Cost-effectiveness of ruxolitinib vs. Best Available Therapy in the treatment of myelofibrosis in Spain


1. Dr. Negrin University Hospital, Las Palmas de Gran Canaria (Spain); 2. Dept. of Hematology, Clinic University Hospital, Valencia (Spain); 3. Cpt. Of Hematology and Hemotherapy, Regional University Hospital, Malaga (Spain); 4. Dept. Of Hematology, 12 delvocablo Hospital, Madrid (Spain); 5. Cytogenetics, Castellon de la Plana (Spain); 6. Neuroradiology, Barcelona (Spain).

Introduction

- Primary myelofibrosis (MF) is a rare philadelphia-negative myeloproliferative neoplasms. Its prevalence is generally estimated at 24,000 people, yielding an estimate of approximately 1,400 patients in Spain.
- MF is associated with significant symptom burden which reflects on high healthcare costs. Recently, direct annual annual costs ranging between $2,400 and $25,576 per patient in the US were estimated.
- Furthermore, a Spanish study reported a mean indirect cost of $86,315 per patient ($168,456 for more symptomatic patients).
- Ruxolitinib is the first JAK1/2 inhibitor approved for the treatment of disease-related splenomegaly or symptoms in patients with MF with evidence of rapid and sustained splenomegaly reduction, symptom improvement and overall survival (OS) increase.

Objective

- To assess the cost-effectiveness of ruxolitinib vs. available therapy (BAT) in MF patients in Spain from a societal perspective.

Materials and methods

Model structure

- A global model built in Microsoft Excel® was adopted to the Spanish setting. The model is structured in two main parts: a decision tree and a 3-health states Markov model (Figure 1).

Figure 1 Decision tree and Markov model health states

- A lifetime horizon of 15 years was considered, based on the NICE ERG recommendations. Cycle length was 20 days. Costs and benefits were discounted at an annual rate of 3%.
- Main inputs of the model include incremental cost-effectiveness (ICER) and cost-utility ratio (ICUR) based on the following outcomes: life years (LYs) gained, quality adjusted life years (QALYs) and total costs.
- Key assumptions and main inputs (Table 1-Table 3) were validated by clinicians experienced in the treatment of BAT.

Table 1: Cost-effectiveness results

<table>
<thead>
<tr>
<th>Cost per patient (€)</th>
<th>LYG</th>
<th>QALYs</th>
<th>ICER</th>
<th>ICUR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruxolitinib</td>
<td>704,504</td>
<td>6.1</td>
<td>4.4</td>
<td>47,159</td>
</tr>
<tr>
<td>BAT</td>
<td>43,425</td>
<td>3.5</td>
<td>2.2</td>
<td>-</td>
</tr>
<tr>
<td>Difference</td>
<td>661,079</td>
<td>2.6</td>
<td>2.2</td>
<td>-</td>
</tr>
</tbody>
</table>

Sensitivity analysis

- A One-Way Sensitivity Analysis (OWSA) and a Probabilistic Sensitivity Analysis (PSA) were run to evaluate the consistency of the results under the uncertainty of the input data.
- The OWSA sequentially introduces a variation of ±20% of the base case value for each input parameter. The Spanish National Health System perspective was also considered as an alternative scenario.
- The PSA ran a Monte Carlo simulation with 1,000 iterations while varying the input values according to predefined probability distributions and their corresponding parameters. For the parameterized survival curves, a Choquetes dissection of the variance/covariance matrix was used to vary the defining parameters. Gamma distributions were used for costs, proportions and utilities while sampling from beta distribution, while a normal distribution was used for baseline utility.

Results

- The ICER and the ICUR of ruxolitinib vs. BAT were €47,159/LYG and €55,635/QALY respectively (Table 4).

Table 4: Cost-effectiveness results

- The OS curve lambda parameter for BAT and the baseline utility values had the greatest impact on the ICUR (Figure 2).

Figure 2: Tornado diagram: ICUR (cost/QALY) variation caused by individual variations of the input parameters

- The OS curve lambda parameter for BAT and the baseline utility values had the greatest impact on the ICUR (Figure 2).

Clinical effectiveness

- Transition probabilities were obtained from the OS curves of the COMFORT-I >5 years’ clinical trial (CT), adjusted to account for the crossover between treatment arms. Parametric extrapolation methods were used to project survival over the 15-year time horizon.
- Utilities were derived from the COMFORT-I CT.

Costs estimation

- Costs included pharmacological treatment, resource use, as well as adverse events (grade 3-4) management, loss of productivity, transformation to AML, and end-of-life costs (Table 2, Table 3).
- Unit costs were derived from Spanish healthcare cost databases. Frequency of use was obtained from the literature and the experts opinion.
- Loss of productivity was estimated based on the age distribution of patients in the COMFORT-ITC and the average annual income from the Spanish National Institute of Statistics. A proportion of 25.1% of patients was assumed to be working in both treatment arms. Mean number of working days/year was estimated in 250 and 260 for ruxolitinib and BAT respectively, yielding a cost per cycle of 263.04 and 231.41 € in each treatment arm.

Table 2: Unit cost, frequency and percentage of patients requiring use of resources

- PSA
- The PSA showed that 95.9% of the iterations fell into the upper-right quadrant of the cost-effectiveness plane, meaning that ruxolitinib is more effective and more costly than BAT.
- Ruxolitinib has 61% probability of being cost-effective at the threshold established by the NICE for oncology drugs that meet End-of-Life (eLC) criteria ($61,500/QALY) (Table 3).

Figure 3: Cost-effectiveness scatterplot (a) and acceptability curves (b) of ruxolitinib vs. BAT

Conclusions

- According to this analysis ruxolitinib is an effective therapeutic option and can be regarded as cost-effective in comparison with BAT for the treatment of MF-related symptoms in Spain.

References