HTA110

Acceptance of Cure Assumptions in NICE Oncology Technology Appraisals: Remission Impossible?

Morgan J,[1] Shanley L,[1] Halford E,[1] Woodhouse F[2]

[1]Costello Medical, London, UK; [2]Costello Medical, Cambridge, UK

Objective

To reinvestigate the use and acceptance of cure assumptions in cost-effectiveness analyses submitted in recent NICE technology appraisals of oncology products.

Background

- Novel oncology treatments, such as chimeric antigen receptor T-cell therapies, immuno-oncology therapies and targeted treatments, offer the potential for long-term survival and even cure.[1]
- An analysis conducted in 2021 suggested early attempts at incorporating cure modelling in submissions to the National Institute for Health and Care Excellence (NICE) were not widely accepted.[2] Since then, further guidance on the use of cure modelling has been published by NICE, in the form of Technical Support Document 21 (TSD21).[3]
- The current analysis investigated whether cure modelling has gained greater acceptance in recent NICE appraisals for oncology products.

Methods

- The NICE website was searched on the 16th May 2024 for completed technology appraisals in oncology. The ten most recent appraisals which included a cure assumption in the manufacturer's cost-effectiveness analysis were identified. From these ten appraisals, information regarding the cure modelling approach, acceptance and key criticisms from external assessment groups and committees, and final recommendation, was extracted.

Results

- Ten appraisals explicitly incorporating a cure assumption in the cost-effectiveness analysis were identified after searching the 45 most recent oncology appraisals. A summary of the key details of these 10 appraisals is presented in **Table 1**. This is a similar rate to the previous analysis conducted in 2021, where 10/44 appraisals searched included a cure assumption, albeit published over a longer time frame than the current analysis (20 versus 14 months, respectively).[2]
- In the current analysis, four appraisals utilised mixture cure models and six modelled cure where survival was informed by general population mortality after a specific timepoint for a proportion of patients (**Figure 1**). Methods used across appraisals identified in the 2021 analysis were similar.
- NICE committees considered the modelled cure assumption to be acceptable in the majority (n=7) of the appraisals in the current analysis, compared with only three appraisals in the analysis conducted in 2021 (**Figure 1**).[2]
- Despite increasing acceptance of cure modelling, concerns remain around limited trial follow-up (n=7) and lack of an observed survival plateau (n=2) to validate cure rates. Another key source of uncertainty is the mortality and utility experienced by cured patients (n=4), which is often deemed 'optimistic' or overestimated (**Table 1**).
- TSD21 was cited in six appraisals (including all four appraisals that utilised mixture cure modelling) as supporting methodology for cure modelling, notably in justifying the need for more flexible parametric models and to improve statistical and visual fit. In five of these appraisals, committees ultimately agreed with the modelled cure assumption.
- Clinical opinion remained an important source of justification in the majority of appraisals (n=7), validating aspects of cure modelling such as the cure fraction, estimates of mortality and utility in the cured population and plausibility of the extrapolated survival curves.
- All but one appraisal resulted in a positive recommendation, with two interventions receiving conditional approval through the Cancer Drugs Fund to generate further long-term data.

Conclusion

Cure assumptions appear to be increasingly considered appropriate for NICE decision-making: 78% of evaluated cure assumptions were ultimately accepted by NICE committees, compared with just 30% three years ago.

Despite this, uncertainty when modelling cure remains, particularly regarding the availability of long-term trial data and the adjustment of mortality and utility values.

Clinical expectation of cure remains an important factor in committees' acceptance of cure assumptions in the face of uncertainty. Recently published guidance on methodological aspects of cure modelling appears to have lent methodological support and likely contributed to its increasing acceptance in NICE oncology appraisals.

TABLE 1

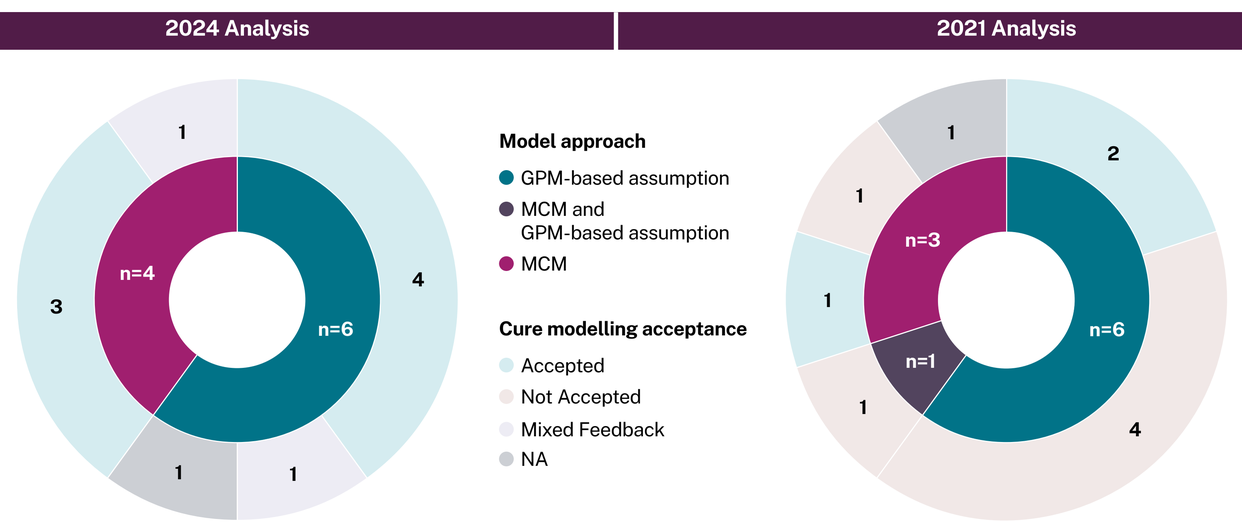
Summary of technology appraisals that included a cure assumption in the cost-effectiveness analysis

				Rationale		Criticisms				
ID	Indication	Model approach	Cure assumption	TSD21 cited	Clinical opinion	Limited follow-up /evidence of plateau	Utility/mortality in cured patients	Cure modelling accepted	Appraisal Outcome
TA975	Tisagenlecleucel in r/r B-cell ALL in young adults	MCM	EFS and OS extrapolated using MCMs. OS bounded by SMR-adjusted GPM. Patients alive at 5 years follow EFS utility	✓	✓	✓		✓	Recommended
TA967	Pembrolizumab in r/r classical Hodgkin lymphoma 2L+	GPM	Patients alive at 4 years with successful SCT follow GP utility and mortality. Patients with unsuccessful or no SCT follow disease-specific transitions		✓	✓	✓	✓	Recommended
TA962	Olaparib in BRCA+ advanced ovarian, fallopian or peritoneal cancer 1L+	MCM and standard parametric models	PFS1 modelled using MCM; PFS2 and OS modelled using standard parametric extrapolations. PFS2 and OS constrained to be ≥ PFS1 and PFS2, respectively	✓	✓	✓		✓	Recommended
TA947	Loncastuximab tesirine in r/r DLBCL and HGBL 2L+	GPM	In scenario analyses, PFS at 2, 5, and 10 years follow SMR-adjusted GPM and GP utility		✓	✓	✓	Mixed	Recommended
TA946	Olaparib with bevacizumab for advanced ovarian, fallopian or peritoneal cancer	MCM and standard parametric models	PFS1 modelled using MCM, PFS2 and OS modelled using standard parametric extrapolations. PFS2 and OS constrained to ≥ PFS1 and PFS2, respectively	✓	✓	✓		Mixed	Recommended
TA927	Glofitamab in r/r DLBCL 2L+	GPM	In PD and PF health states, long-term remission assumed at 2 and 3.5 years, respectively. Long-term remission associated with 10% decrement from GP utility, and SMR-adjusted GPM	✓		✓	✓	✓	Recommended
TA895	Axicabtagene ciloleucel in r/r LBCL after 1L chemo	MCM	EFS and OS extrapolated using MCMs	✓	✓	✓		✓	Recommended (CDF)
TA893	Brexucabtagene autoleucel in r/r LBCL 26 years+	GPM	Patients alive at 3 years assumed cured, with SMR-adjusted background mortality and GP utility	✓	Unclear[a]		✓	✓	Recommended (CDF)
TA883	Tafasitamab with lenalidomide in r/r BCL ASCT ineligible	GPM	Scenarios included fixed cure points defined at 2 years or on crossing of OS and PFS curves. Cured patients followed GPM			✓		NA[b]	Not Recommended
TA876	Nivolumab with platinum doublet chemotherapy for neoadjuvant or resectable NSCLC	GPM	95% of patients who remain event-free for at least 5 years achieve functional cure, with no risk of progression and GPM		✓	✓		✓	Recommended

[a]Cure definition is cited as being covered during clinical expert interviews, however it is unclear exactly what was validated and how this validation was utilised; [b]Cure assumption not included in company base case and not discussed by the committee.

FIGURE 1

Cure assumptions in the 10 most recent NICE health technology appraisals of oncology therapies versus appraisals identified in the 2021 analysis



Abbreviations: ALL: acute lymphoblastic leukaemia; **ASCT:** autologous stem cell transplant; **BCL:** B-cell lymphoma; **CDF:** Cancer Drugs Fund; **DLBCL:** diffuse large B-cell lymphoma; **EFS:** event-free survival; **GP:** general population; **GPM:** general population mortality; **HGBL:** high grade B-cell lymphoma; **ID:** identification; **L:** line; **LBCL:** large B-cell lymphoma; **MCM:** mixture cure model; **NA:** not applicable; **NICE:** National Institute for Health and Care Excellence; **NSCLC:** non-small cell lung cancer; **OS:** overall survival; **PD:** progressed disease; **PF:** progression-free; **PFS:** progression-free survival; **r/r:** relapsed/refractory; **SCT:** stem cell therapy; **SMR:** standardised mortality ratio; **TA:** technology appraisal; **TSD21:** Technical Support Document 21.

References: [1]Michielin O, et al. Evolving impact of long-term survival results on metastatic melanoma treatment. Journal for ImmunoTherapy of Cancer 2020, Volume 8, e000948; [2]Micallef J, et al. Capturing The Value Of Potentially Curative Oncology Therapies: Lessons From The Use And Acceptance Of Cure Modelling Assumptions In NICE Technology Appraisals. Value in Health 2022, Volume 25, Issue 1, S171–S172; [3]Rutherford M, et al. NICE DSU Technical Support Document 21: Flexible Methods for Survival Analysis. The Decision Support Unit, 2020, 1–97.
Acknowledgements: The authors thank Amie Ennew, Costello Medical, for graphic design assistance. We also thank Alex Porteous, Costello Medical, for their review and editorial assistance in the preparation of this poster.

Presented at ISPOR Europe 2024 | Barcelona, Spain | 17–20 November