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

Carlos González, MD, PhD; Raquel Almodóvar, MD; Teresa Caloto, PhD, MPH; María Echeave, MSc; Isabel Elías, MSc; Tom Tencer, PhD
1Department of Rheumatology, Gregorio Marañón University Hospital, Madrid, Spain; 2Department of Rheumatology, Fundación de Alcorcón University Hospital, Madrid, Spain; 3Department of Health Economics, Celgene Corporation, Madrid, Spain; 4Pharmacoconomics & Outcomes Research Ibérica, Madrid, Spain; 5Celgene 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 interphalangeal joints.1 Patients with PsA have a diminished capacity to carry out daily activities and a reduced quality of life.1,2

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.3

Apremilast is an oral immunomodulator with anti-inflammatory activities used to treat adult patients with 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 biologics in patients with active PsA who have failed to respond to or are intolerant of conventional DMARDs.5

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 biologics 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

1. 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.

2. 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%).

3. All-cause overall mortality was adjusted with a hazard ratio (HR) associated with PsA (1.36).6

4. Resource consumption was estimated by an expert panel, and biological doses were taken from the summary of products. The Spanish National Health System (NSH) perspective was considered, including the following costs: drug acquisition (ex-factory price) with mandatory deduction7, administration (for parenteral drugs), and monitoring costs. Unit costs (€, 2014) were obtained from national databases8 (Table 1).

5. 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.

6. One-way deterministic and probabilistic sensitivity analyses were performed to test model robustness.

Table 1. Costs (€ 2014)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Ex-Factory Pricea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apremilast (Otezla®)</td>
<td>30 mg BD, 56 tablets – oral</td>
</tr>
<tr>
<td>Adalimumab (Humira®)</td>
<td>40 mg, 2 injections 0.8 mL – SC</td>
</tr>
<tr>
<td>Etanercept (Enbrel®)</td>
<td>50 mg, 4 injections 1 mL – SC</td>
</tr>
<tr>
<td>Golimumab (Simponi®)</td>
<td>100 mg, 1 injection 0.5 mL – SC</td>
</tr>
<tr>
<td>Infliximab (Remsima®)</td>
<td>100 mg, 1 vial – IV</td>
</tr>
</tbody>
</table>

Administration for Parenteral Drug

<table>
<thead>
<tr>
<th>Drug per infusion (0.5 hour–2 hours)</th>
<th>Unit Costb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nusea personal</td>
<td>€20.87/hour</td>
</tr>
</tbody>
</table>

Monitoring (Detailed Consumption Provided for Expert Panel)

| Apremilast | €18.02 |
| Apremilast, etanercept, golimumab, and infliximab | €476.10 |

RESULTS

At 20 years, the use of apremilast before biological drugs showed higher effectiveness (0.19 QALYs) than the sequence with biological drugs only (0.12 QALYs). The strategy with apremilast implied lower total costs (€209,372). Placing apremilast before biologics is a dominant strategy.

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base Case Parameters</th>
<th>Sensitivity Analysis Parameters</th>
<th>Incremental Total Cost (€)</th>
<th>Incremental QALY</th>
<th>Incremental Cost-effectiveness Ratio (€/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time horizon</td>
<td>20 years</td>
<td>10 years</td>
<td>-5,541</td>
<td>-0.06</td>
<td>Dominant</td>
</tr>
<tr>
<td>Drug order in</td>
<td></td>
<td></td>
<td>-5,603</td>
<td>0.36</td>
<td>Dominant</td>
</tr>
<tr>
<td>A &gt;I &gt;E &gt;G</td>
<td></td>
<td></td>
<td>-5,976</td>
<td>0.17</td>
<td>Dominant</td>
</tr>
<tr>
<td>Mortality</td>
<td>HR for PsA: 1.36</td>
<td>No HR for PsA</td>
<td>-6,378</td>
<td>0.07</td>
<td>Dominant</td>
</tr>
<tr>
<td>BSC cost</td>
<td>1,091.69 €</td>
<td></td>
<td>-12,659</td>
<td>0.06</td>
<td>Dominant</td>
</tr>
</tbody>
</table>

All additional: T=etanercept; G=golimumab; I=infliximab

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

LIMITATIONS

One of the limitations is the 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 biologics in patients with active PsA who have failed to respond to or are intolerant of conventional DMARDs is a cost-saving strategy for the Spanish NHS.

REFERENCES


This study was sponsored by Celgene Corporation.

Presented at: the SPOR 18th Annual European Congress; 7–11 November 2015; Milan, Italy.
Cost-Utility Analysis of Apremilast for the Treatment of Psoriatic Arthritis Patients in Spain

Carlos González, MD, PhD1; Raquel Almodóvar, MD2; Teresa Caloto, PhD, MPH3; María Echave, MSc4; Isabel Elías, MSc4; Tom Tencer, PhD5

BACKGROUND

Patients with PsA have a diminished capacity to carry out daily activities and a reduced quality of life.1-3

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 earlier treatments.

METHODS

A Markov model was developed to compare 2 treatment sequences for a 20-year time horizon (monthly cycle simulations).1-3

Comparator Sequence

Intervention Sequence

Adalimumab

Apremilast

In/f_liximab

Adalimumab

Etanercept

In/f_liximab

Etanercept

Golimumab

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

RESULTS

The strategy with apremilast showed higher effectiveness and lower total costs than the biological drugs (Table 2).

<table>
<thead>
<tr>
<th>Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity Analysis Parameters</td>
</tr>
<tr>
<td>Incremental Effectiveness</td>
</tr>
<tr>
<td>Incremental Cost-effectiveness Ratio (€/QALY)</td>
</tr>
<tr>
<td>Lower cost and death</td>
</tr>
<tr>
<td>Dominant</td>
</tr>
<tr>
<td>Lower cost and death</td>
</tr>
<tr>
<td>Dominant</td>
</tr>
<tr>
<td>Lower cost and death</td>
</tr>
<tr>
<td>Dominant</td>
</tr>
<tr>
<td>Lifetime (40 years)</td>
</tr>
<tr>
<td>Dominant</td>
</tr>
<tr>
<td>Discount rate</td>
</tr>
<tr>
<td>-€422</td>
</tr>
<tr>
<td>Dominant</td>
</tr>
</tbody>
</table>

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.

One of the limitations should be treatment efficacy, as no studies performed included all current therapies.

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 price used for apremilast was equivalent to the price submitted to the Spanish Health Technology Assessment during the price and reimbursement process (€820.00).

The price used for the biologicals was based on information from published literature.

One-way deterministic and probabilistic sensitivity analyses were performed to test model robustness.

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 price6 with mandatory deduction7), administration (for parenteral drugs), and monitoring costs. Unit costs (€, 2014) were obtained from national databases8 (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)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Ex-Factory Pricea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apremilast (Otezla®) 30 mg BID, 56 tablets – oral</td>
<td>€820.00</td>
</tr>
<tr>
<td>Adalimumab (Humira®) 40 mg, 2 injections 0.8 mL – SC</td>
<td>€1,028.29</td>
</tr>
<tr>
<td>Etanercept (Enbrel®) 50 mg, 4 injections 1 mL – SC</td>
<td>€947.22</td>
</tr>
<tr>
<td>Golimumab (Simponi®) 50 mg, 1 injection 0.5 mL – SC</td>
<td>€1,117.00</td>
</tr>
<tr>
<td>Infliximab (Remsima®) 100 mg, 1 vial – IV</td>
<td>€439.75</td>
</tr>
</tbody>
</table>

SC=subcutaneous; IV=intravenous.

- An annual discount rate of 3% was applied for costs and outcomes. 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**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base Case Parameters</th>
<th>Sensitivity Analysis Parameters</th>
<th>Incremental Total Cost (€)</th>
<th>Incremental QALY</th>
<th>Incremental Cost-effectiveness Ratio (€/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td></td>
<td></td>
<td>-6,541</td>
<td>0.06</td>
<td>Dominant</td>
</tr>
<tr>
<td>Time horizon</td>
<td>20 years</td>
<td>10 years</td>
<td>-6,503</td>
<td>-0.12</td>
<td>Lower cost and effectiveness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lifetime (40 years)</td>
<td>-6,339</td>
<td>0.36</td>
<td>Dominant</td>
</tr>
<tr>
<td>Discount rate</td>
<td>3%</td>
<td>0%</td>
<td>-6,976</td>
<td>0.17</td>
<td>Dominant</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5%</td>
<td>-6,283</td>
<td>0.02</td>
<td>Dominant</td>
</tr>
<tr>
<td>Drug order in biologics sequence</td>
<td>A &gt;I &gt;E &gt;G</td>
<td>E &gt;G &gt;A &gt;I</td>
<td>-6,378</td>
<td>0.07</td>
<td>Dominant</td>
</tr>
<tr>
<td>Efficacy measure</td>
<td>PsARC</td>
<td>ACR20</td>
<td>-6,541</td>
<td>0.06</td>
<td>Dominant</td>
</tr>
<tr>
<td>Mortality</td>
<td>HR for PsA: 1.36</td>
<td>No HR for PsA</td>
<td>-6,558</td>
<td>0.07</td>
<td>Dominant</td>
</tr>
<tr>
<td>BSC cost</td>
<td>1,091.69 €</td>
<td>50%</td>
<td>-422</td>
<td>0.60</td>
<td>Dominant</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-50%</td>
<td>-12,659</td>
<td>0.06</td>
<td>Dominant</td>
</tr>
</tbody>
</table>

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

- In the probabilistic sensitivity analyses, administration of apremilast before biologics 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](image)

**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


This study was sponsored by Celgene Corporation.
Presented at: the ISPOR 18th Annual European Congress; 7–11 November 2015; Milan, Italy.