EE281

Cost-effectiveness analysis of bimekizumab in patients with Axial Spondyloarthritis (axSpA) in Greece

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Objectives

To assess the cost-effectiveness of bimekizumab compared to secukinumab for patients with axial spondyloarthritis (axSpA) in Greece, including both non-radiographic axSpA (nr-axSpA) and radiographic axSpA (r-axSpA) populations.

Background

- AxSpA is a chronic inflammatory rheumatic and musculoskeletal disease[1] primarily affecting the spine and sacroiliac joints[2,3] resulting in severe chronic inflammatory back pain, severe fatigue, and significant stiffness leading to loss of physical function[4,5].
- Prevalence of adults with axSpA in Greece is estimated at 0.24%, thus approximately 22,059 patients[6,7] while the incidence at 0.005% (440 patients)[8].
- Over 50%–65% of patients with axSpA do not achieve clinical response [defined as 40% improvement in Assessment of Spondylarthritis international Society (ASAS40) scale at 24 weeks] after receiving a tumor necrosis factor alpha inhibitor (TNFi) as first line therapy, while 58%–64% patients receiving interleukin (IL)-17Ai do not reach ASAS40 response after 16 weeks of treatment[9].
- Bimekizumab is the first humanised IgG1/κ monoclonal antibody designed to selectively inhibit IL-17F in addition to IL-17A, targeting all three dimers (IL-17A/A, IL-17A/F and IL-17F/F)[10], thus offering an advantageous and unique approach to axSpA management. On April 26, 2023, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion, recommending the approval of bimekizumab for the treatment of patients with axSpA[11].

Methods

Patient Population and Treatment

- The analysis covers two populations (nr-axSpA and r-axSpA). Baseline characteristics of the patients entering the model are aligned with the values reported at baseline of the BE-MOBILE trials, AS0010 for nr-axSpA[12-14] and AS0011 for r-axSpA[14-16].
- Secukinumab was chosen as the comparator for this analysis due to its status as the most widely marketed anti-IL therapy for managing patients with nr-axSpA and r-axSpA in the Greek market.
- For nr-axSpA, secukinumab 150mg was used, while a dose of 300mg was used in r-axSpA patients, based on clinical expert estimates, indicating that up to 60% of patients would receive the higher dose.
- Conventional care was included as the second line in the analysis. Dosing scheme and the percentage of patients on each treatment is provided in Table 1.

Model Overview

- A decision tree was used for the first year starting with the assessment phase of bimekizumab or the comparator, for a period of 12 to 20 weeks, as per treatment-specific prescribing guideline (NICE 2021), and mimicking the treatment pathway separately for initial responders (R1) and initial non-responders (NR1) until the end of the first year (Figure 1). As from the second year, survivors of the first phase entered a Markov state-transition model (Figure 2).
- The treatment response assessment criterion of ankylosing spondylitis disease activity score (ASDAS)-MI was used in the analysis, among the criteria available from the network meta-analysis (NMA) for both populations. This selection was done in line with the therapeutic protocols published by the Greek Ministry of Health[17].
- A rate equal to 11% and 33% of annual discontinuation was used in the analysis for nr-axSpA and r-axSpA, respectively (TA718[18] and TA383[19]).
- The risk of serious infections was taken from TA718[18] for secukinumab and BE MOBILE[12-16] (converted into an annual probability) for bimekizumab (Table 2).
- A recent mapping algorithm, using data from the Portuguese registry Reuma.pt[20,21], predicted baseline utility values that were approximately 0.1-point lower than those observed in BE MOBILE trials, with 0.46 for nr-axSpA (vs. 0.56 from BE MOBILE 1) and 0.45 for r-axSpA (vs. 0.57 from BE MOBILE 2).
- Mortality rates from Greek life tables were adjusted using the World Health Organization (WHO) data[22] and were incorporated into a decision tree and Markov model. Gender-specific probabilities were converted to mortality rates and adjusted by standardised mortality ratios (SMR) of 1.63 for men and 1.38 for women, as per Bakland et al. (2011)[23], consistent with the York model (NICE TA383[19]) and prior technology appraisals (TA407[24], TA718[18]).

Costs and Data Analysis

- From the perspective of a public payer, the analysis considered only direct costs related to drug acquisition, monitoring, and disease management (€, 2023) (Table 3).
- The treatment acquisition costs were calculated based on their ex-factory prices as they were published in the latest drug price bulletin issued by the Greek ministry of health[25], after applying the relevant discounts provided in the corresponding legislation (official government gazette, law 115/7.8.2017).
- For conventional care (CC), the final reimbursement prices were retrieved from the positive list for the reimbursement of medicines[26].
- An annual discount rate of 3.5% was applied for both costs and Quality-adjusted life-years (QALYs) estimation.
- The model outcomes were expressed as incremental cost-effectiveness ratios (ICERs) per QALY gained, using a willingness-to-pay (WTP) threshold of €51,000 per QALY. This threshold, based on published recommendations[27-29], represents three times the gross domestic product (GDP) per capita and is commonly used in countries without a specific cost-effectiveness threshold.
- The robustness of the cost-effectiveness results was evaluated using sensitivity analyses to accommodate variation in the model parameters.

Results

Base-Case Analysis

- For nr-axSpA patients, the analysis showed that over a lifetime horizon, the total discounted lifetime cost per patient was estimated at €124,778 for bimekizumab and €113,750 for secukinumab. In terms of health outcomes, bimekizumab was found to be associated with 10.210 QALYs, while the QALYs for secukinumab was 9.895 (Table 4).
- For r-axSpA patients over a lifetime horizon, bimekizumab incurred a total discounted lifetime cost of €134,843 per patient and yielded 9.830 QALYs, compared to secukinumab (150mg: €125,154 and 9.694 QALYs; 300mg: €127,610 and 9.694 QALYs) (Table 4).
- The ICER for bimekizumab was €34,893 per QALY gained, compared to secukinumab 150 mg in nr-axSpA patients, and €53,087 per QALY gained, compared to secukinumab 300 mg in r-axSpA patients (Table 4).

Sensitivity Analyses

- The deterministic sensitivity analysis (DSA) confirmed the cost-effectiveness of bimekizumab.
- Findings of probabilistic sensitivity analysis indicated that bimekizumab incurred higher incremental costs and outcomes compared to secukinumab in axSpA patients with probabilistic ICERs supporting the robustness of the deterministic base case results and rendering bimekizumab as a cost-effective therapy (Figure 3).

Conclusions

The analysis suggests that the additional therapeutic benefits of bimekizumab makes it a cost-efficient treatment option, in Greece, despite its incrementally higher costs.

Summary

Analysis Population:
Greek adults with axial spondyloarthritis

Base case analysis comparator:
Secukinumab 150mg for nr-axSpA
Secukinumab 300mg for r-axSpA

Analysis year:
2023

Analysis results:
ICER of €34,893 per QALY for nr-axSpA
ICER of €53,087 per QALY for r-axSpA

Figure 1 Cost-effectiveness plane: Bimekizumab vs. Secukinumab

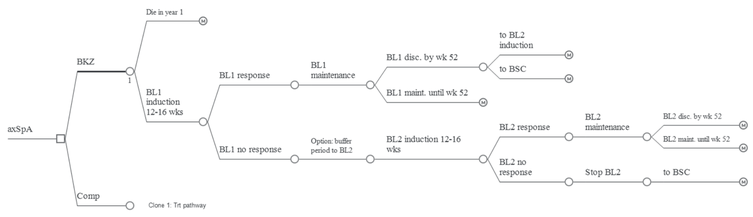


Figure 2 Cost-effectiveness plane: Bimekizumab vs. Secukinumab

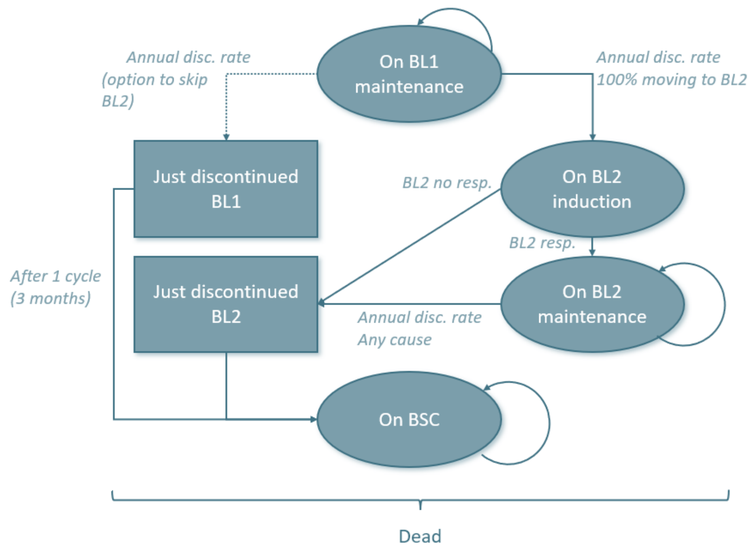


Table 4 Base case analysis results

	Total QALYs	Total Costs	Incremental QALYs	Incremental Costs	ICER per QALY gained
nr-axSpA patients					
Bimekizumab	10.210	€126,407	-	-	-
Secukinumab 150mg	9.895	€115,422	0.315	€10,985	€34,893
r-axSpA patients					
Bimekizumab	9.830	€136,705	-	-	-
Secukinumab 300mg	9.694	€129,460	0.136	€7,244	€53,087

Table 1 Dosing scheme and % of patients using conventional care

Conventional care	Dosing schedule	% of patients
Meloxicam	15 mg once daily	1%
Diclofenac sodium	150 mg once daily	15%
Celecoxib	400 mg once daily	10%
Ibuprofen	1,600 mg once daily	18%
Indometacin	150 mg once daily	9%
Naproxen	1,000 mg once daily	8%
Etericoxib	120 mg once daily	40%

Table 2 Table 2: Risk of adverse events: Annual probability of serious infections

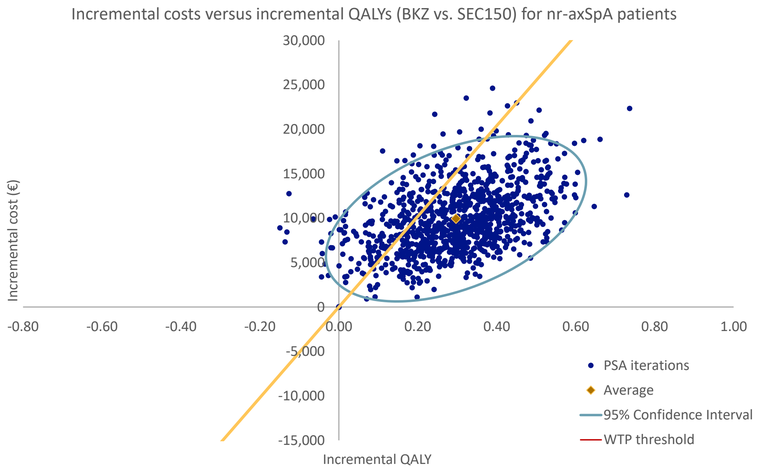
Technology	nr-axSpA	r-axSpA	Source
Bimekizumab	0.0191	0.0206	BE MOBILE[12-16]
Conventional Care	0.0000	0.0000	Assumption
Secukinumab	0.0149	0.0149	TA718[18]

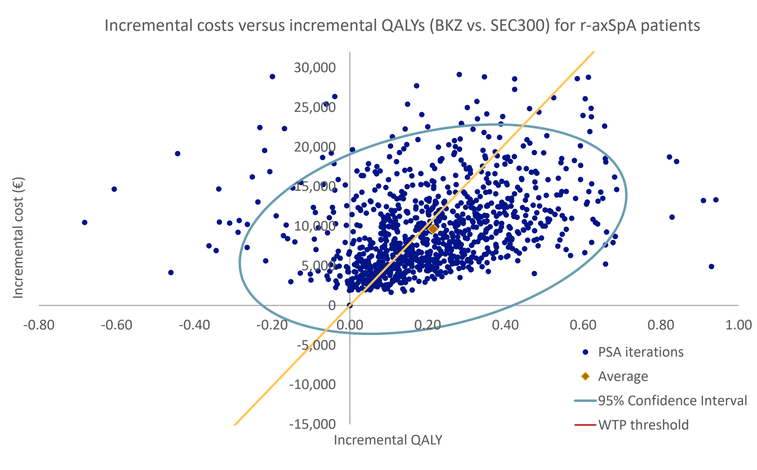
Table 3 Costs used in the analysis

Drug acquisition costs for the different treatments[1]			
Treatment	**Pack size**	**Dose (mg) per vial/ syringe/ tablet**	**Cost per pack (Ex-Factory price)**
Bimekizumab	2	160	€ 2,147.55
Ixekizumab	2	80	€ 1,701.87
Secukinumab	2	150	€ 852.15
Upadacitinib	28	15	€ 673.82
Conventional Care[2]			
Treatment	**Pack size**	**Dose (mg) per vial/ syringe/ tablet**	**Cost per pack (Insurance price)**
Meloxicam	30	15	€ 3.00
Diclofenac sodium	20	50	€ 2.07
Celecoxib	10	200	€ 4.14
Ibuprofen	20	600	€ 1.52
Indometacin	20	75	€ 7.98
Naproxen	28	500	€ 6.04
Treatment monitoring[3]			
Service		**Unit cost per service**	
Rheumatologist		€ 10.00	
Full blood count		€ 1.69	
Erythrocyte Sedimentation Rate		€ 1.00	
Liver Function Test		€ 5.92	
C-reactive Protein		€ 1.92	
Urea and Electrolytes Test		€ 4.30	
TB Heaf Test		€ 1.50	
Antinuclear antibody		€ 7.35	
Double-stranded DNA test		€ 12.75	
MRI		€ 115.01	
Chest Radiograph		€ 3.44	
Disease Management costs: HAQ-related (3 months)[4]			**Mean**
		Intercept	€ 1,239.58
Adverse event cost[5]			**Mean**
		Serious infections	€ 1,563.00

Sources: [1] Drug price bulletin issued by the Greek ministry of health[25]; [2] Positive list for the reimbursement of medicines issued by the Greek ministry of health[25]; [3] Unit costs derived from Government Gazette (FEK 1181B'/8-5-2014) and EOPYY official website[30]; [4] TA383[19], £ 1,284.19 in year 2016 inflated to 2023 GBP (£) values (ONS. Consumer Prices Index, Special Aggregate: 06 Health 2016-2023 = 1.210) and converted to Greek euros (€) based on economic database of Organization for Economic Co-operation and] Development[31] (using the latest available Purchasing Power Parities [PPP] ratio in US dollars for health indicator: US$ = €0.528 for Greece and US$ = £0.664 for UK); [5] Data associated with the inpatient management, were retrieved from both local clinical experts and the list of DRG issued by the Greek Ministry of Health[32]. Costs related to the outpatient management, were calculated by combining healthcare resource consumption, according to local clinical expert estimates and unit costs. Unit costs associated with each input extracted from Government Gazette (FEK 1181B'/8-5-2014) and EOPYY official website[30].

Figure 3 Cost-effectiveness plane: Bimekizumab vs. Secukinumab





ASAS: Assessment of Spondylarthritis international Society; ASDAS-MI: ankylosing spondylitis disease activity score major improvement; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; b/tsDMARDs: biologic/targeted synthetic disease-modifying antirheumatic drugs; CC: conventional care; cDMARDs: conventional disease-modifying antirheumatic drugs; CHMP: Committee for Medicinal Products for Human Use; DSA: deterministic sensitivity analyses; health-related quality of life; EMA: European Medicines Agency; GDP: gross domestic product; HRQoL: health-related quality of life; ICER: incremental cost-effectiveness ratio; IgG1: immunoglobulin G1; IL: Interleukin; JAKs: Janus kinase inhibitors; nr-axSpA: non-radiographic axSpA; NR1: initial non-responders; NSAIDs: non-steroidal anti-inflammatory drugs; QALY: quality-adjusted life-year; R1: initial responders; r-axSpA: radiographic axSpA; SMR: standardised mortality ratios; TNFi: tumor necrosis factor-alpha inhibitors; WHO: World Health Organization; WTP: willingness-to-pay.

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Available from: http://www.moh.gov.gr. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **KM, RS, KV, FM**; Drafting of the publication, or revising it critically for important intellectual content: **KM, RS, DD, DT, PC, SP, KV, FM, KG, LN, WD**; Medical writing: **RS**; Final approval of the publication: **DD, DT, PC, SP, KV, FM, KG, WD**. **Author Disclosures: MK, RS:** employees of ECONCARE LP which had contracts with UCB, Abbvie, Leo, BMS. **DT:** no conflict of interest. **SP:** Research grants and/or consultant's fees from Abbvie, Boehringer, Pfizer, UCB, Eli-Lilly, BIANEΣ, ELPEN, Genesis, Sobi, Demo, Yansen. **VK, FM**: employee of UCB, Greece. **GK:** Payments from Aristotle University, Thessaloniki. Contract with Pfizer via University of the Peloponnese. 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