Imagia Canexia Health™

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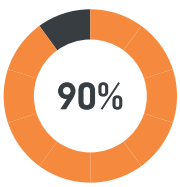
Lessons from a National Liquid Biopsy Program to Provide Access to Cancer Testing and Treatment During COVID-19

Introduction

COVID-19 created a crisis for cancer patients who have faced extraordinary uncertainty since March 2020. In Canada, for example, the fourth wave of the pandemic resulted in additional rounds of surgery cancellations in September 2021.

For cancer patients, some tissue biopsy delays can be offset by a minimally-invasive blood draw to enable oncologists to select targeted treatment options and monitor disease progression. Circulating tumour DNA (ctDNA) testing is already widely deployed throughout the United States, but is not yet standard of care in many places in the world. In exceptional cases, for example, Canadian patients who are able to access this testing through an oncologist must wait for blood samples to be shipped over the border, analyzed in US labs, and then for results to arrive weeks later. This current scenario costs thousands of dollars per patient and is not accessible to all patients who would benefit.

In response, with a strategic investment from Canada's Digital Technology Supercluster, a pilot project to bring ctDNA testing into the Canadian health system was launched in July 2020, reaching more than 3,000 cancer patients with advanced breast, lung, and colorectal cancer. The ability to conduct the blood test at a local laboratory broadened access to rural and underserved populations, removing geography as a barrier to informed cancer treatment decisions. Such testing also kept high-risk patients out of hospitals and other healthcare settings.



Adoption Rate

470+
Ordering Oncologists

3200+
Patients

100+
Institutions

11%
Remote Communities

Objectives

- Provide timely molecular testing to more than 3,000 Canadian patients with metastatic or advanced lung, breast and colorectal cancers in a time of need (in absence or lack of tissue biopsy testing)
- Provide testing to remote communities outside of large cities and cancer centers
- To establish Canadian liquid biopsy testing infrastructure across Canada
- To gain provincial coverage for liquid biopsy testing

Led by Imagia Canexia Health, this federally funded consortium pilot project demonstrated that access to **blood-based testing for cancer treatment** selection should be expanded throughout Canada, and in other locales, to become a **first-line alternative to surgical procedures** whenever medically indicated. This paper highlights key findings from this national program with the aim of sharing lessons learned and recommendations for replication in other locales.

Logistics and Method

Canada is the second largest country in the world by area, with population centres stretching across the entire country. Due to Canada's geographical features and structural factors, testing would ideally be done in a local or regional facility.

Due to the condensed time frame of Project ACTT, liquid biopsy testing was centrally performed at Imagia Canexia Health's CLIA, CAP and DAP-accredited laboratory in Vancouver, British Columbia. Project collaborators, including LifeLabs, GenoLife, Ichor Blood Services, Eastern Ontario Regional Laboratory Association, and hospital systems across Canada, drew blood in their local facilities and shipped two tubes of blood to Imagia Canexia Health for testing.

The Project ACTT consortium understood that central liquid biopsy testing is not a long-term solution for Canada. Therefore, as part of the initiative, Imagia Canexia Health helped local laboratory partners implement liquid biopsy testing in-house as a proof-of-concept with the aim of replicating a sustainable testing infrastructure model across the country and globally.

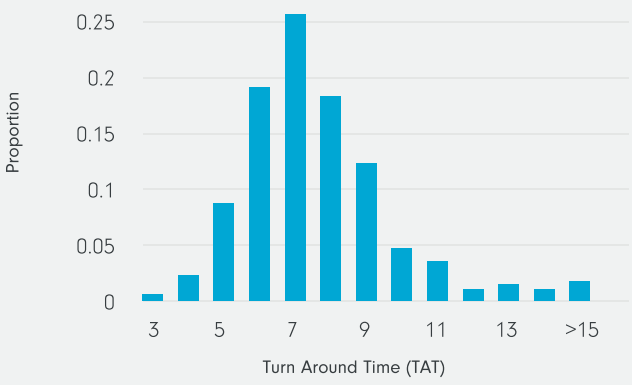
Using Imagia Canexia Health's liquid biopsy assay, Follow It®, extracted DNA was amplified using the multiplex amplicon-based hotspot 30 or 38 gene panel and sequenced. An in-house developed bioinformatics pipeline and reporting platform were used to identify pathogenic single nucleotide variants (SNVs), indels (insertions and deletions), and gene amplifications.

Key Findings

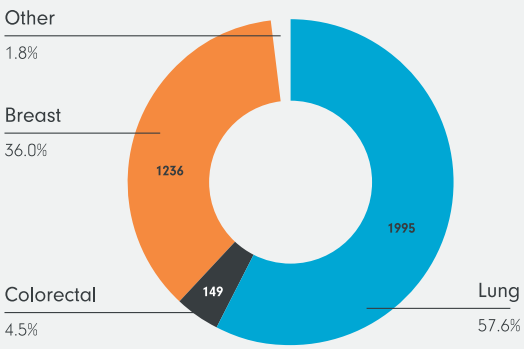
Oncologists overwhelmingly responded to the pilot project, with a 90% adoption rate among solid tumor oncologists working in more than 100 institutions.

The project reached patients in 12 provinces and territories, with the highest participation in Ontario, Quebec, and British Columbia. The pilot also exceeded its target of reaching patients in remote and rural areas, with 11% of samples received outside of major urban centres. In terms of sample Turnaround time (TAT), the median from sample receipt to report send out was 7 days (3-29 days).

Sample receipt to report send out



Cancer Types Tested (Cumulative)



Breast Cancer

Tested 1,236 metastatic or advanced breast cancer patient cfDNA samples. 48.5% of samples harboured pathogenic ctDNA mutations with the most commonly mutated genes being TP53 (23%), PIK3CA (19%), ESR1 (18%), AKT1 (2%), MET (2%) and ERBB2 (2%).

Over 50% of the samples were identified as hormone positive, with greater than 60% harboring PIK3CA and ESR1 ctDNA mutations.

Studies have shown that metastatic PIK3CA mutated ER-positive/ HER2-negative tumors are predictive to respond to alpelisib therapy and have FDA and Health Canada approval.

Gene	Cases	% of cases
TP53	**279**	**23**
PIK3CA	**231**	**19**
ESR1	**223**	**18**
AKT1	**29**	**2**
MET	**22**	**2**
ERBB2	**19**	**2**
GNAS	**18**	**1**
KRAS	**17**	**1**
EGFR	**9**	**1**
PTEN	**7**	**1**
BRAF	**5**	**<1**
IDH1	**4**	**<1**
KIT	**4**	**<1**
POLE	**4**	**<1**
IDH2	**2**	**<1**
HRAS	**2**	**<1**
FGER2	**2**	**<1**
RET	**2**	**<1**
Other genes (one case each)	**5**	**<1**
No Reported Variants	**637**	**52**
Number of Samples	**1236**	**NA**

Lung Cancer

Tested 1,995 lung cancer patient cfDNA samples. 55% of samples harboured pathogenic ctDNA mutations with the most commonly mutated genes being TP53 (35%), EGFR (16%), KRAS (12%), MET (4%), PIK3CA (2%) and BRAF (2%). KRAS-G12C (40%) and KRAS-G12V (18%) were the most commonly observed KRAS mutations.

Non-small cell lung cancer harbouring KRAS-G12C mutations have been predicted to respond to sotorasib therapy and have FDA and Health Canada approval as 2021.

Gene	Cases	% of cases
TP53	**708**	**35**
EGFR	**319**	**16**
KRAS	**238**	**12**
MET	**79**	**4**
PIK3CA	**39**	**2**
BRAF	**36**	**2**
GNAS	**31**	**2**
ERBB2	**27**	**1**
CTNNB1	**26**	**1**
[DH2	**12**	**1**
RET	**11**	**1**
NRAS	**9**	**<1**
KIT	**9**	**<1**
ALK	**8**	**<1**
IDH1	**7**	**<1**
STK11	**5**	**<1**
PDGERA	**4**	**<1**
HRAS	**3**	**<1**
MAP2K1	**3**	**<1**
MAP2K2	**3**	**<1**
PTEN	**3**	**<1**
POLE	**2**	**<1**
AKT1	**2**	**<1**
FGER3	**2**	**<1**
Other genes (one case each)	**2**	**<1**
No Reported Variants	**904**	**45**
Number of Samples	**1995**	**NA**

Colorectal Cancer

Tested 149 colorectal cancer patient cfDNA samples. 64% of samples harboured pathogenic ctDNA mutations with the most commonly mutated genes being TP53 (50%), KRAS (31%), PIK3CA (7%), BRAF (5%) and MAP2K1 (3%). KRAS-G13D (20%), KRAS-G12V (15%), KRAS-G12D (11%) in total accounted for 46% of KRAS mutations observed. Chemotherapy based on 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX) remains first line treatment for CRC, but studies have shown the KRAS-G12D mutation is predictive of inferior response to treatment. MRTX849, a KRAS-G12C inhibitor is currently in phase 1 clinical trial for CRC.

Gene	Cases	% of cases
TP53	**74**	**50**
KRAS	**46**	**31**
PIK3CA	**11**	**7**
BRAF	**8**	**5**
MAP2K1	**5**	**3**
CTNNB1	**3**	**2**
NRAS	**3**	**2**
AKT1	**3**	**2**
MET	**2**	**1**
Other genes (one case each)	**5**	**3**
No Reported Variants	**54**	**36**
Number of Samples	**149**	**NA**

Gene Content

SNVs & Indels (37 genes)						CNVs* (9 genes)		MSI*
AKT1	ALK	AR	BRAF	CTNNB1	DICER1	CCNE1	EGFR	21 Loci
DDR2	EGFR	ERBB2	ESR1	FGFR1	FGFR2	ERBB2	FGFR1	
FGFR3	FOXL2	GNA11	GNAQ	GNAS	HRAS	FGFR2	KIT	
IDH1	IDH2	KIT	KRAS	MAP2k1	MAP2K2	KRAS	MET	
MET	NRAS	NTRK1	NTRK3	PDGFRA	PIK3CA	PIK3CA		
POLE	PTCH1	PTEN	RET	ROS1	STK11			
TP53*								

CNVs*: Detecting amplifications only | TP53*: Full gene (all exons) covered | MSI*: Needs orthogonal validation.

Recommendations:

Project ACTT demonstrated that innovation in cancer testing can minimize the collateral damage of COVID-19 on cancer patients, demonstrating that this long-term solution can be adopted as standard of care anywhere in the world.

Based on our experience with Project ACTT, here are recommendations to replicate such an initiative within a national health system:

- Recruit a strong network of ecosystem partners. This includes collaborators from academic research hospitals, clinical laboratories, local and federal health ministry departments, technology companies, patient advocacy groups, and strategic investment sources. This type of initiative requires systemic support from launch through implementation, through building infrastructure for sustainable testing over the long term.
- Through Project ACTT, four laboratories implemented Imagia Canexia Health NGS liquid biopsy technology.
- Early on, identify the data required to make the clinical and health economics case for reimbursement for ctDNA testing. If ctDNA testing is not covered by public or private payors in your locale, health economic and clinical utility studies must be a core component of your project. Consult with experts on the types of data that will be required to prove the economic and clinical utility case in your locality and collect that data from project onset.
- Educate key stakeholders early in the program – especially oncologists. While ctDNA testing is not new in the US, it is not standard of care in much of the world. Consider what resources will be needed to develop educational content and webinars for audiences including oncologists and patient advocacy groups.

Further Results:

- The overall success rate of blood sample testing was high: 99.3% of samples that arrived at Imagia Canexia Health's lab were viable for testing.
- Within the project's three cancer types (breast, lung, colorectal), in ~50% of cases, one or more mutations were identified, reflecting published frequencies of detectable mutations in plasma of these patients.
- The spectrum of detected mutations included both frequently mutated genes in respective cancer types (such as PIK3CA in breast, EGFR in lung and KRAS in colorectal), as well as many other less frequently altered genes.
- During the project, one or more clinical trials were recommended for 76% of participants.
- Approximately 37% of mutation-positive cases received recommendations regarding FDA approved Tier I/II targeted treatments, such as EGFR inhibitors in lung cancer, and panitumumab and cetuximab in colorectal cancer based on KRAS mutation status.

One of the main objectives of Project ACTT was to perform a Health Technology Assessment for reimbursement submissions to Provincial payers. This is key since coverage through public funding is necessary for liquid biopsy technologies to be equally accessible to all Canadians. **To this end, Project ACTT was able to generate broad advocacy with 15 support letters sent to federal government from oncologists, pathologists, patient groups, and lab directors.**

Imagia Canexia Health engaged with a leading health economics institute to develop a health economics model that could inform such funding decisions. Preliminary findings suggest that if implemented, Follow It testing could result in significant cost savings to the public health care system.

About Imagia Canexia Health

Imagia Canexia Health (ICH) is a genomics-based cancer treatment testing company that accelerates access to precision care by combining AI expertise with advanced molecular biopsy solutions. Leveraging AI-based informatics for treatment selection and monitoring, oncologists now have leading clinical decision support right at their fingertips. With a network of over 20 hospitals and reference labs worldwide, ICH ensures that doctors have the right insights to deliver cost-effective cancer testing to patients no matter where they seek treatment. Join ICH in closing the health-equity gap in cancer.

Imagia Canexia Health™

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