Comparative Effectiveness of Panitumumab Versus Cetuximab in Patients with Chemo-refractory Wild-type KRAS Metastatic Colorectal Cancer

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ISPOR 2016
Outline

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Scope of the Problem

• Approval of novel agents in metastatic colorectal cancer (mCRC) has resulted in a dramatic improvement in longevity of patients.

• Cost of care in these patient population is more than $100,000 per year for the first two years.

• Use of novel agents is the major contributor to the improved survival and rising costs.

• Use of same class agents with similar efficacy, different administration schedule, and different toxicity profile can lower the cost of care without a detriment on the outcome.
EGFR Blocking Antibodies in Colorectal Cancer

- Cetuximab and Panitumumab are anti-epidermal growth factor receptor (EGFR) monoclonal antibodies with approval in multiple lines of therapy in mCRC.

- KRAS mutation is predictive of “lack of efficacy” in mCRC and thus both drugs are indicated only in patients with KRAS wild-type.

- Roughly 50% of patients with mCRC have wild type KRAS.
Motivation and Objective

• Cetuximab and panitumumab have similar efficacy in a head-to-head trial, however their administration schedule and toxicity are different.

• Does differences in the administration schedule and toxicity provide a cost advantage for one drug over the other?

• To answer the question we performed an analysis of comparative effectiveness study of panitumumab and cetuximab as monotherapy in chemo-refractory mCRC patients with wild-type KRAS from US societal perspective.
Model Overview

- Time horizon: 2 years
- Cycle unit: month
- Base case discounting rate: 3%
Methods

• Survival estimates
  – Effectiveness data were drawn from ASPECCT clinical trial\textsuperscript{a}.
  – Transition probabilities were calculated by using DEALE method.

• Health utility estimates
  – Utilities were derived from literature of comparable patient population.

Methods (Continued)

• Cost estimates

  – Drug cost was taken from Veteran Affairs Federal Fee Schedule.
  – Cost for drug administration and toxicities treatment were derived from literature, or Medicare reimbursement rate.
  – Included grade 3/4 toxicities that have significant difference between the two groups: skin rash, hypomagnesaemia, hypokalemia; and infusion reaction (all grades).
  – All costs were converted to 2015 US dollars using the Medical CPI.
Methods: Progressive Disease State

• When patients had disease progression, they would receive one further round of treatment with either regorafenib or TAS-102.

• Survival data for regorafenib or TAS-102 were taken from two separate clinical trials, with comparable patient population.

• Upon failure of regorafenib or TAS-102 we assumed that patients were placed on best supportive care until death.
Model Inputs: Effectiveness and Administration

- **Base case: 61-year-old male**

<table>
<thead>
<tr>
<th></th>
<th>Panitumumab</th>
<th>Cetuximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median progression-free survival (month)</td>
<td>4.1</td>
<td>4.4</td>
</tr>
<tr>
<td>Median overall survival (month)</td>
<td>10.4</td>
<td>10</td>
</tr>
<tr>
<td>Dosage and administration</td>
<td>6 mg/kg every 14 days as an IV</td>
<td>400 mg/m² initial dose followed by 250 mg/m² per week as IV</td>
</tr>
<tr>
<td>Dose required for the base case (per month)</td>
<td>1086 mg</td>
<td>2411 mg (first month) 2097 mg (following month)</td>
</tr>
</tbody>
</table>

a. ASPECCT trial 2014
b. FDA approved label
## Model Inputs: Cost

<table>
<thead>
<tr>
<th></th>
<th>Panitumumab</th>
<th>Cetuximab</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Direct cost</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>$9,613</td>
<td>$12,521 (1st month)</td>
<td>VA FFS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$10,888</td>
<td></td>
</tr>
<tr>
<td>Administration</td>
<td>$272</td>
<td>$544</td>
<td>Medicare</td>
</tr>
<tr>
<td>Premedication</td>
<td>$4</td>
<td>$100</td>
<td>VA FFS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$40</td>
<td></td>
</tr>
<tr>
<td>Toxicities treatment</td>
<td>$178</td>
<td>$510</td>
<td>Literature</td>
</tr>
<tr>
<td></td>
<td>$99</td>
<td>$58</td>
<td>Medicare</td>
</tr>
<tr>
<td>Best supportive care</td>
<td></td>
<td>$2,557</td>
<td>Literature</td>
</tr>
<tr>
<td><strong>Indirect cost</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caregiver cost of PFS</td>
<td>$1,640</td>
<td></td>
<td>Literature</td>
</tr>
<tr>
<td>Caregiver cost of PD</td>
<td>$2,823</td>
<td></td>
<td>Literature</td>
</tr>
</tbody>
</table>

All in 2015 dollar
# Model Inputs: Health Utility

<table>
<thead>
<tr>
<th></th>
<th>Panitumumab</th>
<th>Cetuximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS</td>
<td>0.753</td>
<td>0.745</td>
</tr>
<tr>
<td>PD</td>
<td>0.65</td>
<td>0.65</td>
</tr>
</tbody>
</table>
## Results: Base Case

<table>
<thead>
<tr>
<th></th>
<th>Panitumumab</th>
<th>Cetuximab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total cost</strong></td>
<td>$63,021</td>
<td>$70,084</td>
</tr>
<tr>
<td><strong>Total survival (month)</strong></td>
<td>7.84</td>
<td>7.92</td>
</tr>
<tr>
<td><strong>Total quality-adjusted life year (QALY)</strong></td>
<td>0.44</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>Net monetary benefit</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>$3,648</td>
<td>$ (2,624)</td>
</tr>
<tr>
<td><strong>Incremental net monetary benefit</strong></td>
<td></td>
<td><strong>$6,272</strong></td>
</tr>
</tbody>
</table>

<sup>a</sup> Using a willingness-to-pay threshold of $150,000.

*ICER for Cetuximab: $1,337,737 per QALY*
One-way Sensitivity Analysis

Panitumumab Incremental NMB (vs Cetuximab)

Drug Cost (Cetuximab, 95%CI)
PFS Utility (Cetuximab, +/-20%)
Drug Cost (Panitumumab, +/-20%)
PFS Utility (Panitumumab, +/-20%)
Median PFS (Cetuximab, 95%CI)
Median PFS (Panitumumab, 95%CI)
Median OS (Panitumumab, 95%CI)
Median OS (Cetuximab, 95%CI)
PD Utility (+/-20%)
Caregiver Cost (PD, +/-20%)
End of life care cost (+/-20%)
Chemo Admin Cost (+/-20%)
AE Cost (Cetuximab, +/-20%)
AE Cost (Panitumumab, +/-20%)
Discount rate (1%-5%)
caregiver Cost (PFS, +/-20%)

Base case INMB: $6,271
Limitations and Caveats

• Every economical analysis is based on multiple estimations and assumptions and this study is not an exception.

• The costs used in this study is based on the publicly available data and thus our analysis provides robust output that is generalizable to the US healthcare setting.

• Similarly resource utilization such as duration of hospitalization, number of outpatient visits, and medication costs are estimation and not directly captured. We used a panel of experts to verify these assumptions.
Discussion

• In the US, effectiveness and toxicities are considered the gold standard for choice of treatment regimen. However, the rising cost of cancer care is forcing providers and policy makers to consider other data points in treatment selection.

• While the ASPECTCT trial showed a similar effectiveness and safety profile of the two agents, our results indicate that panitumumab can lower the cost of care from societal perspective in chemo-refractory setting, with minimal compromise in QALY.
Conclusion

- Panitumumab and Cetuximab have equivalent efficacy and safety profile in patients with chemo-refractory mCRC and we show that panitumumab is less costly in these patient population.

- Physician practices and hospitals should consider the results for their decisions in formulary choice and contracting.
Future Direction

• Both panitumumab and cetuximab combined with chemotherapy have indications in earlier lines of therapy in patients with KRAS wild-type metastatic colorectal cancers.

• Panitumumab and cetuximab in combination with chemotherapy are not compared head to head in first line setting and assessing their comparative effectiveness is planned in near future.

• Development and pricing of biosimilars may have a significant impact on the findings of this study as our sensitivity analysis indicates that our model is sensitive to the drug costs.