Cost-effectiveness of Cetuximab and Panitumumab in First-line Treatment for Patients with KRAS Wild-Type Metastatic Colorectal Cancer in Ontario

Emmanuel Ewara, Dr. Greg Zaric, Dr. Stephen Welch, Dr. Sisira Sarma.
Bevacizumab (Avastin®)

- Beva+ FOLFIRI: Used in current clinical practice in 1st line treatment for patients with MCRC in Ontario.

- Bevacizumab + FOLFOX/FOLFIRI:
  ORR, PFS, and OS compared to Chemo alone
Cetuximab (Erbitux®) and Panitumumab (Vecitibix®)

- Only effective in KRAS-WT patients.
- Currently funded in Ontario:
  - Cetuximab: 2\textsuperscript{nd} line, 3\textsuperscript{rd} line with Irinotecan
  - Panitumumab: 3\textsuperscript{rd} line

- RCTs: Addition to FOLFIRI/FOLFOX in first line
  ORR, PFS, and OS compared to chemo alone
To evaluate the cost-effectiveness of the use of cetuximab or panitumumab plus FOLFIRI compared bevacizumab plus FOLFIRI, as first-line treatment for KRAS wild-type MCRC patients from the perspective of the Ontario Healthcare Payer.
3. Methods: Model Structure

- We developed a decision analytic model to simulate the lifetime clinical and economic consequences of MCRC patients.
3. **Methods: Model M1**

- **First-Line Beva + FOLIRI**
  - **FOLFOX**
    - **Panitumumab**
    - **Cancer Free**
    - **Best Supportive Care**
  - **Dead**
3. Methods: Models M2 and M3

- First-Line RX
- FOLFOX
- Best Supportive Care
- Cancer Free
- Dead
1. Patient-level data: ICES-CD link program.
   • Cohort of interest: 1,216 with MCRC and received Beva+ FOLFIRI as 1st line RX

2. Phase III and IV RCT data
2. **Methods: Data Sources - Treatment Efficacy**

### Progression Free Survival

![Progression Free Survival Graph](image)

- **Cetuximab - Van Cutsem et al. 2009**
- **Panitumumab - Douillard et al. 2010**
- **Bevacizumab - ICES Real World Data**

**Cetuximab + FOLFIRI:** Van Cutsem et al. Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer. N Engl J Med. 2009;360(14)

**Panitumumab + FOLFIRI:** Douillard et al. Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: the PRIME study. J Clin Oncol. 2010;28(31)
2. Methods: Data Sources – Real World vs. RCT

Progression Free Survival: Bevacizumab + FOLFIRI

• Estimated monthly state-dependent transition probabilities from Kaplan-Meier survival estimates.

• Parametric distributions were fit to each curve to extrapolate survival.
  – Monthly probabilities determined using scale and shape parameters

• Mortality unrelated to cancer progression was obtained from Statistics Canada Life Tables for age-dependent mortality
• Average monthly, state-dependent direct medical costs:

- Ontario Health Insurance Plan (OHIP)
- Ontario Drug Benefit (ODB)
- CIHI Discharge Abstract Database (CIHI-DAD)
- Home Care Database (HCD)
- National Ambulatory Care Reporting System (NACRS)
- New Drug Funding Program (NDFP)

- Physician Services
- ODB Drugs
- Hospitalizations
- Home care Services
- ER Visits, Cancer Clinic Visits
- Cancer Drugs

• Utility values obtained from literature review.
• Costs and utilities were discounted at 5%.
## Results: Base Case

<table>
<thead>
<tr>
<th>Treatment Strategy</th>
<th>Cost</th>
<th>QALY</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab + FOLFIRI</td>
<td>$150,573</td>
<td>1.749</td>
<td></td>
</tr>
<tr>
<td>Cetuximab + FOLFIRI</td>
<td>$153,731</td>
<td>1.741</td>
<td>Dominated</td>
</tr>
<tr>
<td>Panitumumab + FOLFIRI</td>
<td>$173,931</td>
<td>1.716</td>
<td>Dominated</td>
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</tbody>
</table>

Incremental Cost Effectiveness Ratio (ICER) = Incremental Cost / Incremental Effect
Results: Deterministic Sensitivity Analysis: Panitumumab vs. Bevacizumab

- More Costly, Less Effective
- Less Costly, More Effective
- More Costly, More Effective
- Less Costly, Less Effective

Cost

Effect

ICER >> $100,000/QALY

Dominated

$100,000/QALY
Results: Deterministic Sensitivity Analysis: Cetuximab vs. Bevacizumab - Utility

- More Costly, More Effective
- More Costly, Less Effective
- Less Costly, Less Effective
- Less Costly, More Effective

ICER < $50,000/QALY
4. Results: Deterministic Sensitivity Analysis: Cetuximab vs. Bevacizumab – Progression and Cost

- More Costly, Less Effective
- More Costly, More Effective
- Less Costly, Less Effective
- Less Costly, More Effective

Cost: $100,000/QALY, $50,000/QALY

Effect: Scatter plot with data points indicating a positive correlation between cost and effect.
Results: Scenario Analysis - Panitumumab

More Costly, Less Effective

More Costly, More Effective

Cost

Effect

ICER < $100K/QALY
Cost: Decr by 45%
Prog: Decr by 10%

Dominated

Dominant
Cost: Decr by 50%
Prog: Decr by 10%

Less Costly, More Effective

$100,000/QALY
Results: Scenario Analysis - Cetuximab

- **Effect**
  - More Costly, Less Effective
  - Dominated
  - ICER < $100K/QALY
    - Cost: Decr by 10%
    - Prog: Decr by 5%
  - Dominant
    - Cost: Decr by 15%
    - Prog: Decr by 5%
  - More Costly, More Effective
  - $100,000/QALY

- **Cost**
  - Less Costly, More Effective

- **Effect**
  - Less Costly, More Effective
4. Results: Probabilistic Sensitivity Analysis

Scatter Plot: Cetuximab vs. Bevacizumab

More Costly, Less Effective

Less Costly, Less Effective

Dominant $\rightarrow 0.4 \% \quad$ ICER$< \$100,000/QALY \rightarrow 0\% \quad$ ICER$< \$200,000/QALY \rightarrow 0\%
Results: Probabilistic Sensitivity Analysis

Scatter Plot: Panitumumab vs. Bevacizumab

More Costly, Less Effective

Less Costly, Less Effective

Dominant $\rightarrow$ 0.2%  
ICER< $100,000/QALY $\rightarrow$ 0%  
ICER< $200,000/QALY $\rightarrow$ 0.1%
• For KRAS-WT patients current clinical practice of Bevacizumab + FOLFIRI represents the most cost-effective treatment option.

• Panitumumab should not be considered for use in first line.
  – Dominated or ICER >> $100,000/QALY

• Cetuximab + FOLFIRI: similar to Beva + FOLFIRI in terms of cost and effect.
  – Scenarios where ICER < $50,000/QALY.
Discussion: Limitations

• No head-to-head study comparing all three treatment options.
  – Indirect comparisons with real world and RCT data

• Unable to find cetuximab specific utility value → implications on ICER

• Surrogate marker developed to determine the beginning of BSC state → State costs may not be accurate
• We were able to investigate cost-effectiveness using survival estimates from real world data in alongside as data from published RCTs.

• It is important to validate survival estimates derived from “real world” data with RCT data
  – as observational studies may tend to overestimate survival compared to RCT

• CD-Link data can be utilized to conduct Ontario-specific CEAs.
Acknowledgments:
Dr. Sisira Sarma and Dr. Greg Zaric, Western University
Department of Epidemiology and Biostatistics, Western University
Ontario Institute for Cancer Research.

Thank You
2. Methods: Data Sources: Clinical Trials

- **Cetuximab + FOLFIRI:**

- **Panitumumab + FOLFIRI:**

- **FOLFOX:**

- **3rd line Panitumumab and BSC**
### Results: One Way Deterministic Sensitivity Analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment Strategy</th>
<th>Parameter</th>
<th>-20%</th>
<th>-10%</th>
<th>+10%</th>
<th>+20%</th>
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</thead>
<tbody>
<tr>
<td>Bevacizumab + FOLFIRI</td>
<td>Cetuximab + FOLFIRI</td>
<td>-20%</td>
<td>Less costly, less effective</td>
<td>Less costly, less effective</td>
<td>$167,676</td>
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<td></td>
<td>Cetuximab + FOLFIRI</td>
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<tr>
<td>Cetuximab + FOLFIRI</td>
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<td>Utility of Bevacizumab</td>
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<td>$40,194</td>
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<td>Utility of Cetuximab</td>
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</tbody>
</table>
4. Results: Probabilistic Sensitivity Analysis

Probability of being cost-effective compared to Bevacizumab + FOLFIRI

- Panitumumab + FOLFIRI: 0.003%
- Cetuximab + FOLFIRI: 0.008%