, GSK, and Union. **AA:** Has served as a research investigator and/or scientific advisor to AbbVie, Almirall, Arcutis, ASLAN, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly, EPI, Incyte, Janssen, LEO Pharma, Nimbus, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sun Pharma, Sanofi, and UCB Pharma. **ML:** Employee of Mount Sinai and receives research funds from: AbbVie, Amgen, Arcutis, Avotres Therapeutics, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen Research & Development, LLC, Ortho Dermatologics, Regeneron, and UCB Pharma; consultant for Aditum Bio, Almirall, AltruBio Inc., AnaptysBio, Arcutis Inc., Aristea Therapeutics, Arrive Technologies, Avotres Therapeutics, BiomX, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant, Dr. Reddy's Laboratories, Evelo Biosciences, Evommune, Inc., Facilitatation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Helsinn Therapeutics, Hexima Ltd., LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Seanergy, and Verrica. **KG:** Received consulting fees from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, and UCB Pharma; research support from AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and UCB Pharma. **CL:** Speaker (honoraria) for AbbVie, Celgene, Eli Lilly, and Novartis; served as an investigator for AbbVie, Actavis, Amgen, Boehringer Ingelheim, Celgene, Coherus, Corrona, Dermira, Eli Lilly, Galderma, Glenmark, Janssen, LEO Pharma, Merck (MSD), Novartis, Novella, Pfizer, Sandoz, Stiefel, and Wyeth; served on scientific advisory boards for AbbVie, Amgen, Boehringer Ingelheim, Dermira, Eli Lilly, Janssen, LEO Pharma, Pfizer, Sandoz, UCB Pharma, and Vitae. **NNG:** Former employee and shareholder of UCB Pharma. **VT, SV, SK:** Employees of UCB Pharma. **AK:** Speaker (honoraria) or consulting fees from: AbbVie, Almirall, Beiersdorf, Biogen-Idec, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Hexal, Janssen-Cilag, LEO Pharma, MSD, Novartis, Pfizer, Sanofi, and UCB Pharma. **Acknowledgements:** These studies were funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to these studies. The authors acknowledge Susanne Wiegratz, MSc, UCB Pharma, Monheim, Germany for publication coordination, Poppy Wilson, MBiol, Costello Medical, London, UK for medical writing and editorial assistance and the Design team at Costello Medical for graphic design assistance. All costs associated with development of this poster were funded by UCB Pharma. RBW is supported by the NIHR Manchester Biomedical Centre.

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Conclusions

Reinforcing head-to-head results,[6,7] BKZ was associated with a greater cumulative benefit in patients with moderate to severe psoriasis compared to other anti-ILs.

Over one year, both BKZ doses were associated with patients achieving PASI outcomes for a numerically higher number of days than the comparators, and significantly more days than for BRO, GUS, SEC, and UST.