# A Matching-Adjusted Indirect Comparison of the Efficacy of Bimekizumab and Ixekizumab at 52 Weeks for the Treatment of Radiographic Axial Spondyloarthritis

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#### **Objective**

This matching-adjusted indirect comparison (MAIC) analysis assessed the relative efficacy of bimekizumab versus ixekizumab in patients with radiographic axial spondyloarthritis (r-axSpA) at Week 52.

# Background

- Bimekizumab, a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated consistent and sustained efficacy to Week 52 across the full spectrum of axSpA.<sup>1,2</sup>
- A previous network meta-analysis established similar relative efficacy for Assessment of SpondyloArthritis international Society (ASAS) outcomes at Weeks 12–16 with subcutaneous bimekizumab 160 mg every four weeks (Q4W), versus subcutaneous ixekizumab 80 mg Q4W, an IL-17A-only inhibitor, in patients with r-axSpA (i.e. ankylosing spondylitis<sup>3</sup>).<sup>4</sup>

### Methods

- Individual patient data from BE MOBILE 2 (bimekizumab 160 mg; NCT03928743; n=220) were matched to pooled summary data from COAST-V and COAST-W (ixekizumab 80 mg following starting dose at Week 0; NCT02696785, NCT02696798; n=195) (**Table 1**).
- COAST-V and COAST-W trials were conducted in TNFi-naive and TNFi-experienced patients, respectively; 16.7% of patients in BE MOBILE 2 were TNFi-experienced (Table 1).
- To adjust for cross-trial differences, patients from BE MOBILE 2 were reweighted to match baseline characteristics in the ixekizumab trials. The target population is therefore that of the COAST-V/COAST-W trials.
- Weights, determined by propensity score, were based on age, sex, ethnicity, previous TNFi exposure, weight, time from diagnosis and baseline ASDAS and BASFI.
- These were identified as important effect modifiers and prognostic factors by clinician consensus and literature review, but are limited to those characteristics reported by the COAST trials.
- 52-week outcomes were recalculated for ASAS20. ASAS40, BASDAI50 and BASDAI change from baseline as pre-specified outcomes for this MAIC.
- Odds ratios (OR) or mean differences (MD) were estimated alongside 95% confidence intervals (CI) based on robust sandwich estimates of the standard error. Effective sample size (ESS) was estimated to assess the overlap between BE MOBILE 2 and COAST-V/COAST-W trial populations.
- These analyses followed the MAIC methodology described by Signorovitch et al.,<sup>5</sup> in accordance with the NICE Decision Support Unit Technical Support Document 18.6

#### Results

• With bimekizumab (ESS=45), patients may have a significantly greater likelihood of achieving ASAS20 (p=0.023), ASAS40 (p=0.035), BASDAI50 (p=0.025), and of achieving greater reductions from baseline in BASDAI (p=0.042) than with ixekizumab at Week 52 (Figure 1, Figure 2 and Table 2).

#### Limitations

- The reduced ESS for bimekizumab following reweighting (ESS=45, reduced from N=220 [20.5%]) indicates limited overlap between trial populations, likely due to the higher number of patients with previous TNFi exposure included for ixekizumab.
- An unanchored MAIC analysis does not utilise a common control arm or randomisation to balance effect modifiers and prognostic factors, and bias can result from unreported but important characteristics.

## Conclusions

Patients with r-axSpA treated with bimekizumab 160 mg Q4W may have a significantly greater likelihood of long-term response in ASAS and BASDAI outcomes versus ixekizumab 80 mg Q4W at Week 52, but analyses were limited by poor overlap in trial populations and potential bias from unreported effect modifiers and prognostic factors.

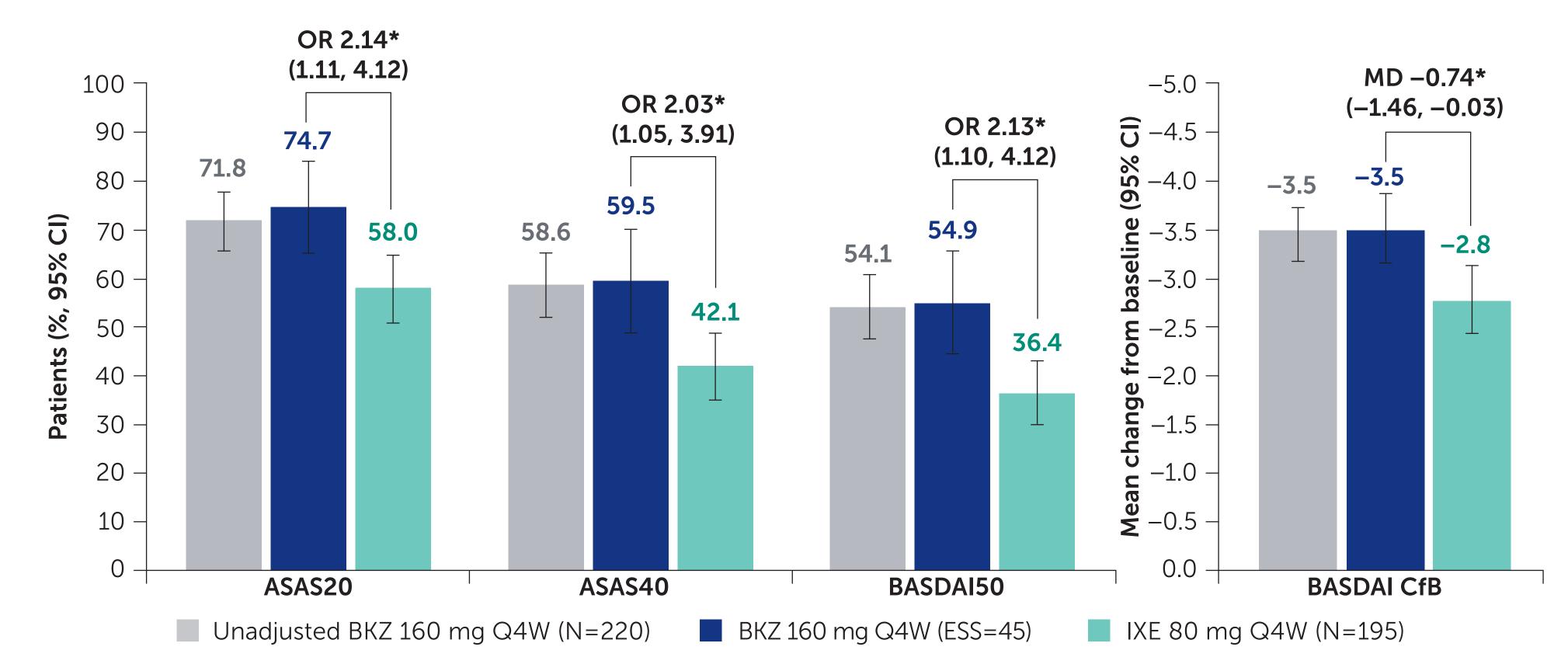
#### **Methodology Summary** Unbalanced trial populations **Balanced MAIC populations** Apply weights based on baseline: Recalculate BE MOBILE 2 Age, sex, ethnicity, previous TNFi exposure, weight, (ESS=45) outcomes time from diagnosis, ASDAS and BASFI **Bimekizumab Ixekizumab** Bimekizumab **Ixekizumab** 160 mg Q4W 160 mg Q4W 80 mg Q4W 80 mg Q4W ASAS20 BE MOBILE 2 COAST-V and COAST-V and BE MOBILE 2 (N=221)COAST-W (N=195)COAST-W (N=195)(ESS=45)ASAS40 BASDAI50 BASDAI change from baseline Compare reweighted bimekizumab versus ixekizumab efficacy outcomes at Week 52

Table 1 Baseline characteristics of patients with r-axSpA in relevant BKZ and IXE randomised controlled trials

Trial	Unadjusted BE MOBILE 2	Adjusted BE MOBILE 2	Unadjusted COAST-V	Unadjusted COAST-W
Treatment	<b>BKZ 160 mg Q4W</b>	BKZ 160 mg Q4W	IXE 80 mg Q4W	IXE 80 mg Q4W
N	221	45	81	114
Age, years, mean (SD)	41.0 (12.1)	44.7 (12.9)	41.0 (12.1)	47.4 (13.4)
Male, %	72.4	81.5	84	79.8
White, %	80.1	73.7	64	80.5
Previous TNFi exposure, %	16.7	58.5	0	100
Weight, kg, mean (SD)	80.0 (19.1)	82.2 (18.1)	77.6 (14.7)	85.5 (20.2)
Time from diagnosis, years, mean (SD)	6.7 (8.3)	9.4 (8.6)	8.3 (9.6)	10.1 (7.8)
ASDAS, mean (SD)	3.7 (0.8)	4.0 (0.8)	3.7 (0.7)	4.2 (0.9)
BASFI, mean (SD)	5.3 (2.2)	6.9 (1.8)	6.1 (1.8)	7.4 (1.8)

Only matching variables are reported. Unadjusted values reported as presented in the published trial manuscripts.

Adjusted outcomes for BKZ vs IXE at Week 52 Figure 1

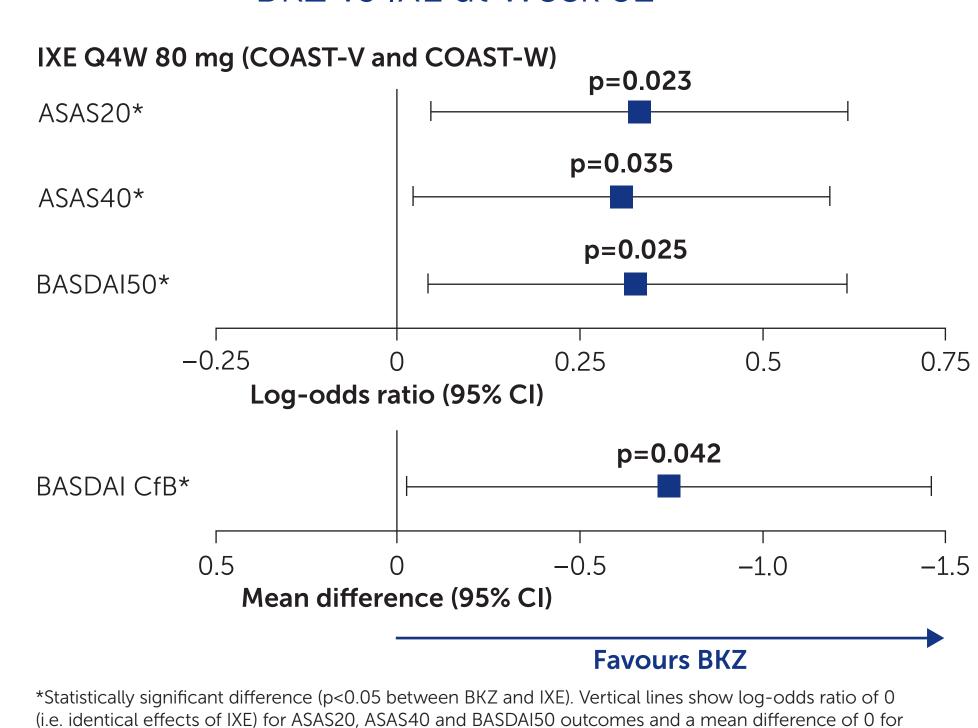


\*Statistically significant difference (p<0.05 between BKZ and IXE). Error bars represent 95% CI

Table 2 Unadjusted response rates for IXE at Week 52

	Unadjusted COAST-V	Unadjusted COAST-W
Treatment	IXE 80 mg Q4W	IXE 80 mg Q4W
N	81	114
<b>ASAS20</b> , % (95% CI)	65.4 (54.9, 76.0)	52.6 (43.4, 61.9)
<b>ASAS40</b> , % (95% CI)	53.1 (42.1, 64.1)	34.2 (25.4, 43.0)
<b>BASDAI50</b> , % (95% CI)	49.4 (38.3, 60.4)	27.2 (18.9, 35.5)
BASDAI CfB, mean (95% CI)	-3.3 (-3.9, -2.8)	-2.4 (-2.9, -2.0)

Figure 2 Odds ratios for relevant outcomes for BKZ vs IXE at Week 52



BASDAI CfB. Error bars represent 95% Cl.

**ASAS:** Assessment of SpondyloArthritis international Society; **ASAS20/40:** ASAS  $\geq$ 20/40% improvement; **ASDAI:** Bath Ankylosing Spondylitis Disease Activity Index; **BASDAI50:**  $\geq$ 50% improvement in BASDAI; **BASFI:** Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; CfB: change from baseline; CI: confidence interval; ESS: effective sample size; IL: interleukin; IXE: ixekizumab; MAIC: matching-adjusted indirect comparison; MD: mean difference; NICE: National Institute of Health and Care Excellence; OR: odds ratio; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; SD: standard deviation; TNFi: tumour necrosis factor inhibitor.

