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ORIGINAL RESEARCH ARTICLE

Cost-Effectiveness Analysis of Abrocitinib Compared with Other Systemic Treatments for Severe Atopic Dermatitis in Spain

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Abstract

Introduction Atopic dermatitis (AD) is a chronic, inflammatory skin disease characterized by itchy, painful, and dry skin. Despite the great number of available therapies, economic evaluations are still needed to provide evidence on their cost efficiency. This research aimed to evaluate the cost effectiveness of the Janus kinase (JAK) inhibitor abrocitinib (200 mg) compared with dupilumab (300 mg), tralokinumab (300 mg), baricitinib (2 and 4 mg), and upadacitinib (15 and 30 mg) for the treatment of patients with severe AD from the Spanish National Health System (NHS) perspective.

Methods A hybrid model consisting of a decision tree linked to a Markov model was developed to estimate costs, quality-adjusted life-years (QALYs), total years in response and incremental cost-per-QALY gained (willingness-to-pay [WTP] threshold: €25,000/QALY). Adults with severe AD entered the decision tree and response (75% reduction in baseline Eczema Area and Severity Index score, EASI-75) was considered at 16 and 52 weeks. After this time, patients entered the Markov model (remainder of the 10-year time horizon), which consisted of three health states: maintenance with active therapy, subsequent treatment, or death. All costs were presented in 2022 euros (€). Additionally, cost per number-needed-to-treat (NNT) was calculated for abrocitinib and dupilumab based on a head-to-head post-hoc analysis.

Results Abrocitinib 200 mg was dominant (i.e., lower incremental costs and higher incremental benefit) compared with all studied alternatives (dupilumab 300 mg, tralokinumab 300 mg, baricitinib 2 and 4 mg, upadacitinib 15 and 30 mg) with a QALYs gain of 0.49, 0.60, 0.64, 0.43, 0.45, and 0.08, respectively, and per-person costs savings of €22,097, €24,140, €14,825, €7,116, €12,805, and €45,189, respectively. Considering the WTP threshold, abrocitinib was dominant or cost effective compared with all alternatives for most simulations. Additionally, abrocitinib was dominant compared with all alternatives when evaluating the cost effectiveness over a 5-year time horizon. NNT showed that abrocitinib was dominant versus dupilumab.

Conclusions The results of the study show that abrocitinib is a cost-effective therapy compared with other JAK inhibitors and biological therapies from the Spanish NHS perspective.

Key Points for Decision Makers

The analysis reveals that, when compared with other JAK inhibitors (baricitinib and upadacitinib) and biological treatment alternatives (dupilumab and tralokinumab), abrocitinib is a dominant therapy for the treatment of severe atopic dermatitis (AD) for the Spanish NHS, with lower costs and higher clinical benefits.

Abrocitinib's cost effectiveness, alongside its high efficacy and favorable safety profile, demonstrate its value as a treatment for severe AD.

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1 Introduction

Atopic dermatitis (AD) is a common chronic, relapsing inflammatory skin disease characterized by itchy, painful, and dry skin that affects up to 15% of children and 5% of adults worldwide [1, 2]. The severe form of the disease can affect up to 10% of that population [2]. In Spain, the estimated prevalence of severe AD in the general population aged ≥ 6 years is 0.10% [3]. Clinical manifestations of AD (mainly pruritus and pain) can negatively impact patients' quality of life, leading to impaired sleep and subsequent daytime tiredness and irritability, especially in those with severe forms of the disease [4, 5]. In fact, patients with AD frequently report negative effects on physical, emotional, and social life domains [6, 7]. In addition, AD has been associated with other atopic diseases, including asthma, allergic rhinitis, and food allergies [7]. Overall, AD imposes a high burden that might increase associated economic costs and healthcare resource utilization [4, 5]. No laboratory test for the diagnosis of AD exists. Instead, AD is diagnosed by clinical examination and its severity is classified with validated clinical tools like the Eczema Area and Severity Index (EASI) [8].

AD management aims to reduce symptoms and severity and improve long-term disease control [6]. Classical therapies for AD include emollients, topical corticosteroids and calcineurin inhibitors, and phototherapy, which have been the main treatment options for decades [9]. Moderate-to-severe cases require systemic therapies with immunosuppressants or corticosteroids [10]; however, their use is not indicated in the long term due to the emergence of adverse effects [10, 11]. The growing knowledge of the disease at a molecular level has led to the development of biological therapies targeting type 2 immune pathways IL-4 and IL-13 cytokines [7]. In this context, the monoclonal antibody dupilumab, the first biological therapy approved for treating patients with AD, has shown to have a positive benefit–risk profile [12]. However, responses to the therapy in some patients are not satisfactory [13], or patients may develop adverse events and need to discontinue. Other biologics targeting only IL-13, such as tralokinumab, have also been developed and are now approved in Europe [14]. As an alternative to biological therapies, the Janus kinase (JAK) inhibitors abrocitinib [15, 16], baricitinib [17], and upadacitinib [18–20] have been recently approved for use in moderate-to-severe AD, offering some advantages over biological therapies as they are orally available and have a rapid onset of action, especially with itch relief, and have potential to reach superior efficacy on endpoints compared with dupilumab [9].

Given the myriad of available therapies for severe AD, economic evaluations are needed to provide evidence on efficiency and help the National Health System (NHS) in decision making. The aim of this research was to evaluate, from the perspective of the Spanish NHS, the cost effectiveness of the JAK inhibitor abrocitinib (200 mg) compared with dupilumab (300 mg), tralokinumab (300 mg), baricitinib (2 and 4 mg), and upadacitinib (15 and 30 mg) for the treatment of patients with severe AD who showed an inadequate response or inability to tolerate topical treatments or required systemic treatment to control the disease. Additionally, cost per number-needed-to-treat (NNT) for abrocitinib and dupilumab were calculated based on a head-to-head study, as this is a widely used tool in medical decision making and may increase understanding and relevance of cost-effectiveness analysis findings [21].

2 Methods

2.1 Model Structure

The cost-effectiveness analysis was conducted using a hybrid model composed of a decision tree that captures short-term outcomes followed by a Markov model programmed in Excel, with a 10-year time horizon, to capture long-term outcomes. The structure of the model aims to capture the long-term treatment of a chronic condition such as AD. The design and implementation of the model was significantly informed by published literature [22] and other publicly available documentation reviewing and critiquing recent pharmacoeconomic modeling of treatments for AD [23, 24].

The model evaluated the costs and outcomes of adults with severe AD inadequately controlled with topical therapy or for whom topical therapies were medically inadvisable or required systemic treatment to control the disease. Patients entered the model through the decision tree (Fig. 1a), where they received abrocitinib or one of the comparators in combination with topical drug therapy. Response to treatment was assessed at 16 weeks as most of the included trials assessed their primary efficacy endpoint in this time period. Treatment response was defined by a ≥ 75% reduction in EASI score (EASI-75) after a patient began treatment. If patients responded to treatment and did not discontinue, they continued receiving the same intervention until week 52, when the response was again evaluated. If patients did not respond to treatment at any node of the decision tree, they were considered to stop treatment and start subsequent therapy.

After 52 weeks, patients entered the Markov model (Fig. 1b) for long-term maintenance treatment, which consisted of three health states: maintenance with active therapy (abrocitinib or a comparator), subsequent treatment (in case of discontinuation or loss of response), or death. The simulation was conducted on a 6-month cycle length (with

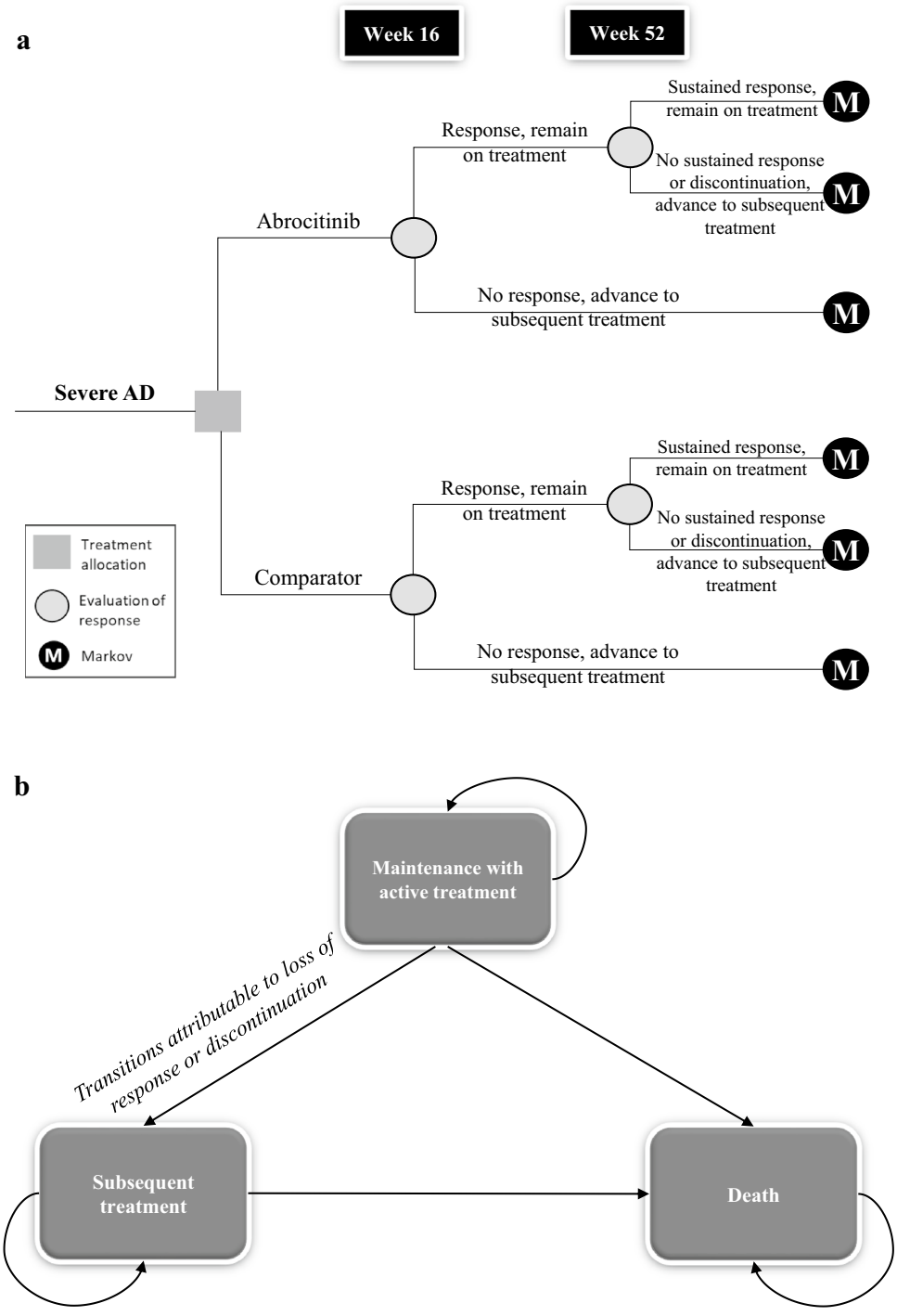

Fig. 1 Abrocitinib cost-effectiveness model structure. **a** Decision tree (until week 52); **b** Markov model (52+ weeks). *AD* atopic dermatitis

half-cycle correction) for the remainder of the time horizon. Patients who were still administered abrocitinib or a comparator following the first 52 weeks of treatment were treated continuously with that product until loss of response or treatment discontinuation (response was re-assessed after each cycle). When this occurred, patients transitioned to subsequent treatment, where they remained until death. Transition to death state (absorbing state) was possible from any health state.

The modelled population had a mean age of 34 years at the start of the model, based on the mean age of participants in abrocitinib studies [25]. The model considered age-dependent mortality data for the Spanish population obtained from the National Institute of Statistics mortality

tables [27]. The presence of AD did not increase the likelihood of death.

All data inputs were validated by a panel including three Spanish clinical experts (two dermatologists and one hospital pharmacist) through an advisory board and follow-up one-to-one consultations [28].

2.2 Efficacy

Key efficacy inputs used in the model included the time to onset of response, the response at 16 and 52 weeks (decision tree), the annual loss of treatment response (Markov model), and the discontinuation both in the year of treatment initiation and each year after that (decision tree and Markov model).

As described above, the response was defined as EASI-75 score (Table 1). The model assumed patients in treatment with JAK inhibitors begin experiencing therapeutic benefits at 8 weeks, as supported by clinical trial results that suggest response to abrocitinib commonly emerges within 4 weeks and has typically plateaued by 8 weeks [29]. For injectable medications (dupilumab and tralokinumab), it was assumed responders begin experiencing benefits at 16 weeks, as supported by clinical studies [29, 30].

Response rates are detailed in Table 1. The percentage of responders at 16 weeks was derived from a network meta-analysis for abrocitinib 200 mg, dupilumab 300 mg, tralokinumab 300 mg, and baricitinib 2 and 4 mg [31]. For upadacitinib 15 and 30 mg, response rates were derived from the AD-Up study [19].

Loss of treatment response beyond 52 weeks was assumed to occur at the same rate observed between 16–52 weeks (derived with reference to the proportion of week 16

Table 1 Clinical inputs

Treatment	Measure	References
Response rate at 16 weeks[a]		
Abrocitinib 200 mg	74.3%	Assumptions based on Silverberg et al. [31] and JADE COMPARE (data on file) [26]
Dupilumab 300 mg	61.5%	
Tralokinumab 300 mg	49.3%	
Baricitinib 2 mg	41.3%	
Baricitinib 4 mg	47.3%	
Upadacitinib 15 mg	67.7%	Assumptions based on Reich et al. [19] and JADE COMPARE (data on file) [26]
Upadacitinib 30 mg	80.7%	
Sustained response at 52 weeks among 16-week responders		
Abrocitinib 200 mg	94.7%	JADE EXTEND (data on file) [32]
Dupilumab 300 mg	82.1%	NICE Dupilumab [35]
Tralokinumab 300 mg	82.1%[b]	Assumption
Baricitinib 2 mg	82.9%[c]	Assumption
Baricitinib 4 mg	92.1%[d]	Assumption
Upadacitinib 15 mg	78.6%	Silverberg et al. [36]
Upadacitinib 30 mg	89.5%	Silverberg et al. [36]
Annual discontinuation probability		
16–52 weeks	6.9%	JADE EXTEND (data on file) [32]
52 weeks+	6.3%	CADTH Dupixent [23]
Utility weights		
Baseline utility	0.6156	Simpson et al. [34]
Treatment responders	0.8772	Simpson et al. [34]
Treatment non-responders	0.7777	Simpson et al. [34]
Subsequent treatment	0.6084	Simpson et al. [34]

[a]Efficacy data for the subgroup of adult patients with severe AD were only available for abrocitinib and dupilumab [26]. For comparators for which disaggregated data were unavailable for the adult-severe AD profile, the observed proportion of adult patients and change in response observed between patients with moderate-severe AD and those with severe AD was applied to the response rates obtained from the network meta-analysis (NMA) [31] or Reich et al. [19], based on JADE COMPARE [26]. For baricitinib and upadacitinib, the change observed for abrocitinib was applied, and for tralokinumab, the change from dupilumab was applied.

[b]The same rate as for dupilumab is assumed

[c]Assumed to be the mean between the rate of abrocitinib 100 mg and upadacitinib 15 mg

[d]Assumed to be the mean between the rate of abrocitinib 200 mg and upadacitinib 30 mg

responders who sustained response at week 52 based on the clinical trials of each comparator).

2.3 Treatment Discontinuation

Due to the lack of treatment discontinuation rates for each treatment, it was assumed to be the same for all comparators: 6.9% of patients discontinued during the first 52 weeks (based on rates observed for EASI-75 responders discontinuing abrocitinib 200 mg in JADE EXTEND) [32], and 6.3% discontinued each subsequent year (based on results from LIBERTY AD SOLO for dupilumab) [23].

2.4 Utility Values

The analysis applied health state utilities based on EuroQol instrument (EQ-5D-3L) data collected in two dupilumab phase III clinical trials for adults with moderate-to-severe AD [33] (Table 1), in line with NICE recommendations [24]. EQ-5D-3L is a standardized health-related quality of life (HRQoL) questionnaire which evaluates five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) in three levels of severity. Utilities reported range from 0 (death) to 1 (perfect health).

In addition, the model applied adjustment factors that accounted for the HRQoL impact of Spanish cohort aging [34]. Population norms were applied multiplicatively to treatment state utilities to reflect the aging of the cohort beyond its average age upon initiation of treatment and the resultant decline in baseline utility over time.

2.5 Cost

Costs included drug-related costs (acquisition and administration), adverse events (AEs) management, testing, medical visits and hospitalizations, and cost of subsequent treatment. All costs were presented in 2022 euros (€).

Drug costs were calculated using list prices obtained from the database of the Official College of Pharmacists [37] (the rebate established in Spanish Royal Decree-Law 8/2010 was applied [37]). In addition, a one-time cost of training patients to self-administer injectable products (specialized nursing visit) was included for dupilumab and tralokinumab (Table 2). No administration costs were considered for oral therapies.

Annual testing was assumed to be the same for all comparators. For AE management, the model included those experienced by at least 5% of participants in clinical trials for any comparator [29, 38–41]. Frequencies of AEs were annualized (Table S1, see electronic supplementary material [ESM]). AEs were assumed to be usually managed through a visit to a dermatologist or an ophthalmologist for allergic conjunctivitis (Table 2).

The model also accounted for the costs of primary care visits, emergency room visits, and hospitalizations depending on treatment response. The average annual utilization of each resource was derived from a longitudinal, non-interventional, retrospective cohort study in Canadian patients with AD [42], and Spanish unitary costs [43] were applied (Table 2).

For subsequent treatment, experts assumed an average cost between biological drugs and JAK inhibitors, considering the highest price of each category, in order not to underestimate the cost of this state (Table 2).

2.6 Model Outputs

The model reported outputs including total costs, years in response, years in subsequent therapy and quality-adjusted life-years (QALYs). The incremental cost per QALY gained was calculated. A willingness-to-pay (WTP) threshold of €25,000 per QALY gained was considered in line with the Spanish guidelines [44]. If the incremental cost-effectiveness ratio (ICER) of the treatment was below the WTP threshold, then it was considered a cost-effective alternative. When the intervention was both clinically superior and cost saving, it was referred to as an economically 'dominant' strategy. The opposite was a 'dominated' strategy. Another option is that an alternative was less costly, but also less effective.

Both costs and outcomes were discounted at 3% per year according to the local recommendations for economic evaluation of health technologies [45, 46].

2.7 Sensitivity Analyses

One-way sensitivity analysis (OWSA), scenario and probabilistic sensitivity analyses (PSA) were carried out to identify the most influential parameters and test the robustness of the results.

OWSA was performed to investigate the impact of individual model parameters used in the base-case analysis on model outcomes, using the hypothetical increases or decreases of 20%. Finally, results were compared with the base case in a tornado diagram.

The PSA was conducted using a Montecarlo simulation with 1000 iterations. A PSA simultaneously sets all inputs to a value randomly sampled from the appropriate distribution (Table S2, see ESM). When uncertainty data were not reported, the standard error was assumed to be 10% of the mean.

A scenario analysis was performed for a 5-year time horizon. To further account for the structural uncertainty, alternative scenarios were constructed to assess the impact of variations in discontinuation rates on cost effectiveness (i.e. maintaining the values of abrocitinib for 16–52 weeks and dupilumab for +52 weeks and increasing the other values

Table 2 Cost inputs

Cost type	Unit cost	Monthly cost	Loading dose cost	Administration cost	References
Drug costs					
Abrocitinib 200 mg	€31.73	€965.71			BotPlus [37], eSalud [43]
Dupilumab 300 mg	€560.34	€1218.24	€1120.68	€72.06	
Tralokinumab 150 mg	€280.17	€1218.24	€1120.68	€72.06	
Baricitinib 2 mg	€25.77	€784.37			
Baricitinib 4 mg	€25.77	€784.37			
Upadacitinib 15 mg	€31.08	€946.00			
Upadacitinib 30 mg	€62.16	€1892.00			
Subsequent treatment (monthly cost)[a]	€1555.12				Assumption
Test (annual cost)[b]	€394.28				eSalud [43]
AE management	€83.86 (ophthalmology visit) for allergic conjunctivitis/€74.68 (dermatology visit) for all other AE				eSalud [43]

Visits and hospitalizations by type of response	Responders utilization (annual)	Non-responder utilization (annual)	Cost per visit	
Hospitalization	0.30	0.50	€3059.93	Data on file [42], eSalud [43]
Emergency room visit	0.60	1.30	€268.38	
Primary care visits	9.80	21.20	€41.60	

AE adverse event

[a]Average cost of JAK inhibitor and biologic of highest price

[b]Annual testing includes: 1 renal function test, 1 lipid profile, 1 complete blood count, 1 liver function test, 1 tuberculosis test and 1 hepatitis B and C test. Same costs considered for all the pharmacological therapies included in the model

by 10% [scenario 1] or decreasing the other values by 2% [scenario 2]; using the same values for the same drug type, and increasing or decreasing the others by 2% [scenario 3 and 4]; Table S3, see ESM).

2.8 Number-Needed-to-Treat (NNT) and Cost Per Responder Analysis

The NNT is an outcome measure commonly used in clinical settings, providing a quick, short-hand approach to estimating relative efficacy of different treatments [47]. The NNT corresponds to the average number of patients who need to be treated with a particular therapy to achieve one extra positive outcome when compared with another therapy or placebo. The ideal NNT is 1 because it implies every patient treated will achieve the stated clinical benefit. The higher the NNT, the less effective the intervention [48].

$$\text{NNT} = \frac{1}{(\text{probability of treatment response} - \text{probability of placebo response})}$$

NNT is often used as a tool in medical decision-making [47]. For this reason, we additionally included an analysis of the cost per NNT for abrocitinib 200 mg and dupilumab 300 mg based on EASI-75 responders from a post-hoc analysis of patients with severe AD from the JADE COMPARE study [21, 49], as these are the unique treatments that have been compared in a head-to-head study. Firstly, the NNT for achieving an EASI-75 response was obtained using the difference in response for active treatment (abrocitinib 200 mg or dupilumab 300 mg) versus placebo at 12 and 16 weeks, where the NNT is calculated as the inverse of the probability of response to the active treatment minus the probability of response to placebo.

The cost per NNT for each drug was obtained by multiplying the annual cost of each therapy over the first year of treatment by its NNT (at 12 and 16 weeks).

Additionally, NNT for abrocitinib versus dupilumab was calculated. An incremental cost per additional patient with clinically meaningful outcome was calculated as the difference in annual drug costs (abrocitinib vs dupilumab) multiplied by the corresponding NNT. When the difference

in total cost is negative and the NNT is positive, the incremental cost per additional patient is denoted as 'dominant'.

3 Results

3.1 Base-Case Results

In the base-case analysis, abrocitinib 200 mg was dominant versus all alternatives (dupilumab 300 mg, tralokinumab 300 mg, baricitinib 2 mg, baricitinib 4 mg, upadacitinib 15 mg, and upadacitinib 30 mg), generating a QALYs gain of 0.49, 0.60, 0.64, 0.43, 0.45, and 0.08 with cost savings of €22,097.46, €24,139.97, €14,825.26, €7116.25, €12,805.37, and €45,189.39, respectively. Moreover, abrocitinib 200 mg led to an increase in response time versus comparators of 2.08, 2.55, 2.75, 1.84, 2.00, and 0.38 years, respectively. Table 3 contains the detailed base-case results.

3.2 Sensitivity Analyses

Sensitivity analyses confirmed the robustness of the results. Changes in parameters analyzed in the OWSA did not affect the results of dominance. The PSA showed that abrocitinib was dominant or cost effective versus all comparators for most of the simulations performed, considering the WTP threshold of €25,000 per QALY gained (Table 4).

3.3 Scenario Analyses

When evaluating the cost effectiveness over a 5-year time horizon, abrocitinib was dominant versus all comparators (dupilumab 300 mg, tralokinumab 300 mg, baricitinib 2 mg, baricitinib 4 mg, upadacitinib 15 mg, and upadacitinib 30 mg), generating a QALYs gain of 0.27, 0.35, 0.37, 0.27, 0.22, and 0.01 with per-person cost savings of €13,984, €15,503, €7910, €3867, €6023, and €30,839, respectively. Table 5 describes the model results for a 5-year time

Table 3 Base-case results

Results	Abrocitinib 200 mg	Dupilumab 300 mg	Tralokinumab 300 mg	Baricitinib 2 mg	Baricitinib 4 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Costs							
Pharmacological	€132,241	€152,652	€154,389	€144,947	€137,906	€143,507	€177,023
Drug administration	€0	€72	€72	€0	€0	€0	€0
Adverse events	€518	€487	€423	€492	€520	€526	€657
Testing costs	€1625	€968	€799	€702	€1002	€965	€1507
Medical visits and hospitalization	€18,883	€21,186	€21,724	€21,951	€20,956	€21,074	€19,270
Total costs	€153,267	€175,365	€177,407	€168,092	€160,383	€166,073	€198,457
Total QALYs	6.33	5.84	5.73	5.70	5.90	5.88	6.25
Years in response	4.43	2.35	1.89	1.68	2.59	2.43	4.05
Years in subsequent therapy	5.55	7.62	8.09	8.30	7.39	7.55	5.93
ΔCost (abrocitinib vs)		− €22,097	− €24,140	− €14,825	− €7116	− €12,805	− €45,189
ΔQALYs (abrocitinib vs)		0.49	0.60	0.64	0.43	0.45	0.08
ICER (abrocitinib vs)		Dominant	Dominant	Dominant	Dominant	Dominant	Dominant

ICER incremental cost-effectiveness ratio, *QALYs* quality-adjusted life-years

Table 4 PSA results of the base case

Results	Abrocitinib 200 mg vs					
	Dupilumab 300 mg	Tralokinumab 300 mg	Baricitinib 2 mg	Baricitinib 4 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Dominant	88.2%	88.8%	85.5%	70.2%	86.4%	60.9%
Cost effective	0.4%	0.7%	3.4%	11.7%	1.7%	0.0%
Not cost effective	0.0%	0.0%	0.3%	5.9%	0.7%	0.0%
Less costly, less effective	11.4%	10.4%	10.5%	8.6%	10.3%	39.1%
Dominated	0.0%	0.1%	0.3%	3.6%	0.9%	0.0%

PSA probabilistic sensitivity analysis

horizon. PSA results demonstrated the robustness of the analysis (Table S4, see ESM).

Table 6 presents the results of the scenarios related to changes in discontinuation values. In all scenarios, abrocitinib was found to be dominant over all alternatives.

3.4 NNT Analysis

The cost per NNT of abrocitinib and dupilumab versus placebo is shown in Table 7. Abrocitinib had the lowest NNT compared with placebo to achieve an additional EASI-75 responder for both week 12 and week 16, demonstrating its sustainability of the response. As the EASI-75 response time increases, costs per NNT increase for both therapies, being lower for abrocitinib than for dupilumab in both cases.

When compared with dupilumab, the annual cost of abrocitinib was lower (−€4,151.04), with an NNT for EASI-75 responders of 4.37 for week 12 responders and 8.00 for week 16 responders, so abrocitinib was dominant compared with dupilumab as it was associated with lower costs and favorable clinical outcomes (Table 8).

4 Discussion

This analysis has shown that abrocitinib 200 mg is dominant (i.e., lower incremental costs and higher incremental benefit) compared with currently available alternatives, with QALY gains ranging from 0.08 to 0.64 and costs savings of €7116.25–€45,189.39. The cost difference was mainly explained by lower abrocitinib acquisition costs and lower medical visits and hospitalization costs for patients treated with abrocitinib. Regarding differences in clinical results, abrocitinib significantly increased time in response versus comparators, delaying the loss of response and the transition to subsequent therapy, and increasing QALYs.

Table 5 5-year time horizon deterministic results

Results	Abrocitinib 200 mg	Dupilumab 300 mg	Tralokinumab 150 mg	Baricitinib 2 mg	Baricitinib 4 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Total QALYs	3.54	3.27	3.18	3.16	3.27	3.31	3.52
Total costs	€78,280	€92,264	€93,783	€86,190	€82,147	€84,303	€109,120
ΔCost		− €13,984	− €15,503	− €7910	− €3867	− €6023	− €30,839
ΔQALYs		0.27	0.35	0.37	0.27	0.22	0.01
ICER		Dominant	Dominant	Dominant	Dominant	Dominant	Dominant

ICER incremental cost-effectiveness ratio, *QALYs* quality-adjusted life-years

Table 6 Deterministic results of scenarios with different discontinuation rates

Discontinuation scenario[a]	Abrocitinib 200 mg vs					
	Dupilumab 300 mg	Tralokinumab 300 mg	Baricitinib 2 mg	Baricitinib 4 mg	Upadacitinib 15 mg	Upadacitinib 30 mg
Scenario 1	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant
Scenario 2	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant
Scenario 3	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant
Scenario 4	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant

[a]Discontinuation scenarios: (1) maintaining the values of abrocitinib for 16–52 weeks (6.9%) and dupilumab for + 52 weeks (6.3%) and increasing the other values by 10%; (2) maintaining the values of abrocitinib for 16–52 weeks (6.9%) and dupilumab for + 52 weeks (6.3%) and decreasing the other values by 2%; (3) using the same values for the same drug type, and increasing the others by 2%; (4) using the same values for the same drug type, and decreasing the others by 2%

Table 7 NNT and cost per NNT by treatment response assessment period

Drug	Week 12 responders		Week 16 responders	
	NNT EASI-75 (95% CI)	Cost per NNT	NNT EASI-75 (95% CI)	Cost per NNT
Abrocitinib 200 mg	1.51 (1.28–1.73)	€17,478.91	1.88 (1.51–2.32)	€21,742.06
Dupilumab 300 mg	2.30 (1.79–3.05)	€36,266.27	2.45 (1.85–3.38)	€38,577.35

CI confidence interval, *EASI-75* 75% reduction in baseline Eczema Area and Severity Index score, *NNT* number needed to treat

Table 8 NNT and incremental costs per patient comparing abrocitinib with dupilumab

Drug	NNT EASI-75 (95% CI) week 12 responders	NNT EASI-75 (95% CI) week 16 responders	Cost difference	Incremental cost per additional patient with outcome
Abrocitinib vs dupilumab	4.37 (2.78–9.19)	8.00 (3.94–587.81)	− €4151.04	Dominant

CI confidence interval, *EASI-75* 75% reduction in baseline Eczema Area and Severity Index score, *NNT* number needed to treat

The probabilistic analysis confirmed deterministic results while allowing for full, simultaneous parameter variation. In addition, the scenario analyses confirmed the base-case results, demonstrating that abrocitinib is a dominant alternative in Spain, even with shorter time horizons or different discontinuation rates.

To the best of our knowledge, this is the first study to evaluate the cost effectiveness of abrocitinib versus currently available therapies for treating AD in Spain. This is also the first study to date to compare the cost per NNT of a JAK inhibitor versus a biologic for severe AD in Spain. As we have seen, treating severe AD patients with abrocitinib would result in more patients with improved outcomes at a lower cost. This calculation of cost per unit of clinical effectiveness is an approach clinicians and healthcare decision makers understand well. However, the value of this measure cannot be placed in relation to an established threshold of how much it is reasonable to invest per health outcome, unlike in cost-effectiveness models. It is therefore useful to have both methodologies available to complement health decisions [50].

Abrocitinib economic evaluation data are still scarce in the literature. In a previous study conducted in the US, the cost effectiveness of abrocitinib (using an average of the net prices of baricitinib and upadacitinib as a placeholder) versus the standard of care and dupilumab in patients with moderate-to-severe AD was evaluated; the authors reported a cost per QALY gained for the base case of US$148,300 for abrocitinib compared with the standard of care, resulting in a cost-effective alternative at a threshold of US$100,000–US$150,000. However, abrocitinib was not cost effective (US$303,400 per QALY gained) compared with dupilumab [51, 52]. It is worth noting that marketed prices for abrocitinib were not available at the time of the study. Moreover, cost effectiveness was estimated using a Markov model previously developed for dupilumab [51], which could explain, at least in part, the differences observed with respect to our study. In contrast, the analysis conducted by the Canadian Agency for Drugs and Technologies in Health showed that abrocitinib 200 mg was dominant versus dupilumab for the treatment of adults with moderate-to-severe AD, in line with our results [53]. Another study reported a post-hoc economic analysis of abrocitinib versus placebo or dupilumab using data from the clinical trials JADE MONO-2 [16] and JADE COMPARE [29], showing a reduction in overall work impairment and associated costs at week 12 in patients treated with abrocitinib compared with those receiving placebo, as reported in JADE MONO-2. Moreover, the mean number of physician visits in JADE COMPARE at week 16 was lower for abrocitinib (0.9) versus dupilumab (1.3) and placebo (1.6) [54]. These results are in line with the lower medical visits and hospitalization costs of abrocitinib versus dupilumab in our model.

A recent meta-analysis showed that abrocitinib is one of the most effective alternatives in improving Investigator's Global Assessment (IGA) and EASI scores while being a safe option for treating patients with moderate-to-severe AD [55, 56]. In line with this evidence, our analysis showed that patients treated with abrocitinib were more years in response than those treated with the alternatives. Regarding the impact of AD on patients' lives, recently published studies analyzed patient-reported outcomes in adults and adolescents with moderate-to-severe AD and showed that abrocitinib improved AD symptoms (itch severity, pain, erythema), sleep disturbance, depression, and anxiety, increasing general health-related quality of life in these patients [57, 58]. Consistent with these studies, our analysis showed that patients who received abrocitinib obtained a better response to treatment, translating into a higher number of QALYs and, therefore, a better quality of life.

Our model is subject to limitations. Firstly, efficacy data for the severe subgroup was not available for all treatments, so it was estimated by applying ratios of overall versus subpopulation response based on original data from JADE COMPARE of abrocitinib for JAK inhibitor and from dupilumab for tralokinumab. Moreover, response rates at 16 weeks for upadacitinib were not available from the network meta-analysis (NMA), so clinical trial data were used. However, the response rates of each drug were varied in the OWSA and had no significant impact on abrocitinib dominance. Secondly, treatment discontinuation was assumed to be the same for all treatments. However, a sensitivity analysis was performed including variations in discontinuation rates, noting that it does not impact dominance results. Thirdly, the model does not explicitly account for treatment sequencing; it assumes use of a basket of treatments (subsequent treatments), the cost of which is calculated as the mean between the JAK inhibitor and the biologic with the highest price. Nevertheless, the model aims not to compare sequences of treatment but to compare abrocitinib against its comparators

in the same treatment line. Furthermore, applying the same cost of subsequent therapy for all treatments, the only thing that influences it is the length of time patients are on subsequent therapy, which is lower for abrocitinib (as patients are on response longer). Another limitation is that resources consumption used for the estimation of medical visits and hospitalizations were derived from a Canadian study. Nevertheless, the expert panel validated the annual number of visits as representative of the Spanish environment. Finally, health state utilities were derived from two clinical trials for adults with AD but were not Spanish data. However, these health-state utilities are in line with NICE recommendations and were validated by Spanish clinical experts.

5 Conclusion

Abrocitinib is a dominant therapy compared with other JAK inhibitors and biological therapies for the Spanish NHS. These results might help decision making at a regulatory level regarding the use of abrocitinib in routine clinical practice.

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Declarations

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Conflicts of interest This analysis was sponsored by Pfizer, S.L.U., Spain. Arumi, Hernández-Martín, Herrera-Lasso, Llevat, De Lossada Juste, and Rebollo Laserna are employees of Pfizer (Spain). Aceituno Mata, Bellmunt, and Prades disclose that they are paid consultants to Outcomes10, a company paid by Pfizer to assist with the writing of this manuscript. Herranz Pinto has served as investigator and/or speaker for Abbvie, Almirall, Bristol Myers Squibb, Janssen, Leopharma, Lilly, Novartis, Pfizer, Regeneron, Sandoz, Sanofi, and UCB pharma. Campos Dominguez has served as speaker for Sanofi and Abbvie and as investigator for Abbvie. Romero Jimenez declares no conflicts of interest.

Availability of data and material Data are available from the corresponding author upon reasonable request.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Code availability The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions RMRJ, PHP, MCD validated the parameters and provided data about local management of patients. SAM, AB and MP performed the analysis. All authors participated in the interpretation of the results. The first draft of the manuscript was primarily written by SAM and AB, and all authors provided comment and revision on subsequent versions of the manuscript. All authors reviewed and approved the final manuscript.

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