A matching-adjusted indirect comparison of the efficacy of bimekizumab and guselkumab at 52 weeks for the treatment of psoriatic arthritis

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Synopsis

- Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has shown efficacy and tolerability in patients with active psoriatic arthritis (PsA) for 52 weeks in two Phase 3 trials: BE OPTIMAL1 (NCT03895203) and BE COMPLETE2 (NCT03896581).
- Guselkumab (GUS), an IL-23 inhibitor, has demonstrated 48 to 52-week efficacy and safety in patients with PsA in the DISCOVER 2 (NCT03158285)[3] and COSMOS (NCT03796858)[4] Phase 3 trials.
- Due to the absence of direct comparison trials or control arms to compare the efficacy of BKZ and GUS in PsA, a matching-adjusted indirect comparison (MAIC) was conducted to evaluate the relative efficacy of BKZ 160 mg every 4 weeks (Q4W) compared to GUS 100mg Q4W or Q8W at 52 weeks in bio-n and tumor necrosis factor inhibitor-experienced (TNFi-exp) (Q8W only) patients with PsA.
- The EMA label for GUS recommends the Q4W dose for patients at higher risk of joint damage.[5]

Objective

To assess the 52-week comparative efficacy of BKZ 160 mg Q4W vs GUS 100 mg Q4/8W in patients with PsA who are biologic disease-modifying anti-rheumatic drug-naïve (bio-n) or TNFi-exp.

Methods

- Relevant trials were identified as part of a systematic literature review.[6]
- The MAIC method was followed in accordance with Signorovitch et al.[7] and the National Institute for Health and Care Excellence Decision Support Unit Technical Support Document 18 (NICE DSU TSD 18).[8]
- **Figure 1** shows how individual patient data (IPD) from BKZ trials were matched to GUS trials.
- BKZ trial patients were reweighted to match the baseline characteristics (**Table 1**) of the GUS trial patients; weights were determined using a logistic regression based on sex, age, methotrexate use (MTX), Health Assessment Questionnaire-Disability Index (HAQ-DI), proportion of patients with psoriasis affecting ≥3% body surface area (BSA ≥3%), swollen and tender joint counts (SJC/TJC), and time since PsA diagnosis. The adjustment variables were selected based on expert consensus (n=5).
- Recalculated BKZ 52-week outcomes for American College of Rheumatology (ACR) 20/50/70 and minimal disease activity (MDA) index (non-responder imputation [NRI]) were compared to GUS outcomes via non-placebo-adjusted comparisons and were reported as odds ratios (ORs). The likelihood of outcome (e.g., greater or worse) was determined by the exclusion of value 1 from the 95% CIs. All analyses were conducted with R version 3.6.2 using the program provided in the NICE DSU TSD 18.

Results

- In bio-n patients, the post-matching effective sample sizes (ESSs) for BKZ were 155 (36% of original sample size [OSS]) and 142 (33% of OSS) for the comparisons to GUS Q4W and Q8W, respectively (**Figure 2 A–B** and **Figure 3 A–B**).
- BKZ had a greater likelihood of achieving ACR50, ACR70 and MDA outcomes than GUS Q4W at 52 weeks.
- BKZ had a greater likelihood of achieving ACR70 and MDA outcomes than GUS Q8W at 52 weeks.
- In TNFi-exp patients, the post-matching ESS for BKZ was 181 (68% of OSS) for comparison to GUS Q8W (**Figure 2C** and **Figure 3C**).
- BKZ had a greater likelihood of achieving ACR20, ACR50, ACR70, and MDA outcomes than GUS Q8W at 52 weeks.
- The MAIC-adjusted ORs did not differ greatly to the unadjusted ORS for any outcome.

Conclusions

Using MAIC methodology, bio-n patients treated with BKZ had a higher probability of achieving higher treatment thresholds (ACR70 and MDA) compared to GUS Q4W and Q8W.

TNFi-exp patients treated with BKZ had a higher probability of achieving all ACR and MDA responses compared to those receiving GUS Q8W.

The MAIC findings at 52 weeks are consistent with a recent NMA suggesting better efficacy of BKZ against GUS on joint outcomes at 16 to 24 weeks.

Figure 1 Summary of MAIC method

- MAICs use IPD from trials of one treatment to match baseline aggregate statistics reported from trials of another treatment.
- By using an approach similar to propensity score weighting, treatment outcomes can be compared across balanced trial populations after matching.

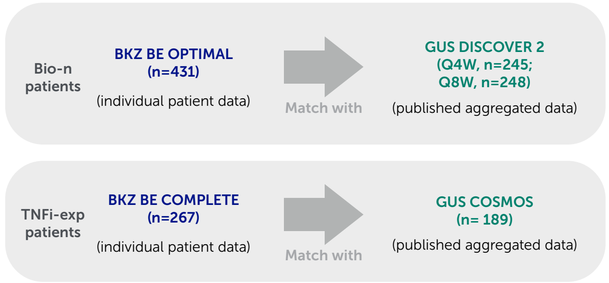
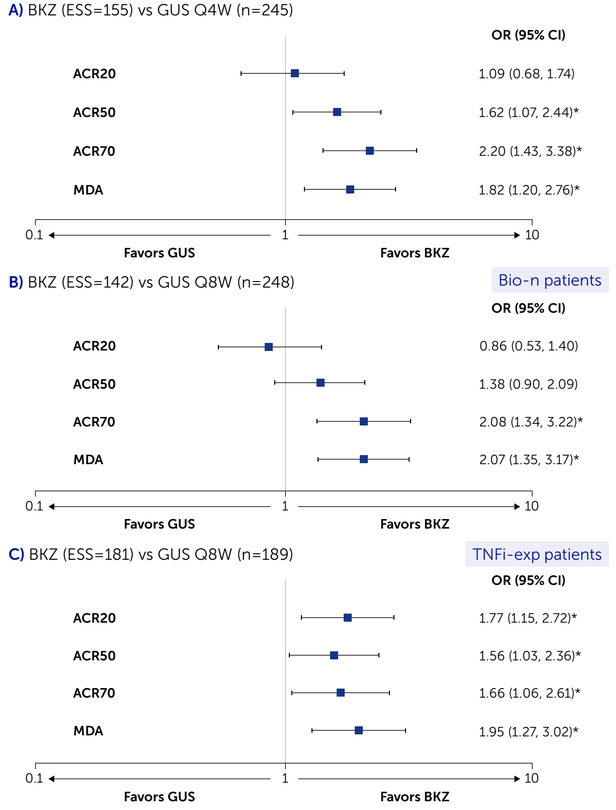


Table 1 Patient baseline characteristics before matching

Mean (SD) unless stated	Bio-n			TNFi-exp	
	BE OPTIMAL N=431	DISCOVER 2 Q4W N=245	DISCOVER 2 Q8W N=248	BE COMPLETE N=267	COSMOS Q8W N=189
Age, years	49 (13)	46 (12)	45 (12)	50 (12)	49 (12)
Male, %	47	58	52	49	46
Time since diagnosis, years	6.0 (7.3)	5.5 (5.9)	5.1 (5.5)	9.6 (9.9)	8.3 (7.8)
MTX use, %	59	69	69	45	Not reported
SJC (of 66 joints)	9.0 (6.2)	12.9 (7.8)	11.7 (6.8)	9.7 (7.5)	10.0 (7.0)
TJC (of 68 joints)	16.8 (11.8)	22.4 (13.5)	19.8 (11.9)	18.4 (13.5)	21.0 (13.0)
HAQ-DI score	0.82 (0.59)	1.2 (0.6)	1.3 (0.6)	0.97 (0.59)	1.3 (0.6)
BSA ≥3%, %	50	75	71	66	70

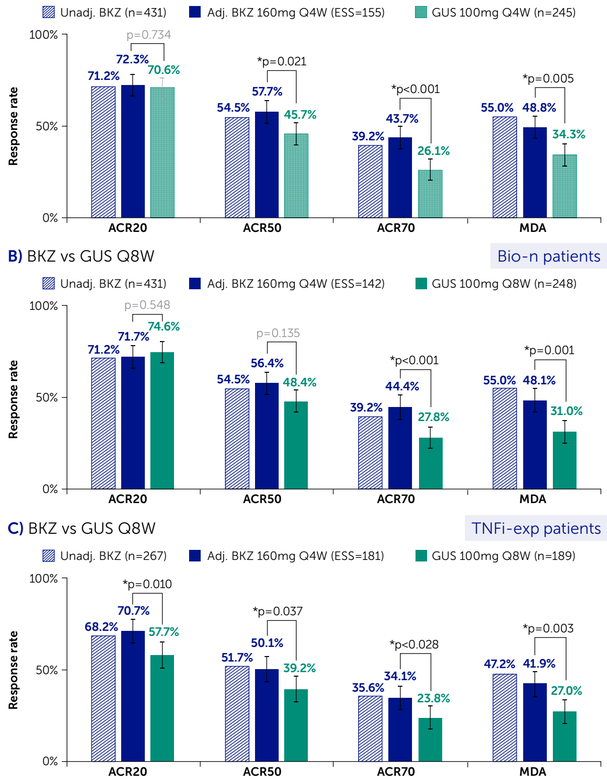
*Only 48-week efficacy data for GUS was available from the COSMOS trial.

Figure 2 Matching-adjusted odds ratio comparison of BKZ vs GUS at Week 52 (NRI)



A) BKZ 160 mg Q4W vs GUS 100 mg Q4W in bio-n patients with PsA, B) BKZ 160 mg Q4W vs GUS 100 mg Q8W in bio-n patients with PsA, C) BKZ 160 mg Q4W vs GUS 100 mg Q8W in TNFi-exp patients with PsA. *Indicates statistical significance. Figures show a logarithmic scale. No comparison for BKZ vs GUS Q4W in TNFi-exp patients due to the lack of reported outcomes for TNFi-exp patients using GUS Q4W.

Figure 3 Matching-adjusted response rates of BKZ vs GUS in patients with active PsA at Week 52 (NRI)



A) BKZ 160 mg Q4W vs GUS 100 mg Q4W in bio-n patients with PsA, B) BKZ 160 mg Q4W vs GUS 100 mg Q8W in bio-n patients with PsA, C) BKZ 160 mg Q4W vs GUS 100 mg Q8W in TNFi-exp patients with PsA. *Indicates statistical significance. No comparison for BKZ vs GUS Q4W in TNFi-exp patients due to the lack of reported outcomes for TNFi-exp patients using GUS Q4W.

ACR: American College of Rheumatology; **ACR20/50/70:** at least a 20/50/70% improvement in ACR response; **bio-n:** biologic disease-modifying anti-rheumatic drug-naïve; **BMI:** body mass index; **BKZ:** bimekizumab; **BSA:** body surface area; **CI:** confidence interval; **csDMARD:** conventional synthetic disease-modifying anti-rheumatic drug; **EMA:** European Medicines Agency; **ESS:** effective sample size; **GUS:** guselkumab; **HAQ-DI:** Health Assessment Questionnaire–Disability Index; **IL:** interleukin; **IPD:** individual patient data; **MAIC:** matching adjusted indirect comparison; **MDA:** minimal disease activity; **MTX:** methotrexate; **NICE DSU TSD 18:** National Institute for Health and Care Excellence Decision Support Unit Technical Support Document 18; **NMA:** network meta-analysis; **NRI:** non-responder imputation; **OR:** odds ratio; **PsA:** psoriatic arthritis; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SD:** standard deviation; **SJC:** swollen joint count; **TJC:** tender joint count; **TNFi-exp:** tumor necrosis factor inhibitor-experienced; **VAS:** visual analogue score; **Unadj:** unadjusted.

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