Did OS Immaturity Preclude From Receiving a Positive Recommendation: A Review of Recent Oncology NICE Technical Appraisals?

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Background and Objective

- Overall survival (OS) is a key driver in health-economic evaluation in oncology.[1,5]
- Immature OS results in higher uncertainty for long-term survival extrapolation in health-economic evaluations. Mature OS can lead to more accurate extrapolation of long-term benefit and therefore is desirable from a reimbursement perspective.[2–5]
- This research aimed at describing the relationship between the level of OS maturity within different National Institute for Health and Care Excellence (NICE) technology appraisals (TAs) and the corresponding recommendation status.

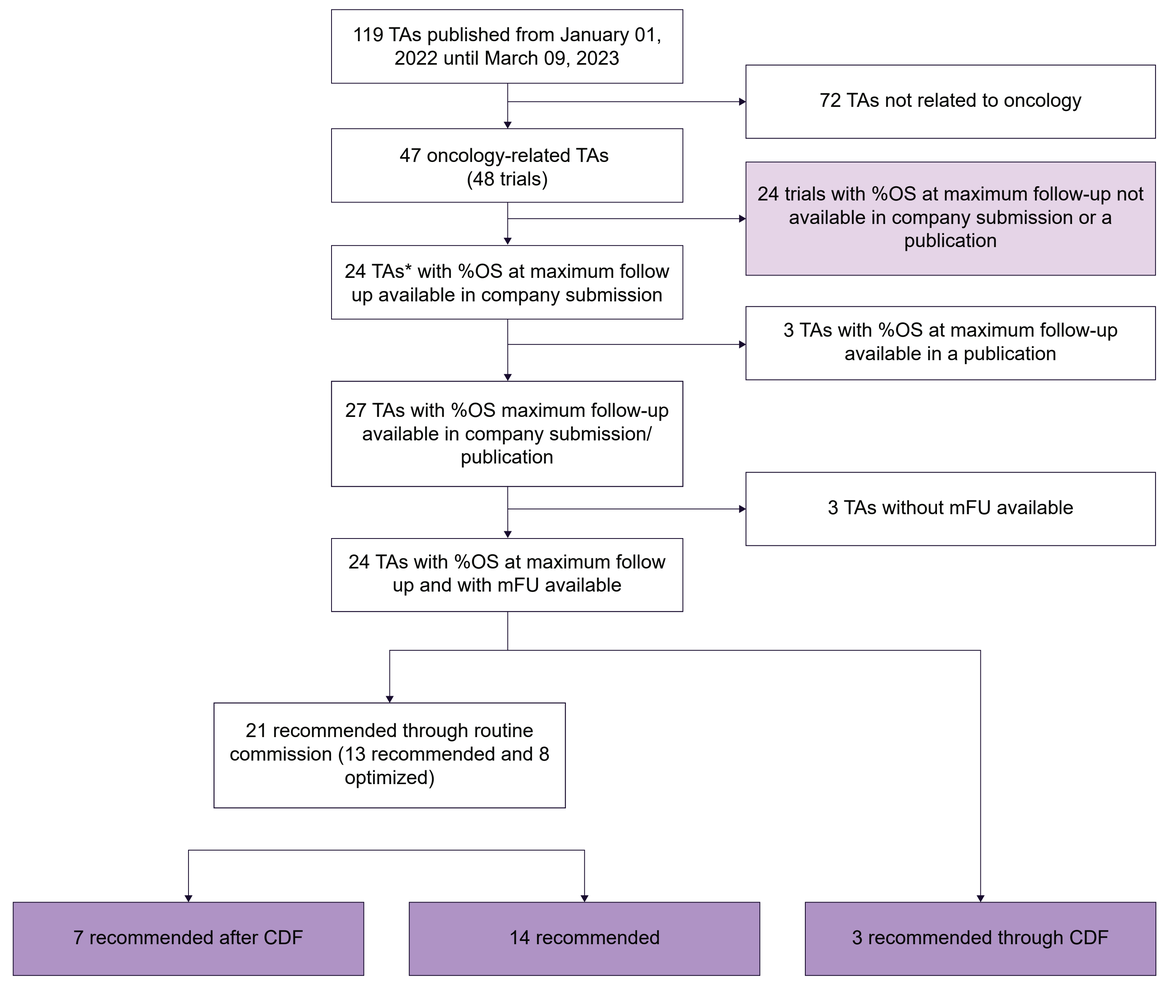
Methods

- Single TAs published by NICE between January 01, 2022 and March 09, 2023, only for oncology products and excluding terminated TAs, were identified.[6]
- The range of OS (i.e., percentage surviving at the end of the trial follow-up) was collected in 10% increments through a visual assessment, to avoid requiring digitizing each of the OS curves while capturing the required information for the analysis.
- The range of OS at the end of the clinical trial follow-up and the corresponding median follow-up time were collected from the company's submission in the first committee papers or clinical trial publication if such information was redacted from the TA. Only clinical trial publications corresponding to the same follow-up as in the company submissions were considered in the latter case.
- The recommendation status was captured from the NICE website.[7]
- OS was considered immature if less than 50% of the patients were dead at the end of the trial follow-up.[5]

Results

- A total of 47 oncology TAs were reviewed among 119 TAs published within the defined period. TA866 included 2 clinical trials; thus, the 47 TAs correspond to 48 clinical trials (**Figure 1**).

Figure 1. PRISMA flow chart



*One TA included one trial with the %OS at maximum follow-up available and one trial with the %OS at maximum follow-up not available.
TAs in purple were included in the analysis.
CDF, Cancer Drugs Fund; mFU, median follow-up; OS, overall survival; TA, technology appraisal.

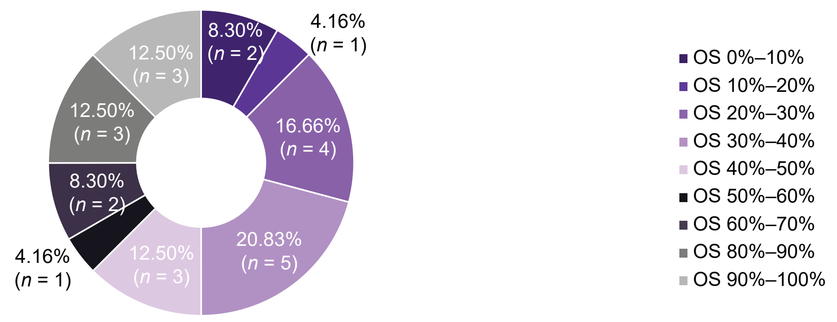
- OS and the associated median follow-up for OS were publicly available for 24 TAs (dark purple in **Figure 1**). All TAs received a recommendation for reimbursement through routine commissioning or CDF. Reported OS at maximum follow-up ranged anywhere from 0%–10% to 90%–100% (**Table 1**; **Figure 2**).

Table 1. TAs including %OS and median follow-up in the company's submission in the first committee papers

Reference number	%OS at maximum follow-up	Median follow-up (months)	Recommendations	Cancer subtype
TA874	80%–90%	28.2	Recommended	Lymphoma
TA872	50%–60%	15.4	Recommended (after CDF)	Lymphoma
TA870	20%–30%	85	Recommended (after CDF)	Myeloma
TA866	0%–10%	7.4	Recommended	Colorectal (metastatic)
TA862	80%–90%	16.2	Recommended (after CDF)	Breast (metastatic)
TA855	30%–40%	14.16	Recommended	Lung (advanced)
TA851	80%–90%	37.8	Recommended	Breast (adjuvant/neoadjuvant)
TA849	0%–10%	22.9	Recommended	Hepatocellular (advanced)
TA836	10%–20%	73.3	Recommended (after CDF)	Breast (advanced)
TA833	90%–100%	19.5	Recommended	Waldenstrom's macroglobulinaemia
TA830	90%–100%	30.1	Recommended	Renal (adjuvant)
TA827	20%–30%	51.7	Recommended	Leukemia
TA823	60%–70%	32.2	Recommended (through CDF)	Lung (adjuvant)
TA819	20%–30%	8.38	Recommended	Breast (advanced, metastatic)
TA818	20%–30%	29.7	Recommended	Mesothelioma
TA798	40%–50%	61.6	Recommended (after CDF)	Lung (advanced)
TA796	60%–70%	26.6	Recommended (after CDF)	Leukemia
TA788	40%–50%	19.6	Recommended	Urothelial (advanced, metastatic)
TA786	30%–40%	14	Recommended	Breast (advanced)
TA781	40%–50%	15.3	Recommended (through CDF)	Lung (advanced, metastatic)
TA780	30%–40%	60	Recommended (after CDF)	Renal (metastatic)
TA770	30%–40%	14.3	Recommended (after CDF)	Lung (metastatic)
TA765	30%–40%	20.5	Recommended	Leukemia
TA763	90%–100%	29.2	Recommended	Myeloma

CDF, Cancer Drug Fund; OS, overall survival; TA, technology appraisal.

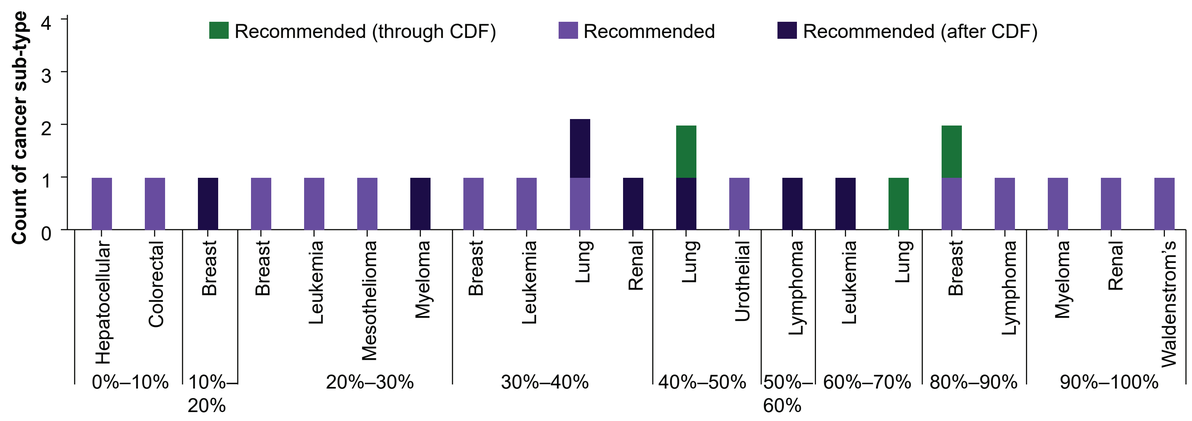
Figure 2. Number of TAs as a function of %OS range at the trial maximum follow-up



OS, overall survival; TA, technology appraisal.

- Of those recommended for routine commissioning (after Cancer Drugs Fund [CDF] or not) (*n* = 21/24), nine reported OS between 20% and 40% and six reported OS over 80% (**Figure 3**).
- Those TAs receiving recommendation for routine commissioning following CDF review (*n* = 7/21) reported OS from 10% to 70% indicating immaturity of OS may be acceptable at the time of review following CDF exit (**Figure 3**).
- The most common cancer types were lung (*n* = 5) and breast (*n* = 5) cancers. For TAs related to lung cancer, the OS ranged from 30% to 70%. A recommendation of reimbursement through CDF was decided for the TA with the OS ranging from 60% to 70% (in adjuvant setting). For the two TAs with OS ranging from 40% to 50%, one led to a recommendation of reimbursement through CDF while the other one led to a recommendation for routine commissioning after a CDF exit. OS ranging from 30% to 40% corresponded to two TAs with a recommendation for routine commissioning, including one exiting CDF (**Figure 3**).

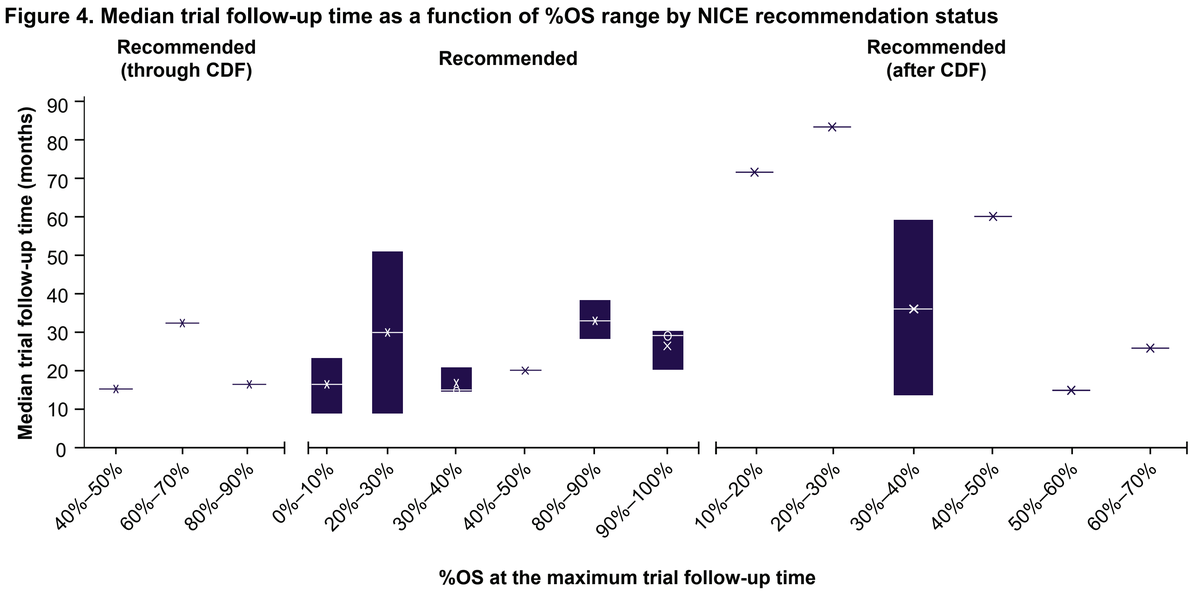
Figure 3. NICE recommendation status by %OS range at the trial maximum follow-up by cancer type



CDF, Cancer Drug Funds; NICE, National Institute for Health and Care Excellence; OS, overall survival.

- The average median follow-up (*n* = 24) is 31 months (from 7.4 to 85). The median follow-up logically tended to be higher for the TAs corresponding to a positive recommendation exiting CDF (48 months) than that for the TAs corresponding to a positive recommendation through CDF (21 months) or not through CDF (24 months) (**Figure 4**).

Figure 4. Median trial follow-up time as a function of %OS range by NICE recommendation status



When the median trial follow-up time of only one TA is available for a given %OS at the maximum trial follow-up time, one point is represented, while if the median trial follow-up time for several TAs are available for a given %OS at the maximum follow-up, the range of median trial follow-up time is represented as a bar.
CDF, Cancer Drug Funds; NICE, National Institute for Health and Care Excellence; OS, overall survival, TA, technology appraisal.

- Among the TAs for which it is mentioned that the submission was done without OS (*n* = 6/47), only one was not recommended while others received a recommendation for reimbursement (routine commissioning *n* = 4; through CDF *n* = 1).

Limitations

- Obviously, the OS maturity is not the only parameter to impact the recommendation for reimbursement, so the analysis mainly intended to evaluate whether having OS immature would preclude from receiving a positive recommendation.
- A further step would be to help identifying the different approaches to reach a positive recommendation when OS is immature.
- Cancer stage and type-level of unmet needs, among other factors can impact acceptance of immature OS data (e.g., adjuvant indications).
- An assessment of recommendation for routine commissioning versus CDF against the level of maturity of OS could help understand further the drivers for interim funding via CDF. However, that was not in the scope of this work.
- The OS data collected for this analysis were from the company's submission in the first committee papers, as such that the results do not include any additional data submitted to NICE during that given submission.
- Only half of the TAs included clinical trial OS and median trial follow-up time in the company's submission in the first committee papers. As a consequence, the results might not be representative of the TAs in which the OS information was redacted.
- A more detailed analysis of the median trial follow-up time at the time of submission would be needed as it differs between cancer stage and type.

Conclusions

- **In recent NICE oncology TAs, OS could be immature for different reasons, including good prognosis during the trial follow-up.**
- **OS immaturity did not preclude from receiving a recommendation for reimbursement in routine commissioning or through CDF.**

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CONFLICTS OF INTEREST

AP and HS: Sanofi —employees, may hold stock and/or stock options in the company.

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