Use of Single-arm Trials in NICE Reviews of Oncology Drugs

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Introduction

- Single-arm trials have been increasingly used to support oncology technology appraisals by the National Institute for Health and Care Excellence (NICE), despite known limitations in providing comparative evidence.
- In the absence of relative treatment efficacy directly available from trials, alternative approaches are available to generate indirect evidence using external controls.
- The use of external comparator data in past NICE submissions and their acceptance are of interest to the future submissions based on single-arm trials.

Objectives

- To assess the frequency of oncology NICE technology appraisals based on single-arm trials, the approach to generating comparative evidence, and recommendations from the committee review

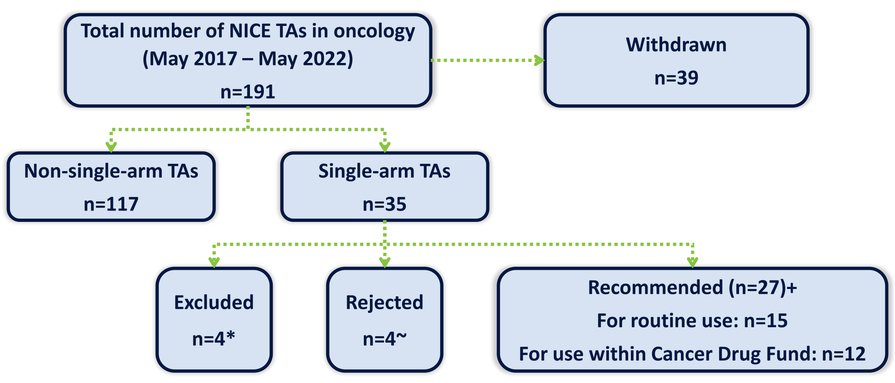
Methods

- We reviewed publicly available NICE recommendations identified on the https://www.nice.org.uk/ website from May 2017 to May 2022, including technology appraisal guidance and committee papers.
- A total of 191 unique technology appraisals in oncology were identified.
- Full-text screening of the committee papers and technology appraisal guidance was conducted by a single investigator, and the abstracted data were validated by a second investigator.
- Information on drug of interest, indication, trial design, external comparator data, and committee commentaries was extracted.

Results

- Of the 191 final appraisals, 35 (18%) used only single-arm trials as primary clinical evidence. For those new drugs supported by single-arm trials, the percentage recommended for routine use or Cancer Drug Fund was 77% (n=27). See **Figure 1**.

Figure 1. Characteristics of NICE Appraisals for Oncology based on Single-arm Trials

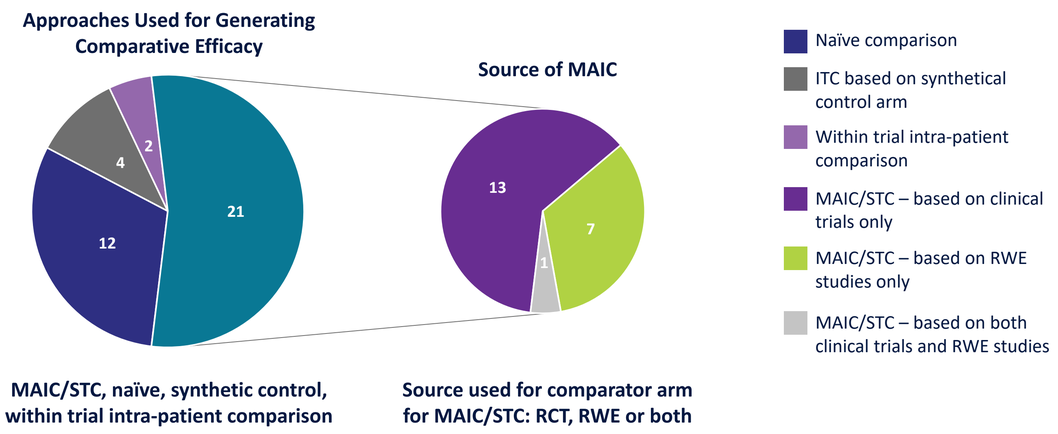


*TA517 was replaced by TA691 and therefore was excluded from the analysis. TA428, TA450, and TA739 were excluded as manufacturers submitted RCTs in addition to single-arm trials while RCTs were used as primary source for decisions.
~Three rejections from initial submission. Decision for TA491 was replaced by TA795 and the latter was rejected in the June 2022 update.
+Decision for TA487 was replaced by TA796 and decision for TA592 was replaced by TA802. Both replacements in June 2022 changes the original recommendation for use within Cancer Drug Fund to routine use.

Abbreviations: NICE = National Institute for Health and Care Excellence; RCT = randomized controlled trial; TA = technology appraisal

- Most single-arm trial-based submissions (78%; 21 of 27) applied matching-adjusted indirect comparison (MAIC) or simulated treatment comparison (STC) to generate external comparator data. Among them, more MAICs/STCs used clinical trials than real-world evidence (13 vs. 7) as external controls, with one study based on both. The rest utilized synthetic control (n=4) or within-trial intra-patient comparisons (n=2) in addition to naïve comparison (n=12). Some studies adopted more than one method (**Figure 2**).

Figure 2. Approaches Used for Generating Comparative Efficacy in the NICE Appraisals for Oncology Single-arm Trials



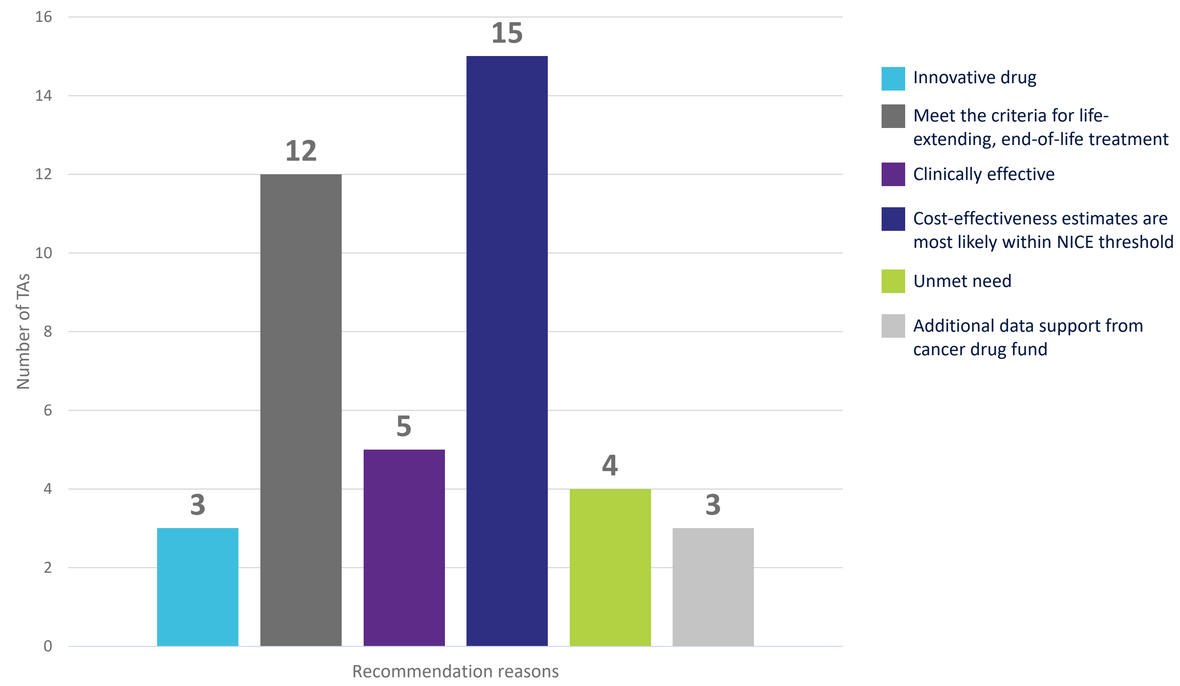
Six TAs reported using both naïve comparison and MAIC approach. One TA used all three approaches, including naïve comparison, MAIC and ITC based on synthetic control arm.

Abbreviations: ITC = indirect treatment comparison; MAIC = matching adjusted indirect compassion; NICE = National Institute for Health and Care Excellence; RWE = real-world evidence; STC = simulated treatment comparison; TA = technology appraisal

Results (cont.)

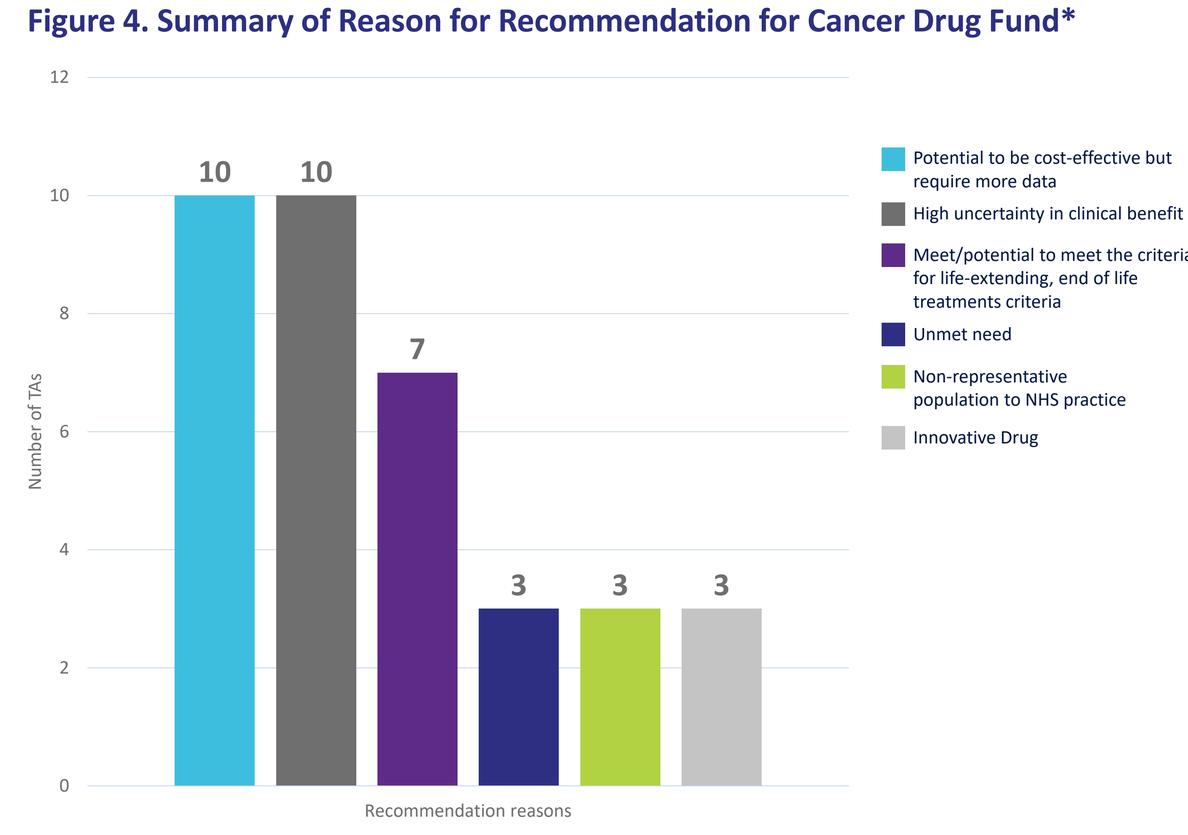
- About half of the recommendations are for routine use with the dominant reasons being "cost-effectiveness estimates are most likely within NICE threshold" and "meet the criteria for life-extending, end of life treatment" (**Figure 3**). For the other half that were recommended under the Cancer Drug Fund, the most frequently listed reasons are "potential to be cost-effective but require more data" and "high uncertainty in clinical benefits" (**Figure 4**).

Figure 3. Summary of Reason for Recommendation for Routine Use*



*Reasons were not mutually exclusive; multiple reasons were commonly cited for one technology appraisal.
Abbreviations: NICE = National Institute for Health and Care Excellence; TA = technology appraisal

Figure 4. Summary of Reason for Recommendation for Cancer Drug Fund*



*Reasons were not mutually exclusive; multiple reasons were commonly cited for one technology appraisal.
Abbreviations: NHS = National Health Service; NICE = National Institute for Health and Care Excellence; TA = technology appraisal

- The common reason of all four rejection decisions was the quality of submitted indirect comparison was not robust, which lead to incremental cost-defectiveness ratios higher than the commonly accepted threshold of £30,000 per quality-adjusted life year. The studies applied landmark analysis of its own trial, STCs using another clinical trial, and MAIC with real-world evidence (n=2).

Discussion

- In spite of uncertainty around clinical evidence based on single-arm trials, the recent acceptance rate by NICE for oncology drugs is encouraging, which provides opportunity for new drugs that meet the life-extending and end of life category but may not have randomized control trials available at the moment.
- In this context, leveraging valid approaches to generate relatively robust external control data is important to help address the uncertainty around relative treatment effect and smooth out the reimbursement decision making.

References

National Institute for Health and Care Excellence.
[TA802, TA796, TA795, TA783, TA781, TA779, TA760, TA742, TA739, TA722, TA716, TA704, TA691, TA677, TA644, TA643, TA630, TA628, TA604, TA592, TA589, TA571, TA567, TA559, TA554, TA540, TA539, TA530, TA524, TA517, TA491, TA489, TA487, TA478, TA462, TA451, TA450, TA428]. https://www.nice.org.uk/guidance

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