CONCLUSIONS

- All NICE appraisals in the last two years where cure assumptions have been applied (n=11) were evaluating oncology treatments. All 11 treatments were recommended by NICE.
- NICE and the ERG/EAG typically considered the cure assumption to be uncertain, due to trial data immaturity, small patient populations, cure timepoint variability and uncertainty around extrapolations.
- Ultimately cost-effectiveness was the key deciding factor. Uncertainty around the cure assumption was deemed acceptable in most cases if the medicine was cost-effective.

OBJECTIVES

- Curative therapies have the potential to restore patient health and significantly improve survival.
- However, cure assumptions in HTA appraisals can be complex to represent in an economic model and support with robust evidence.
- The aim of this research was to investigate how cure assumptions have been clinically justified, modelled and considered by Evidence Review Group (ERG)/External Assessment Groups (EAG) and NICE Committees in recent NICE technology appraisals across all therapy areas.

METHODS

- A targeted review of all NICE single technology appraisals (STAs) published on the NICE website in the last two years (March 2021 to March 2023) was conducted.
- The term ‘cure’ was searched on the NICE website and the resulting list of appraisals were reviewed to ensure only those STAs where a cure assumption was applied were included in the review.
- Data extracted included details of the cure assumption, clinical trial and/or other data supporting the cure assumption, cure modelling approach and HTA feedback on the cure assumptions (including conclusions from the ERG/EAG and NICE Committee).

RESULTS

Table 1: Overview of identified NICE appraisals incorporating a cure assumption

<table>
<thead>
<tr>
<th>ST/TA</th>
<th>Appraisal</th>
<th>Cancer</th>
<th>Cure model</th>
<th>OS/EFS</th>
<th>Patient characteristics</th>
<th>Cure timepoint</th>
<th>Feedback from HTA</th>
<th>NICE Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA747</td>
<td>Mucormycosis in combination for unresectable diffuse large B-cell lymphoma</td>
<td>3 years</td>
<td>Immature OS data from pivotal trial so cure assumptions informed by NIV and validated by clinical experts</td>
<td>Not validated/presented supported assumption</td>
<td>ERG reviewed cure assumption in light of new evidence</td>
<td>NICE satisfied that even with removal of cure assumption all STAs reached threshold</td>
<td>Recommended within MA</td>
<td></td>
</tr>
<tr>
<td>TA748</td>
<td>Pemetrexed and bevacizumab for unresectable non-small cell lung cancer</td>
<td>2 years</td>
<td>Clinical experts validated cure assumption</td>
<td>ERG accepted cure assumption on survival in decision-making</td>
<td>Recommended within MA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA749</td>
<td>Alectinib for advanced or relapsed ALK-positive non-small cell lung cancer</td>
<td>5 years</td>
<td>Clinical experts validated cure assumption</td>
<td>ERG accepted cure assumption on survival in decision-making</td>
<td>Recommended within MA</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A total of 11 appraisals were identified in the search (Table 1). Although the search was not limited to oncology therapies, all 11 appraisals were in oncology. In all 11 appraisals, NICE issued a positive recommendation (3 recommendations within full label population, 3 restricted recommendations and 3 recommended in the Cancer Drugs Fund - Figure 2).

Most appraisals (54.5%, n=6) applied a cure assumption after patients were progression-free for 5 years, while 27.3% (n=3) of appraisals used 2 years. The remaining two appraisals applied cure assumptions at 3 years and 30 months (Figure 1).

There were largely two types of approaches to cure modelling noted in the reviewed appraisals. In one approach, general population mortality rate was assumed in all (or nearly all) patients after the cure timepoint. This approach was applied in the majority of appraisals (72.7%, n=8). The other approach was the development of a mixture-cure model which was applied in 27.3% (n=3) of appraisals.

Across the 11 appraisals, MCMs were generally accepted and in some cases ERG/NICE requested this approach. Common challenges with incorporating a cure assumption included immature trial data to support a cure assumption, small trial patient populations at the cure timepoint, exploration of variable cure timepoints, uncertainty around survival extrapolations and in some appraisals assuming GPM after cure timepoint was not considered clinically plausible.