Plasma-Based Comprehensive Genomic Profiling DNA Assays for Non–Small Cell Lung Cancer

Recommendation

NOVEMBER 2024

Ontario Health

Final Recommendation

Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends publicly funding plasma-based comprehensive genomic profiling DNA assays (liquid biopsy testing) for individuals diagnosed with non–small cell lung cancer who have an insufficient tissue sample or difficult-to-reach tumour tissue and for those who are otherwise unable to undergo tissue biopsy.

Rationale for the Recommendation

The Ontario Health Technology Advisory Committee made the above recommendation after considering the clinical, economic, and patient preferences and values evidence reported in the health technology assessment[1] and the recommendation of a subcommittee, the Ontario Genetics Advisory Committee.

The committee members agreed that the evidence supported that liquid biopsy testing (a blood test to determine the genetic make-up of cancer tumours) is effective at identifying actionable genomic alterations (specific genetic or molecular changes in tumour DNA that predict response to targeted therapies) that are missed by tissue testing (which involves a tissue biopsy) because of insufficient tissue sampling or the tumour being difficult to reach. Further, the committee acknowledged that liquid biopsy testing should not replace tissue testing in all cases of non–small cell lung cancer (NSCLC) since tissue testing has superior sensitivity compared to liquid biopsy testing. The committee recognized that the accurate and timely identification of actionable genomic alterations can facilitate access to targeted NSCLC treatments.

The committee noted that using liquid biopsy testing for people with insufficient tissue for tissue testing was the preferred implementation approach based on the cost-effectiveness and budget impact results of the health technology assessment. Testing all people with NSCLC using both tissue and liquid biopsy testing (either sequentially or in parallel) may detect more people with actionable genomic alterations but may also lead to unnecessary liquid biopsy testing in cases where tissue testing results are truly negative. Contributing to the committee's decision is the recognized potential for liquid biopsy testing to be performed in Ontario laboratories, which will likely reduce the costs of this service compared with those of commercial and out-of-country laboratories.

The committee considered the lived experiences of people with NSCLC and their families and other care partners, who described the perceived social, clinical, and safety benefits of liquid biopsy testing. In particular, the committee noted that people with NSCLC valued the noninvasive nature of liquid biopsy testing and the importance of receiving the most appropriate treatment option available.

Committee members recognized the importance of providing timely comprehensive genomic profiling results to guide treatment decisions for people with locally advanced or metastatic NSCLC (stage IIIB or IV), which reduces life expectancy. Additionally, they acknowledged the ability of targeted therapies to extend life expectancy in people with advanced NSCLC with actionable genomic alterations identified via tissue or liquid biopsy testing. The committee recognized that the available clinical evidence is based primarily on studies of people with advanced NSCLC. Consequently, there is a limited understanding of the performance of liquid biopsy testing in earlier stages of the disease. However, the committee highlighted that limiting access to liquid biopsy testing to people with advanced NSCLC may lead to delays in starting targeted therapy for those who present at earlier stages of the disease. In making their

recommendation, the committee recognized the importance of avoiding unnecessary procedures and that the decision of whether tumour tissue is insufficient or difficult to reach, or whether a patient is unable to undergo tissue biopsy, would be based on the surgeon or treating team's judgment after considering imaging or other diagnostic test results or after having attempted tissue biopsy.

Decision Determinants for Plasma-Based Comprehensive Genomic Profiling DNA Assays for Non–Small Cell Lung Cancer

Overall Clinical Benefit

Analytical Validity

What is the ability of liquid biopsy testing to accurately and reliably identify actionable genomic alterations?

Our assessment indicates that the sensitivity of liquid biopsy testing in detecting actionable genomic alterations ranges from low to moderate (Grading of Recommendations Assessment, Development, and Evaluation [GRADE]: Moderate to High). This sensitivity falls below that of tissue testing. In settings where tumour tissue may have actionable genomic alterations but obtaining a tissue sample is unfeasible or yields insufficient material, liquid biopsy testing has demonstrated the potential to detect these alterations in at least 45% of cases.

Clinical Utility

What is the impact of liquid biopsy test results on patient outcomes and clinical decision-making?

The use of targeted therapies after testing positive for an actionable genomic alteration with liquid biopsy testing could improve the following outcomes: partial response, progressive disease, stable disease, objective response rate, progression-free survival, and overall survival (GRADE: Low to Moderate).

Safety

How safe is the health technology/intervention likely to be?

Liquid biopsy testing is known to be safe because of its minimally invasive nature, requiring only a small blood draw. Compared with tissue testing, it poses fewer risks of complications such as bleeding, pneumothorax (air leaking into the pleural space between the lungs and chest wall) and infection.

Burden of Illness

What is the likely size of the burden of illness pertaining to this health technology/intervention?

About 10,000 new cases of NSCLC are diagnosed annually in Ontario.[2] Of these, about 4,500 are advanced or metastatic nonsquamous NSCLC.

Need

How large is the need for this health technology/intervention?

An estimated 29% to 60% of people with NSCLC will test positive for actionable genomic alterations.

Patient Preferences and Privacy

Patient Preferences and Values

Do patients have specific preferences, values, or needs related to the health condition, health technology/intervention, or life impact that are relevant to this assessment?

Participants valued treatments focused on overall survival with minimal side effects. Those with whom we spoke valued the minimally invasive nature of liquid biopsy testing, and those with experience of both tissue and liquid biopsy testing perceived that the turnaround time for results was quicker for liquid biopsy testing. Participants perceived liquid biopsy testing as having the potential to inform treatment decisions for those with actionable genomic alterations unable to undergo tissue testing because of insufficient or difficult-to-reach tissue.

Autonomy, Privacy, Confidentiality, and/or Other Relevant Ethical Principles as Applicable

Are there concerns regarding accepted ethical or legal standards related to patient autonomy, privacy, confidentiality, or other ethical principles that are relevant to this assessment?

Participants felt that having access to information is an integral part of patient autonomy, and they perceived liquid biopsy testing as an important tool to help them and their families and care partners make informed treatment decisions.

Equity and Patient Care

Equity of Access or Outcomes

Are there disadvantaged populations or populations in need whose access to care or health outcomes might be improved or worsened that are relevant to this assessment?

Access to liquid biopsy testing is presently limited to patients participating in a clinical trial at 1 hospital in Toronto. Making liquid biopsy testing available to all clinically eligible patients without cost and at more locations across the province would increase equity of access.

Patient Care

Are there challenges in the coordination of care for patients or other system-level aspects of patient care (e.g., timeliness of care, care setting) that might be improved or worsened that are relevant to this assessment?

Liquid biopsy testing would provide an option for testing for actionable genomic alterations for patients who have undergone a tissue biopsy that yielded insufficient tissue for sampling and for those who have been assessed as having a tumour that is difficult to reach for tissue biopsy.

Cost-Effectiveness

Economic Evaluation

How efficient is the health technology/intervention likely to be?

For people with locally advanced or metastatic NSCLC (stage IIIB or IV), all 4 of the liquid biopsy testing strategies we assessed were associated with increased costs and increased quality-adjusted life-years (QALYs) compared with current standard care (tissue testing only). The incremental cost-effectiveness ratios (ICERs) for each of the 4 strategies are as follows:

- Liquid biopsy testing only for people with insufficient tissue for tissue testing: $96,738 per QALY gained
- Liquid biopsy testing first for all people, followed by tissue testing only for those with negative results: $147,636 per QALY gained
- Tissue testing first for all people, followed by liquid biopsy testing only for those with negative results: $157,267 per QALY gained
- Combined tissue and liquid biopsy testing for all people: $173,032 per QALY gained

The probability of the “insufficient tissue” strategy being cost-effective is less than 1% at a willingness-to-pay (WTP) of $50,000 per QALY gained and 55% at a WTP of $100,000 per QALY gained.

Feasibility of Adoption Into Health System

Economic Feasibility

How economically feasible is the health technology/intervention?

Publicly funding liquid biopsy testing for people with locally advanced or metastatic NSCLC and insufficient tissue for tissue testing over the next 5 years would lead to an additional cost of $13.72 million. The 5-year budget impact of publicly funding the other liquid biopsy testing strategies ranges from $110.13 million to $134.24 million.

Organizational Feasibility

How organizationally feasible is it to implement the health technology/intervention?

Commercially available comprehensive genomic profiling tests are currently accessible to people with NSCLC who have private insurance coverage or who can pay out of pocket. These tests require samples be sent out of country. However, liquid biopsy testing may be performed at Ontario laboratories in the future.

References

1) Ontario Health. Plasma-based comprehensive genomic profiling DNA assays for non–small cell lung cancer: a health technology assessment. Ont Health Technol Assess Ser [Internet]. 2024 Nov;24(8):1–306. Available from: https://hqontario.ca/evidence-to-improve-care/health-technology-assessment/reviews-and-recommendations/plasma-based-comprehensive-genomic-profiling-dna-assays-for-non-small-cell-lung-cancer
2) Ontario Health (Cancer Care Ontario). Ontario cancer statistics 2022. Ch 1: Estimated current cancer incidence [Internet]. Toronto (ON): Ontario Health; 2022 [cited 2023 Apr 3]. Available from: https://www.cancercareontario.ca/en/data-research/view-data/statistical-reports/ontario-cancer-statistics-2022/ch-1-estimated-current-cancer-incidence-2022

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