Introduction

• Economic evaluations play an important role in reimbursement decision-making by government agencies such as the pan-Canadian Oncology Drug Review (pCODR) and the United Kingdom (UK) National Institute for Health and Care Excellence (NICE).

• In the last decade, many new therapies (e.g. thalidomide, bortezomib, lenalidomide, pomalidomide) have become available for the treatment of relapsed and/or refractory multiple myeloma (RRMM) and significantly improved response rates and survival outcomes. More novel agents are coming to the market or are in development (e.g. carfilzomib, panobinostat, elotuzumab, daratumumab).

• To inform and improve economic evaluations of new therapies for RRMM, it is important to learn from approaches used in the past drug submissions, as well as feedback from the technology health assessments (HTA) agencies.

Objectives

• To identify and summarize previous HTA submissions in RRMM, and use pCODR and NICE’s critiques to formulate recommendations for future economic evaluations.

Methods

• A targeted search of the pCODR and NICE websites was performed to identify previous RRMM economic evaluations since 2007.

• Details of the modelling methods were extracted, including model structure, comparators, data sources for clinical effectiveness, survival extrapolation approach, time horizon, and model assumptions. Critiques from pCODR and NICE were also extracted.

Results/Discussion

• Four submissions in RRMM were identified.1,2,3,4 The drugs evaluated included lenalidomide, bortezomib, and pomalidomide. (Table 1)

• Model structures used included partitioned survival model, semi-Markov model, and discrete-event simulation model, all of which are considered appropriate. All models used a lifetime horizon, which varied from 10 to 30 years.

• Since crossover was allowed in the key clinical trials used to inform the clinical effectiveness, external data were used to adjust the survival estimates in all four economic evaluations.

• Main issues criticized by pCODR and NICE were inappropriate comparators, bias against comparators (e.g. underestimating survival, overstating costs), bias favouring the drug of interest (e.g. not including costs and disutility of adverse events), and validity of health state utility values. (Table 1)

• Three of the evaluations received a positive recommendation, despite of high incremental cost-effectiveness ratios.

• Risk sharing agreements were used in the UK. For lenalidomide, manufacturer agreed to cover the drug cost for people who remain on treatment for more than 26 cycles (normally 2 years).1 For bortezomib, manufacturer rebated the drug cost for people who have less than a partial response after 4 cycles.3

• There may be product listing agreement in Canada for pomalidomide. However, such information is not publicly available.

Table 1: Summary of past economic evaluations submitted to pCODR and NICE for RRMM

<table>
<thead>
<tr>
<th>Drug</th>
<th>HTA submission</th>
<th>Patient population</th>
<th>HTA recommendation</th>
<th>Comparators</th>
<th>Model structure</th>
<th>Time horizon</th>
<th>Data source for clinical effectiveness</th>
<th>Method/Data used to adjust crossover</th>
<th>QoL</th>
<th>CE result</th>
<th>HTA agency appraisal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pom/LDex</td>
<td>pCODR, Aug 2014</td>
<td>Patients who have had at least 2 prior treatments, including lenalidomide and bortezomib</td>
<td>Recommended conditional on CE being improved</td>
<td>BSC (a combination of therapies weighted by average usage)</td>
<td>Partitioned survival model</td>
<td>10 years</td>
<td>Comparisons: observational studies (Golding et al. 2013; Tanent et al. 2013); equal efficacy assumed for comparators based on MM-003 post-hoc analysis and clinical expert opinions</td>
<td>Not available</td>
<td>Not available</td>
<td>Inappropriate comparator (HDex as more appropriate)</td>
<td>in the long term</td>
</tr>
<tr>
<td>Pom/LDex</td>
<td>NICE TA338, March 2015</td>
<td>Patients who have had at least 2 prior treatments, including lenalidomide and bortezomib</td>
<td>Not recommended</td>
<td>Bortezomib/HDex</td>
<td>Semi-Markov partitioned survival model</td>
<td>Life (25 years)</td>
<td>Indirect comparison for Len/Dex vs. bortezomib</td>
<td>Statistical methods used: two-stage Wedbull, and RPSPFTM method</td>
<td>Multivariate regression analysis using EQ-SD data from MM-003</td>
<td>Submitter’s base case result: $132,217/QALY to $172,430/QALY</td>
<td>Fitted curve for lenes compared to OS curve for dex should be adjusted to predict mean rather than median OS</td>
</tr>
<tr>
<td>Len/Dex</td>
<td>NICE TA171, June 2009</td>
<td>People who had received at least one prior therapy</td>
<td>Recommended for people who have received 2 or more prior therapies</td>
<td>HDex</td>
<td>Discrete-event simulation model</td>
<td>Lifetime (30 years)</td>
<td>External CE analysis in newly diagnosed MM (van Agthoven et al. 2004)</td>
<td>UK Medical Research Council MM trials</td>
<td>Extreme CE analysis in newly diagnosed MM (van Agthoven et al. 2004)</td>
<td>Eligibility criteria not appropriate</td>
<td></td>
</tr>
<tr>
<td>Bortezomib</td>
<td>NICE TA120, Oct 2007</td>
<td>People at first or subsequent relapse</td>
<td>Recommended for people at first relapse (received one prior therapy)</td>
<td>HDex</td>
<td>Semi-Markov state transition model</td>
<td>Lifetime (15 years)</td>
<td>APEX-RCT (bortezomib vs. HDex)</td>
<td>Mayo Observational Study</td>
<td>Submitter’s base case result: £31,000/LY at first relapse (£38,950/QALY), £77,000/LY and £107,000/LY at second relapse only and third relapse only</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion

• The findings of this study suggest that most problems identified by pCODR and NICE could be avoided if the submissions conform to the method guidance set by the reimbursement authorities.

• It is helpful to include patient access schemes in the model for HTA agencies to explore.

References

Seeihandout for complete list.

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A Symbol of Excellence

PRM87: WHAT MAKES A GOOD ECONOMIC EVALUATION IN RELAPSED AND REFRACTORY MULTIPLE MYELOMA: A REVIEW OF REIMBURSEMENT SUBMISSIONS TO PCODR AND NICE

Chun Mei Li, Nancy Rixebrugh, Andrew Briggs - ICON Health Economics, Toronto, ON, Canada
References:


3. NICE TA171 (2009). TA171: Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy.

