Comparative Efficacy of Bimekizumab in Biologic/Targeted Synthetic DMARD-Naïve Patients with Axial Spondyloarthritis: Results from a Systematic Literature Review and Network Meta-Analysis

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Presented at ISPOR 2023 | May 7–10 | Boston, MA

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Objective

This network meta-analysis (NMA) assesses the efficacy of bimekizumab 160 mg/4 weeks (Q4W) in non-radiographic axial spondyloarthritis (nr-axSpA) and ankylosing spondylitis (AS) compared with approved biologic/targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs).

Background

- Axial spondyloarthritis (axSpA) is an inflammatory rheumatic disease that affects the axial skeleton, causing severe pain, stiffness, and fatigue.[1] axSpA comprises nr-axSpA and AS, also known as radiographic axSpA.[2]
- Non-steroidal anti-inflammatory drugs (NSAIDs) are the first line of pharmacological treatment. Following NSAID failure/intolerance/contraindication, available therapies include b/tsDMARDs; tumour necrosis factor alpha (TNF-α), interleukin (IL)-17A, and Janus kinase (JAK) inhibitors.[3]
- Bimekizumab is a selective inhibitor of IL-17F in addition to IL-17A, that has recently demonstrated significant and rapid improvements in efficacy outcomes vs placebo in patients with nr-axSpA and AS (BE MOBILE 1 and BE MOBILE 2 Phase 3 trial programme).[4]

Methods

Systematic literature review and feasibility assessment

- A systematic literature review (SLR) was conducted to identify randomized placebo-controlled trials in axSpA up to April 2022 (in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA] guidelines).
- Two reviewers performed screening and data extraction; any conflicts between reviewers were resolved via consensus.
- A feasibility assessment was performed to determine which of the identified trials were suitable for synthesis within a meta-analysis framework in either a predominantly (>50%) b/tsDMARD-naïve or b/tsDMARD-experienced network (Table 1).

Network meta-analysis

- Separate NMAs were run for the separate b/tsDMARD networks
- Bayesian fixed-effect (nr-axSpA) and fixed effect placebo-adjusted (AS) NMAs were conducted; models were selected based on best model fit.
- Efficacy outcomes at 12–16 weeks included Assessment in Spondyloarthritis International Society (ASAS) partial remission (PR), ASAS20, and ASAS40 response rates.
- Due to the proven efficacy of TNF-α inhibitors in axSpA, TNF-α inhibitors were pooled as a single drug class.[5]
- Results are presented as odds ratios (OR) and 95% credible intervals (CrI), and overall ranking is expressed as a surface under the cumulative ranking curve (SUCRA) value ranging from 0 to 100%, with higher values indicating higher ranked treatments.

Results

Of the 62 trials identified by the SLR:

- 33 trials were available for the predominantly b/tsDMARD-naïve network **(Figure 1)**
  - In nr-axSpA, 9 trials reported ASAS PR, and 10 reported ASAS20 and ASAS40
  - In AS, 16 trials reported ASAS PR, 23 reported ASAS20, and 21 reported ASAS40
- 10 trials were available for the b/tsDMARD-experienced network
  - The network was not feasible for nr-axSpA (n=2 trials)
  - In AS, 6 trials reported ASAS PR, 8 reported ASAS20, and 8 reported ASAS40

Predominantly b/tsDMARD-naïve (~90% of patients were b/tsDMARD-naïve in this network)

- nr-axSpA (n=10)
  - Bimekizumab was ranked first of six comparators for ASAS PR (77%), first of seven (92%) for ASAS20, and second of seven (76%) for ASAS40 **(Figure 2)**.
  - Bimekizumab was associated with significantly higher ASAS20 vs secukinumab 150 mg no LD (OR 2.18, 95% CrI: 1.13, 4.24) and secukinumab 150 mg with LD (OR 2.31, 95% CrI: 1.20, 4.53).
- AS (n=23)
  - Bimekizumab ranked third of seven comparators (79%) for ASAS PR, and fourth of eight for ASAS20 (57%) and ASAS40 (58%) **(Figure 2)**.
  - ASAS PR was significantly higher with bimekizumab vs secukinumab 150 mg with LD (OR 1.65, 95% CrI: 1.08, 2.51), and ASAS40 was significantly higher with bimekizumab vs secukinumab 150 mg no LD (OR 1.60, 95% CrI: 1.00, 2.60).

No other significant differences between bimekizumab and comparators were observed for either nr-axSpA or AS.

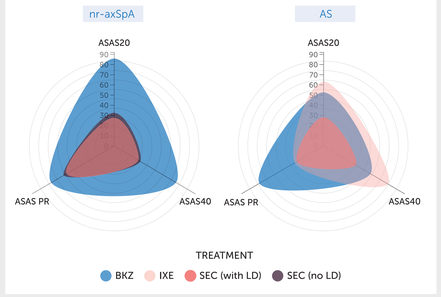
b/tsDMARD-experienced (100% of patients were b/tsDMARD-experienced in this network)

- nr-axSpA: network not feasible
- AS (n=8)
  - Bimekizumab was ranked second of seven comparators for ASAS20 (65%) and fourth of seven for ASAS40 (63%). The network was not feasible for ASAS PR **(Table 2)**.

Summary

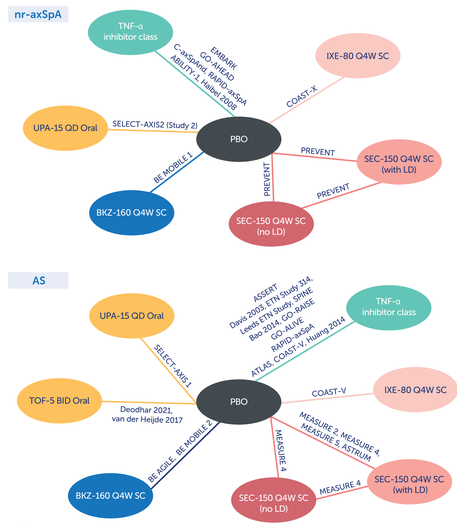
- This NMA synthesises available efficacy evidence for approved b/tsDMARDs in patients with nr-axSpA or AS.
- Bimekizumab achieved significantly higher response rates compared with secukinumab 150 mg for ASAS40 and ASAS PR in AS, and ASAS20 in nr-axSpA, ranking highly in nr-axSpA. It was associated with similar response rates compared with other b/tsDMARDs.
- SUCRA values are presented below for ASAS PR, ASAS20, and ASAS40 for bimekizumab and IL-17A inhibitors (secukinumab and ixekizumab [latter only for AS due to data availability]), with higher values on the chart indicating a higher treatment ranking.

Radar charts of SUCRA values for bimekizumab and IL-17A inhibitors in nr-axSpA and AS for ASAS PR, ASAS20, and ASAS40[†‡¶]



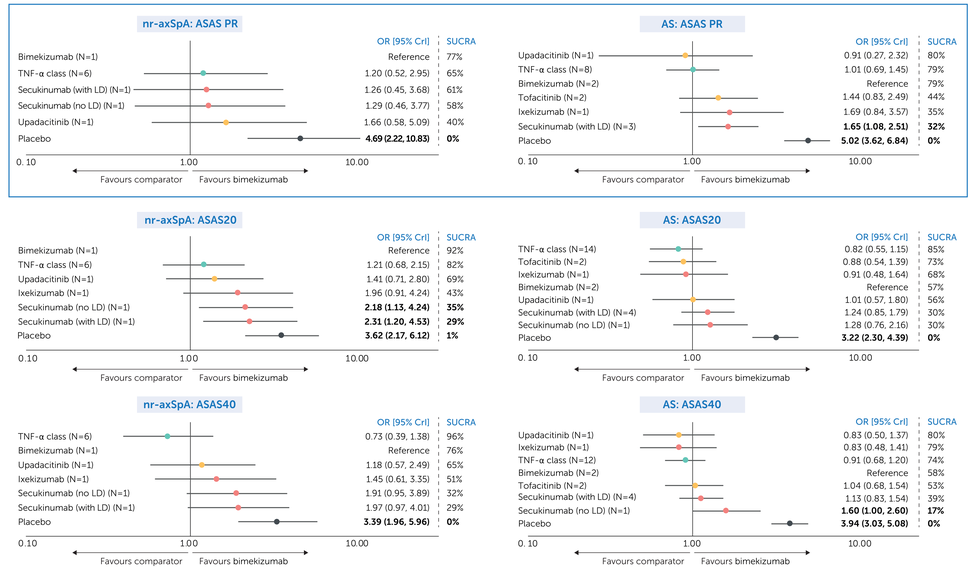
[†]The chart axis represents the SUCRA value and individual spokes denote the results for each outcome (ASAS PR, ASAS20, and ASAS40); [‡]SUCRA values are missing for IXE in the nr-axSpA network and SEC (no LD) in the AS network; [¶]The chart presents SUCRA values for bimekizumab and IL-17A inhibitors (secukinumab and ixekizumab [latter only for AS due to data availability]); please see SUCRA values in individual forest plots for bimekizumab's ranking compared with other analysed b/tsDMARDs (TNF-α and JAK inhibitors).

Figure 1 Evidence networks for ASAS40 in nr-axSpA and AS – predominantly b/tsDMARD-naïve network[†‡]



[†]Presented network diagrams are for ASAS40 outcomes in the predominantly b/tsDMARD-naïve network. Interventions in the TNF-α inhibitor class for nr-axSpA are ETN-25 BIW or 50 QW SC, GOL-50 Q4W SC, CZP-200 Q2W or 400 Q4W SC, and ADA-40 Q2W SC. Interventions in the TNF-α inhibitor class for AS are IFX-5 IV Q6W, ETN-25 BIW or 50 QW SC, GOL-50 Q4W SC, GOL-2Q8W IV, CZP-200 Q2W or 400 Q4W SC, and ADA-40 Q2W SC.

Figure 2 Bimekizumab vs comparators for ASAS PR, ASAS20, and ASAS40 – predominantly b/tsDMARD-naïve network (ORs [95% CrI] and SUCRA values)[†‡]



[†]Results expressed as ORs; higher ORs indicate better outcomes for bimekizumab. Bold denotes significance based on 95% CrI; [‡]N numbers refer to number of trials.

Table 1 Eligibility criteria for study inclusion in the NMA[†]

	Inclusion criteria	Exclusion criteria/comment
Population	Adult patients (≥18 years) with nr-axSpA or AS, who have an inadequate response to, intolerance of, or contraindication to NSAID therapy • **Predominantly b/tsDMARD-naïve network:** >50% patients b/tsDMARD-naïve[¶] • **b/tsDMARD-experienced network:** 100% patients b/tsDMARD-experienced[‡]	• Studies in NSAID-naïve patients, or those still receiving their first NSAID were excluded[††] • Studies with mixed nr-axSpA and AS populations were excluded if subgroup data not reported separately
Interventions[‡‡]	IL-17 inhibitors • Bimekizumab 160 mg Q4W • IXE 80 mg Q4W • SEC 150 mg Q4W (with or without an initial 150 mg QW loading dose at Weeks 0, 1, 2, 3 and 4; referred to as 'with LD' or 'no LD', respectively)	• Brodalumab was excluded as only licensed for axSpA in Japan and limited published trial data • In AS, marketing authorisation allows for an increase in the SEC dose to 300 mg Q4W, however this is conditional on prior clinical response to the SEC 150 mg; SEC 300 mg is not yet licensed for nr-axSpA
	TNF-α inhibitors: • ADA 40 mg Q2W • CZP 200 mg Q2W or 400 mg Q4W • ETN 50 mg QW or 25 mg BIW • GOL 50 mg Q4W SC or 2 mg/kg Q8W IV • IFX 5 mg IV Q6W	Biosimilars were excluded
	JAK inhibitors • TOF 5 mg BID oral • UPA 15 mg QD oral	Filgotinib was excluded as Phase 3 trials have been withdrawn and the drug development programme terminated at the time of analysis[6,7]
	Aforementioned treatments may be administered in conjunction with conventional care without biologic treatment	–
Comparators[‡‡]	Above interventions or PBO	PBO assumed to represent conventional care without biologic treatment, given that patients may be receiving background treatment in addition to the study drug
Outcomes	ASAS PR, ASAS20, ASAS40	Outcomes measured at 12–16 weeks and prior to any treatment arm cross-over
Study design	Placebo or active controlled RCTs with ≥10 patients randomized to treatment arm (or subgroup)	• Minimum of 12 weeks follow-up and up to 16 weeks • Outcome data at timepoints after cross-over are excluded

[†]NMA eligibility criteria were applied to studies identified in the SLR to ensure that the trial data could be synthesised within a meta-analysis framework. This poster presents key ASAS outcomes; [‡]Or it can reasonably be assumed that >50% of patients were bDMARD-naïve; [¶]Or the trial reported subgroup data for b/tsDMARD-naïve patients; [††]Or the trial reported subgroup data for b/tsDMARD-experienced patients; [‡‡]If the publication is unclear, it is assumed that patients participating in RCTs for IL-17, TNF-α, or JAK inhibitors will have failed on ≥1 NSAID; [§§]Doses/schedule as per marketing authorisation/pending marketing authorisation.

Abbreviations: ADA: adalimumab; ASAS: Assessment in Spondyloarthritis International Society; AS: ankylosing spondylitis; BID: twice daily; BIM: twice-weekly; BIW: twice weekly; BKZ: bimekizumab; b/tsDMARD: biologic/targeted synthetic disease-modifying antirheumatic drugs; CrI: credible interval; CZP: certolizumab pegol; ETN: etanercept; GOL: golimumab; IFX: infliximab; IL: interleukin; IV: intravenous; IXE: ixekizumab; JAK: Janus kinase; LD: loading dose; NMA: network meta-analysis; nr-axSpA: non-radiographic axial spondyloarthritis; NSAID: non-steroidal anti-inflammatory drug; OR: odds ratio; PBO: placebo; PR: partial remission; QD: once daily; QW: once weekly; QXW: every X weeks; RCT: randomized controlled trial; SC: subcutaneous; SEC: secukinumab; SUCRA: surface under the cumulative ranking curve; TNF-α: tumour necrosis factor alpha; TOF: tofacitinib; UPA: upadacitinib.

Table 2 Odds ratios and SUCRA values for ASAS20 and ASAS40 in b/tsDMARD-experienced patients with AS[†]

Treatment	ASAS20		ASAS40[‡]	
	OR (95% CrI)	SUCRA	OR (95% CrI)	SUCRA
Upadacitinib	0.81 (0.31, 2.27)	84%	0.84 (0.40, 1.80)	76%
Bimekizumab	Reference	65%	Reference	63%
Secukinumab (no LD)	1.04 (0.30, 3.86)	62%	1.79 (0.64, 5.53)	29%
Secukinumab (with LD)	1.12 (0.40, 3.31)	56%	0.84 (0.38, 1.87)	75%
TNF-α inhibitor class[¶]	1.33 (0.28, 7.39)	47%	0.72 (0.19, 2.34)	81%
Ixekizumab	1.51 (0.50, 4.57)	35%	1.92 (0.86, 4.53)	25%
Placebo	**2.72 (1.12, 7.01)**	3%	**3.26 (1.63, 6.56)**	1%

[†]Bold denotes statistically significant in favour of bimekizumab; [‡]Ordered by ASAS20 SUCRA ranking; [¶]Includes certolizumab pegol only.

Strengths and limitations

The current analysis provides a comprehensive and up-to-date synthesis of available efficacy evidence for approved b/tsDMARD treatments for patients with nr-axSpA or AS, including the recent Phase 2 and 3 trials of bimekizumab. This analysis also provides new evidence in b/tsDMARD-experienced patients, albeit with low trial and patient numbers (and hence analyses should be interpreted with caution). Limitations of the analysis include different patient populations, mixed patient populations (100% b/tsDMARD naïve only vs mixed), short-term efficacy analyses (12–16 weeks), and some trials being ~20 years older than others.

Conclusion

At week 12-16, bimekizumab achieved significantly higher response rates compared with secukinumab 150 mg in nr-axSpA (ASAS20 only) and AS (ASAS40 and ASAS PR only), and ranked highly in nr-axSpA. Bimekizumab was associated with similar response rates compared with other b/tsDMARDs across remaining outcomes. The analysis provides evidence for bimekizumab being an efficacious alternative in the management of patients across the axSpA spectrum.

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Author Disclosures: AD: Speakers bureau for Janssen, Novartis and Pfizer; consultant for AbbVie, Amgen, Aurinia, BMS, Eli Lilly, Janssen, MoonLake, Novartis, Pfizer and UCB Pharma; grant/research support from AbbVie, BMS, Celgene, Eli Lilly, MoonLake, Novartis, Pfizer and UCB Pharma; PMM: Personal fees from AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, GSK, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB Pharma; NH: Consultant for AbbVie, Amgen, Eli Lilly, Janssen, Merck, Novartis and UCB Pharma; MFM, VT, DW: employees of UCB Pharma; MEO: employee of ICERA Consulting Ltd; DS: employee of Source HE; LSG: Grants from Novartis and UCB Pharma paid to institution; consulting fees from AbbVie, Acelyrin, Eli Lilly, Fresenius Kabi, Janssen, Novartis, Pfizer, and UCB Pharma.

Acknowledgements: This study was funded by UCB Pharma. Medical writing and editorial services were provided by Source HE and funded by UCB Pharma. Review management was provided by Costello Medical and funded by UCB Pharma.

Institutions: 1. Oregon Health & Science University, Oregon, US; 2. University College London, London, UK; 3. UCB Pharma, Copenhagen, Denmark; 4. UCB Pharma, Colombes, France; 5. UCB Pharma, Brussels, Belgium; 6. ICERA Consulting Ltd, Swindon, UK; 7. Source Health Economics, Oxford, UK; 8. University of California, San Francisco, US