COMPARISON OF UTILITY COST IN THREE COMMERCIALLY AVAILABLE PRECISION MEDICINE APPROACHES IN ONCOLOGY

Kenneth Russell1, Iaak Janssens2, Andrew Dean3, William Gallagher4, Alejandro Hernandez5, Andreas Voss5, Gordon Stamp5
1- Caris Life Sciences, Basel, Switzerland; 2 - Department of Oncology, Limburg Oncology Center, Belgium; 3 - St. John of God Hospital, Subiaco, Australia; 4 - UCD School of Biomolecular and Biomedical Science, UCD Conway Institute, University College Dublin, Dublin, Ireland; 5 - Imperial College School of Investigative Medicine, Hammersmith Campus, London, United Kingdom

Abstract

BACKGROUND: The introduction of molecular profiling as standard of care in cancer has led to the launch of a number of commercial precision medicine services, which differ largely in their approaches. It can be difficult for payers, providers, and patients to distinguish between these services and determine which testing is most appropriate for an individual case. An understanding of the clinical utility and the utility cost (to find one patient with clinical benefit) of the different approaches can help to set expectations for all stakeholders involved.

OBJECTIVES: The aim of this study is to define the utility cost of three leading commercially available oncology precision medicine approaches, Caris Molecular Intelligence® (CMI), FoundationOne® and PCDx™.

METHODS: A systematic review of all published clinical evidence for the three services was performed, to determine the number of patients treated in line with the profiling results and the clinical benefit resulting from these treatment choices. Utility cost was defined as the list price divided by the fraction of patients treated based upon the profiling results and the clinical benefit in treated patients.

RESULTS: Based on the number of profiled patients treated and the corresponding number of patients with clinical benefit, 34% of CMI-profiled patients had clinical benefit (184 of 543 profiled patients), compared to 46% of those profiled with FoundationOne® (166 of 2,675 profiled patients) and 11% profiled using PCDx™ (19 of 168 profiled patients). Utility cost was calculated as $19,118 for CMI, $43,866 for PCDx™ and $96,667 for FoundationOne®.

CONCLUSIONS: The results of this study show that the multiplex approach of CMI brings the highest clinical utility, based on the use of conventional chemotherapies in the majority of patients profiled. A few clinical utility means that almost 20% of FoundationOne® must be purchased to find one patient who benefits.

Background

• Molecular tumor profiling for patients with advanced or recurrent solid tumors is increasingly adopted as standard of care in oncology, as it has been demonstrated that improved clinical outcomes can result from selection of the optimal therapy for individual patients.
• Initial large scale attempts to profile patients in the hope of directing them to molecularly matched clinical trials have highlighted that only a small proportion of patients have actionable alterations which are suitable for enrolment into a trial.
• For oncologists who are actively integrating tumor profiling into their patient’s care today, it can be challenging to understand the differences in clinical utility and benefit between numerous available molecular profiling services. The often considerable costs of the patient’s treatment require justification.
• The aim of this study is to compare and contrast the clinical utility of 3 commercial approaches, to show that not all approaches to precision medicine are the same in terms of quality and cost-effectiveness.

Methods

• Three commercially available services were included in this analysis – Caris Molecular Intelligence® from Caris Life Sciences, FoundationOne® from Roche/ Foundation Medicine, PCDx™ from Paradigm Dx.
• Key differences between molecular profiling services lie in the range and scope of platforms used to assess biomarkers.
• Caris Molecular Intelligence® (CMI) – multiplex profiling service comprised of immunohistochemistry (IHC), next-generation sequencing (NGS), RNA sequencing and in situ hybridization (ISH).
• FoundationOne® (FMI) – NGS only
• PCDx™ – Multiplex service comprised of IHC and NGS
• A comprehensive review of all published data was performed for details on number of patients profiled, treated, evaluable and with clinical benefit.
• Data from a comparison of commercially available services was based on 534 patients profiled as part of physician-led studies for CMI, 2675 patients profiled using FMI, and 168 patients profiled by PCDx.
• It is assumed that patients who are not evaluable did not have clinical benefit.

Methods – Model for Calculation of Utility Cost

• Clinical utility is defined as the usefulness of a test for clinical practice and is distinct from clinical validity, which is how well the test can determine the presence, absence, or risk of a disease.
• The model assumes that the clinical utility of a molecular profiling approach must demonstrate whether they lead to a reconsideration of the treatment plan and whether this improves the clinical outcome in profiled patients.
• Utility cost was defined as the list price divided by the fraction of patients treated based upon the profiling results and the clinical benefit in treated patients.
• The utility cost is a reflection of the clinical utility and indicates the cost needed to treat one patient with clinical benefit.
• Statistical analysis (unpaired t-tests) was performed using GraphPad®

Results

• Seventy-seven percent (411 of 534) of patients profiled with CMI were treated in line with the report. Of these, 88% (365 of 416) were evaluable. Fifty percent of evaluable patients (184 of 365) had clinical benefit. The overall clinical utility was 34% (184 of 543 profiled patients).
• Nineteen percent (469 of 2,675) of patients profiled using FMI were treated in line with the profiling findings. Of these, 98% (488 of 499) were evaluable. The four percent of evaluable patients (166 of 488) had clinical benefit. This represents an overall clinical utility of 6% (166 of 2,675 profiled patients).
• Twenty-six percent (44 of 168) of patients profiled using PCDx were treated in line with the report, of whom all were considered evaluable. Forty-three percent of treated patients had clinical benefit, representing an overall clinical utility of 11% (19 of 168 profiled patients).

Results – Graphical Representation of Clinical Utility in 100 profiled patients

• In a hypothetical population of 100 patients, significantly more patients are treated with CMI compared to FMI (p<0.001; 95% CI 0.47 to 0.69) or PCDx® (p<0.001; 95% CI 0.39 to 0.53).
• There was no significant difference between patients treated when FMI and PCDx® were used as the profiling approach (p=0.280; 95% CI -0.19 to 0.05).
• Significantly more patients of the overall cohort profiled experience clinical benefit when using CMI compared to FMI (p=0.0001, 95% CI 0.17 to 0.39) or PCDx® (p=0.0001, 95% CI 0.13 to 0.35).
• There was no significant difference between levels of profiled patients with clinical benefit when FMI and PCDx® were used as the profiling approach (p=0.2995; 95% CI -0.12 to 0.04).

Conclusions

• Significantly more patients are treated using CMI’s multiplex profiling approach, which provides the most comprehensive information (on which chemotherapies, hormone therapies and immunotherapies to use as well as which targeted therapies are suitable) compared to those focused on targeted therapies alone.
• The impact on treatment choice is directly dependent on the panel of biomarkers tested, the frequency of those biomarkers in the population and the level of evidence presented to the oncologist in support of a change in treatment decision.
• The individual patient’s likelihood of clinical benefit within the whole profiled patient group is the most critical measure for a patient and their oncologist when setting expectations of what a molecular profile can offer.
• The cost of profiling does not include any consideration for the recommended therapies, which would further extend the gap in cost given the high price of targeted therapies compared to conventional cytotoxic agents.
• The value of profiling should not be considered as a reflection of the unit cost but rather the amount that needs to be invested to bring clinical benefit to a single patient.
• Precision medicine using a sequencing-only approach brings such low clinical utility that the costs seem unsustainable outside of a research setting.

Study Highlights – Utility Cost Differences Between Profiling Approaches

• The Utility Cost (or the cost of profiling per patient treated with clinical benefit) using CMI at $19,118 and is less than a quarter of the equivalent cost of $96,667 using FMI’s NGS only approach and half that of PCDx® ($43,866).

Table: Utility Cost Differences Between Profiling Approaches

<table>
<thead>
<tr>
<th>Service</th>
<th>List Price ($)</th>
<th>% of Patients Treated</th>
<th>Percentage Clinical Benefit</th>
<th>Utility Cost ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caris Molecular Intelligence®</td>
<td>$6,500</td>
<td>77</td>
<td>$8,442</td>
<td>$19,118</td>
</tr>
<tr>
<td>FoundationOne®</td>
<td>$5,800</td>
<td>19</td>
<td>$30,526</td>
<td>$96,667</td>
</tr>
<tr>
<td>PCDx™</td>
<td>$4,800</td>
<td>26</td>
<td>$18,462</td>
<td>$43,866</td>
</tr>
</tbody>
</table>

References

2. Accessed online on 16 October 2017 at https://www.oncologist.com/articles/articles/2015/7/1179/079/c7a47f4db3051e/177f;

ParadigmOne\textsuperscript{™}

ParadigmOne\textsuperscript{™} is a multiplex service comprised of IHC and NGS.

Accessed online on 16 October 2017 at https://amjmc.com/articles/articles/2015/7/1179/079/c7a47f4db3051e/177f;

Lessons for Molecular Diagnoses.
