Capturing The Value Of Potentially Curative Oncology Therapies: Lessons From The Use And Acceptance Of Cure Modelling Assumptions In NICE Technology Appraisals

Micallef J1, New E1, Satija A1, Subramaniyan SV1, Porteous A1

1. Costello Medical, London, UK

OBJECTIVE

To explore the use and acceptance of cure assumptions in cost-effectiveness analyses as part of National Institute for Health and Care Excellence (NICE) health technology appraisals of oncology therapies.

BACKGROUND

- Novel oncology treatments, such as chimeric antigen receptor T-cell (CAR-T) therapies, immune-oncology therapies and highly effective targeted treatments have emerged in the last few years as potential treatments for a variety of cancers. Due to their novel mechanism of action, these treatments may offer long-term survival and even cure.1

- Owing to this potential, these treatments often exhibit complex survival functions which standard methods for survival extrapolation may not adequately reflect. Accordingly, cure assumptions behave a proportion of the modelled population are implicitly or explicitly assumed to achieve long-term survival in line with the general population) are becoming increasingly common in cost-effectiveness analyses submitted as part of NICE appraisals.

METHODS

- The NICE website was searched on 20th May 2021 until the ten most recent completed technology appraisals for oncology therapies where the manufacturer’s cost-effectiveness analysis included a cure assumption were identified.

- Information relating to the choice of modelling approach (including the Evidence Review Group comments and Appraisal Committee response) was extracted from these ten appraisals.

RESULTS

- Ten appraisals incorporating a cure assumption into the manufacturer’s cost-effectiveness analyses were identified after searching the ten most recent oncology appraisals.

- These appraisals utilised mixture cure models (MCMs) and six modelled cure (three explicitly, three implicitly) where survival was informed by general population mortality (GPM) after a certain timepoint for a proportion of patients (Figure 1). One appraisal used a combination of MCM and GPM-based assumptions.

- A summary of the key features of these ten appraisals is presented in Table 1.

- Manufacturers justified the use of cure-based modelling approaches by claiming that standard methods for survival extrapolation may not accurately reflect the survival profile of patients who had received novel oncology treatments.

CONCLUSIONS

- Cure assumptions were included in a quarter of the most recent oncology appraisals to NICE but were rarely considered appropriate for decision-making.

- The absence of long-term trial survival data, or the lack of an observed plateau, and the reliance on surrogate outcomes, such as progression-free survival. For MCMs, limited data follow-up can result in a wide range of possible cure fractions, introducing additional uncertainty.

- Appraisal Committees considered generalisability external data with long-term follow-up, precedence from previous appraisals in the same indication and clinical expert opinion more robust justifications for cure versus short-term observed survival profiles.

- For non-MCM approaches, Appraisal Committees cited methodological concerns with the external choice of the proportion of patients who were considered cured and the timepoint beyond which patients are considered cured (N=2).

- In appraisals where a GPM-based assumption was solely used to model cure (N=9), evidence review groups commented the consideration of an MCM to model cure in most cases (4/6).

1. The modelled cure assumption was rejected in the majority (N=7) of appraisals (Table 1). Table 1 summarises the criticisms frequently associated with cure assumptions, which included limited data follow-up, the lack of an observed plateau, and the reliance on surrogate outcomes, such as progression-free survival. For MCMs, limited data follow-up can result in a wide range of possible cure fractions, introducing additional uncertainty.

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References


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Table 1: Summary of appraisals that included a cure assumption in the cost-effectiveness analysis

<table>
<thead>
<tr>
<th>Appraisal number</th>
<th>Interaction</th>
<th>Indication</th>
<th>Modelling approach used</th>
<th>Cure assumption</th>
<th>Modelled cure (N=7)</th>
<th>GPM-based assumptions (N=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA649</td>
<td>Ongoing</td>
<td>Multiple myeloma</td>
<td>Explicit cure (N=3)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>TA661</td>
<td>Relapsed</td>
<td>Multiple myeloma</td>
<td>Implicit cure (N=4)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>TA677</td>
<td>Ante-grade</td>
<td>Glioblastoma</td>
<td>Explicit cure (N=3)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>TA673</td>
<td>Glioblastoma</td>
<td>Glioblastoma</td>
<td>Implicit cure (N=4)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>TA670</td>
<td>Glioblastoma</td>
<td>Glioblastoma</td>
<td>Implicit cure (N=4)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>TA676</td>
<td>Plaque-like</td>
<td>Multiple myeloma</td>
<td>Implicit cure (N=4)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>TA654</td>
<td>Advanced</td>
<td>Multiple myeloma</td>
<td>Implicit cure (N=4)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>TA640</td>
<td>Advanced</td>
<td>Multiple myeloma</td>
<td>Implicit cure (N=4)</td>
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<td>Yes</td>
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<tr>
<td>TA641</td>
<td>Advanced</td>
<td>Multiple myeloma</td>
<td>Implicit cure (N=4)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>TA645</td>
<td>Advanced</td>
<td>Multiple myeloma</td>
<td>Implicit cure (N=4)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>TA648</td>
<td>Advanced</td>
<td>Multiple myeloma</td>
<td>Implicit cure (N=4)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

1. Trastuzumab emtansine with carboplatin
2. Pembrolizumab
3. Galectin-3
4. Gilteritinib
5. Pembrolizumab with pembrolizumab
6. Pembrolizumab with pembrolizumab
7. Pembrolizumab with pembrolizumab

1. The company capped overall survival by subject to GPM (N=7) of appraisals. This happened at approximately 36 months, with an increase in the use of MCMs was not appropriate and the ERG agreed that that GPMs were explored. However, both the Extrapolations of OS and PFS using functionally cured after treatment with CAR-T and immuno-oncology therapies and may not adequately reflect. Accordingly, cure assumptions (including the Evidence Review Group comments and Appraisal Committee response) were extracted from these ten appraisals.

RESULTS

Ten appraisals incorporating a cure assumption into the manufacturer's cost-effectiveness analyses were identified after searching the ten most recent oncology appraisals. These appraisals utilized mixture cure models (MCMs) and six modelled cure (three explicitly, three implicitly) where survival was informed by general population mortality (GPM) after a certain timepoint for a proportion of patients (Figure 1). One appraisal used a combination of MCM and GPM-based assumptions.

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