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Cost-effectiveness of mepolizumab vs anti-interleukin-5/5r biologic therapies for the treatment of adults with severe asthma with an eosinophilic phenotype: a Chilean healthcare system perspective

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ABSTRACT

Aim: Asthma is a heterogeneous respiratory condition often classified into distinct phenotypes. Severe asthma, characterized by uncontrolled symptoms despite optimal treatment, imposes a significant burden on healthcare systems, particularly in low- and middle-income countries. This study evaluates the cost-effectiveness of mepolizumab compared with other interleukin (IL)-5 pathway inhibitors, benralizumab and reslizumab, in treating severe asthma with an eosinophilic phenotype in Chile.

Materials and methods: A Markov cohort model was developed to compare mepolizumab (100 mg subcutaneously every four weeks) with benralizumab (30 mg subcutaneously every four weeks for the first three doses, every eight weeks subsequently) and reslizumab (3 mg/kg intravenously every four weeks), both as add-on therapies to standard care. Data from the Mepolizumab as Adjunctive Therapy in Patients with Severe Asthma (MENSA) clinical trial and a network meta-analysis were used. Utility values were extracted using the EuroQoL 5-Dimension questionnaire (EQ-5D-5L) questionnaire. Probabilistic and one-way sensitivity analyses assessed model robustness.

Results: Mepolizumab demonstrated dominance with probability over 95% when compared with benralizumab and reslizumab. Cost savings ranged from 37,000 United States dollars (USD) to 104,000 USD, with an increase of 0.52 to 0.55 quality-adjusted life years. Mepolizumab was also associated with a lower incidence of exacerbations and asthma-related deaths. Sensitivity analyses confirmed the stability of the model outcomes across key parameters.

Limitations: Limitations of the economic model are related to the lack of direct comparisons between mepolizumab and other biologics. Additionally, the absence of data on continuation criteria required estimating relative risks for the overall population.

Conclusions: Mepolizumab offers greater efficacy and cost savings compared to benralizumab and reslizumab for eosinophilic asthma, providing essential insights for improving asthma management and informing healthcare policies in Chile.

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Introduction

Asthma is a complex respiratory condition characterized by symptoms, such as wheezing, shortness of breath, chest tightness, and coughing, alongside variable expiratory airflow limitation. Severe asthma is defined as disease that remains uncontrolled despite adherence to optimal treatment with high-dose inhaled corticosteroids and long-acting β_2-agonists (ICS/LABAs)[1].

The burden of asthma is particularly pronounced in low- and middle-income countries, where the majority of asthma-related fatalities occur[1]. In South America, the overall prevalence of asthma is 4.9% while in Chile, the prevalence of self-reported asthma diagnosis was 5.4% in those aged 15 years or more[2,3]. Although no estimates are available for the prevalence of severe asthma in Chile, according to the Global Initiative for Asthma (GINA), severe asthma accounts for 3.7% of the overall asthma population[1].

Asthma treatment in Chile includes use of ICS/LABAs, short-acting β_2-agonists (SABAs), and oral

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corticosteroids (OCSs)[4]. However, this represents suboptimal care for patients with severe asthma; biologic therapies are not included[4]. The 2024 GINA report outlines specific recommendations for patients with severe asthma who do not respond adequately to optimized maximum therapy, and may benefit from the use of add-on biologic therapies[1]. Each of these biologics targets specific pathways implicated in the inflammatory processes underlying severe asthma, where the cytokines interleukin (IL)-4, IL-5, and IL-13 are the key drivers and their inhibition provides tailored treatment strategies for achieving better disease control[5].

In the case of IL-5, it regulates the proliferation, maturation, activation, recruitment, and survival of eosinophils[5]. Eosinophilia is characterized by an elevated absolute eosinophil count greater than 450 to 550 cells/μL in peripheral blood, which results from impaired regulation of these cells[6,7]. It is estimated that about 50% of all severe asthma cases are classified as eosinophilic[8]. In the context of the Latin America, a study conducted in Brazil showed that the percentage of patients with a blood eosinophil count exceeding 300 cells/mm^3 was 40.0%[9]. Evidence suggests that IL-5 plays a role in asthma beyond its involvement with eosinophils, as its inhibition exerts negative effects on immunological processes[10]. Targeting this signaling pathway has led to the development of three monoclonal antibodies[11]. Mepolizumab and reslizumab inhibit circulating IL-5, which prevents it from binding to the IL-5 receptor on effector cells, particularly eosinophils. In contrast, benralizumab targets the alpha subunit of the IL-5 receptor on eosinophils, basophils, and innate lymphoid cells type 2, effectively blocking IL-5 from attaching to its receptor[11,12].

The importance of phenotype-specific treatment approaches is highlighted by data reported in the prevalence of the eosinophilic phenotype among severe asthma patients (PREPARE) study, that investigated severe asthma phenotypes in five Latin American countries (Argentina, Chile, Colombia, Costa Rica, and Mexico)[13]. In the preceding year, 52% of participants experienced at least one severe exacerbation, and 44% required OCS treatment. Elevated blood eosinophil counts were observed in 44% of participants (≥300 cells/μL) and 76% of participants (≥150 cells/μL), while 58% of participants exhibited serum immunoglobulin E levels exceeding 100 IU/mL. Notably, 50% of participants reported uncontrolled asthma[13].

In Chile, the economic burden of asthma is significant, with annual treatment costs estimated at approximately 15 million United States dollars (USD)[14]. Thus, cost-effective technologies able to decrease the economic burden are needed, particularly for severe asthma. This study aimed to assess the cost-effectiveness of anti-IL5/5 receptor treatments available in Chile in the treatment of severe asthma with eosinophilic phenotype (SAEP) when used as add-on therapies to standard of care (SoC), from the public healthcare system perspective.

Methods

Population

The overall simulated patient population corresponds to the population in the mepolizumab as adjunctive therapy in patients with severe asthma (MENSA) clinical trial, which assessed the clinical efficacy and tolerability of mepolizumab[15]. The MENSA trial enrolled patients with uncontrolled asthma at GINA treatment step 4 and moving up to step 5, and patients at step 5[15]. Considering the approved indication and data availability, the base case populations in the comparisons versus benralizumab and reslizumab were adult-only patients with an Asthma Control Questionnaire (ACQ) score ≥1.5 (poorly controlled asthma) and blood eosinophils ≥400 cells/μL at baseline. Subgroup analyses included patients with ACQ scores ≥1.5 and blood eosinophils ≥150 cells/μL or ≥300 cells/μL at baseline. In the absence of any head-to-head trials directly comparing mepolizumab versus benralizumab or reslizumab, data from a network meta-analysis (NMA) was used[16].

Interventions

The intervention consisted of a subcutaneous administration of 100 mg of mepolizumab once every four weeks provided in healthcare facilities. Mepolizumab was compared with benralizumab 30 mg subcutaneously every four weeks for the first three doses, followed by 30 mg every eight weeks, and reslizumab 3 mg/kg of body weight once every four weeks intravenously, using data from the NMA[16]. All interventions were used as add-on therapies to SoC for asthma management and according to their respective approved labels. The following groups and comparators were considered: base case (ACQ ≥1.5 & >400 eosinophils/μL) – comparators, benralizumab and reslizumab; subgroup A (ACQ ≥1.5 & >150 eosinophils/μL) – comparator, benralizumab; subgroup B (ACQ ≥1.5 & >300 eosinophils/μL)

– comparator, benralizumab. Comparative data are reported in Supplementary Table S1.

According to national reports and clinical expert judgment, SoC, as currently provided by the Chilean health system, consists of a combined therapy of high-dose ICS/LABA plus SABA and OCS for all patients with SAEP[4].

Model structure

The model used follows a similar structure from a previous study, in which mepolizumab + SoC was compared to SoC alone[17]. The disease's natural history was modeled using a 4-state Markov cohort model (two states representing patients on and off treatment and two states for death: death from other causes and asthma-related deaths), as presented in Figure 1.

Patients entered the evaluation with diagnosed persistent, uncontrolled SAEP despite best SoC. At each 4-week cycle, patients could discontinue biologic treatment and move to an off-treatment health state, remain in the same health state or transition to death (asthma-related or due to other causes). While on the on-treatment or off-treatment health states, patients could experience a clinically significant exacerbation. Exacerbations were not treated as a health state, but observed as transient events occurring over time in an asthma symptom health state. During each cycle patients could experience one of three types of exacerbation: exacerbations requiring OCS burst, an emergency room visit or hospitalization. The rate of clinically significant exacerbations depends upon the therapy a patient is receiving. The impact of each type of exacerbation was implemented by applying a utility decrement and a cost to treat the exacerbation. Patients who discontinued biologic treatment were transitioned to SoC.

Time horizon, cycle length and discount rate

A lifetime horizon was adopted, with the effect of biological treatment assumed to persist throughout. The model cycle length was set at 4 weeks, consistent with the visit schedule and measurements from clinical trials[15,18]. Clinical experts also concurred that this duration would accurately capture the time frame of likely asthma symptom and exacerbation occurrence. In accordance with Chilean guidelines for economic evaluation, an annual discount rate of 3% was applied to both costs and outcomes[19].

Model inputs

Model parameters are presented in Supplementary Table S1. Patient demographics, including age and gender distribution, were derived from the MENSA clinical trial, while body weight distribution, necessary for reslizumab dose calculation, was obtained from the National Institute for Health and Care Excellence (NICE) technology appraisal guidance document number 479 (NICE TA479)[20].

In the absence of head-to-head trials directly comparing mepolizumab versus benralizumab or reslizumab, a NMA comparing licensed doses of these treatments was previously conducted in a frequentist framework[16]. This NMA compared the relative efficacy of these biologics in

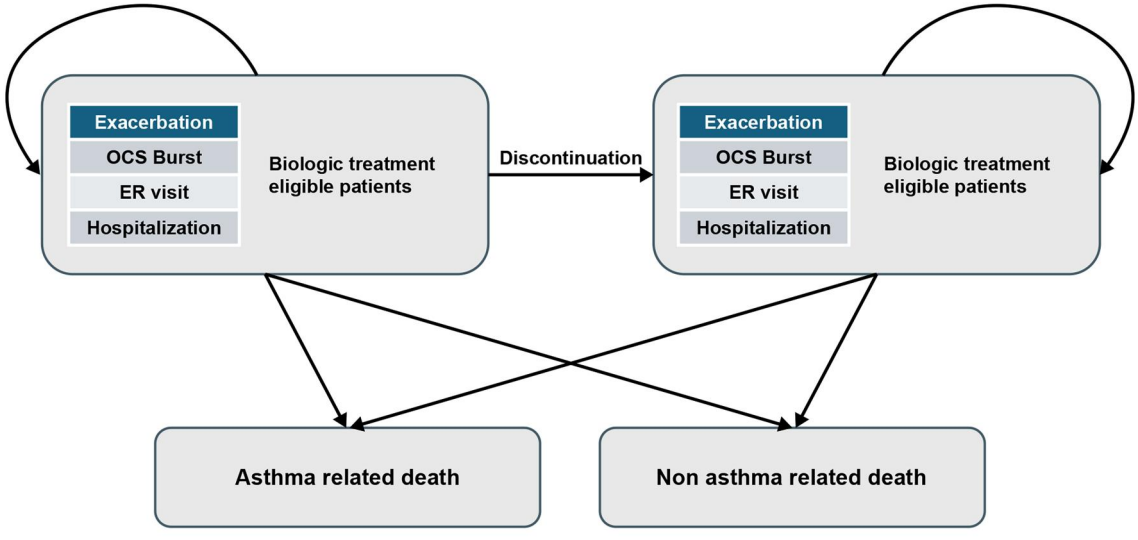


Figure 1. Markov model structure, regardless of subgroup analyses.
Abbreviations. ER, emergency room; OCS, oral corticosteroid.

severe asthma by synthesizing data from available randomized controlled trials through a common comparator (placebo); the primary efficacy outcomes assessed were the reduction in clinically significant exacerbations and improvements in asthma control[16].

The patient populations in the clinical trials for these biologics varied, particularly in terms of blood eosinophil thresholds for inclusion. Since blood eosinophils serve as an effect modifier for all three treatments, any comparison must account for these differences. Furthermore, as the benralizumab and reslizumab trials only included patients with an ACQ score $\geq$1.5, the NMA excluded patients with an ACQ score $<$1.5 at baseline from the mepolizumab trials.

The exacerbation results of the NMA, presented as rate ratios, are presented in Supplementary Table S1. These rate ratios were applied to the baseline exacerbation rate of SoC from the subgroup in the MENSA trial, which most closely aligns with the NMA subgroup.

Utility values were obtained from the mepolizumab add-on therapy on health-related quality of life and markers of asthma control in severe eosinophilic asthma (MUSCA) trial where health-related quality of life was evaluated for mepolizumab + SoC and SoC alone using the EuroQoL 5-Dimension questionnaire (EQ-5D-5L) questionnaire. Data were collected at baseline, week 12, and week 24 in the trial[21]. Disutilities for benralizumab and reslizumab versus mepolizumab were based on ACQ score mapping using the fractional polynomial regression with baseline data from MENSA[22].

Asthma-related mortality was assumed to occur only in cases where hospitalization was required for the treatment of an exacerbation. The probability of death following an exacerbation was modeled as age-dependent, based on the study by Roberts et al. (2013), which considers both in-hospital mortality and deaths occurring post-discharge[23].

Drug costs (biologics and SoC) were obtained from tender public records, while costs associated with asthma exacerbation were derived from previous publications[17,24]. It was assumed that discontinuation rates would be equal across all treatment comparators.

All costs were expressed in 2024 Chilean pesos and converted to USD using a conversion rate of 937.46 Chilean pesos to 1 USD (average rate between January and September 2024)[25].

Study outcomes

The primary outcomes of the cost-effectiveness model are the total and incremental costs and quality-adjusted life years (QALYs) gained. The base case estimate is presented as incremental costs per QALY gained over a lifetime horizon. Additionally, total number of clinically significant exacerbations, asthma-related mortality and life years are shown, including incremental costs per exacerbation.

Net health benefit, expressed as the difference between incremental QALYs and the ratio calculated from incremental costs and the predefined willingness to pay threshold, was also estimated. A willingness to pay threshold of 16,000.68 USD was established. Positive values were defined as cost-effective under the willingness to pay threshold[26,27].

Sensitivity analyses

A deterministic one-way sensitivity analysis and a probabilistic sensitivity analysis were conducted to explore the second-order uncertainty in the model's results. For the one-way sensitivity analysis, each parameter was assigned a "low" and "high" value (Supplementary Table S1), where the low value represents the lower bound of the 95% confidence interval (CI), and the high value represents the upper bound. In the absence of CI data, it was assumed that the standard error would be 20% of the mean of the parameters. The estimated standard error was used to predict the upper and lower limits of the CI for the parameters. A tornado plot was developed to graphically present the parameters that have the greatest impact on the incremental cost-effectiveness ratio (ICER), with the parameters driving the most variation in the results displayed at the top and those with lesser influence shown further down.

The probabilistic sensitivity analysis was conducted by simultaneously varying each parameter, with the resulting incremental outcomes recorded as part of each "simulation." A total of 1,000 Monte Carlo simulations were performed, generating a distribution of incremental outcomes to assess the robustness of the cost-effectiveness results. A beta distribution was applied to vary parameters that needed to remain bounded between 0 and 1, such as proportions, utilities, and disutilities, while a gamma distribution was used for all other parameters, including costs and relative risks (RRs). Treatment acquisition costs did not vary in the sensitivity analyses.

Results

Overall results

In the base case analysis (patients with ACQ $\geq$ 1.5 & $>$400 eosinophils/μL), mepolizumab + SoC showed a

Table 1. Effectiveness results.

	OCS burst (mean per patient)	ER visit (mean per patient)	Hospitalization (mean per patient)	Asthma-related deaths (%)
Base case				
Mepolizumab	12.96	0.94	1.67	20.01
Benralizumab	16.72	1.21	2.16	23.52
Reslizumab	16.72	1.21	2.16	23.52
Subgroup A: ACQ $\geq$ 1.5 & >150 eosinophils/μL				
Mepolizumab	12.46	1.27	1.33	15.46
Benralizumab	15.50	1.58	1.66	17.86
Subgroup B: ACQ $\geq$ 1.5 & >300 eosinophils/μL				
Mepolizumab	12.67	0.94	1.62	18.84
Benralizumab	16.10	1.19	2.05	22.01

Abbreviations. ACQ, Asthma Control Questionnaire; ER, emergency room; OCS, oral corticosteroid.

Table 2. Base case and subgroup analysis results.

	Total cost (USD)	Total QALYs	Incremental costs (USD)	Incremental QALYs	ICER (USD/QALY)	Net health benefit*
Base case						
Mepolizumab	113,349.57	14.69	Reference	Reference	Reference	Reference
Benralizumab	150,042.80	14.16	−36,693.23	0.52	Dominant	2.82
Reslizumab	217,197.17	14.14	−103,847.61	0.55	Dominant	7.04
Subgroup A: ACQ $\geq$ 1.5 & >150 eosinophils/μL						
Mepolizumab	113,200.71	14.79	Reference	Reference	Reference	Reference
Benralizumab	150,622.82	14.32	−37,422.11	0.47	Dominant	2.81
Subgroup B: ACQ $\geq$ 1.5 & >300 eosinophils/μL						
Mepolizumab	113,014.22	14.65	Reference	Reference	Reference	Reference
Benralizumab	149,819.82	14.11	−36,805.60	0.54	Dominant	2.83

Abbreviations. ACQ, Asthma Control Questionnaire; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life years; USD, US dollars. *Considering a willingness to pay of 16.000,68 USD.

lower incidence of exacerbations and asthma-related deaths (Table 1) with a gain in QALYs of 0.52 and 0.55, along with cost savings of 37,000 and 104,000 USD when compared to benralizumab and reslizumab, respectively. In this way, mepolizumab was found to be more effective and less costly than either of the comparators (Table 2).

As previously described, two subgroups were analyzed: subgroup A (ACQ $\geq$ 1.5 and >150 eosinophils/μL) and subgroup B (ACQ $\geq$ 1.5 and >300 eosinophils/μL). Comparators were selected based on data availability. Consistent with the base case findings, mepolizumab + SoC demonstrated a consistent increase in QALYs over benralizumab in both subgroups, ranging from 0.47 to 0.54 and cost savings of −37,000 (Table 2).

Table 2 also presents the results estimated through the net health benefit analysis. In the base case scenario, mepolizumab promoted a net benefit of 2.82 and 7.04, when compared to benralizumab and reslizumab, respectively. In the subgroup analyses, net benefit was similar to the base case scenario; mepolizumab promoted a net benefit of 2.81 and 2.83, when compared to benralizumab, in subgroups A and B, respectively. These results indicate mepolizumab to be cost-effective, at a willingness to pay threshold of 16,000.68 USD. In addition, the highest values were observed in comparison with reslizumab.

One-way sensitivity analyses

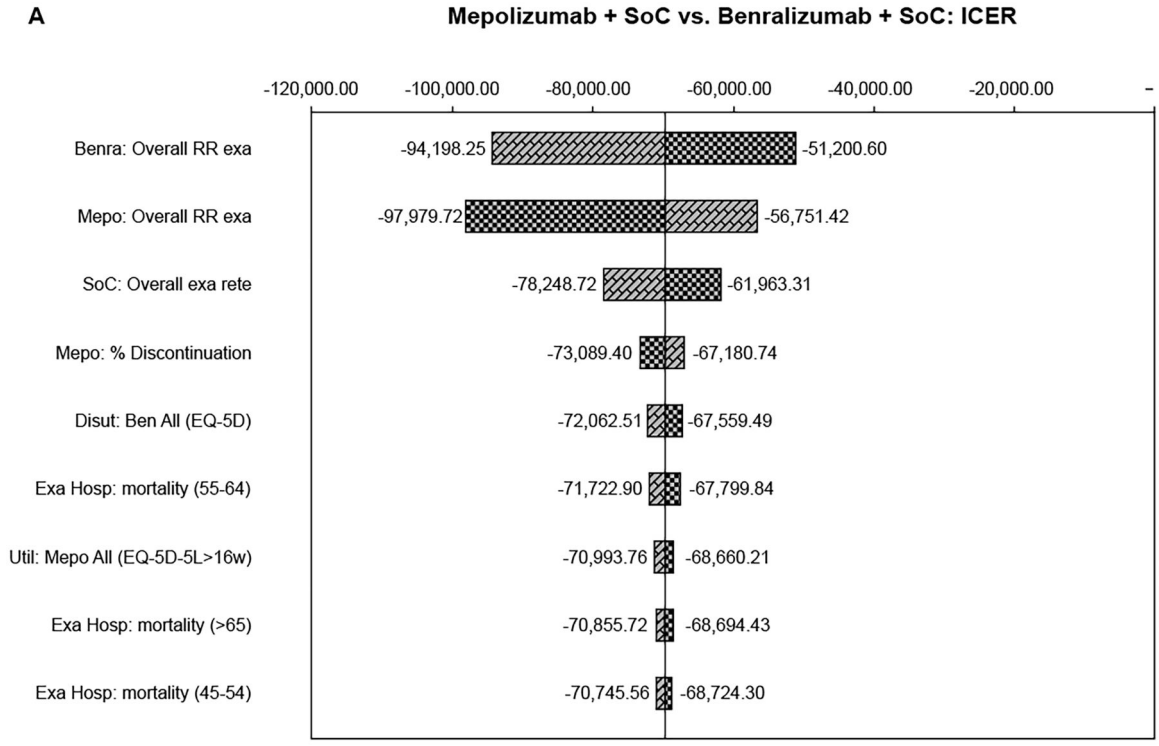
In the one-way sensitivity analysis for the base case, the main drivers of uncertainty in the model results were the exacerbation RR versus placebo for mepolizumab, benralizumab, and reslizumab, as well as the exacerbation rate for SoC (Figure 2A,B). No parameters were able to reverse the effects of mepolizumab compared to benralizumab and reslizumab.

Probabilistic sensitivity analyses

When comparing mepolizumab with benralizumab and reslizumab in the base case, both clouds of interactions in the scatterplot remained mostly in the fourth quadrant which suggest greater effectiveness and lower cost (Figure 3). The probability of dominance was greater than 95% in relation to both comparators. This finding further confirmed the results observed in the base case.

Discussion

The base case analysis demonstrated that mepolizumab is associated with cost savings of 37,000 USD and 104,000 USD, alongside a gain of 0.52 and 0.55 QALYs compared to benralizumab and reslizumab, respectively. The probabilistic sensitivity analyses comparing mepolizumab to benralizumab and reslizumab



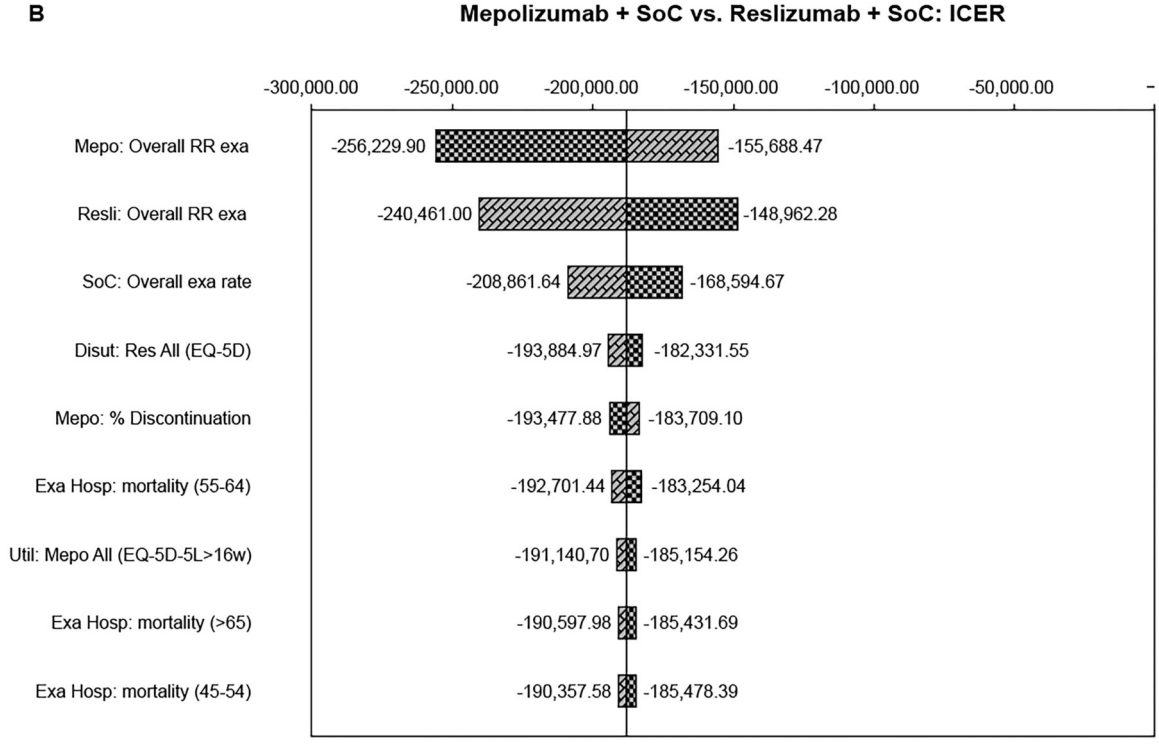


Figure 2. One-way sensitivity analysis tornado diagram for the base case for (A) mepolizumab vs. benralizumab and (B) mepolizumab vs. reslizumab.

The tornado diagram illustrates the variability of the ICER in response to changes in the specified parameters. Lighter shading represents the impact on the ICER when the parameter is set to its proposed lower limit, while darker shading indicates the effect when the parameter is adjusted to its upper limit. Abbreviations. Ben, benralizumab; Benra, benralizumab; Disut, disutility; EQ-5D, EuroQoL 5-Dimension questionnaire; Exa, exacerbation; Hosp, hospitalization; ICER, incremental cost-effectiveness ratio; Mepo, mepolizumab; Res, reslizumab; Resli, reslizumab; RR, risk ratio; SoC, standard of care; Util, utility; w, weeks.

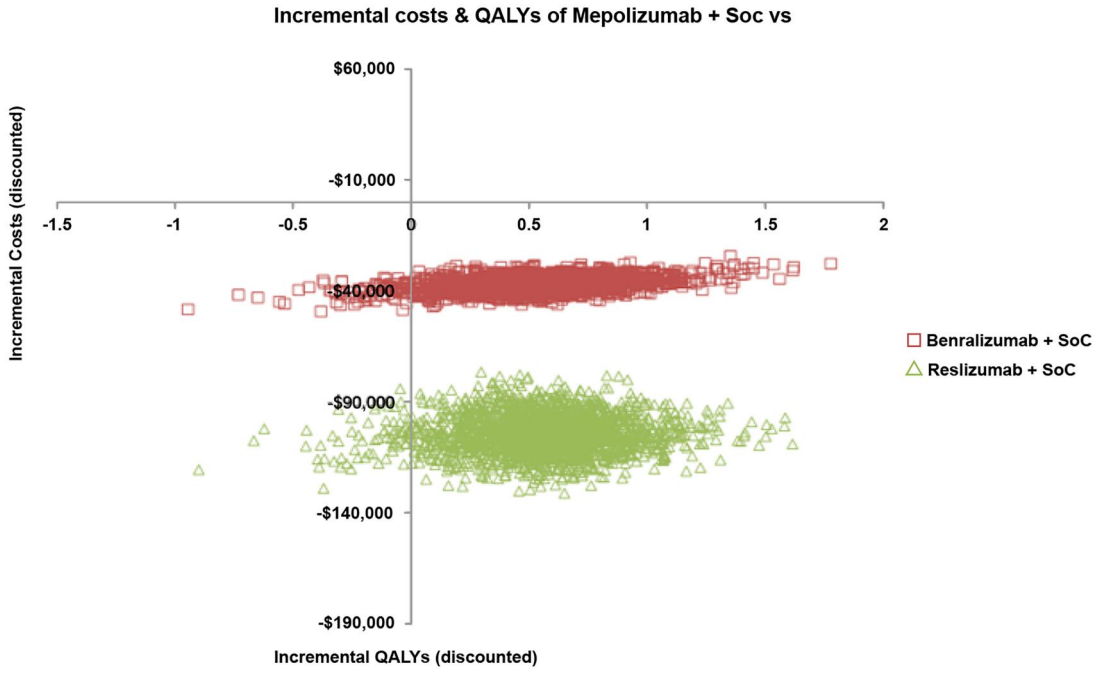


Figure 3. Probabilistic sensitivity analysis incremental cost-effectiveness plane for the base case.
Abbreviations. QALYs, quality-adjusted life years; SoC, standard of care; vs, versus.

further reinforced the base case findings. The one-way sensitivity analysis revealed that variations in key model parameters had minimal impact on the base case results. A significant driver of the model's estimates was the difference in treatment effectiveness between patients receiving mepolizumab versus those on benralizumab and reslizumab.

Clinical and economic benefits of mepolizumab use to manage severe asthma have been previously reported. In a Spanish study, there was a notable reduction in exacerbations per person from a mean of 3.1 to 0.7 12 months after initiating mepolizumab treatment[28]. Furthermore, Asthma Control Test (ACT) scores rose from 14.9 to 21.5 (higher ACT scores correlate with improvements in asthma control, with scores $\geq$ 20 indicating well-controlled asthma[29,30], and the proportion of OCS-dependent patients reduced substantially, from 53.3% to 13.3%, after 12 months of mepolizumab therapy. In this period, hospitalization costs also saw a remarkable decline of 94%, from 4,063.9 euros (EUR) before treatment to 238.6 EUR afterward ($p = 0.0003$), which translates to approximately 4,515.51 USD to 264.09 USD, respectively. Overall costs also decreased significantly, from a median of 2,423.1 EUR prior to treatment to 1,177.5 EUR after treatment, excluding mepolizumab costs, equivalent to about 2,697.05 USD and 1,303.17 USD, respectively. Despite the differences in the monetary values, this study aligns with our findings that adding mepolizumab to SoC for SAEP results in reduced medical costs related to asthma exacerbations and overall healthcare resource utilization, within a cost-effective range[28]. Mepolizumab was also associated with a significantly lower incidence of exacerbations and asthma-related deaths in eosinophilic subgroups. When analyzing both subgroups – those with an ACQ of 1.5 or higher with either >150 eosinophils/μL or >300 eosinophils/μL – mepolizumab also proved to be cost-effective compared to benralizumab.

The multi-country, bi-directional, self-controlled observational cohort Nucala Effectiveness Study (NEST) took place in Colombia, Chile, India, Türkiye, Saudi Arabia, the United Arab Emirates, Kuwait, Oman, and Qatar. NEST investigated the effectiveness of mepolizumab in individuals with severe asthma across countries that had previously been less represented in real-world research. The findings indicated that mepolizumab effectively alleviated the burden of severe asthma by significantly decreasing clinically relevant exacerbations, lowering OCS use and healthcare resource utilization, and enhancing lung function and asthma management. These improvements may lead to better health-related quality of life for patients with severe asthma and a high dependence on OCS in these countries[31].

Another study conducted in Spain evaluated the economic and health-related impacts of mepolizumab, benralizumab, and reslizumab as add-on therapies to SoC, estimating direct costs and QALYs over a five-year time horizon[32]. Additionally, two scenarios were

analyzed: one comparing the effectiveness of mepolizumab versus benralizumab in patients with blood eosinophil counts of ≥300 cells/μL, and the other comparing mepolizumab to reslizumab in patients with blood eosinophil counts of ≥400 cells/μL. Consistent with our findings, despite the longer time horizon, the model demonstrated that mepolizumab offers reduced costs and greater benefits compared to benralizumab and reslizumab. Notably, in five years, treatment with mepolizumab led to an increase of 0.076 QALYs compared to benralizumab and 0.075 compared to reslizumab, resulting in estimated cost savings of around 3,524.86 USD and 8,635.36 USD per patient, respectively. As in our study, these results were robust across multiple sensitivity analyses[32].

Ali et al. (2024) analyzed the cost-effectiveness of dupilumab versus omalizumab, mepolizumab, and benralizumab also as an add-on therapy to SoC to manage adults with severe asthma in Colombia. Considering a 5-year time horizon, dupilumab was considered dominant against omalizumab 450 mg and 600 mg, mepolizumab 100 mg, and benralizumab 30 mg. In comparison to mepolizumab (100 mg), an ICER per QALY gained of −5.429 USD was reported[33]. Although these results pertain to patients diagnosed with severe asthma, they do not specifically address those with an eosinophilic phenotype. Consequently, despite being conducted in a Latin American context, these findings may not be directly comparable.

The primary limitations of our model originate from the comparison of mepolizumab with other biologic treatments. Due to the lack of direct head-to-head evidence, the relative efficacy of mepolizumab versus benralizumab and reslizumab was derived from indirect comparisons. For these comparisons, limited subgroup data were available, allowing valid comparisons in only three patient subgroups. Furthermore, there was no publicly available evidence regarding the use of continuation criteria for these interventions. Consequently, the relative risks of exacerbations for benralizumab + SoC and reslizumab + SoC versus SoC alone could only be estimated for all patients, irrespective of treatment response. A key strength of this model lies in its alignment with the methodology used in the United Kingdom NICE submission for omalizumab, enabling thorough incorporation of feedback from independent reviewers and integration of higher-quality evidence to substantiate the OCS-sparing potential of mepolizumab. The model's structure has also been endorsed by multiple health technology assessment agencies to support the evaluation of mepolizumab in adults with SAEP. The findings presented in this study are robust, offering valuable support for the decision-making process in health technology assessment.

Conclusion

Mepolizumab offers greater efficacy and cost savings compared to benralizumab and reslizumab for eosinophilic asthma in Chile. The analysis indicates savings ranging from 37,000 USD to 104,000 USD alongside QALY gains of 0.52 to 0.55. Results from both probabilistic and one-way sensitivity analyses highlight the influence of treatment effectiveness and associated costs on the ICER. Furthermore, mepolizumab was associated with a lower incidence of exacerbations and asthma-related mortality.

Transparency

Declaration of funding

This study was funded by GSK (221788).

Declaration of financial/other relationships

In accordance with Taylor & Francis policy and ethical obligation as researchers, the authors are reporting the following conflict of interest: FMdS, CRM and VG are employed by GSK and do not hold financial equities in GSK. JR is employed by GSK and holds financial equities in GSK. MAE declares that he has received fees from Novartis, MSD, Abbvie, Boehringer Ingelheim, Pfizer, Roche, Astellas, Takeda, Biomarin for services as speaker, consultancy or participation in advisory boards. He has also received fees from the Interamerican Bank of development, World Bank, Ministry of Health of Belize, Center for Global Development and Americas Health Foundation, for consultancy services. He has been granted by research grantes from ANID Chile. CB declares that he has received grants or contracts from AstraZeneca, BMS, Boehringer Ingelheim, Novartis, PTC Pharmaceuticals, Roche Diagnostic, Sanofi Pasteur, Tecnofarma; received fees for scientific consulting services from CECAN and Storm Chile and was provided support for attending meetings and/or travel by ESMO and Sanofi. We have disclosed those interests fully to Taylor & Francis, and we have in place an approved plan for managing any potential conflicts arising from that involvement.

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Author contributions

FMdS, CRM and JR, study concept and design; FMdS, data acquisition; FMdS, CRM, VG, MAE, CB and JR, data analysis and interpretation; all authors, drafting of the manuscript/critical revision of the paper for important intellectual content and approval of the final version to be submitted.

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Data availability statement

The data that support the findings of this study are available from the corresponding author, FMdS, upon reasonable request.

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