Policy Paper- BEAT Cancer Coalition

July 2022

Executive Summary

The treatment landscape for cancer has evolved significantly over the past few decades, with a shift towards personalized healthcare for individual patients. Cancer therapies are now being developed based on key molecular drivers within the genomic profile of individual tumours. Despite these advancements, patients today still suffer from the one-size-fits-all approach to treatment, lacking access to advanced diagnostics and being subjected to sequential rounds of therapy that may or may not be successful. It is essential to ensure the patients can access the right treatments at the right time, using the tools that are now available, and thus give cancer patients their best chance at a healthy life and lead to improved patient outcomes

To capitalize on innovation, equitable access to advanced diagnostic testing and innovative therapies is crucial. This means access regardless of location, age, disability, income, or any other factors.

The BEAT Cancer Coalition recommends that governments enable equitable access to the appropriate advanced molecular diagnostic testing through comprehensive genomic profiling (CGP), for all cancer patients across Canada, to give them the best chance at a long and healthy life.

The Coalition proposes that decision-makers develop resilient and sustainable access processes and infrastructure for evaluating new diagnostic technologies and for ensuring that they reach patients as quickly as possible. This will be essential not only for meeting today's needs, but in order to meet the pace of innovation that following to guide governments' decisions and laboratory implementation, such as:

1. Increase the level of comprehensive genomic profiling standards across Canada such as defining CGP as panels that evaluate 50 or more genes or genetic alterations that are either known oncologic drivers or have the potential to be
2. That CGP for patients with tumour types having 5+ genes (NSCLC, CRC, breast, CUP) known to have targetable mutations for immediate public coverage in all provinces, and testing should be standard of care for those defined patient groups.
3. That while solid tissue testing is still the most commonly used, increase the availability and access to liquid (blood) biopsy to detect genetic alterations. Access could start in priority patient populations such as for patients who are unable to undergo tissue biopsy for any reason.

These initial steps are part of a larger path towards a state of equitable access to advanced molecular diagnostics which enables access to the technology of today and a future mechanism to ensure sustainable access and a pathway forward for the technology of tomorrow. This commitment is what will change the world for and offer hope to Canadian cancer patients.

Introduction

The treatment landscape for cancer has evolved significantly over the past few decades, with a shift towards personalized healthcare for individual patients. Cancer therapies are now being developed based on key molecular drivers within the genomic profile of individual tumours. Despite these advancements, patients today still suffer from the one-size-fits-all approach to treatment, lacking access to advanced diagnostics and being subjected to sequential rounds of therapy that may or may not be successful. It is essential to ensure the right patients can access the right treatments at the right time, using the tools that are now available, and thus give cancer patients their best chance at a healthy life.

The Bringing Equitable Access to Advanced Molecular Testing (BEAT) Cancer Coalition is a collaborative group of stakeholders including patient organizations, clinicians, pathologists, professional organizations, academics, and industry working towards a common vision:

> *"All Canadian oncology patients, regardless of where they live, should receive timely and appropriate advanced molecular testing in order to receive the optimal therapy for them, giving them the greatest chance of treatment success and the greatest opportunity to live their best life."*

This paper presents an overview of the value of advanced molecular diagnosis through comprehensive genomic profiling (CGP) for oncology patients and for the Canadian healthcare system, and provides recommendations for Canada's provincial healthcare administrators to support their decision-making, resourcing, and implementing CGP, towards the shared goal of better patient outcomes within a sustainable healthcare system.

Personalized Healthcare for Cancer Patients

Cancer therapies are rapidly advancing, developed based on key molecular drivers present within the genomic profile of an individual patient's tumour, rather than the tumour's location in the body. This is the foundation for the concept of personalized healthcare[1] in cancer care and precision oncology.

Personalized Healthcare (PHC) is based on the observation that patients with the same diagnosis may have different underlying causes of disease and may react to the same treatment in different ways. PHC is a holistic approach to care delivery, enabled by high-medical-value diagnostic solutions, meaningful data, advanced analytics, and digital technologies to improve R&D, optimize health outcomes for individuals, and deliver value and sustainability for the overall healthcare system[2]. PHC is the approach that will change the landscape for patients, and bring them hope for their futures.

Innovative companies work to advance modern medicine through investment in innovative treatments, diagnostics and novel approaches to care. The Canadian healthcare system now needs to similarly invest to keep up with the pace of change. This not only benefits patients, but can result in system-wide savings in multiple areas within healthcare, including drug and hospital expenditures.

[1] The terms 'personalized medicine', 'personalized health care', 'precision medicine', and 'precision oncology' are often used interchangeably, however throughout their paper we will utilize 'personalized healthcare'

[2] https://www.roche.com/dam/jcr:8ce4417d-c5b7-4d8d-9e43-83e5182a849c/en/13_Position_Personalised_Healthcare_reviewed_April_2020.pdf

In cancer care, PHC and precision oncology can allow healthcare providers (HCPs) to avoid unnecessary, ineffective and/or potentially harmful oncology treatments, and instead can better allow them to tailor care plans and provide the right treatment from the start. This early, appropriate treatment benefits patients and optimizes the system's investment of both HCP time and financial resources, both of which are at a premium in today's healthcare system.

In order to fully embrace PHC, we need to expand our capacity for advanced molecular diagnostics to be beyond reimbursing diagnostic tests, but instead to be inclusive of the test(s), expertise required to perform them, systems enabled to interpret results and deliver them in an action-oriented manner to Canadian healthcare stakeholders

Tumour Drivers and Comprehensive Genomic Profiling

Traditionally, molecular drivers in tumours are identified by panels that look for a limited or small number of genes. These panels target only the most common mutations associated with specific tumour types. However, they present challenges that can result in missed opportunities for precision medicine: narrow coverage of gene sequences; inability to detect some of the main classes of genomic alterations; inability to capture genome-wide changes (e.g., tumour mutational burden, microsatellite instability or minimal residual disease); and lack of adaptability for keeping pace with a quickly-evolving list of genomic biomarkers required to make treatment decisions[3]. Additionally, they maintain the focus on the physical tumour site, rather than on molecular drivers and actionability (i.e., tumour-site-agnostic).

Advanced diagnostics such as comprehensive genomic profiling (CGP) enable the rapid analysis of a tumour's complete molecular profile to enable diagnosis, surveillance, treatment decisions, health coverage for innovative options, and clinical trial eligibility. CGP uses next-generation sequencing (NGS), a technique that enables high-throughput sequencing of nucleic acids in a fast and cost-efficient manner, allowing novel and known genomic marker detection for individual patients across all cancer types.

By enabling personalized healthcare, CGP not only provides patients with the right treatments, but also saves the time and money that are often spent on ineffective treatments with the current one-size-fits-all approach to cancer care[4]. CGP is the technology of today - not of tomorrow - and should be available to patients to support their care.

Haydn's Story

March 1st, 2021 was the day Haydn' life changed. After awakening from a diagnostic procedure, he was brought into a private room and told that they found a a likely malignant tumour Haydn was able to avail himself of molecular testing which reported that he had been diagnosed with stage III colorectal cancer, more specifically with Lynch syndrome which would avail himself of more precision options for his care. Without the upfront testing for his tumour, and appropriate molecular diagnostics, Haydn does not learn the intricacies of his condition, and cannot be directed to more appropriate and impactful treatment options. Investing in these kinds of tests allowed his medical team to develop a personalized approach to treating Haydn's disease, and that upfront investment has inspired Haydn to look to dedicate his coming years to investing back into the system, studying to enter medical school. To learn

[3] Final_CGP_Report_Dec23.pdf
[4] https://www.roche.com/about/priorities/personalised_healthcare/comprehensive-genomic-profiling.htm

At present, three primary access challenges exist for CGP:

1) **Infrastructure:** Access to CGP panels may be dependent on where you live. Additionally, there is not an accepted definition of "comprehensive", so the scale of a CGP panel and/or the provided tumour profile information may vary considerably depending on where a patient accesses care. Human resources required to deliver CGP and its insights represent an additional infrastructure associated barrier to implementation.
2) **Funding/Coverage:** Public funding for molecular profiling is disparate across the country, and is largely single-biomarker and tumour-site based rather than technology-based and tumour-agnostic. In many cases there is a lack of transparency and no clear path for CGP technologies to be covered.
3) **Education / Awareness:** The healthcare ecosystem is composed of stakeholders with significant educational gaps with respect to comprehensive genomic profiling, the impact it can have within a patient journey, along with the availability across therapeutic areas and provinces

In addition, the pace of change makes it difficult to know how to identify and when to evaluate new technologies, necessitating a continuous process. A key example is the development of liquid (blood) biopsy testing. As the system struggles to successfully adopt comprehensive profiling of solid tumour tissue, technology continues to innovate, developing the ability to detect circulating tumour DNA in blood, making sample collection much less invasive and time consuming for patients while also avoiding risk of adverse events which can add considerable cost to the health care system.

It is evident that the rapid advances in genomics present unique challenges to decision-makers, including payers and HTA bodies. The value assessment for CGP can be challenging given the current budget silos which make it difficult to showcase the overall impact of CGP testing on healthcare systems, patients, and society. Additionally, legacy technology assessment methods and the data required to inform HTA recommendations may not be applicable when evaluating diagnostics like CGP for several reasons (e.g., non-traditional data, lack of regulatory guidelines or standardization, speed of innovation, etc.)[5].

A more holistic assessment approach integrating the economic and social impact of molecular testing is necessary to ensure that better patient-centric investment decisions are made. There is an urgent need for payers to build a framework for incorporating CGP into funding decisions[6].

A recent report (*"Determining Priority Access to Comprehensive Genomic Profiling for Canadian Patients with Cancer"*) succinctly stated that, "[a] plan for publicly funding CGP in patients with cancer is crucial for enabling our healthcare system to keep pace with rapidly evolving molecular testing needs." This report identified five key recommendations:

- All patients with advanced or metastatic solid tumours should have access to CGP where deemed necessary or valuable by their clinician.
- Given budgetary constraints, tumour types that currently have five or more genes linked to approved or pipeline therapies should be prioritized for CGP funding to replace current limited testing modalities (lung cancer, colorectal cancer, breast cancer, cancer of unknown primary).
- Decision-makers must remain cognizant of the many other tumour types which will soon reach the five-biomarker threshold and be able to respond quickly or proactively to provide CGP funding for these

[5] https://www.nature.com/articles/gim2013110
[6] Final_CGP_Report_Dec23.pdf

patients (e.g., bladder cancer, cancer of the bile duct, gastrointestinal stromal tumours, melanoma, ovarian cancer, pancreatic cancer, prostate cancer).

- Any patient with an advanced or metastatic solid tumour who is refractory to standard therapy or is lacking treatment options that could extend survival should be prioritized for CGP.
- Stakeholders should collaborate to establish a new framework for assessing the value of CGP and new genomic biomarker-matched therapies that consider non-traditional methodologies[7].

BEAT-Cancer Coalition Position Statement

The BEAT-Cancer Coalition and its members support the recommendations of the *Determining Priority Access to Comprehensive Genomic Profiling for Canadian Patients with Cancer* report, and offer their support to governments in developing an appropriate, rapid, responsive, and patient-centered approach to evaluating NGS technologies and CGP, and to providing public funding for such testing for all Canadian cancer patients.

The Coalition proposes **that decision-makers develop a resilient and sustainable access process for evaluating new diagnostic technologies, and ensuring that they reach patients as quickly as possible. This will be essential not only for meeting today's needs, but in order to meet the pace of innovation.** This process should be transparent, it should include an opportunity for innovators to seek early advice on the evaluation process, and it should include a consultative component to ensure innovators, patients, and HCPs can all contribute. It will be critical for the system to keep up with innovations and adapt processes to include real world evidence and system-wide approaches to the concept of value in these technologies.

Initial steps to help guide governments' decisions and laboratory implementation should be:

1. **That CGP be defined as panels that evaluate 50 or more genetic alterations that are either known oncologic drivers or have the potential to be.** This would ensure that all currently - and imminently - actionable mutations are detected, while also supporting labs in developing the infrastructure & capacity to move away from hotspot panels towards comprehensive panels. This commits to sustainability so that patients have access to all information and all options important for their care and their futures.
2. **That, as proposed in the report (above), CGP for patients with tumour types having 5+ actionable mutations (NSCLC, CRC, breast, CUP[8]) be targeted for immediate public coverage in all provinces, and testing should be standard of care for those defined patient groups.** Future-looking cancer care should (a) immediately provide coverage for any other tumour types that reach this threshold, and (b) strive to become tumour-agnostic. Decision-making processes and testing guidelines should encourage system change from the current tumour-site-specific to a tumour-agnostic approach.
3. That while solid tissue testing is still considered the gold standard, **liquid (blood) biopsy is highly effective in detecting genetic alterations, and should be an available, funded option for high value patient segments such as those who are unable to undergo tissue biopsy for any reason.**

Laboratories, institutions and governments are recognizing the importance of sustainable funding for laboratory infrastructure and are investing in innovative diagnostic technologies which can significantly benefit patients,

[7] Final_CGP_Report_Dec23.pdf

[8] These tumour types include patients with advanced/metastatic non-squamous non-small cell lung cancer (NSCLC); metastatic colorectal cancer (CRC); metastatic breast cancer at one point in their disease course; and Cancer of Unknown Primary (CUP).

HCPs, and the healthcare system. We have an opportunity -- and an obligation -- to maximize that investment by ensuring that all patients and their care providers have access to the technology and to the information generated by the testing as rapidly and seamlessly as possible.

The path towards a state of equitable access to advanced molecular diagnostics needs a multi faceted approach that enables access to the technology of today and the mechanism to ensure sustainable access and a pathway forward for the technology of tomorrow. This commitment will change the world for and offer hope to Canadian cancer patients.

Appendix: About BEAT Cancer Coalition

The Bringing Equitable Access to Advanced Molecular Testing (BEAT) Cancer Coalition is a collaborative group of stakeholders including patient organizations, clinicians, pathologists, professional organizations, academics and industry working towards a common vision:

"All Canadian oncology patients, regardless of where they live, should receive timely and appropriate advanced molecular testing in order to receive the optimal therapy for them, giving them the greatest chance of treatment success and the greatest opportunity to live their best life."

The BEAT-Cancer Coalition aims to educate, shape policy, and improve public access to advanced molecular diagnostic testing for all oncology patients. The Coalition's core principle is collaboration towards achieving the aforementioned vision, and it acknowledges the ongoing work through a number of initiatives aimed towards a similar goal.

Members:
For a full list of members, visit https://www.beatcancercoalition.com/members

Terms Glossary:

Comprehensive genomic profiling: Laboratory methods used to learn about all the genes in a person or in a specific cell type, and the way those genes interact with each other and with the environment. Comprehensive genomic profiling may be used to find out why some people get certain diseases while others do not, or why people react in different ways to the same drug. It may also be used to help develop new ways to diagnose, treat, and prevent diseases, such as cancer.

Liquid biopsy: A test done on a sample of blood to look for cancer cells from a tumor that are circulating in the blood or for pieces of DNA / RNA from tumor cells that are in the blood. A liquid biopsy may be used to help find cancer at an early stage. It may also be used to help plan treatment or to find out how well treatment is working or if cancer has come back. Being able to take multiple samples of blood over time may also help doctors understand what kind of molecular changes are taking place in a tumor

Personalized healthcare: a holistic approach to care delivery, enabled by high-medical-value diagnostic solutions, meaningful data, advanced analytics, and digital technologies to improve R&D, optimize health outcomes for individuals, and deliver value and sustainability for the overall healthcare system. Often used colloquial terms: 'personalized medicine', 'personalized health care', 'precision medicine', and 'precision oncology'

Next Generation Sequencing (NGS): refers to large-scale DNA sequencing technology that allows for querying the entire genome (whole genome), the exons within all known genes (whole exome), or only exons of selected genes (target panel)

Precision Medicine: a specific health technology which utilize information about a patient's tumour to inform diagnosis, plan treatment, understand response or inform prognosis