Economic Analysis of Rituximab in Combination with Cyclophosphamide, Vincristine and Prednisolone in the Treatment of Patients with Advanced Follicular Lymphoma in Portugal

INTRODUCTION

- Non-Hodgkin’s lymphoma (NHL) is the 5th most common cancer in most countries, with an estimated 1.5 cases worldwide in 2000.
- Incidence estimates for NHL vary ten to twelve fold across countries, ranging from 1.6 to 17.1 new cases per 100,000 persons per year among men and 0.7 to 11.7 new cases per 100,000 persons per year among women.
- In Portugal, an estimated total number of new cases and deaths by NHL in 2002 among men was 622 and 284, respectively, and 533 cases and 264 deaths among women.
- More men than women are diagnosed with NHL and incidence increases with age.
- Rituximab is a monoclonal antibody that binds specifically to the transmembrane antigen, CD20, a non-glycosylated phosphoprotein, located on pre-B and mature B lymphocytes. The antigen is expressed on >95% of all B cell non-Hodgkin’s lymphomas.

OBJECTIVE

- Evaluate costs and benefits of rituximab in combination with cyclophosphamide/ vincristine/ prednisolone chemotherapy regimen (R-CVP) versus CVP alone in previously untreated patients with indolent NHL.

METHODS

Pharmacoeconomic model

A Markov model with 3 health states: “Progression Free Survival” (PFS), “Progression” and “Death” (Figure 1) was used to estimate the cost-effectiveness (Life Years Gained – LYG) and cost-utility (Quality Adjusted Life Years – QALYs) of R-CVP regimen versus CVP alone.

Population

A hypothetical cohort of Portuguese patients of both genders aged 18 years or above with follicular NHL, Ann Arbor stage III or IV, International Working Formulation B, C or D categories (1-3 follicular scales of World Health Organization), global state of the Eastern Cooperative Oncology Group (ECOG) score between 0 and 2 and with measurable and previously untreated disease.

Model assumptions

- Comparators: R-CVP and CVP (pivotal clinical trial M39021).
- All patients enter the model in the PFS health state, having completed treatment with either R-CVP or CVP alone. The transition to other health states is performed in 1 month length cycles with a standard half-cycle correction.
- Based on the published data, with a median follow-up of 30 months, no clinically significant toxicity between the two regimens (CVP and R-CVP) was observed, so the costs of treating adverse events was not considered.
- The mean age of patients entering the model is assumed to be 53 years (this is comparable to the mean age of patients in the pivotal clinical trial M39021).
- The “Progression” health state represents the survival, costs and quality of life of a patient from the time of relapse after 1st line therapy (or non-response to 1st line therapy) to death, including 2nd and later line treatments, remissions and relapses.
- Time horizon: 10 years with possible extrapolation of survival curves to 300 months (25 years) through Log-logistic function (Figure 2 and Figure 3).
- 5% annual discount rate for costs and consequences (QALYs, LYG).
- Portuguese National Health System (NHS) perspective (direct medical costs supported by NHS) was applied.

RESULTS

- The base-case analysis (10 years) show that (Table 2):
  - The total cost per patient was lower with CVP (€ 88,373) vs. R-CVP (€ 88,373) vs. R-CVP (€ 99,899);
  - LYG and QALYs per patient were higher with R-CVP (6.596 and 4.045, respectively), representing increases of 1.655 in LYG and 1.308 in QALYs;
  - In this scenario R-CVP remains a cost-effective alternative to CVP and the incremental cost per QALY gained was € 6,006.

- Probabilistic sensitivity analysis (± 20% variation considering resource consumption and costs) resulting in € 30,000/QALY “willingness-to-pay” threshold and a time horizon of 10 and 25 years, R-CVP in some simulations is “dominant” (Figure 4 and Figure 5). This analysis confirmed the robustness of the model, once the results obtained were similar to the base-case analysis results (Table 2).

CONCLUSIONS

The results of this pharmacoeconomic analysis demonstrates that the combination R-CVP in previously untreated NHL patients improves life expectancy and is a cost-effective alternative to CVP in Portugal.

REFERENCES

5. Lymphoma: Pathology, Diagnosis and Treatment; Edited by Robert Marcus, John W. Sweetenham and Michael E. Williams, Cambridge University 2007.
7. Pharmacoeconomic model

Figure 1: Markov model diagram

Table 1: Summary of costs used in the model

<table>
<thead>
<tr>
<th>Costs</th>
<th>CVP</th>
<th>R-CVP</th>
</tr>
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<tbody>
<tr>
<td>Treatment costs</td>
<td>€ 88,373</td>
<td>€ 99,899</td>
</tr>
<tr>
<td>Incremental cost per QALY gained</td>
<td>€ 6,006</td>
<td></td>
</tr>
</tbody>
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Table 2: Econometric analysis and probabilistic sensitivity analysis at 10 and 25 years

<table>
<thead>
<tr>
<th>Year</th>
<th>Baseline analysis</th>
<th>Probabilistic sensitivity analysis</th>
</tr>
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<tbody>
<tr>
<td>Total Cost</td>
<td>Incremental</td>
<td>Total LYG</td>
</tr>
<tr>
<td>CVP</td>
<td>€ 88,373</td>
<td>€ 99,899</td>
</tr>
<tr>
<td>R-CVP</td>
<td>€ 88,373</td>
<td>€ 99,899</td>
</tr>
</tbody>
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Figure 2: Fitted log-logistic function plotted against Kaplan-Meier survival curves from 30-month clinical trial M39021 data for the CVP and R-CVP arms.

Figure 3: KAF plot of the Monte Carlo simulation: 10 year analysis.

Figure 4: KAF plot of the Monte Carlo simulation: 25 year analysis.

Figure 5: Scatter plot of the Monte Carlo simulation: 25 year analysis.

Figure 6: Scatter plot of the Monte Carlo simulation: 25 year analysis.