I. Introduction

Melanoma is a public health concern because of the aggressiveness and high mortality in the advanced stage. In Spain, the incidence adjusted per 100,000 inhabitants is 5.5 for men and 5.3 for women, with approximately 850 deaths every year.4

No approved chemotherapy agents for advanced melanoma have provided an additional survival benefit as compared to the standard of care for most patients (dacarbazine) in the past 30 years, being 2 to 6 months the median overall survival (OS) for advanced melanoma patients on treatment.6

Ipilimumab obtained CHMP positive opinion in 2011 and has improved the OS in a number of studies.5 Therefore, it is necessary to evaluate the overall costs and survival benefits associated to ipilimumab with respect to the standard of care for most patients (dacarbazine) in advanced melanoma patients.

II. Methods

Model description

A 3-health states Markov model (Figure 1) with 3-week cycles was developed. All patients started in stable state. Transition probabilities were based on progression-free survival (PFS) and OS data from clinical trials.

Figure 1. Health states

Costs estimation

Direct costs included: drug acquisition and administration, disease and AEs management. Unit costs were derived from Spanish healthcare cost databases (€, 2013).14

Drug acquisition and administration

First line (dacarbazine, dacarbazine) and second-line (dacarbazine, paclitaxel, temozolomide, fotemustine, vemurafenib, ipilimumab) drug costs were considered (Table 1). The costs of second-line drugs were added to each treatment arm by taking a weighted average cost based on market share.

Table 1. Cost per cycle model (€/day)

<table>
<thead>
<tr>
<th>Drug (mg/kg)</th>
<th>Target dose (mg)</th>
<th>Drug cost (€)</th>
<th>Administration cost (€)</th>
<th>Total cost (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPI (10 mg/kg)</td>
<td>210</td>
<td>668</td>
<td>16,779</td>
<td></td>
</tr>
<tr>
<td>Dacarbazine (80 mg/m²)</td>
<td>1,520</td>
<td>22</td>
<td>260</td>
<td></td>
</tr>
<tr>
<td>Paclitaxel (260 mg/m²)</td>
<td>458</td>
<td>1,239</td>
<td>268</td>
<td></td>
</tr>
<tr>
<td>Temozolomide (200 mg/m²)</td>
<td>306</td>
<td>599</td>
<td>501</td>
<td></td>
</tr>
<tr>
<td>Fotemustine (130 mg/m²)</td>
<td>180</td>
<td>791</td>
<td>1,363</td>
<td></td>
</tr>
<tr>
<td>Vemurafenib (240 mg)</td>
<td>1,920</td>
<td>6,410</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

• Median patient weight: 76 kg, mean patient body surface area: 1.7 m².
• Drug dose and drug dose reduction were assumed.
• Administration (100 %): ipilimumab, vemurafenib, fotemustine, temozolomide.
• Administration was divided: i.v. (10 %) and o.s. (90 %).
• Administration was divided: i.v.

• For drugs with a double-pricing system (like ipilimumab), costs were based upon the official notified prices in Spain.

Disease management

Resource use was derived from a physician’s survey on resource use associated with the treatment of melanoma in Europe. Disease management, best supportive care, terminal care and home care costs were included considering medical visits, hospital stay, laboratory tests, radiology tests and pain control drugs.

AEs management

Grade 3-4 AEs (ipilimumab and dacarbazine: infection, sepsis, thrombocytopenia, anemia, neutropenia, diarrhea, vomiting, pain, nausea, leukopenia, fatigue, rash, hypothyroidism, pyrosis; vemurafenib: colitis, stomatitis, intestitis, hypothyrosis, hypophysis, adrenals, insufficiency, hepatitis) frequencies from observational CA184-338 study7 were considered.

The proportion of in-patient versus out-patient was estimated by the clinicians. The in-patient cost was based on the resource use estimated by clinicians multiplying by unit costs; the out-patient cost was based on aggregated costs.

Conclusions

Ipilimumab is a cost-effective alternative compared with dacarbazine for previously untreated patients with advanced melanoma in Spain providing an additional two-years survival benefit related to dacarbazine over the model time horizon.

References

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