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Cost-effectiveness analysis of bimekizumab in patients with active psoriatic arthritis (PsA) in Greece

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Objectives

To demonstrate the cost-effectiveness of bimekizumab, a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, against biologic/targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) for patients with active psoriatic arthritis (PsA) in Greece.

Background

- PsA is included in the group of peripheral spondyloarthritis (SpA) diseases, and it is a chronic immune-mediated inflammatory disease, usually seronegative for rheumatoid factor, involving both the skin and musculoskeletal system[1,2].
- In Greece, prevalence of adults with PsA is estimated at 0.17%, thus approximately 15,206 patients [3,4,5] while the incidence at 0.003% [6,7] (277 patients).
- The suboptimal management of PsA, marked by inadequate response or intolerance to initial advanced therapy, frequent switching due to lack of efficacy or adverse events, and the significant financial and social burden on patients, underscores the urgent need for additional therapeutic options to improve clinical outcomes [8,9,10].
- Bimekizumab is a humanized immunoglobulin G1 (IgG1) monoclonal antibody that selectively inhibits IL-17F in addition to IL-17A and has demonstrated sustained clinical efficacy and tolerability for up to two years in patients with PsA[11], thus offering an advantageous and unique approach to PsA management.
- On April 26, 2023, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency's (EMA) issued a positive opinion, recommending the approval of bimekizumab for the treatment of patients with active PsA.

Methods

Patient Population and Treatment

- According to local clinical experts, 64% of total PsA patients have prior exposure to one or more tumor necrosis factor-alpha inhibitors (TNFi); thus, TNFi-experienced patients were chosen for the analysis, based on BE COMPLETE phase 3 trial population of bimekizumab [12,13].
- As only TNFi-experienced patients were included in the analysis, secukinumab 300mg was used as comparator, reflecting its licensed posology.
- Scenario analyses were conducted comparing bimekizumab with the latest recently available b/tsDMARDs in the PsA market (ixekizumab and risankizumab) and two available Janus kinase inhibitors (tofacitinib and upadacitinib) for managing adult Greek PsA patients.
- The dose and frequency of administration of bimekizumab and its comparators were modelled according to EMA licensed dosing schedules that are commonly followed by the Greek clinical practice, based on clinical experts' opinion (Table 1).
- A mix of DMARD treatments was used concurrently by patients being treated with b/tsDMARDs and by those who are on Standard of Care (conventional DMARDs [cDMARDs]) in the model, based on local clinical experts estimates (Table 2).

Model Overview

- A previously peer-reviewed and published Markov model with a lifetime horizon was locally adapted and utilized, evaluating treatment response based on American College of Rheumatology 50% (ACR50) and Psoriasis Area and Severity Index (PASI) changes (Figure 1).
- Patients initiate first-line treatment in a 12- to 16-week trial phase, during which ACR50 response is assessed, with response probabilities derived from BE OPTIMAL, BE COMPLETE, and 16-week interim network meta-analysis (NMA) data, determining whether patients continue treatment or transition to best supportive care (BSC)[12,14] (Table 3).
- PASI response is assessed at the end of the induction phase (response of PASI75), and during the maintenance phase. Patients remain in their response state, switching therapies if necessary, until treatment discontinuation at which point their Health Assessment Questionnaire Disability Index (HAQ-DI) and PASI scores revert to baseline values, initiating a new induction phase or moving to best supportive care[15,16] (Table 3).
- During the maintenance phase, patients may switch therapies based on the probability of discontinuation (16.5% based on literature[15,16]), which allows for treatment stopping due to relapse or adverse events, for example.
- The utilities used in the analysis were estimated using HAQ-DI and PASI scores, based on a regression equation from Rodgers et al. used in the original 'York model'[15].
- As PsA is associated with higher mortality compared with the general population, life table mortality rates for males and for females were accelerated using a hazard ratio of 1.05 based on a prospective study of PsA[17]. Annual mortality rates for the general population of Greece were sourced from the official website of the World Health Organisation (WHO)[18].

Costs and Data Analysis

- Following a public payer perspective, only direct costs pertaining to drug acquisition, monitoring and disease management were considered (€, 2023) (Table 4).
- 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[19], after applying the relevant discounts provided in the corresponding legislation (official government gazette, law 115/7.8.2017).
- A 3.5% annual discount rate was applied for both costs and Quality-Adjusted Life-Years (QALYs) estimation.
- The cost-effectiveness of bimekizumab over secukinumab was evaluated by calculating the incremental cost effectiveness ratio (ICER) per QALY gained.
- In the absence of an official willingness-to-pay (WTP) threshold for Greece, the current analysis used a WTP of €51,000 per QALY, based on published recommendations and studies[20,21,22], which equates to three times the gross domestic product (GDP) per capita, a common practice in countries without a defined threshold to assess cost-effectiveness.
- The robustness of the cost-effectiveness analysis results was tested by a set of deterministic sensitivity analyses (DSAs) and scenario analyses.
- Probabilistic sensitivity analysis was also performed by attaching probability distributions to input parameters.

Results

Base-Case Analysis

- Bimekizumab was found to be more effective, providing an additional 0.54 QALYs, but also more expensive by €14,117 compared to secukinumab 300mg (Table 5).
- The resulting ICER of the comparison was estimated at €26,264 per QALY, remaining below Greece's WTP threshold of €51,000.

Scenario and Sensitivity Analyses

- Based on the results of each analysis, treatment with bimekizumab was estimated to be a cost-effective strategy versus ixekizumab, tofacitinib, upadacitinib and Risankizumab, over a WTP threshold of €51,000 (Table 5).
- All sensitivity analyses confirmed these cost-effectiveness estimates.
- Probabilistic sensitivity analysis showed that, bimekizumab was associated with more incremental costs and outcomes, compared to Secukinumab (Figure 2).

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 active psoriatic arthritis

Base case analysis comparator:
Secukinumab
Scenario analysis comparator:
Ixekizumab, Risankizumab, Tofacitinib and Upadacitinib

Analysis year:
2023

Analysis results (vs. secukinumab):
ICER of €26,264 per QALY

Table 1 Dosing schedules

Treatment	Dosing schedule
Bimekizumab	160 mg every 4 weeks
Ixekizumab	160 mg for 1 dose and then 80 mg every 4 weeks
Rizankizumab	150mg at weeks 0 and every 12 weeks thereafter
Secukinumab[a]	300 mg at week 0, 1, 2, 3, 4, and monthly thereafter
Tofacitinib	5 mg twice daily
Upadacitinib	15 mg once daily

Note: [a] In line with the SmPC, TNF experienced patients and patients with concurrent moderate-to-severe plaque psoriasis, are assumed to use the 300mg dose. **Source:** EMA licensed dosing schedules.

Table 2 Concurrent medication for PsA patients

Treatment	Dosing schedule	b/ts DMARDs Therapy (% of patients)	Standard of Care (% of patients)
Methotrexate	15 mg once weekly	47.0%	36.3%
Leflunomide	20 mg once daily	10.0%	14.0%
Sulfasalazine	3,000 mg once daily	0.6%	0.3%
Methotrexate sodium	15 mg once weekly	15.8%	20.0%
Hydroxychloroquine	200 mg once daily	0.6%	0.5%

Source: Local clinical experts etimates.

Figure 1 Markov model employed for the cost-effectiveness analysis of Bimekizumab

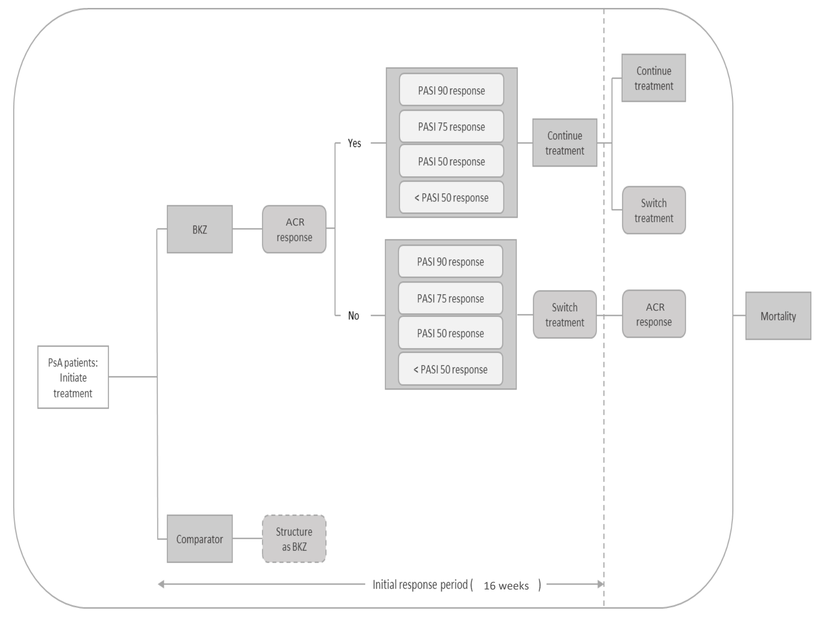


Table 4 Costs used in the analysis

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
Risankizumab	2	75	€ 2,530.70
Secukinumab	2	150	€ 852.15
Tofacitinib	56	5	€ 583.31
Upadacitinib	28	15	€ 673.82

Concurrent medication[2]

Treatment	Pack size	Dose (mg) per vial/ syringe/ tablet	Cost per pack (Insurance price)
Methotrexate	100	2.5	€ 7.58
Leflunomide	30	10	€ 12.82
Sulfasalazine	50	500	€ 5.65
Methotrexate sodium	1	25	€ 29.39
Hydroxychloroquine	30	200	€ 3.73

Treatment monitoring[3]

Service	Unit cost per service
Antinuclear antibody (ANA)	€ 7.35
DNA binding (dsDNA)	€ 12.75
Erythrocyte Sedimentation Rate	€ 1.00
Full blood count	€ 1.69
Liver Function Test	€ 5.92
Tuberculosis Blood Test	€ 1.50
Urea and Electrolytes Test	€ 4.30
Chest Radiograph	€ 3.44

Disease Management costs: HAQ-related (3 months)[4]	Mean
Intercept	€ 233.00
HAQ-DI coefficient	€ 103.00

PASI-subgroup related costs (3 months)[5]	Mean
CONTROLLED Mild to moderate PSO (PASI between 2.5 and 10)[a]	€ 18.12
UNCONTROLLED Mild to moderate PSO (PASI between 2.5 and 10)[b]	€ 224.18
CONTROLLED Moderate to severe PSO (PASI > 10)[a]	€ 18.12
UNCONTROLLED Moderate to severe PSO (PASI > 10)[b]	€ 640.83

Note: [a] Controlled disease indicates PASI 75 responders; [b] Uncontrolled disease indicates PASI 75 non-responders.
Sources: [1] Drug price bulletin issued by the Greek ministry of health[19]; [2] Positive list for the reimbursement of medicines issued by the Greek ministry of health[19]; [3] Unit costs derived from Government Gazette (FEK 1181B'/8-5-2014) and EOPYY official website[23]; [4] Rodgers et al.[5], inflated to 2023 GBP (£) values and converted to Greek euros (€) based on economic database of Organization for Economic Co-operation and Development[24] (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] Hartman et al.[25], inflated to 2023 GBP (£) values and converted to Greek euros (€) based on economic database of Organization for Economic Co-operation and Development[24] (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).

Table 3 Treatment Response - ACR and PASI

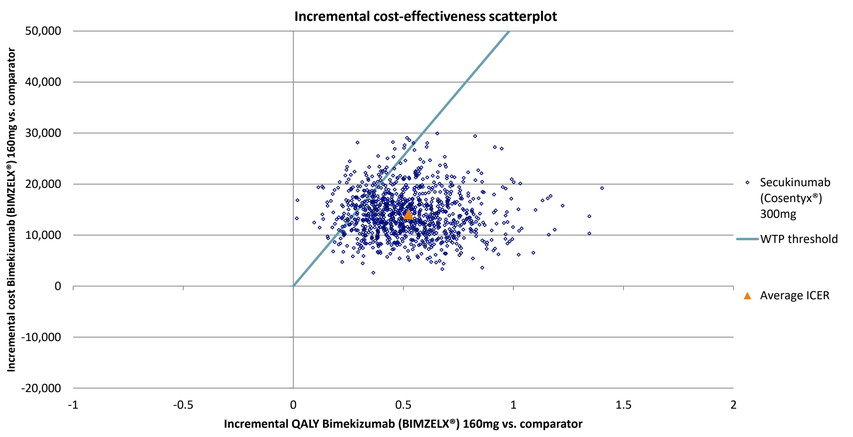
	Probability of ACR response	Probability of PASI75 response	Correlation between PASI75 and ACR
	Mean	Mean	Mean
Bimekizumab	0.490	0.850	0.415
Ixekizumab	0.330	0.500	0.415
Risankizumab	0.190	0.500	0.415
Secukinumab	0.310	0.500	0.415
Tofacitinib	0.230	0.140	0.415
Upadacitinib	0.350	0.360	0.415
Best Supportive Care	0.080	0.080	0.415

Source of ACR50 and PASI scores from NMA. Efficacy and correlation coefficients were estimated using data from the bimekizumab (BIMZELX®) trial[13].

Table 5 Base case and scenario analyses results

	Bimekizumab versus comparator				
	Total Costs	Total QALYs	Incremental Costs	Incremental QALYs	ICER per QALY gained
Bimekizumab	€ 50,083	6.74	-	-	-
Secukinumab	€ 35,967	6.20	€ 14,117	0.54	€ 26,264
Tofacitinib	€ 25,586	5.84	€ 24,498	0.90	€ 27,310
Upadacitinib	€ 30,529	6.13	€ 19,555	0.61	€ 32,122
Ixekizumab	€ 38,058	6.22	€ 12,025	0.51	€ 23,488
Risankizumab	€ 32,726	6.03	€ 17,357	0.70	€ 24,705

Figure 2 Cost-effectiveness plane: Bimekizumab vs. Secukinumab



ACR: American College of Rheumatology; BSC: best supportive care; b/tsDMARDs: biologic/targeted synthetic disease-modifying antirheumatic drugs; CHMP: Committee for Medicinal Products for Human Use; cDMARDs: conventional disease-modifying antirheumatic drugs; DSA: deterministic sensitivity analyses; EMA: European Medicines Agency; GDP: gross domestic product; HAQ-DI: Health Assessment Questionnaire Disability Index; ICER: incremental cost effectiveness ratio; IgG1: immunoglobulin G1; IL: Interleukin; NMA: network meta-analysis; PASI: Psoriasis Area and Severity Index; PsA: psoriatic arthritis; QALYs: Quality-Adjusted Life-Years; SpA: spondyloarthritis; TNFi: tumor necrosis factor-alpha inhibitors; WTP: willingness-to-pay; WHO: World Health Organisation

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Cost-effectiveness analysis of a psoriasis care instruction programme with dithranol compared with UVB phototherapy and inpatient dithranol treatment. Br J Dermatol. 2002 Sep;147(3):538-44. **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, BIANEΞ, ELPEN, Genesis, Sobi, Demo, Yansen. **VK, FM:** employee of UCB, Greece. **GK:** Payments from Aristotle University, Thessaloniki. 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