CANCER: AN ECONOMIC ANALYSIS BASED ON THE CALGB 80405 TRIAL

1 – INTRODUCTION

• Bevacizumab (Avastin) is an anti-angiogenic humanized monoclonal antibody which binds to vascular endothelial growth factor (VEGF) to inhibit angiogenesis for continuous tumour control.

• Avastin is approved in combination with fluoropyrimidine-based chemotherapy for the treatment of patients with epidermal growth factor receptor (EGFR) - expressing, RAS wild-type metastatic colorectal cancer (mCRC) in combination with irinotecan-based chemotherapy, in first-line in combination with FOLFOX, as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan [2].

• Both treatments have been shown to bring similar efficacy for the KRAS wild-type population [3]. However, cetuximab is recognized to be more expensive than bevacizumab in Portugal.

• The objective of this study was to perform a cost-effectiveness analysis comparing bevacizumab versus cetuximab in combination with FOLFOX or FOLFIRI in patients with KRAS wild type mCRC.

2 – METHODS

Model

Partitioned survival model with three health states - free survival (PFS), in progression, death - and weekly cycles

Population

Patients with KRAS wild-type mCRC, 60 years, 69 kgs, 165 cm, 1.76 cm², 57.6% KRAS not mutated

Treatment arms

• Bevacizumab (Avastin): 3 mg/kg every 2 weeks + FOLFOX or FOLFIRI
• Cetuximab (Erbitux): 400 mg/m² initial dose, then 250 mg/m² weekly + FOLFOX or FOLFIRI
• Patients in FOLFOX / FOLFIRI 73.4% / 26.6%.

• FOLFOX every 2 weeks: Oxaliplatin 85 mg/m² on day 1 of each cycle; Leucovorin 200 mg/m² on day 1 and 2 and of each cycle; Fluorouracil: 400 mg/m² on day 1, 2 and 2 of each cycle; Fluorouracil IV: 500 mg/m² on day 1 and 2 of each cycle; FOLFIRI every 2 weeks: Irinotecan: 180 mg/m² on day 1 of each cycle; Leucovorin 200 mg/m² on day 1 of each cycle; Fluorouracil: 400 mg/m² on day 1, 2 and 2 of each cycle; Fluorouracil IV: 3000 mg/m² on day 1 of each cycle (see [48]).

Treatment duration

• Treatment duration has been modelled using PFS estimates as a proxy and adjusting down the curve using a hazard ratio for bevacizumab and cetuximab of 1.5
• Median treatment durations: 9.0 months for bevacizumab and 8.3 months for cetuximab

Time horizon

12 years (after 12 years, less than 1% of patients are expected to be alive)

Efficacy, quality of life and data

• PFS and overall survival (OS) from CALGB 80405 trial
• Gamma / Weibull distributions to extrapolate PFS / OS after trial period.
• QALYs based on EQ-5D questionnaire
• Incidence of grade 3/4 adverse events from CALGB 80405 trial

Costs

• Direct medical costs: drug costs (including wastage), drug administration costs, incidence of grade 3/4 adverse events (AEs), KRAS test, PFS supportive care and treatment of AEs costs.
• Indirect costs were not obtained using Portuguese official sources.

Discount rate

5% per annum in costs and health consequences [4]

Perspective

Portuguese National Health Service (NHS).

3 – RESULTS

• Bevacizumab and cetuximab presented no statistically significant difference in terms of clinical benefit – PFS, OS and QALYs.
• The model predicted total cost of €84,268 or €103,305 for treating a mCRC patient with bevacizumab or cetuximab, respectively (Table 2).
• Acquisition cost of bevacizumab is lower than cetuximab (€15,449/patient) as well as supportive care while on progressive disease (-€4,458/patient); supportive care while on PFS is slightly higher in bevacizumab arm (+€553/patient) and showed the robustness of the results (Figure 2).

4 – CONCLUSIONS

• The proposed model predicts similar health consequences - efficacy - for bevacizumab and cetuximab.
• Bevacizumab treatment results in a cost-saving of €19,000 per mCRC patient to the Portuguese NHS vs cetuximab treatment.
• Major cost drivers are acquisition drug costs and patients’ management in the progression health state.
• The use of bevacizumab in KRAS wild type mCRC patients permit to achieve substantial cost-savings by the Portuguese NHS representing a cut of 39% on the biologic drug costs over a 12-year horizon.

REFERENCES


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Table 1 – Costs and sources

<table>
<thead>
<tr>
<th>Costs</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs</td>
<td></td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>€ 2,057.00/month [5]</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>€ 3,592.00/month [5]</td>
</tr>
<tr>
<td>Oxaliplatin 50 mg - 100 mg</td>
<td>€ 498.6 - € 7.27 [5]</td>
</tr>
<tr>
<td>Irinotecan 40 mg - 300 mg</td>
<td>€ 523.18 - € 18.59 [5]</td>
</tr>
<tr>
<td>Leucovorin 50 mg - 300 mg</td>
<td>€ 1.49 - € 5.57 [5]</td>
</tr>
<tr>
<td>Fluorouracil 500 mg - 1000 mg</td>
<td>€ 1.34 - € 2.16 [5]</td>
</tr>
<tr>
<td>Administration</td>
<td></td>
</tr>
<tr>
<td>Drug infusion</td>
<td>€ 20.20 DRG 99350 [6]</td>
</tr>
<tr>
<td>Supportive care</td>
<td></td>
</tr>
<tr>
<td>PFS/month</td>
<td>€ 292.28/month Expert panel [5, 6, 7]</td>
</tr>
<tr>
<td>Progression/month</td>
<td>€ 1,019.70/month Expert panel [5, 6, 7]</td>
</tr>
<tr>
<td>KRAS test</td>
<td>€ 110.70 DRG 36058 [6]</td>
</tr>
<tr>
<td>AE treatment</td>
<td></td>
</tr>
<tr>
<td>Neupogen (grade 3-4)</td>
<td>€108.15 Expert panel [5, 6, 7]</td>
</tr>
<tr>
<td>Rash (grade 3-4)</td>
<td>€ 432.75 Expert panel [5, 6, 7]</td>
</tr>
<tr>
<td>Ototoxicity (grade 3-4)</td>
<td>€ 2,701.91 Expert panel [5, 6, 7]</td>
</tr>
<tr>
<td>Hyperglycemia (grade 3-4)</td>
<td>€ 520.63 Expert panel [5, 6, 7]</td>
</tr>
<tr>
<td>Gastointestinal events (grade 3-4)</td>
<td>€ 2,701.91 Assumption [diabetes]</td>
</tr>
</tbody>
</table>

Table 2 – Incremental cost analysis (bevacizumab vs cetuximab)

<table>
<thead>
<tr>
<th>Costs</th>
<th>Bevacizumab arm</th>
<th>Cetuximab arm</th>
<th>Incremental (bevacizumab vs cetuximab)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS</td>
<td>€ 45,000</td>
<td>€ 50,629</td>
<td>€ 5,629</td>
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<tr>
<td>Progression</td>
<td>€ 39,238</td>
<td>€ 43,676</td>
<td>-€4,438</td>
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<tr>
<td>Total</td>
<td>€ 84,268</td>
<td>€ 103,305</td>
<td>-€19,037</td>
</tr>
</tbody>
</table>

*Includes acquisition and administration of drugs, KRAS test, PFS supportive care and treatment of AEs costs.

Figure 1 – Cost components

Table 2 – Incremental cost analysis (bevacizumab vs cetuximab)

Figure 2 – Sensitivity analysis

Incremental cost (bevacizumab vs cetuximab)/patient:

Time: 10 years -€17.930 €

Time: 5 years -€13.041 €

Cetuximab cost: -€17.67 €

No wortinag -€20.514 €

Discount rate 0% -€23.332 €

Treatment duration (HR: 1.25) -€19.477 €

Treatment duration (HR: 1.75) -€21.252 €

Cost by health state >20% -€17.330 €

Cost by health state >20% -€19.728 €

FOLFOX/FOLFIRI 50%/50% -€18.334 €

FOLFOX/FOLFIRI 50%/50% -€19.037 €

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