NICE Reconsiderations for Oncology Drugs Based on Single-Arm Trials Referred to the Cancer Drug Fund

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Background

- Submissions based on single-arm trials often raise concerns from the National Institute for Health and Care Excellence (NICE), requiring the generation of additional evidence within the Cancer Drug Fund (CDF). In October 2023, NICE published the approval rate of re-appraisals of all oncology drugs referred to the CDF since 2016.[1]

Objectives

- The objective of this study was to review single-arm trial-based re-appraisals referred to the CDF during the same period and compare them with the NICE publication on re-appraisals of general oncology drugs recommended to CDF with managed access.

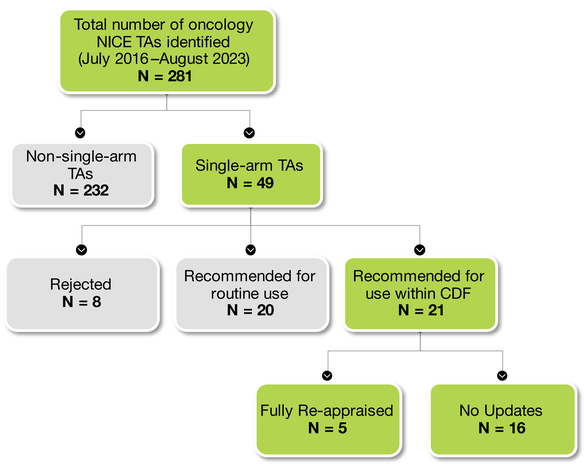
Methods

- Published NICE oncology technology appraisals (TAs) based on single-arm trials from July 2016 through August 2023 were reviewed to identify re-appraisals using evidence from the CDF.
- Full-text screening of the committee papers and guidance was conducted by a single investigator and the abstracted data were validated by a second investigator.
- Information extracted for analysis included the original evidence submitted for initial review, reasons for referring to the CDF, new evidence submitted for re-appraisal while in CDF, and committee commentaries.

Results

- Among 44 single-arm trial-based TAs identified, 21 were referred to the CDF and **five** were fully re-appraised by NICE with additional clinical trials and real-world data from the CDF (**Figure 1**).

Figure 1. Screening Process Chart

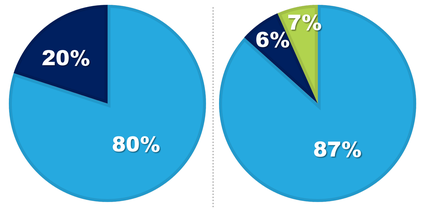


Abbreviation: CDF = Cancer Drug Fund; NICE = National Institute for Health and Care Excellence; TA = technology appraisals

Results (cont'd)

- Four (80%) of the fully re-appraised TAs were recommended for routine use comparing with the NICE published overall rate of 87% (26/30), and one was declined (**Figure 2**).
- Key limitations of the evidence submitted in the original appraisal that was referred to the CDF included immature trial data with limited follow-up, inadequate or low-quality evidence identified for comparators, trial data with limited generalizability to the UK clinical practice, and an estimated ICER above the threshold or with considerable uncertainty (**Figure 3**).
- Further evidence considered during the re-appraisal mainly included updated trial data with longer follow-up and additional data collected from the systemic anti-cancer therapy (SACT) dataset while drugs were available in the CDF. The SACT dataset contains UK real-world clinical-effectiveness data from the CDF population. Input from clinical experts also played an important role when additional evidence from the SACT dataset was considered limited or infeasible (**Figure 4**).
- For the approved TAs, data from the CDF could demonstrate better clinical effectiveness with extended follow-up from the real world, provide evidence on the treatment's life-extending potential and justify acceptability of cost-effectiveness estimates, and better reflect the local patient population and clinical practice. However, limitations due to a lack of comparative evidence normally remain upon exiting the CDF (**Table 1**).
- For the rejected TA, new evidence was more representative of the local population but failed to resolve the uncertainty around the magnitude of the clinical benefit and thus justify high cost-effectiveness estimates.

Figure 2. Comparison of NICE Recommendations for Re-Appraisal of Oncology Drugs Based on Single-Arm Trials and General Oncology Drugs Recommended to CDF with Managed Access* Between July 2016 and August 2023



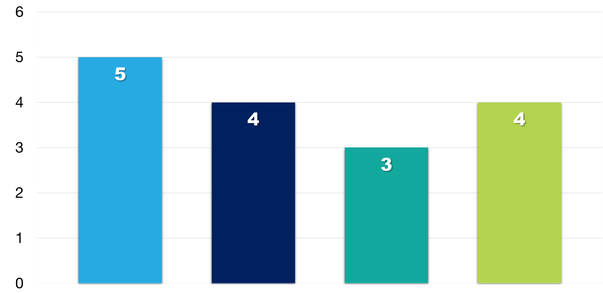
NICE RE-APPRAISAL DECISION	RE-APPRAISAL FOR ONCOLOGY DRUGS BASED ON SINGLE-ARM TRIALS	RE-APPRAISAL FOR ONCOLOGY DRUGS UNDER MAA[1]
Recommended for routing use	4	26
Not approved for routine use	1	2
Terminated/withdraw	0	2

Abbreviation: MAA = Managed Access Agreement; NICE = National Institute for Health and Care Excellence

*Managed Access Agreement is a source of funding for treatments that show clinical promise and where further data collection is needed to resolve uncertainty around their effectiveness

[1] NHS. Cancer Drugs Fund activity update Q4 2022-23. 2023. Accessed April 14, 2024. https://www.england.nhs.uk/long-read/cancer-drugs-fund-activity-update/

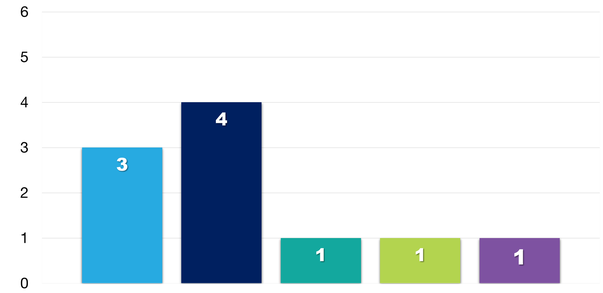
Figure 3. Limitations of Evidence Submitted in the Original Appraisals



APPRAISALS	TA 559	TA 592	TA 487	TA 491	TA 299
Immature OS	✓	✓	✓	✓	✓
Limited/low-quality data for comparators	✓	✓	✓		✓
Trial population was not representative of the UK population/has limited generalizability to the UK clinical practice		✓	✓		✓
ICER above threshold/uncertainty	✓	✓	✓	✓	

Abbreviation: ICER = incremental cost-effectiveness ratio; OS = overall survival; TA = technology appraisal; UK = United Kingdom

Figure 4. Additional Evidence Submitted in Re-Appraisals



RE-APPRAISALS	TA 872	TA 802	TA 796	TA 795	TA 401
Trial with longer F/U	✓	✓		✓	
SACT dataset	✓	✓	✓	✓	
Additional RWE		✓			
Clinical expert's opinion					✓
TLR to support original evidence submitted	✓				

Abbreviations: F/U = follow-up; RWE = real-world evidence; SACT= systemic anti-cancer therapy; TA = technology appraisal; TLR = targeted literature review

Table 1. NICE Re-Appraisal Based on Additional Data from the CDF (2016 – 2023)

Re-appraisal	Initial TA	Reasons for Referring to CDF	Resolved through CDF/Updated findings	NICE Decision on Re-Appraisal
TA 872 (Jan 2019)	TA 559 (Feb 2023)	• Immature OS outcomes due to limited F/U • No direct data comparison	• RWE OS rate from SACT dataset was comparable to trial result and supports routine use • Although still with uncertainty, new ICER is below threshold	Recommend for routine use
TA 802 (Aug 2019)	TA 592 (Jun 2022)	• Limited evidence on life expectancy with SoC and survival benefit from the intervention • High ICER	• New evidence from a trial and a UK RWE on extended life with the intervention meeting end of life criteria • While there is still significant uncertainty in survival vs. SoC, high ICER is more justifiable	Recommend for routine use
TA 796 (Nov 2017)	TA 487 (Jun 2022)	• Trial population not representative of England clinical practice • Not appropriate data source for SoC • Most plausible ICER is above threshold	• Additional clinical data in England population • Acceptable ICER for end-of-life treatment • Uncertainty in ICER due to uncertainty in comparative efficacy as no new data were collected for SoC	Recommend for routine use
TA 795 (Nov 2017)	TA 491 (Jun 2022)	• Limited data to inform long-term benefit • Not a life-extending or end-of-life treatment • Most plausible ICER is substantially above threshold	• Updated trial data with longer F/U demonstrated longer PFS and OS • Uncertainty in comparative efficacy against SoC • Unresolved high ICER above threshold	Not approved for routine use
TA 401 (July 2013)	TA 299 (Aug 2016)	• Limited generalizability of trial to clinical practice • Uncertain OS estimates due to maturity and receipt of further active treatment • Limited data available for comparators and uncertainty about how data was compared*	• Input from clinical experts indicated the unmet need in the patient population • ICERs based on revised key assumptions were within the acceptable ranges	Recommend for routine use

* Data was extracted from TA401 as original TA299 cannot be retrieved.

Abbreviation: CDF = Cancer Drug Fund; F/U= follow up; ICER = incremental cost-effectiveness ratio; NICE = National Institute for Health and Care Excellence; OS = overall survival; PFS = progression-free survival; RWE = real world evidence; SACT = systemic anti-cancer therapy; SoC = standard of care; TA = technology appraisal; UK = United Kingdom.

Conclusions

- For re-appraisals using CDF evidence, single-arm trial-based submissions have a comparable approval rate for routine use versus overall oncology submissions. New evidence from the CDF can reduce uncertainty around data immaturity and generalizability, but it is insufficient to inform comparative effectiveness.

References

1. NHS. Cancer Drugs Fund activity update Q4 2022-23. 2023. Accessed April 14, 2024. https://www.england.nhs.uk/long-read/cancer-drugs-fund-activity-update/
2. NICE Guidance. 10 TAs in total considering replacements: 872, 802, 796, 795, 592, 559, 491, 487, 401, 299

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