Beyond the Biomarker: HTA Challenges for Precision Oncology Technologies in NICE Appraisals

HTA352

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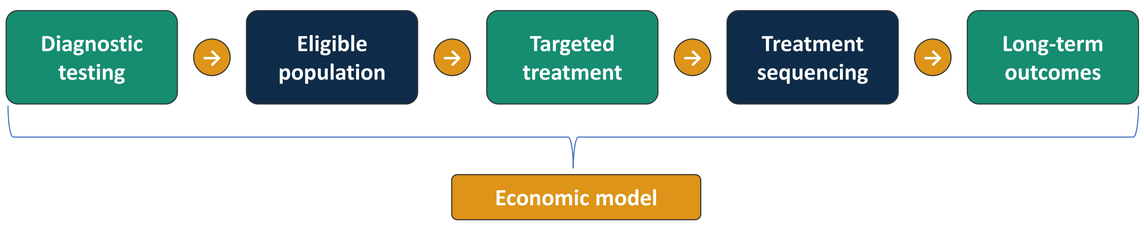
> **Despite frequent evidence uncertainty, NICE recommended 21/23 precision oncology technologies in this selected cohort, 13 of them with restrictions or managed access, amid immature overall survival (15/23) and indirect or external comparisons (17/23).**

1 BACKGROUND

Precision oncology (PO) technologies link treatment eligibility to molecular biomarkers and diagnostic testing, creating interdependent clinical and economic considerations for **health technology assessment (HTA)** (figure 1).

- Small biomarker-defined populations, single-arm studies, and immature survival data increase uncertainty in clinical and economic assessments.
- Rapidly evolving treatment pathways, multiple lines of targeted therapy, and comparator uncertainty complicate relative effectiveness assessments.
- Biomarker testing and patient selection also influence both clinical assessment and economic evaluation, beyond determining treatment eligibility.

Figure 1. PO diagnostic and treatment pathways introduce interdependent inputs into economic evaluation



Key HTA challenge: Integrating diagnostic pathways, relevant comparators, treatment sequencing, and long-term outcome uncertainty into cost-effectiveness evaluations.

2 OBJECTIVES

To examine key HTA challenges in selected NICE PO appraisals, focusing on evidence limitations, and implications for reimbursement and reassessment, by:

1. **Identifying recurring critiques** – NICE concerns relating to clinical evidence generation, diagnostic testing, comparator selection and treatment sequencing.
2. **Comparing patterns** – how evidence limitations and appraisal critiques varied across tumour areas, particularly between NSCLC and breast cancer.
3. **Exploring Decisions** – examining how residual evidence uncertainty was considered in NICE reimbursement recommendations, including population restrictions, managed access and reassessments.

3 METHODS

- **Structured review** of NICE oncology technology appraisals published between January 2020 and December 2025.
- **23 appraisals** selected to capture variation across tumour types, PO archetypes, evidence maturity, and NICE recommendation outcomes.

Search
NICE oncology TAs, 2020–2025

→ **Eligibility**
Biomarker-defined, molecularly stratified, companion diagnostic-linked, or tumour-agnostic technologies

→ **Extraction**
Evidence limitations, diagnostic pathways, comparators, treatment sequencing, and NICE decisions

→ **Included**
23
NICE appraisals

4 RESULTS

Figure 2. Cohort: appraisals by tumour area



NSCLC and breast cancer represented 18/23 (78%) appraisals.

Table 1. Tumour-specific patterns (share of appraisals)

Tumour area	Immature OS	Indirect/external comparison	Testing costed in model	Restricted recommendation (incl. CDF)	CDF recommendation
NSCLC (n=11)	7/11 (64%)	8/11 (73%)	5/11 (45%)	5/11 (45%)	1/11 (9%)
Breast cancer (n=7)	4/7 (57%)	5/7 (71%)	1/7 (14%)	4/7 (57%)	1/7 (14%)
Other* (n=5)	4/5 (80%)	4/5 (80%)	2/5 (40%)	4/5 (80%)	2/5 (40%)
All (n=23)	**15/23 (65%)**	**17/23 (74%)**	**8/23 (35%)**	**13/23 (57%)**	**4/23 (17%)**

NSCLC critiques centred on immature OS and comparator uncertainty; breast cancer critiques on comparator uncertainty and cost-effectiveness in narrower biomarker-defined populations.

Note. Percentages represent the proportion of appraisals within each tumour group; categories are not mutually exclusive.
*Ovarian/fallopian/peritoneal, tumour-agnostic solid tumour, endometrial, multi-tumour and prostate (one each).

Diagnostic considerations, trial evidence and reassessment

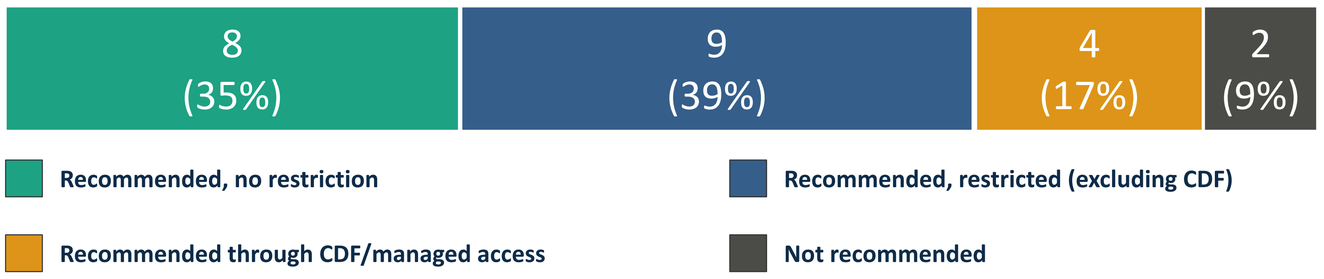
23/23 required biomarker testing diagnostic pathways were described in 21/23

8/23 explicitly included diagnostic testing costs in the model; testing availability (e.g., RET fusion, METex14) was also critiqued

11/23 included single-arm trial evidence; surrogate endpoints were considered across the reviewed appraisals

7/23 appraisals involved reassessment of previously published NICE guidance.

Figure 3. NICE recommendation outcomes across 23 appraisals



21/23 appraisals received positive recommendations, including 13 with restrictions or managed access. Two technologies were not recommended, reflecting unresolved clinical and/or cost-effectiveness uncertainties.

Abbreviations: ALK+, anaplastic lymphoma kinase-positive; CDF, Cancer Drugs Fund; EGFR+, epidermal growth factor receptor mutation-positive; METex14, MET exon 14 skipping; NSCLC, non-small-cell lung cancer; OS, overall survival; PFS, progression-free survival; RET, rearranged during transfection; SACT, Systemic Anti-Cancer Therapy dataset; TA, technology appraisal.

HTA lifecycle: reassessment changed the decision in two case studies

Lorlatinib, untreated ALK+ NSCLC

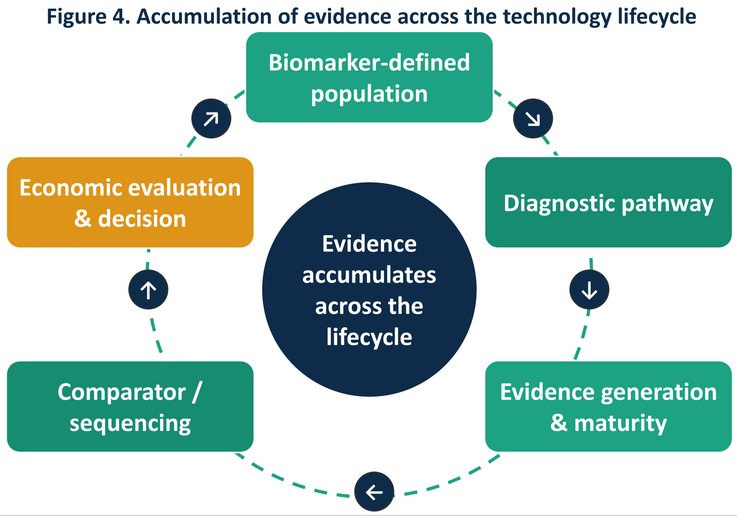
TA909 (2023) Not recommended → More mature PFS evidence; OS remained immature → TA1103 (2025) Recommended

Adjuvant osimertinib, resected EGFR+ NSCLC

TA761 (2022) Managed access → Long-term ADAURA trial + SACT real-world data → TA1043 (2025) Routine commissioning

5 DISCUSSION

Figure 4. Accumulation of evidence across the technology lifecycle



- **Interconnected uncertainty:** Biomarker-defined populations, diagnostic pathways, immature evidence, and comparator limitations create interdependent challenges for clinical and cost-effectiveness assessments (figure 4).
- **Restricted recommendations were more common** than non-recommendations (13/23 vs 2/23).
- **Lifecycle reassessment:** 7/23 appraisals revisited earlier NICE guidance; additional evidence may support changes in recommendations.
- **Limitation:** 23 appraisals selected for representation, not an exhaustive census.

6 CONCLUSION

- **Recurring HTA challenges** in PO appraisals included immature survival evidence, limited comparative data, and diagnostic-linked patient selection.
- **Restricted recommendations were frequent** (13/23), highlighting the importance of managing residual uncertainty.
- **Reassessment may change NICE decisions** as additional clinical and real-world evidence becomes available.
- **HTA implication:** Diagnostic testing, treatment sequencing, and associated costs should be considered alongside clinical evidence.

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