

The Right Treatment for the Right Patient at the Right Time:

Improving access to precision medicine for
patients with lung cancer

In partnership with



About the Lung Health Foundation

We all need to breathe. It is essential to human existence and of vital importance to each and every one of us. But we rarely think about the 22,000 daily breaths we take...until we have trouble taking them.

The Lung Health Foundation is a not-for-profit organization dedicated to helping all Canadians breathe. Our community of donors, patients, researchers, volunteers and professional staff work to ensure Canadians have the healthy lungs, bodies and clean air necessary to breathe. A healthy breath fuels the body and mind; it's something we should not take for granted.

PROMOTING HEALTHY BREATHING

We promote healthy breathing by fighting for policies that protect our air and educate Canadians about what they can do to promote their own lung health.

SUPPORTING THOSE WITH LUNG DISEASE

We support and advocate for those living with conditions that affect the lungs and the ability to breathe, and fight to challenge the stigma and ignorance that can be associated with lung disease.

FINDING FUTURE SOLUTIONS

Through education and research, we work to turn knowledge into action and find cures to diseases that will deliver a future of better breathing for all.

We are helping all Canadians breathe.

About the Breathing Policy Forum Series

Bringing together thought leaders from the public and private sectors, the Breathing Policy Forum Series tackles some of the most urgent and pressing issues facing healthcare today.

Each forum provides strategic opportunities to develop creative and actionable solutions - facilitating collaboration on health and policy issues of growing provincial and national concern, exploring innovative ways of controlling skyrocketing medical costs, improving access to healthcare, and managing the growing burden of chronic disease.

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Letter from the President & CEO

The Lung Health Foundation is very excited about our ongoing Breathing Policy Forum series. This series is aimed at developing creative and actionable solutions that will improve healthcare in Ontario – and it's clear these solutions are needed now more than ever. We are pleased to have partnered with Lung Cancer Canada to dedicate this installment of the series to improving access to cutting edge precision medicine for patients with lung cancer.

The days of one-size-fits-all approaches to medicine are waning. In the case of lung cancer, identifying, defining and investigating mutations, molecular subgroups and lung cancer subtypes has transformed the care landscape. Emerging from these discoveries are more targeted therapies that improve quality of life and overall outcomes for lung cancer patients.

But despite this progress, many Canadian patients are waiting too long for access to these new therapies. We believe that crafting an integrated strategy around precision medicine delivery will require a collaboration between many organizations and entities coming together to address the system barriers, funding silos, and out-of-date policies that are preventing patients' timely access to testing and treatment.

All of these factors have placed many eyes on lung cancer as an example to watch in improving care delivery and have made this a fitting topic for our latest Breathing Policy Forum. This white paper is a result of the ideas and recommendations that came out of this gathering of healthcare providers, patients, thought leaders and government representatives.

Our series of Breathing Policy Forums are a way for the Lung Health Foundation to play a deeper, more profound role in policy, bringing relevant players together to tackle pressing issues facing us here in Ontario and across Canada. To address the issue of precision medicine innovation within the context of competing healthcare priorities and limited healthcare spending, collaboration among many stakeholders is key. The Lung Health Foundation is proud of the role it is playing in advocating for the right treatment, for the right patients, at the right time.

A handwritten signature in black ink, appearing to read "G. Habib". The signature is fluid and cursive, with a long horizontal stroke at the end.

George Habib PRESIDENT & CEO
Lung Health Foundation

The Patient's Perspective:

Barriers to Access

ANNE MARIE CERATO

Patient Advocate, Lung Health Foundation

"I'm a unicorn," says Anne Marie Cerato. "I'm a rarity." Diagnosed with Stage 3A adenocarcinoma in the spring of 2009, Anne Marie was just thirty years old when her now decade-long lung cancer journey began. At the time, she wondered if she would live more than a year or two. "Cancer changed everything," she reflects.

Incredibly, Anne Marie defied survivorship statistics thanks to unprecedented advancements in lung cancer treatment. In fact, her experience with precision medicine has led her to advocate harder than ever for patients' access to the right treatments at the right times.

Anne Marie initially endured six months of intensive traditional lung cancer treatment, experiencing a host of debilitating side effects along the way. So when targeted therapy crizotinib (Xalkori®) entered the picture, it was – comparatively – a breath of fresh air. Anne Marie was able to access the drug as a first line monotherapy through a clinical trial after her tumour tested and found to be ALK-positive. This ALK-inhibitor drug, taken orally at home, kept Anne Marie out of the hospital and boosted her quality of life. Her world was changed.

But what hoops would she have to jump through, had she not been lucky enough to be considered for a clinical trial? Had she not been a part of this study, Anne Marie notes that accessing the drug would have been a long and baffling process. First, her oncologist would have to fill out and fax an Exceptional Access Program application and wait for deliberation. If approved but not privately insured, she would have had to apply for the Trillium Drug Plan and wait once more, typically 19 days according to the Auditor General. In the case of crizotinib, Anne Marie notes that 1,318 days passed between the drug's approval by Health Canada to when it was approved for provincial funding by Ontario.

Lung cancer patients can't wait a year or more for the treatments they need, much less three and a half.

But access is only half of the struggle. Even if Anne Marie had achieved Trillium Drug Plan status, the copay (at 4% of her yearly income at first dispensation) would be a difficult financial burden in the best of situations, let alone during a battle with a cancer that kills more than breast, colorectal and prostate cancers combined.

Each year, more than 10,000 Ontarians are diagnosed with lung cancer. Without access to the right treatments, few will survive to call themselves unicorns.

Moving Forward

Anne Marie's story highlights the life-changing impact of accessing powerful targeted therapies – IF the patient is lucky enough to be considered for a clinical trial, or live in a province with coverage. We know that these therapies aren't making it into the hands of many Ontario patients. What if we looked to other provinces as inspiration for a system that improves the accessibility and affordability of oral cancer drugs?

Crizotinib was approved by the United States Food and Drug Administration in 2011. The drug was approved by Health Canada 243 days later. It would take a further 1,318 days for the drug to be approved for provincial funding by Ontario.

The Clinician's Perspective:

An Urgent Need to Improve Access

DR. ROSALYN JUERGUENS

Associate Professor, Department of Oncology, McMaster University

“It was only in 1995 that we established that treatment for lung cancer made any difference whatsoever,” states Dr. Rosalyn Juergens. At that time, the median survival time for a patient newly diagnosed with lung cancer was just four months. Luckily the bar has moved further ahead, thanks in part due to improved chemotherapy agents and the advent of personalized medicine. But severe inequalities remain.

The targeted therapy that has prolonged Anne Marie’s survivorship is familiar to Dr. Juergens, too. Crizotinib is one of dozens of targeted therapies she has studied and subsequently tracked through the drug approval and funding process in her work as a lung and esophageal cancer specialist.

Like other targeted therapies, this drug’s potential is astonishing. When compared against chemotherapy it offers a dramatic improvement in median survival time. On average, a patient treated with crizotinib lives somewhere between 45 and 48 months. “Not weeks,” notes Dr. Juergens, “Months.” That’s four years on average that someone with ALK-positive lung cancer will live if oncologists like Dr. Juergens can identify the target quickly and get the patient into the right treatment. When compared to the mere 12 months that a patient can expect to survive by undergoing chemotherapy alone, it’s clear that more targeted therapies are prolonging lives.

But it’s not just about the number of days a patient survives, as advocating for access to precision medicine is also about preserving the patient’s quality of life. When recalling the case of osimertinib, a third generation EGFR-targeted therapy undergoing its clinical trial as a first-line treatment, Dr. Juergens notes that its superior brain-penetrant characteristics have been proven to prevent the formation of crippling brain metastases. This allows patients to continue to fight their cancer without significant effects to their mood, personality, and thinking – vital in a disease with a grim prognosis. Despite an unusually quick progression from FDA to Health Canada approval, the drug remains unfunded and with no compassionate access program picking up the slack. Cancer continues to spread to patients’ brains.

Then there’s the issue of simple geography. “It shouldn’t be that you have to come to a Ros Juergens in Hamilton to be able to get access to all the bells and whistles. You should be able to get the same bells and whistles at every single cancer center across the country,” she maintains. The reality is that asking physicians to fill out stacks of paperwork to garner access to these new drugs is difficult at best, and nearly impossible

when they don't even know that the research exists. Outside of a few major Ontario cities and bustling cancer centers, this is often the case.

Moving forward

Dr. Juergens' perspective highlights the fact that a lack of equal access to both oral and IV cancer drugs across the provinces makes treating lung cancer patients even more challenging. What if we found efficiencies that improved the speed of the approval process for cancer drugs, giving oncologists the best tools available in the fight against lung cancer?

Osimertinib was approved by the United States Food and Drug Administration in April of 2018. The drug was approved by Health Canada in July of 2018. It was recommended for funding by pCODR in January of 2019, but remains unfunded.

The Pathologist's Perspective:

Diagnostics and the Disconnect in Decision Making

DR. BRANDON SHEFFIELD

Pathologist, William Osler Health System

Dr. Brandon Sheffield is optimistic about the future of targeted therapies despite the numerous barriers he encounters as an anatomic pathologist. “This field of personalized medicine offers not just a glimmer or a peek, but a huge bay window of hope and opportunity for prolonging and improving the lives of patients living with cancer.”

Before a patient (like Anne Marie) can be prescribed targeted cancer treatments (by an oncologist like Dr. Juergens), samples of the patient’s tissues will find themselves in a lab not unlike Dr. Sheffield’s space at the William Osler Health System. However, whether the patient anxiously waits weeks or just days for their biomarker test results will ultimately depend on their postal code.

Provincial funding is only provided to a small number of reference centers across Ontario – and for the testing of just three biomarkers (EGFR, ALK, and PDL1). To close the gap, health centers mail specimens out to external centers, incurring high costs and extensive administrative delays in the process. For some biomarker testing, the cost will be shouldered by the patient themselves at thousands of dollars out of pocket. When results trickle in, typically four to six weeks later, the aggressive nature of lung cancer may render the entire effort fruitless. It is not uncommon for patients to die awaiting their biomarker results.

For patients fortunate enough to have their samples tested at William Osler, they will experience a rare – unicorn rare – turnaround time of just two days. That’s because the center created their own internal testing system outside of the provincial framework, working even further to extend its testing parameters to include two additional biomarkers (ROS1 and BRAF). Under the William Osler framework, patients will know which targeted treatments their genetics qualify them for from the very first time they meet with their oncologist. This early identification of candidates for targeted therapies greatly maximizes the benefits of the treatment and improves outcomes.

Still, Dr. Sheffield notes that significant gaps will remain until Ontarians gain access to next generation genome sequencing technologies - technologies that make it possible to test for all of the above biomarkers and more (including RET, NTRK, NRG, MET, ERBB2, KRAS et al) in just one test. Unfortunately, there is currently no additional investment in testing technology planned, and no existing framework to support this type of practice in Ontario.

The barriers to a healthy diagnostic system aren’t merely financial. Dr. Sheffield notes

that his team had to fill in around fifty pages of paperwork with each application when his center began testing for the EGFR biomarker. In essence, current lab licensing procedures are a relic of a time when single gene tests were at the cutting edge. That simply won't cut it in a world that is rapidly moving towards tests that can evaluate four hundred genes at once. Multiply those fifty pages times four hundred and the problem with the current state of lab licensing becomes abundantly clear.

Moving forward

Dr. Sheffield's perspective highlights the practical challenges that arise when technology advances faster than policy. What if we could reduce the barriers to timely biomarker testing and identify patients' candidacy for cutting edge therapies without cutting into crucial treatment time?

The Government Perspective:

The Evolution of Evaluation

ALEXANDRA CHAMBERS

Former Director, pan Canadian Oncology Drug Review, Canadian Agency for Drugs and Technologies in Health (CADTH)

“Could the HTA process be faster and more efficient? Absolutely,” pCODR then-director Alex Chambers acknowledges. “I think there are a lot of efficiencies that we could find in the process.” She recognizes the changing nature of precision medicine, but notes the many barriers that regulators face.

The Pan Canadian Oncology Drug Review (pCODR) is working to find efficiencies where it can. Consider pCODR’s newly established process that aligns its reviews with Health Canada. A drug company can now file with Health Canada and pCODR at the same time, with the goal of improving the speed of approvals. While there is much work to be done, it is a positive step forward down a long and winding road.

So what kind of journey does a lifesaving cancer drug go through before it gets into the hands of an oncologist like Dr. Juergens, to prescribe to a patient like Anne Marie? Who are the key players in the drug approval process?

The process begins with Health Canada, which makes a determination on the effect and safety of a drug. This triggers the health technology assessment (HTA) process, which examines the value of the drug in the current healthcare system. It looks at what’s available and how this additional drug may be better than existing options. For example, the process may consider whether a drug’s brain-penetrant qualities – recall the case of osimertinib – make it a better choice than similar therapies already in market for the treatment of lung cancer.

In Canada, Chambers notes, there are three different HTA programs. Two fall within the Canadian Agency for Drugs and Technologies in Health (CADTH): pCODR, which focuses specifically on oncology drugs, and The Common Drug Review, which examines non-oncology drugs. A third program, called INESSS, operates in the province of Québec.

After the HTA assessment, the new drug will go through evaluation with the Pan Canadian Pharmaceutical Alliance, which facilitates national price negotiations. And finally, the ultimate decision of whether to fund a drug is up to individual provinces.

Chambers, providing a different perspective than the other panelists, reminds us of some of the challenges that regulators themselves are confronting throughout the process. First and foremost is the issue of volume and capacity. She highlights the enormous increase in drugs being submitted for recommended funding. “This is tremendous,” she marvels. “It

really is amazing... the number of new drugs coming into the system, and the number of new drugs that we're seeing.”

Unfortunately, this unprecedented volume does pose its own challenges to a system which is not set up in a way that prioritizes drugs based on their patient impact.

Another challenge is the quality of the clinical data. In some cases, pCODR receives non-comparative data, which limits pCODR's ability to fulfill their mandate to examine how the drug compares to what is currently available.

The good news is that Chambers and her team have been working on a pathway for reassessment – a way to introduce a drug into the system and have an opportunity to reassess its value later based on real world evidence (RWE).

Looking to the emerging role of RWE is a critical move, since traditional randomized control trials are challenging to conduct when a pool of patients is small – like in the case of lung cancer patients with rarer driver mutations. “It's a direction that we need to go in,” she says, recognizing the many breakthrough therapies that are in development.

It's clear that Chambers and her team at pCODR are committed to improving the process and taking advantage of some of these opportunities for positive change.

Moving forward

Alex Chambers' perspective highlights a number of challenges within the drug approval process. What if we could build on her team's positive changes to accelerate it, while increasing the role of patient engagement – patients' lived experiences and the real world evidence gathered by their oncologists – in determining the value of new therapies?

Our Policy Recommendations

Our policy recommendations confront lung cancer precision medicine challenges in three key areas: increasing access & affordability, improving the diagnosis and molecular testing system, and finding efficiencies in health technology assessment (HTA) processes/approvals.

Challenge #1: Accessibility & Affordability

In Canada, oral cancer medication is publicly covered by all of the western provinces, Quebec, and the territories. Ontario and the Atlantic provinces are lagging behind in their coverage of important cancer medications.² In Ontario, oral cancer drugs are only covered under the Ontario Drug Benefit (ODB) and the Trillium Drug Program for those age 65+, receiving social assistance, or with limited private insurance.³ In contrast, IV cancer drugs are publicly covered for all Ontarians because they are administered in-hospital.⁴

Consider this: Manitoba's Home Cancer Drug Program

- A program initiated in 2012 that allows all Manitobans to access certain publicly funded oral cancer medication.⁵
- Patients must register with CancerCare Manitoba to receive coverage and be eligible for Manitoba's Pharmacare program.
- Covering the costs of these drugs has yielded overall costs savings to the healthcare system.

RECOMMENDATIONS

1. Improve the speed of approval for cancer drugs. In 2005, the Ministry of Health streamlined its generic drug submission review with Health Canada's process. This has led to increased efficiencies as 90 to 95 percent of generic drug submissions are not required to undergo scientific review by the ministry of health's advisory council, eliminating duplication.⁶
2. Still, brand name drugs must be submitted to the Ministry's expert advisory committee for review, even after Health Canada scientific approval. This process results in an unnecessary regulatory burden on the province.⁷ In addition, pCODR can also re-review scientific data after Health Canada approval, further adding duplication.

3. We recommend coordinating the Ministry of Health's brand name drug approval process with Health Canada's to eliminate unnecessary duplication in the review process. Drugs should still be reviewed for overall compliance. Still, the scientific review process by Ontario's expert advisory committee for drugs that have already gone through the same review by Health Canada should be excluded.
4. Improve the affordability of oral cancer drugs:
 - » Short-term option: develop a system similar to Manitoba's Home Cancer Drug Program whereby all Ontarians are able to access oral cancer drugs regardless of age or income.
 - » Long-term option: National pharmacare

Challenge #2: Diagnosis/ Molecular testing

Early laboratory testing not only helps in improving patient outcomes and rates of survival, but minimizes costs in the long-run by reducing hospital admissions, physician visits, and costs associated with other treatments and tests.⁸ There are three biomarkers that are currently funded in some capacity by the Ontario government-EGFR, ALK, and PDL1. However, these only exist in a small number of reference centers across the province. The result is that specimens need to be mailed to outside centers with the capacity to conduct biomarker testing, causing wait times of up to 6 weeks. Often, patients do not live long enough to see the results of the biomarker tests. A study conducted by Lim et al. (2017) outlines that there is a lack of funding dedicated by the Ontario government towards diagnostic testing. Moreover, over 90% of lung cancer patients are treated in a community setting, and these patients do not have access to timely biomarker testing.

Consider this: Ontario's current licensing process

- Community, hospital, and Public Health Ontario laboratories are regulated by the Laboratory and Specimen Collection Centre Licensing Act.
- The Act mandates that all laboratories are licensed by the Ministry of Health.
- Laboratories who perform cancer biomarker testing in Ontario are accredited through the Institute for Quality Management in Healthcare (IQMH).⁹
- There exist current guidelines by the Canadian Association of Pathologists for the number of cases necessary for laboratories to perform testing.¹⁰ Other requirements for laboratories to run diagnostic tests are around sufficient professional competency.
- Cancer Care Ontario began to include molecular testing in their lung cancer diagnostic pathway as of 2012.¹¹
- In 2014, advocacy related to the limitations around molecular testing resulted in the Ministry of Health approving funding for EGFR analysis in lung cancer.

Helpful Terms and Abbreviations

Precision medicine: Care that optimizes therapeutic benefits for certain patients based on their genetic or molecular profiles. Also called personalized medicine.

Small cell lung cancer: The most common type of lung cancer. The three major types of NSCLC are squamous cell carcinoma, adenocarcinoma, and large cell carcinoma.

Non-small cell lung cancer: A less common type of lung cancer, SCLC accounts for about 10 to 15% of lung cancers. It tends to spread more slowly than other lung cancers.

Molecular (or tumour) testing: Tumor testing is a promising new field in the diagnosis and treatment of lung cancer. It is referred to as molecular, biomarker or genomic testing and is a procedure to look for changes (mutations) in the tumor DNA. A piece of the lung cancer tissue is taken during a biopsy procedure and it is sent to a special laboratory that can identify the genomic profile of the tumor. Based on the result, a specific treatment may be available to target the specific mutation that exists in the tumor cells.

Real world evidence (RWE): In medicine, real world evidence (RWE) refers to evidence obtained from outside the context of randomized controlled trials. In the case of precision lung cancer medicine, randomized controlled trials can be difficult to conduct due to the relatively small pool of patients whose molecular tests results make them candidates for a specific targeted therapy.

CADTH: The Canadian Agency for Drugs and Technologies in Health, or CADTH, is a Canadian national organization that provides research and analysis to healthcare decision-makers.

INESSS: Institut national d'excellence en santé et services sociaux, an independent organization that reports to Québec's Minister of Health and Social services.

NOC: Before a drug can be distributed in Canada, its manufacturer must receive a Notice of Compliance (NOC) from Health Canada. This notification indicates that the manufacturer has complied with Canada's Food and Drug Regulations.

NOC/c: An NOC/c is authorization to market a drug with the condition that the manufacturer undertake additional studies to verify the clinical benefit. The safety of the drug must still be reasonably established.

pCODR: The pan-Canadian Oncology Drug Review (pCODR) is an evidence-based cancer drug review process.

pCPA: The pan-Canadian Pharmaceutical Alliance (pCPA) conducts joint provincial/territorial/federal negotiations for brand name and generic drugs in Canada to achieve greater value for publicly funded drug programs and patients through the use of the combined negotiating power of participating jurisdictions.

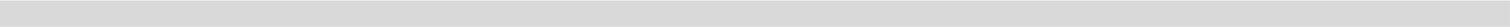
pERC: The Expert Review Committee of pCODR. This group assesses the clinical evidence and cost-effectiveness of cancer drugs in order to make recommendations to the provinces and territories to help guide their drug funding decisions.

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Notes

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