Capturing Added Value in immuno-oncology

Balancing rapid access and new metrics for valuation

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Disclosures: Patrick Hopkinson

- Employment: currently employed by Bristol-Myers Squibb as head of Worldwide Health Economics and Outcomes Research, Markets

- The views expressed in this presentation are personal based on my experience and do not necessarily reflect the views of Bristol-Myers Squibb
Topics

1. Cancer: still a high burden

2. The potential for immuno-oncology treatments to reduce the burden of cancer

3. Challenges and solutions to demonstrating the value of immuno-oncology treatments in oncology
1. Cancer: still a high burden
Despite considerable improvements in outcomes, 1 in 3 people with cancer will not survive more than 5 years.

Cancer in the EU – still the unbeaten disease

- 2.45 million new cases per year
- 1.23 million deaths per year
- 1.26 billion Euros in total costs
- 75 billion Euros in indirect costs

1 in 3 people with cancer today will not survive more than 5 years

Note: all figures above are for all types and stages of cancer

1. Luengo-Fernandez 2013
A considerable burden to our health care systems

- Cancer care accounts for 4% of overall health expenditure in EU27
- Hospitalisations are the main cost driver in all EU countries

Source: Luengo-Fernandez, Lancet Oncol 2013
A substantial cost to society

Source: Luengo-Fernandez, Lancet Oncol 2013

- Productivity losses because of early death: €42.6 billion
- Lost working days: €9.43 billion
- Informal care: €23.2 billion
Caregiver fatigue and depression are also affected by patient's systemic therapies

Barzelloni et al. presented data on fatigue and depression in family caregiver of patients with lung, breast and colorectal cancer.

Fatigue and depression were compared between caregivers of patients treated with oral versus systemically administered therapies.

Measures: FACT-F and Zung Self-rating Depression Scale.

This was true even for caregivers of patients with advanced disease.

FACT-F: Functional assessment of cancer therapy – fatigue, SDS: self-rating depression scale,

2. Potential for immuno-oncology treatments to reduce the burden of cancer
A rapid pace of progress, making treatments available to patients with many different forms of cancer

**EC, European Commission; FDA, Food and Drug Administration**

- Ipilimumab (melanoma)
- Pembrolizumab (melanoma)
- Nivolumab (NSCLC)
- Nivolumab (melanoma)*

*Nivolumab received Japan approval July 2014

EC, European Commission; FDA, Food and Drug Administration
Potential long-term survival for advanced cancer patients who previously had very few treatment options available.

Long term survival from pooled prospective and retrospective ipilimumab studies in advanced melanoma (N = 1861)* - 3 mg/kg is the only registered dose.

**Patients at Risk**

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<th>0</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
<th>72</th>
<th>84</th>
<th>96</th>
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<tr>
<td>3 mg/kg</td>
<td>965</td>
<td>429</td>
<td>127</td>
<td>73</td>
<td>41</td>
<td>29</td>
<td>28</td>
<td>12</td>
<td>8</td>
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<tr>
<td>10 mg/kg</td>
<td>706</td>
<td>316</td>
<td>191</td>
<td>145</td>
<td>118</td>
<td>111</td>
<td>64</td>
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<tr>
<td>Other</td>
<td>190</td>
<td>94</td>
<td>52</td>
<td>36</td>
<td>33</td>
<td>30</td>
<td>28</td>
<td>12</td>
<td>7</td>
<td>1</td>
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**Median, months (95% CI) and 3-yr OS rate, % (95% CI)**

<table>
<thead>
<tr>
<th></th>
<th>Median, months (95% CI)</th>
<th>3-yr OS rate, % (95% CI)</th>
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<tbody>
<tr>
<td>3 mg/kg</td>
<td>11.4 (10.3, 12.5)</td>
<td>21 (17, 24)</td>
</tr>
<tr>
<td>10 mg/kg</td>
<td>11.1 (9.9, 13.0)</td>
<td>24 (21, 28)</td>
</tr>
<tr>
<td>Other</td>
<td>12.4 (10.4, 15.1)</td>
<td>20 (14, 26)</td>
</tr>
</tbody>
</table>

*Non-randomized subset analyses.

This improvement in survival is also considered in the context of safety outcomes

• Yervoy is associated with side effects resulting from excessive activity of the immune system, including severe reactions and inflammation.

• Most will resolve following appropriate treatment and/or stopping on Yervoy.

• The most common individual side effects (affecting > 10% of patients), are
  • diarrhoea
  • rash
  • pruritus (itching)
  • fatigue (tiredness)
  • nausea (feeling sick)
  • vomiting
  • decreased appetite and
  • abdominal pain (stomach ache).

Quality of survival: immuno-oncology treatment shows a positive impact on quality of life

Higher scores indicate better health status. Only time points that had PRO data available for ≥5 pts in either treatment arm are on the graph.
3. Challenges and solutions to demonstrating the value of immunoncology treatments
What are the key HTA challenges in immuno-oncology?

1. A significant proportion of patients remain alive at the end of clinical trials – making measures such as median survival less applicable.

2. An established relationship between traditional intermediate endpoints and survival has not yet been shown for immuno-oncology treatments.

3. Regulatory authorities are approving new medicines on the basis of earlier and less mature evidence.

4. Less familiar adverse events makes real life benefit–risk of new treatments less easy to foresee.

5. Substantial public pressure to approve new therapies.

6. Payers and professionals under pressure to contain costs.

In essence, uncertainty around benefit at the time of assessment is increased along with the pressure to approve rapidly.
Shifting the survival curve for advanced cancers: the need for new approaches to assessing survival

As cancer therapies evolve, the cancer survival curve continues to change.

**Clinicians**: Benefit:Risk

**HTAs**: Effectiveness and Value

**Patients**: Access

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The need for accelerated approval and access decisions: patients lose treatment opportunity during approval process

**Average number of months per step**

- **EMA submission/Start of regulatory assessment**: <1 month
- **CHMP opinion issued**: 12 months
- **EU marketing authorisation granted**: 2 months
- **Time to reimbursement after marketing authorisation granted**: ~10 months

**Average time (months) to reimbursement in**

- Spain: 12.5
- England: 10.8
- Italy: 10
- Germany: 9.2
- France: 8.3
- Scotland: 7.5

*Average for EU5: Spain, England, Italy, Germany, France and Scotland

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1 Beishon M. *Cancer World* 2014; Jan-Feb: 12–17
Categories of value demonstration needed to fully capture benefit

- **Patient benefit**
  - PROs (HRQoL, symptom burden, Tx adherence, Tx satisfaction), long-term safety, quality of survival

- **Real-world effectiveness**
  - Long-term survival extrapolation, network meta-analyses, indirect comparisons, budget impact model, cost-effectiveness analyses

- **Burden of disease**
  - Real world data (observational studies and pt registries)
  - Burden of disease/illness, caregiver burden, morbidity and associated costs

- **Economic value**
  - Economic value of biomarker

- **Relative value demonstration**
  - Relative value comparing % improvement in 1-year survival and monthly Tx costs vs anticancer analogues

PRO = patient reported outcomes; HRQoL = Health Related Quality of Life; Tx = treatment
A broader range of outcomes will need to be given more weight and uncertainty needs to be managed more effectively

- HTA traditionally puts more emphasis on efficacy/effectiveness and safety than on societal or other outcomes – **broader societal outcomes should be also used**
- It is also necessary to move beyond median overall survival and **assess mean overall survival** – area under the survival curve – as well as landmark survival
- Uncertainty around efficacy/effectiveness and safety, particularly in the medium to long-term, can be addressed by **longer follow up after approval**
- Health-related quality of life is often inferred from individual symptoms as these offer a more complete data set – **holistic measures of QoL should be used**
- There are fewer randomised controlled trials (RCTs) and more real-world data and modelling – **this needs to be embraced by decision makers.**
THANK YOU