Cost-Utility Analysis of Apremilast for the Treatment of Psoriatic Arthritis Patients in Spain

Carlos González, MD, PhD[1]; Raquel Almodóvar, MD[2]; Teresa Caloto, PhD, MPH[3]; María Echave, MSc[4]; Isabel Elías, MSc[4]; Tom Tencer, PhD[5]

[1]Department of Rheumatology, Gregorio Marañón University Hospital, Madrid, Spain; [2]Department of Rheumatology, Fundación de Alcorcón University Hospital, Madrid, Spain; [3]Department of Health Economics, Celgene Corporation, Madrid, Spain; [4]Pharmacoeconomics & Outcomes Research Iberia, Madrid, Spain; [5]Celgene Corporation, Warren, NJ, USA

BACKGROUND

- Psoriatic arthritis (PsA) is a type of systemic rheumatic disease associated with psoriasis that involves inflammation of the skin as well as the axial and peripheral terminal interphalangeal joints.[1] Patients with PsA have a diminished capacity to carry out daily activities and a reduced quality of life.[2,3]
- The majority of the recommendations and guidelines suggest the initial use of non-steroidal anti-inflammatory drugs in patients with active PsA, followed by disease-modifying anti-rheumatic drugs (DMARDs), and then biological therapies for patients who fail earlier treatments.
- Apremilast is an oral immunomodulator with anti-inflammatory activities used to treat adult patients with active PsA who cannot take or who have not responded well enough to conventional DMARDs.[4]

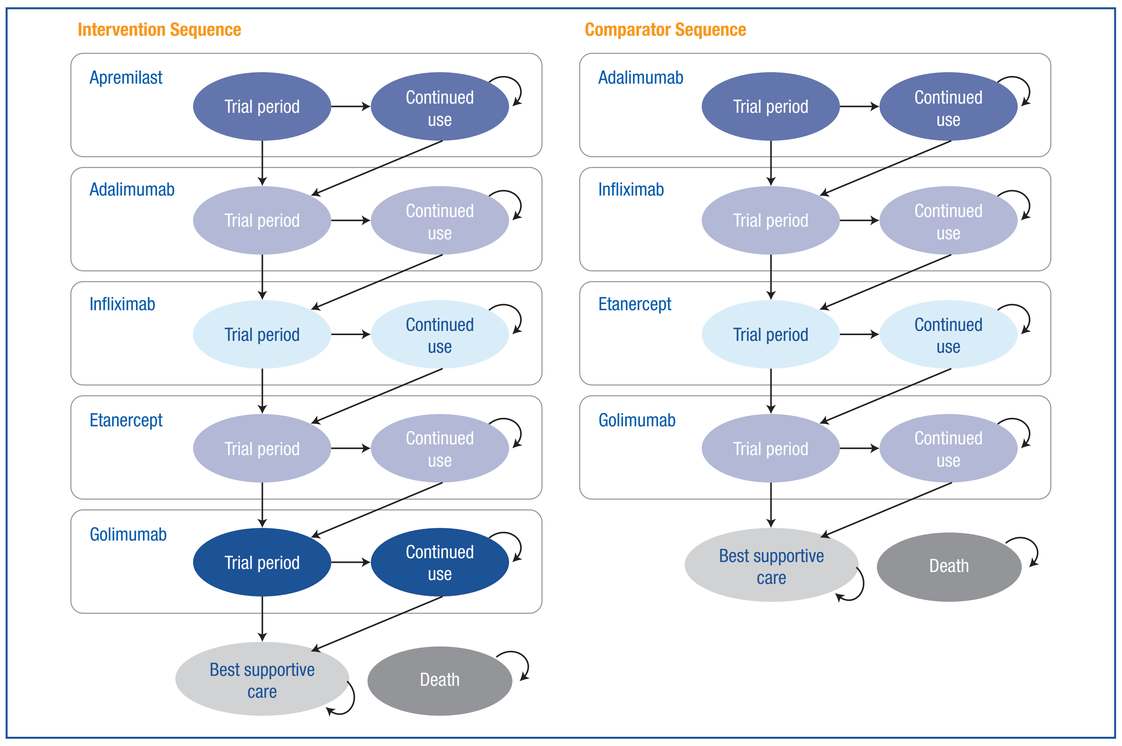
OBJECTIVE

- This cost-utility model was developed from the payer perspective to assess the impact of placing apremilast before biologicals in patients in Spain with active PsA who have failed to respond to or are intolerant of conventional DMARDs.

METHODS

- A Markov model was developed to compare 2 treatment sequences for a 20-year time horizon (monthly cycle duration) (**Figure 1**).
- Treatment strategies consisted of an apremilast before biological drugs sequence compared with a biological drugs only sequence.
- Sequential biologicals were adalimumab, infliximab, etanercept, and golimumab for both strategies. Patients who failed golimumab were assumed to have received best supportive care (BSC).

Figure 1. Markov Model Structure



- The reference cohort was provided by the clinical trial of apremilast, comprising a population with a mean age of 50 years and a mean weight of 85.6 kg.
- The Psoriatic Arthritis Response Criteria (PsARC) were used as the efficacy measure, and the drug response rates were obtained from a meta-analysis: apremilast (48.1%), adalimumab (62.3%), infliximab (78.9%), etanercept (74.1%), and golimumab (79.5%).
- All-cause overall mortality was adjusted with a hazard ratio (HR) associated with PsA (1.36).[5]
- Resource consumption was estimated by an expert panel, and biological doses were taken from the summary of products. The Spanish National Health System (NHS) perspective was considered, including the following costs: drug acquisition (ex-factory price[6] with mandatory deduction[7]), administration (for parenteral drugs), and monitoring costs. Unit costs (€, 2014) were obtained from national databases[8] (**Table 1**).
- The price used for apremilast was equivalent to the price submitted to the Spanish Health Technology Assessment during the price and reimbursement process (€820.00).

Table 1. Costs (€ 2014)

Drug	Ex-Factory Price[6]
Apremilast (Otezla®) 30 mg BID, 56 tablets – oral	€820.00
Adalimumab (Humira®) 40 mg, 2 injections 0.8 mL – SC	€1,028.29
Etanercept (Enbrel®) 50 mg, 4 injections 1 mL – SC	€947.22
Golimumab (Simponi®) 50 mg, 1 injection 0.5 mL – SC	€1,117.00
Infliximab (Remsima®) 100 mg, 1 vial – IV	€439.75
Administration for Parenteral Drug	**Unit Cost[8]**
Drug perfusion (0.5 hour–2 hours)	€156.10
Nurse personnel	€20.87/hour
Monitoring (Detailed Consumption Provided for Expert Panel)	**Annual Cost**
Apremilast	€418.02
Adalimumab, etanercept, golimumab, and infliximab	€476.10

SC=subcutaneous; IV=intravenous.

- An annual discount rate of 3% was applied for costs and outcomes.[9] A PsA baseline utility was corrected based on drug response with published evidence.
- The incremental ratio was calculated in terms of the cost per quality-adjusted life-years (QALYs) gained of the most effective sequence vs. the comparator.
- One-way deterministic and probabilistic sensitivity analyses were performed to test model robustness.

RESULTS

- At 20 years, the use of apremilast before biological drugs showed higher effectiveness (9.19 QALYs) than the sequence with biological drugs only (9.12 QALYs). The strategy with apremilast implied lower total costs (€209,372). Placing apremilast before biologicals is a dominant strategy.
- Results of the sensitivity analyses confirm the robustness of the model.
  - The strategy with apremilast showed higher effectiveness and lower total costs than the biological drugs only sequence in 8 of 9 results and higher effectiveness and total costs in the ninth result (**Table 2**).

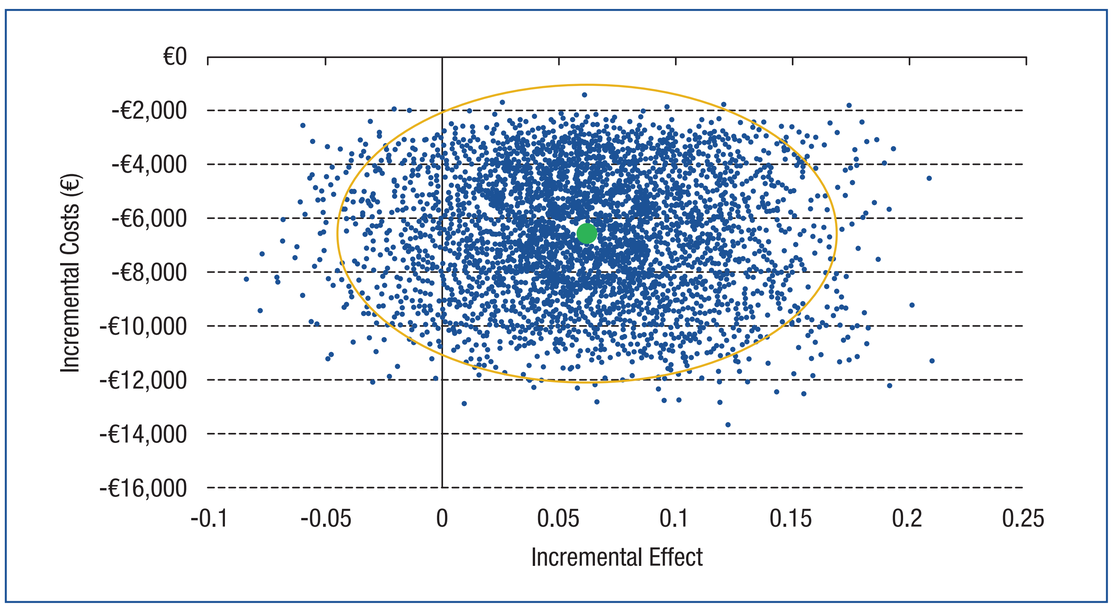
Table 2. One-Way Deterministic Sensitivity Analysis Results

Parameter	Base Case Parameters	Sensitivity Analysis Parameters	Incremental Total Cost (€)	Incremental QALY	Incremental Cost-effectiveness Ratio (€/QALY)
Base case			-6,541	0.06	Dominant
Time horizon	20 years	10 years	-6,503	-0.12	Lower cost and effectiveness
		Lifetime (40 years)	-6,339	0.36	Dominant
Discount rate	3%	0%	-6,976	0.17	Dominant
		5%	-6,283	0.02	Dominant
Drug order in biologics sequence	A >I >E >G	E >G >A >I	-6,378	0.07	Dominant
Efficacy measure	PsARC	ACR20	-6,541	0.06	Dominant
Mortality	HR for PsA: 1.36	No HR for PsA	-6,558	0.07	Dominant
BSC cost	1,091.69 €	-50%	-422	0.06	Dominant
		50%	-12,659	0.06	Dominant

A=adalimumab; E=etanercept; G=golimumab; I=infliximab.

- In the probabilistic sensitivity analyses, administration of apremilast before biologicals was a dominant strategy in 92% of the simulations and provided lower effectiveness and total costs in 8% of the remaining simulations (**Figure 2**).

Figure 2. Cost-effectiveness Plane



LIMITATIONS

- One of the limitations should be treatment efficacy, as no studies performed included all current therapies. However, this has already been solved by performing a meta-analysis.
- Due to the lack of studies, epidemiological data related to mortality and utilities have been considered from studies conducted in countries other than Spain. Nevertheless, based on their experience and knowledge, the expert panel considered that these data were representative of the Spanish population.
- The present model was developed from a third-party payer perspective; thus, it did not include indirect costs that could be useful for a societal analysis.

CONCLUSION

- Administration of apremilast before biologicals in patients with active PsA who have failed to respond to or were intolerant of conventional DMARDs is a cost-saving strategy for the Spanish NHS.

REFERENCES

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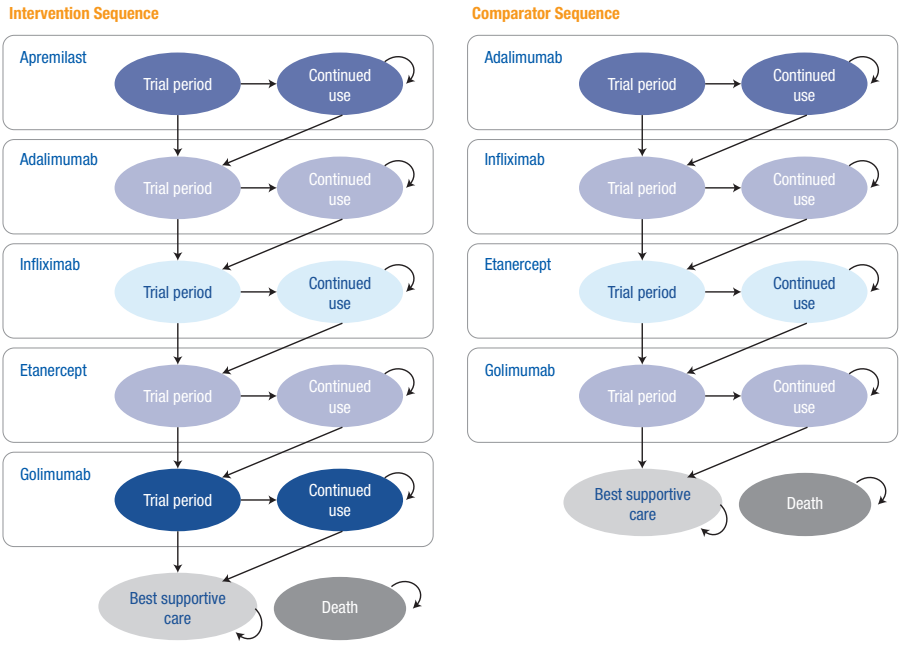

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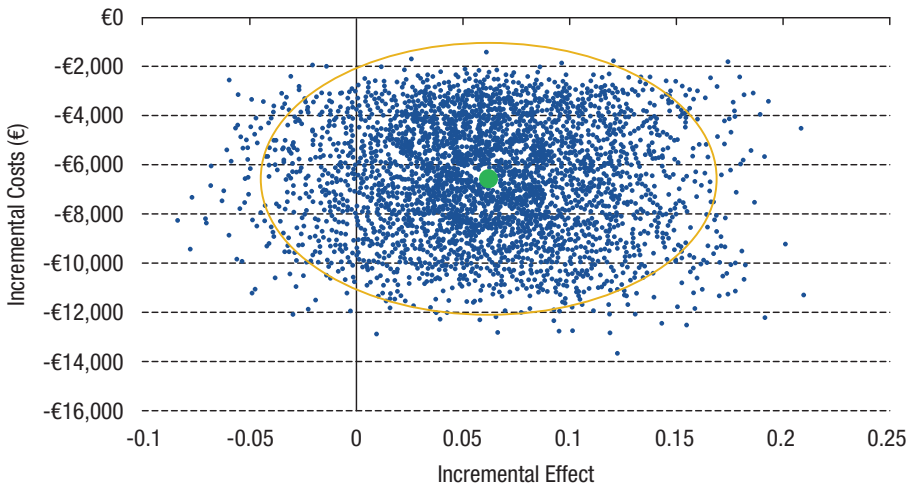

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