THE SAME BUT DIFFERENT: INCONSISTENCIES IN KEY COST-EFFECTIVENESS ASSUMPTIONS FOR CURATIVE THERAPIES ACROSS CLINICALLY SIMILAR NICE APPRAISALS

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BACKGROUND

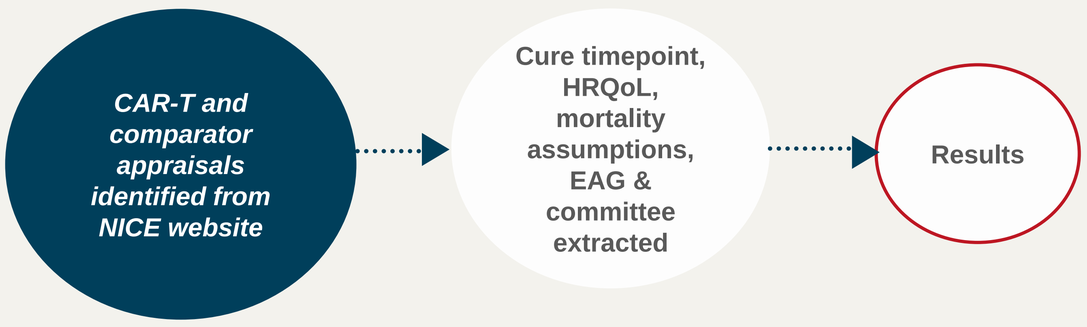
- NICE appraisals in similar therapeutic areas and/or evaluating similar products (e.g. CAR-Ts) are frequently routed to different external assessment groups (EAGs) and can be appraised by different committees.
- This can potentially lead to different preferences regarding key modelling assumptions, particularly those related to cure
- A cure assumption in an economic model is where a proportion of the modelled population are assumed to achieve long-term survival in line with the general population
  - For instance, if patients diagnosed with a particular cancer remain alive beyond a certain timepoint e.g., 2 years, they are assumed to be cured
- In addition to survival, the application of cure assumptions typically extends to the health-related quality of life (HRQoL) of the model population, as it is typically assumed that cured patients will experience the same, or very similar HRQoL to the general population

OBJECTIVE(S)

- To compare the preferred model cure assumptions adopted by NICE committees appraising CAR-Ts and/or their comparator treatments bridging to stem-cell transplant (SCT) in relapsed/refractory leukaemia and lymphoma.

METHODS

- The following data were extracted from technology appraisals (TAs) published on the NICE website:
  - the preferred cure timepoint/fraction assumptions
  - the post-cure health-related quality of life (HRQoL) assumption
  - the post-cure mortality assumption
  - the ERG and committee assigned to the appraisal



DISCUSSION

- In all appraisals that were identified as part of this review, cure assumptions were a key issue discussed at appraisal committee meetings (ACMs) and were typically unresolved after 1 ACM
- It was not always clear from the final appraisal documentation (FAD) published on the NICE website what the final committee preferences were, as often the FADs detailed the uncertainties associated with both the company and EAG's preferred approaches and included statements such as the 'true value likely lies somewhere in between the company's and EAG's preferred mortality estimates'
- There appears to be a lack of consensus regarding the application of cure assumptions for mortality and HRQoL
  - For instance, an EAG argument that came up in 2 appraisals was that it was illogical to assume HRQoL in line with the general population for cured patients if the post-cure mortality assumption was not in line with the general population
  - However, there have been instances where committee have accepted this and the two assumptions have not been treated as mutually exclusive
- It appears that EAGs and committee do not tend to follow precedent set by previous appraisals with regards to the application of cure assumptions, as it is not uncommon for EAGs or committees to opt for preferences which go against what they had accepted previously

RESULTS

- 8 TAs were analysed, of which 2 were targeted leukaemia therapies bridging to SCT, 2 were CAR-T therapies for leukaemia and 4 were CAR-T therapies for lymphoma
- Among the leukaemia TAs the cure timepoint ranged from 3-4 years, with 2 TAs instead assuming cure fractions.
- In lymphoma, the cure timepoint was 5 years, with 2 TAs assuming cure fractions. Standardised mortality ratios (SMRs) of cured patients ranged from 1 to 4, with wide ranging SMRs within the same indication.
- Half of the TAs assumed post-cure HRQoL equal to the general population with the other half assuming a decrement, without consistency across indications.

Table 1: Summary of cure assumptions applied in previous NICE appraisals

TA	Condition	Cure assumption	Post-cure QoL assumption	Post-cure mortality assumption	EAG	Committee
TA893	ALL	3 years	Multiplier of 0.92 applied to the general population	SMR of 3	Sheffield	Committee C
TA554	ALL	Mixture-cure model	EFS health state utility applied	Mixture-cure model	York	Committee C
TA541	ALL	3 years	Utility value of 0.76 (lower than general population)	SMR of 4	York	Committee C
TA450	ALL	4 years	In line with general population	In line with general population	Warwick	Committee A
TA872	Lymphoma	Mixture-cure for OS; 2 years for PFS	In line with general population	In line with general population	Kleijnen Systematic Reviews	Committee C
TA677	Lymphoma	5 years	In line with general population	SMR of 1.09	York	Committee A
TA894	Lymphoma	5 years	PFS health state utility (lower than general population)	SMR between 1.09 and 1.2	Aberdeen	Committee C
TA895	Lymphoma	Mixture-cure model	In line with general population	Mixture-cure model	Aberdeen	Committee C
TA559	Lymphoma	2 years	In line with general population	In line with general population	York	Committee C

Abbreviations: ALL; acute lymphoblastic leukaemia, SMR; standardised mortality ratio, EFS; event-free survival, PFS; progression free survival

CONCLUSIONS

- There is inconsistency in key modelling assumptions preferred by EAGs and/or NICE committees regarding curative therapies
- Differences in cure assumptions will logically lead to differences in cost-effectiveness results and the price achievable for a new therapy.
- A more consistent, structured approach should be considered for centralised application across haematological cancers that considers
  1. the burden of the curative treatment; CAR-T vs. SCT
  2. the relative contribution of disease- vs. treatment-specific post-cure mortality and its temporality
  3. the age of the patient and ability to recover from the disease and treatment.