MULTIPLATFORM TUMOR PROFILING DELIVERS VALUE BASED HEALTH CARE IN REFRACTORY CANCER PATIENTS

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Amended Abstract

BACKGROUND: Caris Molecular Intelligence™ (CMI) is a multiprotocol tumor profiling service helping patients with refractory cancer who are past standard of care to find treatment options. In the UK, the National Institute for Health and Clinical Excellence (NICE) has implemented an end-of-life (EoL) premium since 2009.

OBJECTIVES: The aim of this study is to assess the cost-effectiveness value of CMI in a health system.

METHODS: A model described by McCabe and colleagues is adapted to show the value of CMI. To populate the model, threshold and real-world incremental cost-effectiveness ratio (ICER) data from the health technology assessments performed by NICE in the past year (November 2015-December 2016) were used as comparators. Data collected in a prospective observational study conducted by Caris demonstrated a survival benefit in patients treated in line with the CMI report. An ICER for CMI was calculated based on the demonstrated survival benefit and the clinical utility.

RESULTS: To date, NICE recommendations have consistently used a £50,000 per QALY threshold for these EoL treatments. This equates to a health benefit of 7.3 days of additional benefit per £1,000 expenditure. A CMI unit price of £5,000 was used in the ICER calculation. According to Caris registry data, CMI can extend overall survival by 138 days (or 0.378 years) for health economic evaluation. CMI-guided therapy is administered in 77% of profiled patients, meaning that a decision impact factor of 0.77 could be included in ICER calculation. The ICER for CMI was calculated as Cost of CMI / (QALYs gained x decision impact factor). Based on these assumptions, the ICER for CMI is £17,180 or equivalent to 21.26 days benefit per £1,000 expenditure.

CONCLUSIONS: Data from this model shows that CMI exceeds the threshold opportunity cost and represents value for health care systems that surpass many recently approved drugs.

Background

- The quality-adjusted life-year (QALY) is a generic measure of disease burden, including both the quality and the quantity of life lived. It is used in economic evaluations to assess the value for money of medical interventions. One QALY equates to one year in perfect health.
- In the UK, the National Institute for Health and Clinical Excellence (NICE) has implemented an end-of-life (EoL) premium since 2009.
- NICE’s methods guide attributes a greater weight to QALYs acquired in the later stages of terminal illness if these criteria could be fulfilled:
  - prognosis less than 24 months,
  - small patient population, and
  - life-extension of at least three months compared to current NHS treatment.
- The setting of a threshold for end of life treatment has been described in detail and used in assessment of new treatments and technologies to the healthcare system.
- In the assessment of the cost-effectiveness value of CMI in a health system below, a model described by McCabe and colleagues is adapted to show the value of CMI.
- The aim of this study is to assess the cost-effectiveness value of a multiprotocol tumor profiling service, Caris Molecular Intelligence™ (CMI) in helping patients with refractory cancer who are past standard of care to find treatment options in a health system.
- Caris Life Sciences has established a post-marketing Registry with the aim to complete a series of multicentre prospective observational studies and developing an ongoing oncology molecular profiling-based clinical outcomes database as well as exploring and validating existing and novel biomarkers.
- An initial report from the Caris registry demonstrates that the overall survival of patients with solid cancers treated with drugs associated with potential benefit according to a predictive biomarker panel was longer than in those who received drugs associated with potential lack of benefit.
- The Caris registry is unique in that it gives us the data needed to calculate QALYs gained when patients are treated in line with the CMI report.

Methods

- The average cost per QALY across all positive recommendations since Eol. guidance was introduced in 2009 is approximately £49,000 per QALY.
- To date, these criteria have been met on 36 occasions and the committee recommendations have been consistent with the use of a £50,000 per QALY threshold for these EoL treatments.
- This equates to a health benefit of 7.3 days of additional benefit per £1,000 expenditure by the health care system.
- To populate the model, this threshold cost and real-world incremental cost-effectiveness ratio (ICER) data from the health technology assessments performed by NICE in the past year (November 2015-December 2016) were used as comparators to show the value that CMI offers (all data was accessed on www.nice.org.uk).
- Based on the demonstration that CMI-guided treatments do not cost more than unguided treatment, and the assumption that no profiling would be performed in the baseline case, the costs of CMI are considered to be additive and an ICER for CMI was calculated based on the demonstrated survival benefit and clinical utility.
- A CMI unit price of £5,000 was used in the ICER calculation.

Results – Days Benefit per £1,000 spend on CMI

- In the Caris registry data, the median overall survival in the patients without selection based on matched and unmatched treatment is 93 days.
- The overall survival in patients who received matched therapy only is 1069 days, indicating that CMI can extend overall survival by 138 days (or 0.378 years) for health economic evaluation.
- In addition, CMI can identify the treatments associated with lack of benefit and thus could reduce ineffective spend.
- The median overall survival in the unmatched cohort is 686 days, 245 days (or 0.67 year) less than the median OS in the unselected population.

Note: The reduction of ineffective spend associated with avoiding non-beneficial treatments is an added benefit for CMI that is not included in the calculation of the ICER.

<table>
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<tr>
<th>Drug</th>
<th>ICER Calculation</th>
<th>Days Benefit per £1,000 spend</th>
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<tr>
<td>CarisLifeSciences</td>
<td>£17,180</td>
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Figure 1 - Kaplan Meier Curve of Overall Survival based on treatments administered after Comprehensive Tumor Profiling (CMI)

Figure 2 - Kaplan Meier Curve of Overall Survival Matched and Unmatched Patient Cohorts compared to Survival without treatment selection

Figure 3 - CMI exceeds the NICE threshold for approval in end-of-life cancer care

Results – Calculation of Days Benefit per £1,000 spend on CMI

- CMI-guided therapy is administered in 77% of profiled patients, meaning that a clinical utility factor of 0.77 could be included in ICER calculation.
- The ICER for CMI was calculated as Cost of CMI / (QALYs gained x clinical utility factor).
- Based on these assumptions, the ICER for CMI is £17,180 or equivalent to 21.26 days benefit per £1,000 expenditure.

Conclusions

- The additional cost of performing CMI’s multiprotocol testing is likely to be offset by the additional survival benefits observed, as long as it can be conclusively demonstrated that a tumour profiling service does not confer additional treatment costs.
- Real-world observational data can help to demonstrate the survival benefit needed to model the benefit in return for investment by a health care system.
- The benefit per £1,000 spend for CMI’s multiprotocol profiling service exceeds the threshold for acceptance according to the NICE Eol criteria.
- Additional modeling is needed to estimate the financial impact of avoiding treatments which are not likely to work, and result in shorter survival times.

References