Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

alectinib (Alecensaro)

(Hoffman-La Roche Limited)

Indication: Alecensaro as adjuvant treatment following tumor resection for patients with anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC).

April 30, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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CADTH

Patient Input Template for CADTH Reimbursement Reviews

CADTH Project Number: PC0350-000
Name of Drug: Alectinib (Alecensaro)
Indication: Alecensaro as adjuvant treatment following tumor resection for patients with anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC).
Name of Patient Group: Lung Cancer Canada – Patient Group
Author of Submission: Winky Yau, Coordinator, Medical Affairs

1. About Your Patient Group

Lung Cancer Canada (LCC) is a national charity, focusing its efforts on increasing awareness of lung cancer; providing support and education to persons living with lung cancer, their care partners and loved ones; supporting research; and advocating for improved access and quality of care for all those impacted by the disease across Canada. LCC is a member of the Global Lung Cancer Coalition and the only national organization focusing solely on lung cancer in Canada.

https://www.lungcancercanada.ca/

Lung Cancer Canada is registered with CADTH.

2. Information Gathering

The information discussed throughout this submission consists of the thoughts and experiences of lung cancer patients and those caring for a person living with lung cancer. The clinical basis of this submission is on the results from the recent ALINA clinical trial for alectinib as adjuvant treatment in stage I-IIIB ALK-positive NSCLC patients.

Because alectinib is currently only publicly funded in the stage 4 setting, alongside the novelty of this trial and no clinical trial sites in Canada, LCC had very limited engagement with Canadian patients in this exact indication on the clinical trial. However, as summarized below, LCC was able to speak to 17 Canadian and International patients/caregivers who have experience on alectinib, both in the early-stage (I-IIIB) ALK+ setting and stage IV setting, in which alectinib for metastatic disease is already standard of care in many jurisdictions worldwide.

Only 1 of the patients interviewed (**VK**) received alectinib via the ALINA trial -- a Canadian patient who accessed the trial while living in South Korea at the time. Further details about their access to the drug, line of treatment, duration on alectinib, etc. is summarized in Section 6. All interviews were conducted in April 2024.

Name	Gender	Patient/Caregiver	Age of patient	Date of Diagnosis	Stage & Diagnosis	Location	Contact method
VK	M	Patient	Early 40s	May/June 2019	Stage 2 ALK+ NSCLC	Canada (ON) But was on ALINA while living in South Korea	Interview

SW	F	Patient	39	October 2021	Stage 2B ALK+	USA (Pennsylvania)	Interview
GH	M	Patient	50	September 2018	Stage 3A ALK+	Australia	Interview
KZ	F	Patient	30	March 2021	Stage 3 ALK+	USA (Wisconsin)	Interview
JY	F	Patient	61	June 2021	Stage 3 ALK+	USA (Ohio)	Interview
LR	F	Patient	49	December 2017	Stage 3B ALK+ (now Stage 4)	USA (Virginia)	Interview
KB	M	Patient	65	September 2021	Stage 3 ALK+	United Kingdom	Interview
EN	F	Caregiver	Mid/Late 60s	2014	Stage 1B ALK+ (now likely Stage 4)	Canada (BC)	Interview
HC	F	Patient	45	January 2020	Stage 4 ALK+	Canada (AB)	Interview
JM	F	Caregiver	40	November 2021	Stage 4 ALK+	Canada (MB)	Interview
AN	F	Patient	59	August 2021	Stage 4 ALK+	Canada (ON)	Interview
LJ	F	Patient	43	November 2023	Stage 4 ALK+	Canada (QC)	Interview
BR	F	Patient	49	October 2018	Stage 4 ALK+	USA (Ohio)	Interview
RE	F	Patient	59	December 2020	Stage 4B ALK+	USA (New York)	Interview
KK	M	Patient	73	June 2021	Stage 4 ALK+	United Kingdom	Interview
DE	M	Patient	49	August 2019	Stage 4 ALK+	United Kingdom	Interview
RM	M	Patient	42	November 2022	Stage 4 ALK+	Jersey, Channel Islands, UK	Interview

3. Disease Experience

In March 2021, 36-year-old **SW** noticed a wheezing-like cough that would come and go, but didn't seem urgent enough to seek a doctor. When she visited her primary care physician in September, she noted the persistent cough still hadn't gone away with over-the-counter acid-reflux medications, so SW pushed for a chest x-ray, which revealed a mass in her right lung. Further tests, biopsies and CT scans confirmed SW had stage 2B NSCLC. She had a lobectomy then started 4 rounds of chemotherapy until February 2022, before getting a second opinion from a specialist in ALK+ NSCLC, who suggested the recent data from the ADAURA trial suggested using adjuvant TKIs may have benefit in early-stage patients to prevent recurrence. He suggested SW start alectinib for a 3-year period, and she has been on it ever since, now 2 years later.

Canadian expat, **VK**, had first moved to South Korea in 2008, studying there for 6 years and marrying his now-wife, a Korean citizen. He moved back to Canada in 2014 for a few years to visit family, before eventually moving back to Korea and out of Seoul into a new city with his wife in 2019, living a very healthy and active lifestyle, playing tennis, and traveling around Asia working as a freelance consultant. VK was prepared to start working with a new client in a sterile environment, so he was required to get a full health check as his last one was done 5 years prior. Coincidentally, his doctor found something in the left upper lobe of his lung, which sent VK to a larger hospital for further testing and eventually confirmed he had stage II ALK+ NSCLC. VK notes that he didn't feel any symptoms or any indication of being unwell at the time of diagnosis, but only looking back retrospectively he noticed potential feelings of nausea after running or exercising, and an occasional cough. VK states, "*I was shocked to the core when I was told I had cancer. I had no idea this was coming".* He had a lobectomy before enrolling in the ALINA clinical trial for adjuvant alectinib, and continued on the trial for nearly 2 years until he had to move back to Canada in April 2021 for work purposes.

49-year-old **LR** had always been very active with her background as a dance teacher, teaching several dance classes a week for two decades until she stopped working full-time to raise her kids. In December 2017, she noticed her voice sounded off and felt breathless while talking. After countless medications for asthma, acid reflux, and allergies didn't work, she asked her primary care doctor for an X-ray, after which follow-up CT scans and biopsies confirmed LR had Stage 3B ALK+ NSCLC, which the disease had already spread to her lymph nodes and collar bones. At that time, alectinib had just been approved 6 weeks prior by the FDA, so it was still very new and LR was the very first stage 3 patient put on alectinib as first line treatment in the country. She started alectinib in January 2018, just 4 weeks from her first suspicious x-ray before diagnosis, and has continued to be on it ever since, nearly 6.5 years later, and is still doing very well.

NSCLC is the most common type of lung cancer, accounting for 80-85% of all cases, in which 2-7% of these are positive for ALK alterations. ALK-positive lung cancer patients are typically younger in age and light or never-smokers. In Canada, the current standard of care for metastatic ALK-positive patients is targeted therapy. However, surgery and adjuvant platinum-based chemotherapy remains the recommended treatment protocol for those with early-stage disease. The primary goal for these early-stage patients with resectable disease is cure (i.e., to improve 5-year overall survival). With current practices in the adjuvant treatment landscape for these patients, however, there is an unmet need, as traditional systematic therapies like chemotherapy or radiation has been shown to have limited efficacy in adjuvant treatment.

The most recent results from the ALINA clinical trial, which compared adjuvant treatment with alectinib with the current standard ofc are with chemotherapy, has shown very promising results. 94% of patients on the alectinib arm remained disease-free at the 24-month mark compared to 63% in the chemotherapy arm [1]. Alectinib has shown very impressive results in extending patients' lives while also maintaining or improving their quality of life that were otherwise unimaginable with other therapies. Since starting treatment with alectinib, LR has been on it for nearly 6.5 years and is

still doing very well today, being able to see her son graduate both high school and university, and is now pursuing a PhD program. Having the luxury of being there for important milestones for her kids is something LR says she likely wouldn't have even been around to see had she not gotten access to alectinib. Although physically she's still battling fatigue and loss of muscle mass since her diagnosis, she's still able to walk, go about her activities of daily living, and even recently travelled back to her home country of the Philippines over the summer.

As further explained in Section 6 of this submission, alectinib has helped improve patient outcomes and quality of life.

KB had always been a healthy and active individual, walking and running often, and playing full 18-hole rounds of golf with friends nearly every weekend. When he was diagnosed in September 2021 with stage 3 ALK+ NSCLC, he immediately started first-line treatment with alectinib with no prior treatments. 2.5 years later, he still remains on the treatment and is doing very well. He continues to work 4 days a week and is motivated to keep exercise a daily part of his routine, aiming for 10,000 steps per day, going for walks in his neighborhood after work, and playing golf on the hilly course whenever he can. KB says his close friends are always shocked as he "doesn't look like he has cancer at all", being able to maintain a high quality of life that is comparable to pre-diagnosis.

Patients with the ALK mutation commonly present with brain metastases at diagnosis, this has been observed in about 30% of patients. This involvement can be quite debilitating, affecting quality of life, resulting in a poorer prognosis and reducing already low survival rates even further. While there are existing options to treat metastatic ALK positive patients in the first line, there is also an unmet need for patients with resectable disease to provide treatments that are not just effective maintaining disease-free survival and controlling progression, but also effective in treating CNS involvement. This will reduce the need for other treatments that can result in cognitive side effects further impacting the patient's quality of life further down the line.

Alectinib is an ALK tyrosine kinase inhibitor used for the treatment of patients with ALK-positive non-small cell lung cancer (NSCLC) and has been standard of care for stage IV metastatic patients in Canada, USA, and in many other countries. With the results from ALINA, the expansion of this treatment being utilized in the adjuvant setting for early-stage patients has the potential to improve patient outcomes and have more survivors like LR, VK, SW, and KB. The input below will highlight the profound responses patients have on this treatment which hugely improved the quality of their lives – in all stages of disease, as well as 1st line and beyond. Patients are living longer and better on this treatment and we hope CADTH takes this into consideration and gives alectinib a positive recommendation.

References:

[1] Wu YL, Dziadziuszko R, Ahn JS, Barlesi F, Nishio M, Lee DH, Lee JS, Zhong W, Horinouchi H, Mao W, Hochmair M. Alectinib in Resected ALK-Positive Non–Small-Cell Lung Cancer. New England Journal of Medicine. 2024 Apr 11;390(14):1265-76. DOI: 10.1056/NEJMoa2310532

4. Experiences With Currently Available Treatments

The current standard of treatment for patients with resectable ALK-positive NSCLC is surgery, followed by adjuvant chemotherapy, typically platinum-doublet. Radiation may be used in certain stage II or III cases where lymph nodes are involved, or if surgical resection yields an incomplete resection. As seen with the results from the ALINA trial, the clinical benefit seen with alectinib in the adjuvant setting would become the favoured therapy, inevitably shifting the paradigm of how patients with resectable ALK+ NSCLC are treated. In the case of this submission, other treatment experiences to be discussed in this section are based on that of the patients interviewed, including chemotherapy, radiation, and 2nd line TKIs (after progression on alectinib).

Chemotherapy:

Chemotherapy has been a long-standing and well-documented standard of care for cancer patients. It does see some benefits and has been found to be effective. However, it is limited in its use as a viable long-term treatment option due to its harsh side effects, high risk of recurrence, impact on the individual's functionality, and increases dependence on caregivers in their daily activities. These have been well documented in previous LCC submissions.

Half (8 of 17) of the patients interviewed had experience on chemotherapy prior to starting treatment with alectinib, in which most of them only underwent this form of treatment prior to receiving their biomarker testing results that ultimately showed they were ALK positive, after which they switched to alectinib straight away.

Overall, patients agreed that chemotherapy negatively impacted quality of life and energy levels during treatment, worse than while on alectinib. Fatigue was the number one adverse effect reported by all patients, though the level varied for different individuals, with some feeling more severely debilitated than others.

JY and **EN**, for example, reported that although the fatigue was constant, they were still able to manage it with naps throughout the day to continue going about their day-to-day life (i.e., grocery shopping, cooking, cleaning, etc.) with minimal impact. However, the majority of patients, **KK, LR, BR,** and **SW**, reported that the levels of fatigue they experienced on chemotherapy severely impeded their quality of life, where they felt so sick, dehydrated, nauseous, and doing basic tasks such as walking from the bed to the bathroom felt nearly impossible, like they had just walked a marathon. Tinnitus and hair loss were also side effects reported by 2 individuals. As further discussed in Section 6, when asked to rank their experience on alectinib vs chemotherapy (or other treatments), every single patient favored alectinib over previous treatments.

After scans found a 7.5cm tumour in **JY's** right lung which led to a diagnosis of stage 3 lung cancer in June 2021, JY had surgery to remove her right lobe and 15 lymph nodes, and then began adjuvant chemotherapy with pemetrexed and cisplatin. Although she took some time off for surgery and subsequent recovery, she continued to work from home through her diagnosis and chemotherapy treatment, taking 1-2 days off in the days immediately following infusions, but was still able to continue working while on treatment. JY noted fatigue was the main side effect experienced – she could easily sleep for 13 hours per night and even nap during the day. She also developed tinnitus as a result of chemotherapy as well, which she has since gotten used to, but is still bothersome. As a marathon runner prior to diagnosis, JY had always been very active, and during chemo she couldn't imagine continuing to run due to the fatigue. She still walked outside nearly every day when she felt well enough, and had no issues with Activities of Daily Living (i.e. cooking, cleaning, grocery shopping, bathing).

73-year-old **KK** was diagnosed with Stage 4 NSCLC in Summer 2021 while he was visiting home in the United States since moving to the United Kingdom years ago. He received 1st-line chemotherapy every 2-3 weeks for a year without knowing which biomarker he had. KK says in his interview, "*The chemo had incredibly horrible side effects, my quality of life was pathetic, I couldn't travel back to the UK, and after a year of such treatment I was pretty much willing to give up. I had no appetite, no energy, and no future. Honestly, I felt better on no treatment than I felt while on chemo*". The first 10 days of each cycle were so miserable that he just wanted to stay in bed, his sense of taste was altered, and fatigue was a constant battle. He would then have 4 days feeling better and able to go about normal life, but then the cycle would repeat and he dreaded infusions. After getting an accurate diagnosis identifying his ALK+ biomarker, KK started treatment with alectinib in the UK and has continued to be on it ever since. KK says that his life "completely turned around" with alectinib.

BR and **RM** both also received 1 round of chemotherapy while awaiting their biomarker testing results. BR notes that even the one treatment made her "feel so sick and dehydrated. I couldn't stand it".

EN's mother was diagnosed with stage 1B lung cancer 10 years ago incidentally from a health check required during the process of immigrating to Canada from Hong Kong to be reunited with her son. She had surgery to remove the lobe and 1 lymph node, followed by adjuvant chemotherapy, and was officially declared cancer-free. After moving to Canada a few years later, she remained NED for 7 years until January 2021 when progression yielded small tumours now in both lungs. She started 13 rounds of chemotherapy (pemetrexed and carboplatin) in combination with pembrolizumab immunotherapy. EN recalls his mom was constantly fatigued, but the anti-nausea medication helped. Living alone, she was still independent and able to run errands, grocery shop, cook, etc. However, by January 2022 after a year on the immunotherapy-chemo combination, the treatment wasn't effective in shrinking her tumours and decided to stop treatment since the side effects weren't worth it. Her oncologist then enrolled her into a personal genomics study which found she was ALK+, and subsequently started her on alectinib in March. EN has continued to be on alectinib to this day and is doing very well.

Radiation:

When 49 year-old **BR**'s initial symptoms of mild stomach cramping and shortness of breath while walking upstairs became more severe one night while on vacation with her daughter in Florida, her husband moved up her doctor's appointments to try and find an answer for her discomfort. Though blood tests came back normal, the findings in a lower abdominal CT scan flipped her world upside down. BR had 3 tumours in her spine, 1 lung was completely full of fluid, 7 tumours in her brain, and a hernia which caused the cramping. She had surgery to remove the spinal mets and then did 3 gamma knife radiosurgery procedures in March and April 2019 before she stated alectinib in mid-April, and has continued to be on alectinib ever since. BR recalls that after her 3rd gamma knife procedure, she lost her memory and was no longer able to drive. In addition, prior to alectinib she also had to get her lungs drained once a week, having a total of 8 thoracentesis procedures. She said "*it was very difficult to breathe during this because of all the fluid build-up, and that slowly resolved and I could finally breathe comfortably again since starting alectinib".*

After his diagnosis with stage 3A NSCLC in 2018, **GH** completed 4 rounds of adjuvant chemotherapy in a 3-week cycle, then 25 rounds of radiation daily over 5 weeks, where he fortunately did not have any severe side effects from either treatment. Being a very active individual running 6-8 kms per day, he was still able to continue his activities of daily living with no issues, even continuing to run light 6ks. The only side effects he noted from chemotherapy were fatigue and also exacerbated his existing tinnitus, and with radiation, he had radiation pneumonitis, which is fairly common and did not impede his lifestyle in any way. GH says when he first switched to alectinib on the full dose, the side effects were more significant (as explained in Section 6), but once his oncologist lessened the dosage, his symptoms improved and his quality of life was comparable to pre-diagnosis.

HC had no evident symptoms that led to her diagnosis of lung cancer in 4.5 years ago over the holidays in December 2019, aside from some eye twitching and a few back-to-back dizzy spells, which prompted her to visit her doctor. Shockingly, CT scans found a 2cm primary lung tumour and 5cm brain tumour, which she had a craniotomy to remove and further testing confirmed it was stage 4 ALK+ NSCLC. She had 3 courses of radiation to her brain tumour immediately after surgery alongside her first few weeks on alectinib in January 2020, which has since remained stable but 3 new small spots have popped up as of April 2024.

Unmet needs:

Radiation therapy has been a long-standing treatment for targeting specific tumours around the body, particularly for the brain, and has been very well-documented in past LCC submissions. However, the #1 concern for patients who are ALK+ is CNS disease, as this type of lung cancer is particularly aggressive in spreading to the brain, and current treatments with chemotherapy or radiation are not necessarily preventative against metastases in the brain; however,

alectinib does cross the blood-brain barrier. This is particularly important for patients with early-stage resectable disease, since the primary treatment goal is in the curative intent, and patients cannot afford to wait until their disease has spread elsewhere around the body, progressing them to advanced stages and survival rates are exponentially lower. Alectinib fills this incredibly important gap in current treatment protocols for stage I-III patients.

Other TKIs:

As highlighted in the summary chart in Section 6, 14 out of 17 patients interviewed for this submission are still currently on alectinib as of April 2024. Only 3 patients – **VK, HC**, and **RM** are no longer on the treatment. RM and HC progressed while on alectinib and are currently on 2nd line treatment with lorlatinib, while VK is currently not on any active treatments since stopping his participation in the ALINA clinical trial and moving back to Canada.

In November 2022, **RM** was diagnosed with stage 4 NSCLC when a persistent cough and unexplained weight loss prompted him to go to his general practitioner. He started 1 session of chemotherapy before his genetic testing confirmed he was ALK+, so he began treatment on alectinib for 9 months from January-October 2023. After his tumours stopped responding to the treatment, he started on 2nd line treatment with lorlatinib, which he is still on today in April 2024. His side effects from lorlatinib included some occasional diarrhea and dizziness, and potentially muscle pain. At the time of his interview with Lung Cancer Canada, RM was due to have his first follow-up scan in a few days, so he was unable to compare the effectiveness of lorlatinib to alectinib, but he notes his QOL is nearly the same between both TKIs.

HC started alectinib as her 1st line treatment in January 2020, and had 35 incredible months on it until she progressed in November 2022 and switched to lorlatinib, which she is currently still on in April 2024. Her main side effect experienced with lorlatinib is edema in her hands and feet, but she says this does not necessarily hold her back from going about her day-to-day life, and still enjoys crafting and sewing in her spare time. However, HC is particularly worried about the next step in her journey if she is to progress, as chemotherapy is most likely her only option left, so she is anxious about staying alive and just hoping to keep hearing positive news at each scan.

5. Improved Outcomes

There have been many incredible advancements in lung cancer research in recent years that have changed the treatment paradigm for patients in Canada. ALK alterations account for a relatively small proportion of all NSCLC cases, but in the metastatic setting, alectinib is already the standard of care in Canada for these patients. Promising results from clinical trials testing additional adjuvant approaches in the stage I to IIIA NSCLC setting have shown positive survival benefit, such as CheckMate 816 and ADAURA. With the disheartening survival rates that metastatic patients face, those who are lucky enough to have caught their disease at earlier stages where it is more curable face unique challenges and have values that are different than those with more advanced disease, and the treatment standard already reflects this with the goal of treatment to prolong PFS and provide a potential cure.

Ultimately, patients in this early-stage setting most value a treatment that:

- Effectively treats their disease and manages their symptoms of lung cancer
- Delaying disease progression and settling patients into long-term remission for improved survivorship
- Allowing patients to live longer and maintain their independence and functionality to minimize the burden on their caregivers and loved ones
- Allows patients to have a fulfilling and worthwhile quality of life

- Has manageable side effects

6. Experience With Drug Under Review

Summary of alectinib experience:

Name	Diagnosis Date	Disease Stage	Drug access method	Period on alectinib	Duration on alectinib	Alectinib line of treatment	Still on alectinib?
VK	May/June 2019	2	ALINA Trial (in South Korea)	July 2019 – April 2021	1 year 10 months	1st line adjuvant	No
SW	October 2021	2B	Private Insurance	March 2022 – present	2 years 1 month	1st line adjuvant	Yes
GH	September 2018	3A	Public Coverage	August 2019 – Present	4 years 8 months	1st line adjuvant	Yes
KZ	March 2021	3	Private Insurance + Medicaid	June 2021 – present	2 years 10 months	1st line	Yes
JY	December 2017	3	Private insurance	December 2022 – present	1 year 5 months	2nd line	Yes
LR	December 2017	3	Private Insurance	Jan 2018-present	6 years 3 months	1st line	Yes
KB	September 2021	3 at diagnosis, now 4	NHS public coverage	November 2021 – present	2.5 years	1st line	Yes
EN	2014	1B at diagnosis, now likely 4	Public coverage	March 2022 – present	2 years	2nd line	Yes
HC	January 2020	4	Public coverage	Jan 2020 – Nov 2022	2 years 10 months	1st line adjuvant	No
JM	November 2022	4	Public coverage	December 2022 – April 2023	5 months	1st line	No

AN	August 2021	4	Public Coverage	September 2021 – present	2.5 years	1st line	Yes
LJ	November 2023	4	Out of pocket/Go Fund Me	December 2023 – present	5 months	1st line	Yes
BR	October 2018	4	Private insurance	April 2019 – present	5 years	2nd line	Yes
RE	December 2020	4	Private Insurance	December 2020 – present	3 years 5 months	1st line	Yes
KK	June 2021	4	NHS public coverage	November 2022 – present	1.5 years	1st line	Yes
DE	August 2019	4	Private insurance + NHS	August 2019 – present	4 years 9 months	1st line adjuvant	Yes
RM	November 2022	4	NHS Public Coverage	January - October 2023	9 months	1st line	No

Alectinib has been incredibly successful at treating disease, with some patients even achieving NED status.

7 of the patients interviewed stated that they are currently NED since being on alectinib, all of whom started the treatment as their 1st-line of therapy and are still on it as of April 2024 – **GH, SW, DE, LJ KB, LR,** and **RE**. This is particularly important in showing the survival benefit and, ultimately, showcasing the hopes that cancer patients overall have, especially in the early-stage setting where survival rates are much more promising and the primary goal of treatment is in the curative intent.

After **JY** finished 4 rounds of adjuvant chemotherapy after surgical resection, she wasn't on any treatment, and had scans every 3 months. However one year after finishing chemotherapy, she had recurrence in both lungs and was now at stage 4. She started alectinib in December 2022 quickly afterwards, and has continued to be on it for nearly 1.5 years ever since. On alectinib, her tumours began to shrink by the time of her first scan, and most recently all are now 1cm or smaller.

44-year-old **GH** was just diagnosed with prostate cancer in August 2018 when a pre-surgery CT scan revealed he actually had another primary cancer in his left lung and lymph nodes, which was diagnosed as stage 3A ALK+ NSCLC. After surgeries to remove both cancers, then radiation and chemotherapy aimed at his lung cancer, he remained was cancer-free for 3 months before the lung cancer returned in his lymph nodes. He started adjuvant alectinib shortly afterwards in August 2019, and all his scans have been NED ever since.

When **LJ** was diagnosed in November 2023 with stage 4 NSCLC, she had mets in her bones and shoulder that caused excruciating pain. She was admitted to the hospital for 5 days, was very weak, had a bad cough, inflamed kidneys, and

abdominal pain, and was essentially bedridden. She completed 1 round of radiation to her shoulder before her biomarker testing came back as ALK+ while she was in hospital, and her oncologist started her immediately on alectinib the same day. Her first scan 2.5 months later showed a 75% reduction in the amount of cancer in her body and already felt significantly stronger.

Nearly 5 years ago, 49-year-old **DE** had always been reasonably healthy and was going on a health journey shortly before being diagnosed with lung cancer – he had quit alcohol, ate healthy, went on long (10 mile) walks, and enjoyed hiking with his wife. One day after work while catching up on emails, he suddenly felt off, mentioning it to his wife, then suddenly collapsed and had a full seizure where he lost control of half his face. Thinking he had a stroke, his wife called the paramedics, and DE was taken to the hospital where chest x-rays and brain MRIs found a mass in his brain and lungs. He had a 2nd seizure 3 hours later while in the hospital, so he had surgery 1 month later to remove the 3cm mass in his brain and 2 tumours in his lungs at 2cm each. After the surgery, biomarker testing confirmed he was ALK+ and started adjuvant treatment with alectinib. Within the first 6 months by the time of his 2nd scan, DE had a complete response and was declared NED. He notes that his side effects are minor, and continues to be on the drug alongside anti-seizure medication, and has not had another incidence of seizure since the hospital.

Alectinib has been very durable and has extended patients' lives at an average of 31.8 months.

As summarized above, nearly all patients interviewed were on alectinib for over a year, with the average duration over 2.5 years. It has been extremely successful at extending their progression-free survival, reducing the risk of recurrence, and diminishing the need for traditional, systemic therapies that have limited efficacy and harsh side effects. As mentioned in Section 4, patients who experienced chemotherapy only did so before they received results from biomarker testing, and once they found they were ALK+, they switched treatments to begin alectinib almost immediately. One patient, **LR**, currently continues to be on alectinib and is doing well, even after more than 6 years on the treatment since late 2017.

Only 2 individuals, JM and RM, were treated with alectinib for less than a year, at 5 and 9 months respectively. In **JM's** case, his disease at the time of diagnosis was already very advanced, with mets to both lungs and his spine, and quality of life was extremely poor as he received his diagnosis while hospitalized. He was treated with alectinib for 5 months, which had improved his quality of life during this time, before further progression and ultimately died after a very short 6-month battle with stage 4 lung cancer. For **RM**, alectinib was similarly his first line of treatment once his disease was confirmed ALK+, and he continued to be on it for 9 months between January - October 2023. His cancer was already stage 4 at diagnosis as it was in his lungs, lymph nodes, liver and bones, and physicians told him he only potentially had weeks to months left, which was a huge shock to RM since aside from sudden weight loss and persistent cough, he never felt severely unwell. Alectinib worked very well for him until October when his right lung collapsed and filled with fluid, having 8 litres drained in intensive care. RM started 2nd line treatment with lorlatinib 2 weeks later, which he is still currently on in April 2024.

Both **RM** and **JM** noted in their interviews that although they hoped they'd get more time out of alectinib as they've heard stories of others on the drug for years longer, they were nonetheless happy that they got any extra time out of it, as they were both considered "terminal" patients at diagnosis, particularly for JM who was already very ill with a poor quality of life. RM continues to live a fulfilling life with his 4-year-old daughter as a single parent and even continuing to work to keep himself busy.

Alectinib has seen to relieve symptoms in a relatively quick time frame.

Particularly for patients who were able to notice a drastic change in their health once they started treatment with alectinib, some interviewees noted that they were able to notice the treatment working within a few days to a week of starting the treatment, most notably in **JM**'s case:

After a very delayed and difficult experience getting diagnosed with stage 4 NSCLC, **JM's** 40-year-old husband's quality of life was already very poor. When his initial mild back pain escalated to the severity only a month later where he was in constant pain, couldn't sleep, lie down or sit comfortably, doctors misdiagnosed his symptoms as pneumonia and continued to prescribe steroid injections to no avail. By the time doctors finally confirmed his diagnosis of lung cancer 2 months after initial onset of symptoms, there were already tumours everywhere in both lungs and the spine, the primary tumour being 10cm in 1 lung and rupturing his T4. JM was already bedridden and admitted to the hospital as he couldn't feel his toes or walk, was in severe pain, and was unable to even pull up his pants. He started on alectinib in late December 2022 and although still weak, JM recalls he noticed results from the treatment in a few days. He felt more like himself, was in less pain, and started to get back to his goofy self with his young kids. His first follow-up scan in mid-February showed his all his tumours had shrunk substantially, and JM gradually felt better overtime, tumours were shrinking, and even drove to St. Louis, MI in March with the entire family for his son's baseball tournament, enjoying time with his family and making memories with his children, which JM recalls was incredibly important to him. He was on alectinib for 5 months until he had to be admitted to hospital again in April due to further progression and unfortunately, he died a short 6-months to the day of his diagnosis, on April 27th, 2023.

In September 2023 prior to diagnosis, **LJ**'s only symptom was some shoulder pain she attributed to a yoga injury, but by October, it had become excruciating where she had trouble working and couldn't concentrate. After the diagnosis confirmed stage 4 lung cancer, she had 1 session of radiation done and had agreed to go on a mountain retreat for the weekend the next day, but when she got there, she felt so ill and couldn't participate, lying in the room all weekend. When scans showed masses in her spine, cornea of the left eye, and the primary mass in the center of her chest, she was shocked at her diagnosis and her oncologist started her on alectinib once she was identified as ALK+, and has been on it since December 2020. When she started treatment, RE had so much difficulty breathing, couldn't sleep, and the mass blocking her airway made her life "miserable". Within a week of starting alectinib, her symptoms improved dramatically, and when she went to a retinal specialist a month later, the lesion in her eye had completely resolved. Her first scans in February showed significant improvement and within 9 months, she was declared NED and still continues to be NED in April 2024.

Side effects on alectinib are manageable, and severe AEs improved with dose reduction.

The patients that Lung Cancer Canada had interviewed for this submission have been on alectinib for at a minimum of 5 months and at an average of about 2 years 8 months. The most common AEs reported by those interviewed were fatigue, increased skin sensitivity to sunlight, and gastrointestinal events (constipation or diarrhea). In comparison to adverse events seen with other therapies, such as chemotherapy or radiation, patients consistently stated that these are all relatively minor or side effects that are manageable over time, with simple lifestyle adjustments, or with over-the-counter products, which in turn keep them functional and independent, and carry a lessened burden on care partners as well.

To mitigate the effects of skin sensitivity to sun exposure, patients said that using sunscreen, hats, covering up in long-sleeved clothing, and simply staying away from the sun as much as possible significantly helped reduce the burden of its effects.

Fatigue was also another major patient-reported side effect as with chemotherapy; however overall, patients agreed that the fatigue experienced with alectinib is not nearly as significant as that on chemotherapy, and they learned to manage it over time with the activities they scheduled each day. Some took 1-2 naps throughout the day to maintain their energy levels. For others, the fatigue impacted their motivation to exercise or run errands some days, but no one stated that any of the side effects diminished their functionality or quality of life, nor did it require them to rely solely on caregivers.

Other side effects that some patients noted include skin rash, changes in liver or kidney levels, hormone level changes, weight gain, and muscle weakness/pain. **LJ** recalls when she first started the drug, she had a strong metallic taste in her mouth, particularly when eating dairy or fruit, but that resolved after 2 months. She also found that with alectinib, she has to consistently remain in a state of moderation for "everything" and can't allow herself to reach the extremes in certain instances. For example, she must limit her caffeine, sugar, and alcohol intake to a certain level (i.e., 1 cup of coffee, 2 glasses of champagne, eating a full meal in the morning and evenings), otherwise, she will feel quite ill and the impact/side effects of her medication will be heightened, which takes her 3-4 days to recover from. However, LJ says that after being on alectinib for 5 months and counting, the side effects became more manageable overtime, as it's a matter of learning to listen to her body and working around the side effects.

A few patients, including **SW, EN, GH**, and **RE** had to reduce their dosages due to the intensity of side effects experienced, but these significantly improved once dosages were adjusted. **EN**'s mother had to reduce the dosage of her alectinib due to inflammation of the liver, which had since resolved. Similarly, **SW** reduced her dosage from 1200mg to 900mg after a few months on alectinib due to edema, photosensitivity, and constipation, which all have been less intense and are now much more manageable with simple lifestyle changes. When **GH** was on the full dose, he experienced neuropathy and severe fatigue where getting out of bed required effort and motivation, which improved quite significantly when he reduced the dosage. He also experiences some brain fog, where he notes feeling "*not as mentally sharp and nimble, and also can't multitask anymore*", but this does not impact his ability to continue performing basic tasks at home.

Alectinib allows patients to have a meaningful quality of life that is nearly comparable to pre-diagnosis, including being able to exercise and getting back to old hobbies.

After his lobectomy in 2019, **VK** entered the ALINA trial and received 22 months of alectinib, which he attributes was successful in keeping his NED condition stable. While on the drug, like many other patients mentioned, fatigue was the biggest side effect that had some impact on his life, albeit not significantly. He was still able to continue living independently with his wife, grocery shop, drive himself to appointments, and even exercise. He says that his life since stopping alectinib and moving back to Canada where he is just being monitored via scans every few months is comparable to pre-diagnosis. He continues to work and is looking forward to travelling back to Korea in the next few months to reunite with his wife.

Prior to diagnosis, **JY** had always been very active and healthy. She often ran full and half-marathons, and kept a healthy diet. After a lingering cough led to her stage III diagnosis, she battled with fatigue throughout her cancer journey, but still keeps active as much as possible. She continues to try to walk 4 miles on most days on the treadmill, but still struggles with catching her breath while running and walking up stairs, so she hasn't been able to return to that.

KK had always been an avid hiker while living in the UK with his husband since his retirement in 2017, hiking 8-12 miles a day, even at elevations of 5000-10,000 feet a couple times per week, while also walking 7-8 miles every day. When his quality of life severely diminished while on chemotherapy, he could still walk around the house but was barely able to get out of bed most days. Now, having been on alectinib for 1.5 years, he has the energy and stamina to return to

walking 4-5 miles per day, in addition to pursuing other hobbies that he loves, such as painting. KK is able to travel again, having several trips to Spain, Ireland, and around the UK planned in the next couple of months, meanwhile he couldn't even imagine going to the grocery store while on chemotherapy. He reiterates that alectinib has completely "*changed my life, and although I'm not hiking at high elevations everyday anymore, I'm virtually back to the life I had pre-diagnosis, which I never would have even considered was a possibility before".*

BR has been a stay-at-home mom for over 20 years while she raised her 3 children who are now 26, 23 and 17 years old. After her 3 gamma knife procedures left her with some memory loss and the inability to drive, she is incredibly grateful that her youngest 17-year-old daughter can now drive herself, rather than relying on BR and her husband to get around. Since starting alectinib 5 years ago, she has begun driving short distances locally around town, but still does not go on the highway, so she relies on her husband to run most errands and drive long distances, including to their cottage and accompanying her to oncologist appointments in Cleveland, 2 hours from her home. Since being on alectinib however, she has maintained a good quality of life, is able to care for herself and has no issues doing things around the house, and even restarted some old hobbies such as scrapbooking, crafting, baking, and cooking. Alectinib was "a miracle drug" to BR and so many others who found stability in their treatment for years, and has maintained patients' quality of life, with some even going back to work.

With twin 13-year-old boys, **GH** and his wife have "swapped roles", where she has continued to work full-time while GH takes care of most of the shopping, cooking, and errands around the house. GH says his quality of life now is comparable to his life before cancer, but notes that his goals and values have changed, where he prioritizes his family and finding opportunities to make a difference in the community. Although he does not work anymore, he is still keeping himself very busy and positively contributing to society, joining a lung cancer patient-led charity in the UK where he is now Deputy Chair and focuses his efforts on patient advocacy. He also no longer drives long distances due to the fatigue, but continues to stay active, walking a lot and hiking nearly every weekend. He completed a 3-hour hike over the past weekend and 20 mins of treadmill daily, and although he can't run 6-8km every day anymore like he used to before his diagnosis, GH is still grateful that he found success with alectinib keeping his cancer at bay for nearly 5 years and is hopeful he's able to stay progression-free for years to come.

Exercise had always been a key part of **RE**'s lifestyle, even shortly before her diagnosis with stage 4B lung cancer, where she was out road biking for 60 miles at a time and pushing herself to crazy limits. The daughter of a Phys Ed teacher, she was taught to keep herself active, so when she started feeling out-of-breath while road biking, she just thought she was out of shape and kept pushed herself. But 1.5 months before her diagnosis, she couldn't talk without coughing, had trouble going up/down stairs and performing simple household tasks were difficult. Since starting alectinib, the fatigue is still a constant hurdle she faces, impacting her motivation to get back to exercise. However, she has a great quality of life, is able to do short hikes, maintains her independence, and has no problem performing normal activities of daily living, and has even started kayaking and sailing at her lake house with her husband. RE is also a musician, so she is slowly trying to get back into playing consistently, which is also beneficial for strengthening her lung capacity. RE says that she's incredibly grateful for the extra time that alectinib has given her, and is very excited and sentimental about getting to watch her youngest son get married this June.

Patients are able to return to work or continue working throughout their treatment.

Even throughout his diagnosis, **RM** has continued to work full-time every day, saying that he doesn't necessarily need to financially, but rather to keep himself busy and he enjoys his job. Living only a 10 min walk from work, he feels fortunate that his work colleagues are very understanding and supportive, especially as a single father raising a 4-year-old daughter in the meanwhile.

While in the midst of experiencing portent symptoms of her diagnosis with lung cancer, **LJ** was preparing to move to Canada from her home country of South Africa at the same time. Alectinib has since allowed her stability in her treatment while managing its side effects for her to certainly look forward to working again. Since settling in Montreal, she had continued to work as a consultant for the first 2 months throughout her diagnosis until January 2024, but had stopped after the stress impacted her health and heightened her side effects, as explained previously. However as of April 2024, she has found stability in her treatment and mentions to LCC that she's very eager and feels ready to start working again. In fact, she is travelling to London in early May to reconnect with old colleagues and hopes to plant seeds to start taking on projects again.

SW was a registered nurse doing geriatric home visits, but stopped working in 2015 when her daughter was born in order to raise her. When she started kindergarten a few years ago, she was excited about thinking of going back to work; however, her diagnosis came shortly afterwards, and while on chemotherapy, the idea of returning to work was "out of the picture". SW recalls she often needed help from her family and in-laws to watch her daughter while she was in chemotherapy treatment and her husband was at work. However, after having found stability on alectinib for 2+ years and her daughter now 8 years old, SW says in her interview that she's now able to think about going back to work as she loved her job, potentially looking into daytime work with the local school district.

In October 2019, 2 months after diagnosis, **DE** had his driver's licence revoked as per the UK government's protocol for individuals with neurological diagnoses, which unintentionally forced him to cut back on work in technology sales as driving was important to his duties. After recovering from surgery, he went back to full-time by December 2019, but simply took public transport. Although he loved what he did, DE stopped working full-time in April 2023 and since then, has focused on patient advocacy work with some cancer groups in the United Kingdom, a personal choice to find roles that were more meaningful for him. DE has no issues with daily life, is able to drive again, and even promised himself to start running again to lose some of the weight gained as a side effect of alectinib.

Since her diagnosis nearly 3.5 years ago, **KZ** has really only missed a total of 5-6 days of work and has still continued to work full-time with the government as a paralegal. KZ loves her job and is eager to continue working until her retirement in 3 years' time, given the stability she's found with treatment and continues to maintain NED.

With the long duration of response the drug has shown to have, alectinib has given patients like SW, LJ, KZ, DE, and RM the possibility of returning to work or even continue to work throughout treatment, as the flexible nature of simply taking several pills a day anywhere that's convenient for them allows patients to spend more time recovering, making memories with loved ones and even return to work, helps them adjust more seamlessly to a new "lifestyle". For example, **GH** says in his interview that "*being able to keep being a good, working citizen and contribute to society is a luxury that not all cancer patients have, and being able to have that fulfillment and not worry about financial needs is important"*.

Ultimately, the stability that patients have found with alectinib has allowed them to look forward to goals and wishes for the future, be alive for their children, and even raise money for charity.

Prior to diagnosis, **RM** had always been a very fit and active individual, cycling around his home island of Jersey, a dependency of the UK, and playing soccer often with friends. After the initial shock of receiving a devastating diagnosis of stage IV lung cancer, RM found stability for 9 months with his treatment on alectinib, and then now with lorlatinib. He felt well aside from the minor side effects and maintained his ever-positive mindset to ensure he made a difference with his diagnosis, even while raising a 4-year-old daughter as a single father. In August 2023 while on alectinib, RM actually participated in a race and cycled 100km around the island to raise money for a local charity supporting islanders living

with cancer. He completed the cycling race in a very impressive 4 hours and 26 mins and raising over £7,000 to give back to the community. He noted that being able to make memories with his daughter and modeling for her that "*although faced with a terminal disease, determination and persistence are key to keeping positive and I can't let any barrier stop me from doing what I believe in".* Ultimately, RM is optimistic that he can just keep himself alive to be able to see his daughter grow older, be able to remember her father, and be present for the milestones – seeing her go to school, graduation, getting her driver's licence, and being there for her wedding. Alectinib has allowed patients like RM to find stability in an effective treatment where they can actually foresee a future, have plans to travel more, and set goals for themselves, especially when survival rates are more promising in the stage I-III setting.

Patients with young children also face a similar wish for the future after being faced with a diagnosis of lung cancer – to see their children grow up and be there for the milestones as RM outlined – first day of school, high school and university graduation, getting married, and maybe even having grandchildren one day. Just like RM, **SW** is hoping to live at least 10 more years to see her now-8-year-old daughter turn 18.

30-year-old **KZ** had just given birth to her youngest child a few months prior to getting diagnosed with stage III lung cancer 3 years ago. Being a stay-at-home mom to a 2-year-old at the time and then a newborn, her world flipped upside down, but was very lucky and grateful to have great support from family and friends in town. Her case was non-resectable as it had already spread to her lymph nodes, so she did 6 weeks of chemotherapy and radiation, and then started on alectinib in June 2021. Her day-to-day life was fairly normal and sensitivity to the sun was the only noticeable side effect that she had to manage. Now finding stability on the treatment 3 years later, she's planning on homeschooling her young children, who are now 3 and 5 years old. KZ says that she's hoping to have more kids in the future and is nervous alectinib may cause fetal harm to pregnant women, so that's been very hard on her to wrap her head around. She says to LCC that because she started the treatment when it was still fairly new for early-stage patients, her oncologist plans to take her off at the 3 year mark this June, after which she'll think about growing her family. Being a young parent, KZ's main wish is to still be around for her kids and make memories with them for as long as she can, just like SW and RM.

At the time of her interview in late April, **LJ** was actually travelling across the UK by herself for an introspective trip to find herself and reflect on what the future has in store for her. She says that alectinib has transformed her Quality of Life drastically in that when she started alectinib, being in the hospital, severely fatigued, and bedridden, she couldn't even imagine making the trip to the store for groceries. But as she's now travelling around a new country alone, she's feeling much more like her old self, focused on raising her 5-year-old son, eager to go back to work, and adjust to life in Canada as a recent immigrant with her husband. LJ has taken up old hobbies again, crafting ceramics, doing different therapies to support her mental and physical health, and going on long walks in nature to feel grounded, which she thanks alectinib for giving her the luxury to focus on what's meaningful for her life.

All patients agreed their overall experience with alectinib was significantly better than previous therapies.

LCC asked each patient during their interviews how they would rank their experience with alectinib in comparison to other therapies they've experienced on a scale of 1-10 (i.e., 1 being "*Alectinib was much worse than other therapies/I would prefer other therapies to alectinib"*, 5 being *"about the same*", and 10 being "*Alectinib was much better than other therapies/I would prefer alectinib to other therapies")*.

The average ranking was at **9.7** in strong favour of alectinib. Most agreed that the overall experience with alectinib was much better in terms of manageable side effects, efficacy in treating their disease, and significant improvements in health-related quality of life. It has truly improved the lives of many patients, including the ones interviewed in this submission, and is very effective in targeting their ALK mutations.

One caregiver, **EN**, mentioned that on behalf of his mom who lives with lung cancer, he would rank her experience even higher, at 15, as her quality of life now is actually even better than before her diagnosis. He finds that she has become much more intentional with spending time on activities that she enjoys, and being with loved ones than she did before. She even travelled back to Hong Kong last year on the long 15-hour flight without any problems, and even started attending senior exercise classes at the local community center and over Zoom. He says that her breathing, mobility, and physical strength have improved, and she is now excited to exercise and consistently walks 6 km each day, which was very rare for her prior to diagnosis.

7. Companion Diagnostic Test

Biomarker testing for ALK+ alterations is currently a standard in all provinces across the country. Alectinib does not require additional companion diagnostics.

8. Anything Else?

There is incredible potential in adding adjuvant alectinib to the treatment landscape for early-stage resectable ALK+ lung cancer, where alectinib has already met incredible success in real-world experiences, even outside the ALINA trial, that has extended patients' lives, gives patients their livelihoods back and allows them to plan further down the line for a future that previous therapies could not give them.

Having alectinib available and funded for Canadians impacted by early-stage resectable ALK+ non-small cell lung cancer will be a significant step forward in offering a new adjuvant treatment option aside from traditional chemotherapy. Early-stage patients are lucky to have their disease caught at a stage where potential cure or full recovery is possible, as 75% of lung cancer cases are caught at advanced or metastatic stages. Treating their disease with adjuvant alectinib will extend their lives, maintain DFS and PFS for months to a couple years, as seen with several patients interviewed. Patients were able to live a good and meaningful quality of life, that many even said were very comparable to pre-diagnosis, where they were able to continue or go back to work, get back to old hobbies, and stay active with exercise. The extra time that alectinib has been able to give patients faced with a lung cancer diagnosis is truly unmatched, and allows patients impacted to spend more quality time with loved ones and do the things that are meaningful to them.

The other key benefit of alectinib is that it's effective at treating distant metastasis and protecting the brain as well, which is particularly important for this subset of ALK+ patients, as this type of lung cancer is particularly aggressive in CNS disease progression, which current adjuvant treatments like chemotherapy or radiation do not adequately address.

The current submission is for adjuvant treatment in the early-stage, resectable setting. With the novel results that the ALINA clinical trial had just published in mid-April, it was difficult to find first line patients from the clinical trial for this submission since there were no Canadian trial sites. However, the experiences of this treatment in all lines of therapy have been well documented, and the practice of using targeted therapies for those with actionable mutations is a well-established and well-recognized practice globally. Many other jurisdictions (e.g. FDA, NICE) already have alectinib accessible in the adjuvant setting, either publicly or privately, as highlighted by the geography of patients interviewed. Alectinib is already a standard of care TKI in the stage IV metastatic setting in Canada, so we strongly urge CADTH to extend the availability of alectinib for all patients across all stages with a positive approval in the early-stage resectable setting.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the
   No

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Hoffman-La Roche Canada				X

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Shem Singh
Position: Executive Director
Patient Group: Lung Cancer Canada
Date: April 30th, 2024

CADTH

CADTH Reimbursement Review
Patient Input Template

Name of the Drug and Indication:

Brand name: Alecensaro

Generic name: Alectinib

Indication: ALK-positive NSCLC

Alecensaro as adjuvant treatment following tumour resection in adult patients with Stage IB (4 cm) - IIIA (according to AJCC/UICC 7th edition) anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer.

Name of the Patient Group:

Lung Health Foundation / The Ontario Lung Association

Author of the Submission:

Jess Rogers, Vice President Programs, Research and Public Affairs

1. About Your Patient Group

The Lung Health Foundation (Lung Health Foundation Website) legally known as the Ontario Lung Association, stands as a cornerstone of trust and reliability in the Canadian healthcare and public health systems. We are governed by a dedicated board of directors and supported by a team of approximately 40 employees alongside thousands of passionate volunteers. Together, we work tirelessly to improve the lung health of Canadians, driving positive change and fostering a brighter, healthier future for all. Our work includes:

- offering a diverse range of **programs and services** tailored to individuals living with lung disease or at risk
- investing in impactful **research** and innovation we strive to uncover new insights, treatments, and strategies for combating respiratory illnesses, ultimately driving progress and improving outcomes for individuals across the country
- advocating for change with our **strategic advocacy initiatives and collaborative partnerships**, we champion the interests of individuals living with lung disease,

advocating for improved policies, access to care, and resources to better meet the needs of our community

- **amplifying the voice of people with lived experience** to share their insights and perspectives to inform our work and in processes like patient drug submissions. LHF is registered with esteemed bodies like the Canadian Agency for Drugs and Technologies in Health (CADTH) and the pan-Canadian Oncology Drug Review (pCODR).

In the pursuit of our shared vision, the Lung Health Foundation is honored to serve as a trusted partner and advocate for individuals living with lung conditions, healthcare professionals, researchers and communities nationwide. Together, we will continue to elevate lung health, drive positive change, and build a healthier, more resilient Canada for generations to come.

The Lung Health Foundation serves all Canadians with lung disease and those with an interest in lung health given our tireless work in prevention and screening in addition to management. In order to execute our work, we engage patients as advocates, speakers, and coaches as well as provide direct support to patients and their caregivers through our robust programming including support groups, peer mentorship programs, self-management coaching, education as well as our fitness for breath courses. We often engage healthcare professionals to assist LHF in identifying patients to inform our submissions to CADTH as well.

2. Information Gathering

The information provided from the Lung Health Foundation in this submission builds from our robust experience working directly with people living with lung cancer through our patient and caregiver support programs, lung cancer patient advisory group, our lung cancer patient advocates as well as information obtained from interviews with 3 people living with lung cancer and an online survey completed by 9 people living with lung cancer. The first interview was conducted with a male patient in his 50's who resides in Ottawa, ON, the second interview was conducted with a female patient in her 30's who resides in Vancouver, BC, and the third interview was conducted with a male in his 60's who resides in Toronto, ON. Information on

age, gender and geographical location was not collected from any of the 9 online respondents. All of the online respondents completed the survey in April 2024.

3. Disease Experience

The respondents had varying experiences with their lung cancer diagnosis, but the theme of it being difficult to get an accurate and timely diagnosis was evident among this group. “It's hard to get a diagnosis at an early stage.” One of the interviewees reported that what led him to the emergency department, and eventual lung cancer diagnosis, was severe numbness in his right hand. While there, he mentioned his cough that wouldn’t go away. It was discovered he had a brain tumor (secondary), and after that the primary source was discovered, lung cancer. Another interviewee reported that “during the few months before my lung cancer diagnosis, I had a poor quality of life. I was unable to have full conversations without being abruptly interrupted by coughing fits. During remote work virtual meetings, I often had to be on mute and found it difficult to speak. I had to have other teammates carry on conversations for me. In the evenings, with my partner the cough would be worse and I could only communicate via writing at times. The symptoms did not allow me to work, exercise and socialize like I had before.”

Other symptoms and challenges these patients experienced as a result of their lung cancer were fatigue (61%), shortness of breath (57%), cough (26%), pain (22%), difficulty fighting infection (17%) and chest tightness (13%). Weight loss, diminished appetite, low mood / depressive periods and challenges with physical and emotional intimacy were also noted by

some respondents. When asked whether this condition affected their day-to-day life, some responses included the diseases' negative impact on one's ability to:

- Work (48%)
- Participate in physical activities (30%)
- Do housework (26%)
- Use stairs (22%)
- Go shopping/ do leisure or hobbies / go out for day trips (22%)

As a result of living with lung cancer almost all respondents indicated it had negative impacts on their emotional well-being. Some (44%) feel isolated and struggle to manage their symptoms. Others indicated they feel guilty for the burden they are putting on their family members / friends. One respondent stated his daughter attends all medical appointments with him so that is time-consuming for her and causes her to miss work. Another respondent stated the stigma of living with lung cancer is hard. "If you have breast cancer, everyone gives you sympathy. If you have lung cancer, everyone assumes you were a smoker and brought it on yourself. Many of us never smoked, worked with asbestos, or lived with elevated radon gas. It is NOT our fault."

4. Experiences With Currently Available Treatments

The treatments tried by the respondents included surgery, radiation, chemotherapy, targeted therapy and immunotherapy. The medications tried included Alectinib, Lorlatinib, Maxolone, Gefitinib, Entrectnib, and Tagrisso. Some patients are participating in clinical trials. The benefits experienced with the treatments were: reduced cough, reduced shortness of breath, increased participation in daily activities, ability to exercise, prolonged life, delayed disease progression

and a reduction in the severity of other disease-related symptoms. Patients on oral drugs also value the flexibility the drugs provide in allowing them to work and travel without restrictions. “Once diagnosed, on the right therapy and on the right dosage, I have been able to resume my regular life activities such as working, exercise, traveling, sleeping, and spending time with family and friends. My treatment is taken orally which offers me a convenient way to receive treatment that I can take anywhere. Living with lung cancer is difficult in many ways. What truly makes it a manageable disease is having access to effective, convenient and affordable/covered therapies.”

Some patients reported struggling with lingering side effects. Respondents who received surgery reported deconditioning and chronic fatigue. Some of the side effects reported from radiation were fatigue, skin changes, hair loss and tissue scarring.

With medications, the side effects reported included extreme itching that affects sleep, brain fog, fatigue, nausea, vomiting, mood changes, diminished appetite, weight loss, hair loss, anemia, and neuropathy. Side effects from chemotherapy severely impacted the patients’ quality of life, ability to work and in some cases, the ability to perform activities of daily living.

When asked about challenges with access to treatment, the respondents reported that they struggled with the cost associated with some treatments. They also found it challenging to navigate the healthcare system and in some cases, they were not clear where to go for information and support. Patients on targeted therapy also worry about access to the next line of treatment if or when their current treatment stops working. “I have ALK+ NSCLC diagnosed in 2021. I am a non-smoker. I have been through chemo and radiation but only saw real improvement in my cancer with Alectinib. However, no medication lasts forever and I don't

know what will happen when I have progression as the next drug, Lorlatinib, is not readily available in all provinces."

5. Improved Outcomes

Key treatment outcomes for this group of lung cancer patients included stopping or slowing the progression of the disease with minimal side effects. Regarding side effects, one responded stated that , "I hope for little to no side effects, particularly when it comes to energy levels, and ability to focus. Being able to work, contribute to my community and be with friends & family is important to me. This requires the right energy levels and focus."

Patients would also like to see medications that are effective for advanced disease. Due to the poor outcomes associated with advanced disease, patients describe feeling very anxious about any sign or prospect of disease progression. "ALK-positive affects mainly non-smokers and is treated with inhibitors. These are very expensive but work for years. I have been on Alectinib for 4 years. The next drug when this one stops working is called Lorlatinib and can also be used as 1st line treatment. Alectinib is provincially funded in Ontario but no 2nd line drugs are. These are lifesaving. It is very stressful knowing a 2nd line drug is available but is cost prohibitive."

When choosing therapy, patients are also interested in the efficacy of the medication. One respondent commented that they would be more receptive to side effects if there was strong evidence that the medication would stop or slow down the progression of their lung cancer.

6. Experience With Drug Under Review

Alectinib emerges as a transformative option in lung cancer therapy, offering patients a lifeline of hope and restoration. Seven individuals intimately acquainted with its effects resoundingly

affirm its profound impact on their lives. Across the board, they attest to a marked improvement in their quality of life, echoing the sentiments of a respondent who hailed it as nothing short of a "miracle drug."

Patients on Alectinib report tangible benefits that extend far beyond mere symptom relief. They experience a notable reduction in debilitating symptoms such as coughing and shortness of breath, coupled with an enhanced capacity to engage in daily activities and exercise. For many, Alectinib represents a gateway to newfound freedom, enabling them to sidestep the burdensome regimen of radiation and chemotherapy.

Moreover, the side effects associated with Alectinib, though present, are described as manageable and minor in comparison to the immense gains in well-being. While some patients contend with fatigue, appetite loss, and mild nausea, these effects pale in comparison to the resounding sense of normalcy afforded by Alectinib.

One patient's testimony encapsulates the sentiment shared by many: "Taking targeted therapy Alectinib first line has enabled me to forgo radiation, chemo, and countless doctors' appointments. I have at-home therapy, am able to manage side effects, and have an excellent quality of life 5 years and counting."

Patients acknowledge the financial considerations associated with such medications and emphasize the importance of ensuring equitable access across Canada of approved and effective treatments. They advocate for increased public awareness to destigmatize lung cancer and catalyze advancements in early detection and intervention, ultimately envisioning a world where lung cancer is intercepted in its nascent stages, offering patients a chance at prolonged survival and improved outcomes.

7. Companion Diagnostic Test

LHF consistently hears a common theme from our lung cancer patients and caregivers with respect to the frustration in the lack of access to biomarker testing, the delays in getting biomarker testing as well as the inconsistencies of what biomarker testing is available where across Canada. In our most recent policy forum we tackled this very issue related to the diagnostic to treatment pathway for lung cancer and the significant opportunity for improvement to improve the accuracy and timeliness of diagnosis so that the appropriate treatment can be initiated as quickly as possible. These same themes were reinforced with the ALK-positive patients that participated in our interviews and surveys. Most of the respondents who went through biomarker testing indicated they wished it had been done sooner. Depending on the stage of the cancer diagnosis, biomarker testing was not always an option at diagnosis.

The Lung Health Foundation is committed to raising more awareness about this significant barrier to effective and efficient treatment for people living with lung cancer. The lack of access to and use of biomarker testing is consistently mentioned as a major barrier by the people we work with living with lung cancer as well as the healthcare professionals that work with us.

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

In the realm of lung cancer therapeutics, Alectinib shines as a testament to the transformative power of precision medicine, offering patients not just treatment, but the promise of improved quality of life which the majority of our patients consistently raise as a critical consideration

when balancing benefits and risks when they are working with their physicians to select their treatment options.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it

No

3. **List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review**.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Hoffmann-La Roche Limited			X	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Jess Rogers
Position: Vice President Programs, Research and Public Affairs
Patient Group: Lung Health Foundation (Legal name: Ontario Lung Association)
Date: April 30, 2024

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0350
Generic Drug Name (Brand Name): alectinib (Alecensaro)
Indication: As adjuvant treatment following tumour resection in adult patients with Stage IB (≥4 cm) - IIIA (according to AJCC/UICC 7th edition) anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer.
Name of Clinician Group: OH (CCO) Lung Cancer Drug Advisory Committee
Author of Submission: Dr. Donna Maziak

1. About Your Clinician Group

OH(CCO)'s Cancer Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

Information was gathered by email.

3. Current Treatments and Treatment Goals

The treatment goals include survival, quality of life, prevention of recurrence.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

This is an unmet need as these are often young, otherwise healthy patients with lung cancer with a very high degree of brain tropism, with no known modifiable risk factors. As ALINA demonstrates, the outcomes, even with adjuvant chemotherapy alone, are poor, with 40% relapsing within 2 years, (including 5/12 of the stage 1b's).

The DAC would also like to emphasize that improved CNS DFS is significant.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

In clinical practice, patients would have the option of adjuvant alectinib alone or chemotherapy followed by alectinib. This is the same approach to adjuvant osimertinib.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Patients will be selected based on the presence of ALK rearrangement, which is currently tested for routinely (and tissue isn't an issue with adjuvant setting).

This is for patients with resected stage 2A or higher, or any node positive or T3/T4 or T2 ≥4.0 cm.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Response can be assessed as per the trial protocol. CT imaging can be every 3 to 6 months. Six months is the current standard imaging interval post-surgical resection.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

At 2 years or until disease progression or intolerance.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

This is an oral medication, but prescribed from experienced cancer providers (medical oncologists, respirologists etc.)

6. Additional Information

The ALINA trial compared to chemotherapy, but most appropriate comparison would have included patients who received chemotherapy and compared to no treatment. Expect in clinical practice the receipt of chemotherapy should not exclude patients from receiving alectinib. Receipt of immunotherapy would be exceptionally rare, and only in a circumstance where an incidental ALK positive is found after neoadjuvant therapy, with preoperative testing not being positive for ALK. Adjuvant immunotherapy would not be given.

It is expected that patients who relapse on alectinib would be eligible for second line ALK therapies (if funded - none are), but those who relapse after would be eligible for first line ALK targeted therapy. This approach should be consistent with what is currently funded for osimertinib.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   OH (CCO) provided a secretariat function to the group.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for <u>each clinician</u> who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Donna Maziak
Position: Lead, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 26-04-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Andrew Robinson
Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 26-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Roche	X			
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Peter Ellis
Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 25-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Roche	X			
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Stephanie Brule
Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 26-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 4: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Roche	X			
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Dr. Sara Kuruvilla

Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 26-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 5

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 6

Name: Dr. Natasha Leighl
Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 26-04-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 6

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Roche	X			
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0350-000
Generic Drug Name (Brand Name): Alectinib (Alecensaro)
Indication: Alecensaro as adjuvant treatment following tumor resection for patients with anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC).
Name of Clinician Group: Lung Cancer Canada – Medical Advisory Committee
Author of Submission: Dr Kevin Jao (lead), Dr. Rosalyn Juergens, Dr. Michela Febbraro, Dr. Shaqil Kassam, Dr. Nathalie Daaboul, Dr. Alison Wallace, Dr. Jeffery Rothenstein, Dr Sunil Yadav, Dr. Nicole Bouchard, Dr. Randeep Sangha, Dr. Zhaolin Xu, Dr. Mark Vincent, Dr. Paul Wheatley-Price, Dr. Susana Cheng, Dr. Callista Phillips, Dr. Barbara Melosky, Dr. Ron Burkes, Dr. Quincy Chu, Dr. Cheryl Ho, Dr. Catherine Labbé, Dr. Mahmoud Abdelsalam, Dr. Geoffrey Liu, Dr. Silvana Spadafora, Dr. Biniam Kidane, Dr. David Stewart, Dr. Dorothy Lo, Dr. David Dawe, Dr. Normand Blais, Dr. Stephanie Snow, Dr. Lacey Pitre

1. About Your Clinician Group

Lung Cancer Canada is a national charitable organization that serves as Canada's leading resource for lung cancer education, patient support, research and advocacy. Based in Toronto, Ontario, Lung Cancer Canada has a wide reach that includes both regional and pan-Canadian initiatives. Lung Cancer Canada is a member of the Global Lung Cancer Coalition and is the only organization in Canada focused exclusively on lung cancer.

Website Link: www.lungcancercanada.ca

2. Information Gathering

Information gathered for this submission was based on relevant presented clinical data and expert evidence based review amongst lung cancer medical oncologists across Canada.

3. Current Treatments and Treatment Goals

In Canada, the treatment for Stages IB-IIIA (TNM 7) non-small cell lung cancer (NSCLC) is both stage and biomarker dependent. Current treatment decision in the early stage setting now require Anaplastic Lymphoma Kinase (*ALK)*, Epidermal Growth Factor Receptor (*EGFR*) and PDL1 status in order to select appropriate therapies for patients for which the primary goal is cure (i.e. to improve 5-year overall survival). Canadian practice is aligned with practices around the world, as evidenced from data from both the IASLC Dataset and North America-based National Cancer Database.

For stage IB (TNM7), the primary goal is cure (i.e., to improve 5-year overall survival). To achieve this goal, the standard treatment is complete surgical resection. For this stage, adjuvant platinum-doublet chemotherapy is usually not indicated considering the absence

of demonstrated benefit. In selected cases where disease is considered high risk based on larger T-sizes (more than 4 cm), adjuvant platinum-doublet chemotherapy can be offered to patients. In medically inoperable patients, localized radiation (external beam or stereotactic body radiation) or cryotherapy can be considered as an alternative to surgery

For stage II NSCLC, the primary goal is cure (i.e., to improve 5-year overall survival). To achieve this goal, the standard treatment is complete surgical resection (RO). Thereafter, fit patients are offered adjuvant platinum-doublet chemotherapy. In a small fraction of cases, surgical resection leads to incomplete resection, and adjuvant radiation is potentially offered in this context, which would be given sequentially to adjuvant chemotherapy.

For stage IIIA NSCLC, the primary goal is cure (i.e., to improve 5-year overall survival). To achieve this goal, the standard treatment depends on whether the primary tumour is considered resectable or not, balancing benefits and risks, including peri-operative risks, the ultimate chance of cure, the number of lobes that will be resected (e.g. lobectomy vs pneumonectomy), the number of lymph node stations involved, size of lymph nodes and the long-term residual effects of the operation (e.g. expected residual pulmonary reserve and function after a resection). If surgery is considered reasonable, the next step would depend on whether mediastinal lymph nodes are known to be involved with cancer. If not (T4N0 or T3 or T4N1), medically eligible patients will start with surgery and then proceed to adjuvant platinum-based chemotherapy. For those patients with N2 mediastinal lymph nodes involved, neoadjuvant chemotherapy, sometimes associated with concurrent radiation, followed by complete surgical resection can be offered if the nodal disease is non-bulky and limited in extent. If surgery is not considered reasonable, definitive concurrent chemo-radiation is given, followed by consideration of a year of durvalumab. In a small fraction of cases, surgical resection leads to an incomplete resection, and adjuvant radiation is potentially offered in this context, but sequentially (and not concurrent) with any adjuvant chemotherapy, when feasible.

Adjuvant platinum-doublet chemotherapy given after resection of stage IB-IIIA NSCLC patients typically consists of four cycles of treatment, with each cycle lasting 21 days, for a total of 12 weeks of therapy. CADTH Clinician Group Input Template Page 5 of 28 September 2020 Specific platinum-doublet chemotherapy with the best evidence of efficacy has been with the combination of cisplatin and vinorelbine, but other platinum-doublet combinations have been increasingly used over the recent years such combinations with pemetrexed for non-squamous histology.

More recently, additional approaches have shown survival benefit in patients with stage IB-IIIA NSCLC in which surgical resection is deemed feasible. The use of neoadjuvant Nivolumab in association with chemotherapy has demonstrated improved disease free survival (DFS) in patients with stage IB-IIIA NSCLC based on the CHECKMATE 816 study. This approach is now Health Canada approved and reimbursed across Canada since 2023. The IMpower 010 study demonstrated improved survival with adjuvant Atezolizumab in patients with resected IB-IIIA NSCLC with PDL1 ≥ 50%, and who have had previously received adjuvant platinum-based chemotherapy. Atezolizumab is also Health Canada approved and now reimbursed in Canada since 2023. Eligible patients for these therapies in the clinical setting, however, require that tumors be both *ALK* and *EGFR* wild type.

In patients with tumors that are *EGFR* positive, Osimertinib is Health Canada approved and provincially funded after tumor resection in patients with stage IB-IIIA NSCLC whose tumors have *EGFR* exon 19 deletions or exon 21 (L858R) point mutations. In the ADAURA trial, this specific subgroup of patients benefited from a statistically significant benefit in overall survival with a hazard ratio (HR) of 0.49 (99%CI, 0.34-0.70); p< 0.001. The survival benefit was seen for regardless of stage.

References:

Chansky K, Detterbeck FC, Nicholson AG, Rusch VW, Vallières E, Groome P, Kennedy C, Krasnik M, Peake M, Shemanski L, Bolejack V, Crowley JJ, Asamura H, Rami-Porta R; IASLC Staging and Prognostic Factors Committee, Advisory Boards, and Participating Institutions. The IASLC Lung Cancer Staging Project: External Validation of the Revision of the TNM Stage Groupings in the Eighth Edition of the TNM Classification of Lung Cancer. J Thorac Oncol. 2017 Jul;12(7):1109-1121. doi: 10.1016/j.jtho.2017.04.011. Epub 2017 Apr 28. PMID: 28461257.

Pignon JP, Tribodet H, Scagliotti GV, Douillard JY, Shepherd FA, Stephens RJ, Dunant A, Torri V, Rosell R, Seymour L, Spiro SG, Rolland E, Fossati R, Aubert D, Ding K, Waller D, Le Chevalier T; LACE Collaborative Group. Lung adjuvant cisplatin evaluation: a pooled analysis by the LACE Collaborative Group. J Clin Oncol. 2008 Jul 20;26(21):3552-9.

Forde PM, Spicer J, Lu, S, Provencio M, Mitsudomi MD, Awad M, Felip E, Broderick SR, Brahmer JR, Swanson SJ, Kerr K, Wang C, Ciuleanu TE, Saylors GB, Tanaka E, Ito H, Chen KN, Liberman M, Vokes EE, Taube JM, Dorange C, Cai J, Fiore J, Jarkowski A, Balli D, Sausen M, Pandya D, Calvet CY, Girard N. Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. N Engl J Med 2022 May 26; 386 (21): 1973-1985. doi: 10.1056/NEJMoa2202170. PMID: 35403841

Felip E, Altorki N, Zhou C, Valiières E, Martinez-Marti A, Rittmeyer A, Chella A, Reck M, Goloborodko O, Belleli R, McNally V, Srivastava MK, Bennett E, Gitlitz BJ, Wakelee HA. Overall survival with adjuvant atezolizumab after chemotherapy in resected stage II-IIIA non-small-cell lung cancer (IMPOWER010): a randomized, multicenter, open-label, phase III trial. Ann Oncol 2023. Oct; 34 (10):907-919. doi: 10.1016/j.annonc.2023.07.001. Epub 2023 Jul 17. PMID: 37467930

Yi-Long Wu, M.D., Masahiro Tsuboi, M.D., Jie He, M.D., Thomas John, Ph.D., Christian Grohe, M.D., Margarita Majem, M.D., Jonathan W. Goldman, M.D., Konstantin Laktionov, Ph.D., Sang-We Kim, M.D., Ph.D., Terufumi Kato, M.D., Huu-Vinh Vu, M.D., Ph.D., Shun Lu, M.D., et al., for the ADAURA Investigators* Osimertinib in Resected EGFR-Mutated Non–Small-Cell Lung Cancer. N Engl J Med 2020; 383:1711-1723.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

- The ultimate objective in the adjuvant setting is to provide additional therapies in patients with high risk for recurrence by eliminating micro-metastatic disease. Current traditional therapies include platinum doublet chemotherapy which were shown in large phase 3 randomized trials (such as ANITA and BR10), which have shown increased survival in the range of 8.8-15%, and further validated in the LACE meta-analysis. However, in spite of the addition of adjuvant chemotherapy, recurrence rates still remain dismally high.

- The use of neoadjuvant chemotherapy and nivolumab (as shown in CHECKMATE 816), or adjuvant atezolizumab in NSCLC tumors with PDL1 ≥ 50%, have shown significant survival benefit in patients with resected stage IB-IIIA disease. However, patients with *ALK* or *EGFR* positive tumors were excluded from the former trial, and derived no benefit adjuvant atezolizumab in the latter. Therefore, patients with *ALK* positive NSCLC would not be candidates for these newer and superior therapies compared to standard chemotherapy alone.

- In the ALINA trial, adjuvant Alectinib provides a therapy that is clearly in line with the benefits seen in the ADAURA trial. It is well documented that *ALK* specific tyrosine kinases provide superior survival benefit as compared to chemotherapy in the metastatic setting. In patients with stage IB-IIIA ALK positive NSCLC, Alectinib provided a clear and overwhelmingly significant DFS advantage over the platinum-doublet control arm (HR 0.24; 95% CI: 0.13-0.45). The comparable survival advantage was seen in all stages. Furthermore, CNS disease relapse was significantly improved with Alectinib (HR 0.22; 95% CI: 0.08-0.58), thus preventing a highly morbid complication that is not adequately addressed by adjuvant chemotherapy.

- In this respect, ALINA compares very favorably to the ADAURA trial. Patients with EGFR positive NSCLC are very similar to patients with *ALK* positive NSCLC, in which they are more likely to be lifelong non-smokers, non-squamous histology and younger age, and have higher risk of CNS metastasis. Adjuvant Osimertinib had a remarkably similar DFS at 24 months (HR 0,2; 95% CI: 0.14-0.30) and reduced risk of CNS relapse (HR 0.18; 95% CI: 0.10-0.33). Ultimately, ADAURA showed a statistically significant OS advantage in the Osimertinib arm (HR 0.49; 95% CI: 0.34-0.70). One significant distinction between the two trials is that chemotherapy was mandated in the ALINA trial while chemotherapy was not in the ADAURA trial. This further supports the impressive DFS results and the importance of adjuvant Alectinib as a high degree of patients with *ALK* positive NSCLC will relapse in spite of adjuvant chemotherapy in this population.

References:

Solomon BJ, Ahn JS, Dziadziuszko R, Barlesi F, Nishio M, Lee DH, Lee JS, Zhong WZ, Horinouchi H, Mao W, Hochmair MJ, de Marinis F, Migliorino MR, Bondarenko I, Lohmann TO, Xu T, Cardona Gavaldon A, Bordogna W, Ruf T, Wu YL. LBA2 ALINA:

Efficacy and safety of adjuvant alectinib versus chemotherapy in patients with early-stage ALK+ non-small cell lung cancer (NSCLC). ESMO meeting. October 2023.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

- Based on the ALINA trial design and results, Alectinib should be the current post-operative management of resected Stage IB-IIIA *ALK* positive NSCLC. In this setting, Alectinib instead of platinum-doublet chemotherapy would be the treatment of choice. A correlation with the ADAURA trial can be made as up to 40% of patients did not receive adjuvant platinum-doublet chemotherapy and still maintained a DFS and OS advantage with Osimertinib. Any potential benefit of Alectinib post adjuvant chemotherapy was not evaluated in this study and therefore, no statistical assumptions about efficacy can be made about this treatment sequence. However, as seen in the ADAURA trial, post-operative platinum-doublet chemotherapy followed by adjuvant Osimertinib was both a feasible and effective sequencing of treatments. This approach would be appealing in patients with higher risk disease (i.e stage II or IIIA).

- Alectinib is currently approved as a first line treatment, or in the second line post Crizotinib failure in patients with metastatic *ALK* positive NSCLC. The mechanism of action of Alectinib as well as other 1st, 2nd or 3rd generation *ALK*-TKIs have been previously demonstrated, with clear anti-tumor activity in *ALK* positive NSCLC.

- In response to the question of whether Alectinib will be used as a first-line treatment, it should be clearly noted that the current indication for Alectinib in this submission would be as an adjuvant therapy. The primary goal is to improve cure and thus, reduce the risk of relapse and the necessity to use additional therapies at all. Alectinib is currently the only *ALK*-TKI to demonstrate improved DFS post resection of *ALK* positive NSCLC.

- If accessible, Alectinib would be the standard of care therapy for patients with resected stage IB-IIIA *ALK* positive NSCLC. Since no other therapy (including chemotherapy) has demonstrated the same magnitude of benefit as Alectinib, it would not be recommended to offer other therapies before Alectinib.

- Two years of adjuvant Alectinib will inevitably shift the paradigm of how patients with resected *ALK* positive NSCLC are managed. At the present time, intravenous platinum-doublet chemotherapy for up to 4 cycles is the only current treatment available for this patient population. If funded, patients would be able to access at treatment that significantly reduces the risk of relapse and diminish the need for further therapies.

References:

Peters S, Camidge DR, Shaw AT, Gadgeel S, Ahn JS, Kim DW, Ou SI, Pérol M, Dziadziuszko R, Rosell R, Zeaiter A, Mitry E, Golding S, Balas B, Noe J, Morcos PN, Mok T. Alectinib versus Crizotinib in Untreated ALK-Positive Non-Small-Cell Lung Cancer. N Engl J Med. 2017 Aug 31; 377 (9); 829-838. doi: 10.1056/NEJMoa1704795. Epub 2017 Jun 6.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

- In the subgroup analysis of the intention to treat population of the ALINA trial, all patients treated with Alectinib derived clinical benefit as it pertains to DFS. As pertains to stratification of factor of stage, stage IB, stage II and IIIA patients all benefitted from adjuvant Alectinib (HR 0.21, 0.24 and 0.25 respectively). Alectinib was also superior to chemotherapy when analyzing all other stratification factors including age, sex, race, smoking status or smoking status. Therefore **al**l patients with resected stage IB-IIIA *ALK*-positive NSCLC will benefit from adjuvant Alectinib irrespective of clinical characteristics.

- Typically, patients who are physically fit for surgery would be able to tolerate Alectinib, so we anticipate minimal drop off of patients who meet eligibility requirements and who undergo complete resection.

- Biomarker testing which includes *ALK* testing, either by immunohistochemistry (IHC) or next-generation sequencing (NGS) is now widely available across Canada. In the context of neoadjuvant chemotherapy and nivolumab, adjuvant Atezolizumab or Osimertinib, it is now common practice to have *ALK* rearrangement status either pre or post-operatively before initiating any of the forementioned therapies, particularly in institutions that have initiated reflex testing. No increase in cost for testing for *ALK* rearrangements is anticipated to accommodate for adjuvant use of Alectinib.
- The issues for underdiagnosis of *ALK* positive NSCLC would be either a failure on the part of clinicians to initiate biomarker testing in centers that do not have a reflex testing procedure in place, or a possible technical issue with the testing procedure itself. However, this latter point would be extremely rare given the exceptional sensitivity rate of *ALK* testing in Canada. AIs, based on the CALK trial with ALK IHC, the companion diagnostic of the FDA was changed from FISH to IHC, demonstrating the exemplary work of the Canadian Pathology Community.
- As previously mentioned, the major endpoint for adjuvant therapies is cure. The term “response to therapy” is therefore not an appropriate outcome for this submission. In terms of patients who are most likely to benefit, this was addressed as the first point of this sub-section.

References:

Melosky B, Blais N, Cheema P et al. Standardizing biomarker testing for Canadian patients with advanced lung cancer. *Curr Oncol*. 2018; 25 (1) 73-82. Doi: 10.3747/co.25.3867.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

- The primary outcome of the ALINA trial to determine whether Alectinib has worked is whether disease recurrence has occurred (Disease Free Survival) and whether there is ultimately an overall survival advantage. The use of DFS as a primary endpoint in the ALINA trial is in line with several major phase 3 adjuvant and neoadjuvant trials such as ADAURA, CHECKMATE 816 and IMPOWER 010. In the clinical setting, there is a growing recognition of the importance of preventing disease recurrence. In the context of *ALK* positive disease, recurrence could involve brain or bone metastases which could lead to detrimental symptoms to patients and decreased quality of life, not to mention the psychological impact of living with now incurable disease. Clinicians and patients alike would both agree that preventing disease recurrence is the only real meaningful endpoint in the early stage setting.

  Furthermore, recurrence of *ALK* positive NSCLC would involve reinitiating treatments, either TKIs or chemotherapy. Survival of patients with *ALK* positive NSCLC has been clearly been demonstrated to be measure in years, meaning patients with metastatic disease would be under treatment for many years with both toxicity and financial issues to now be taken into consideration.

References:

T Mok [1], D R Camidge [2], S M Gadgeel [3], R Rosell [4], R Dziadziuszko [5], D-W Kim [6], M Pérol [7], S-H I Ou [8], J S Ahn [9], A T Shaw [10], W Bordogna [11], V Smoljanović [11], M Hilton [11], T Ruf [11], J Noé [11], S Peters. Updated overall survival and final progression-free survival data for patients with treatment-naive advanced ALK-positive non-small-cell lung cancer in the ALEX study. Ann Oncol. 2020 Aug;31 (8): 1056-1064.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

- The primary reason for drug discontinuation is the presence of disease recurrence. A second reason for discontinuation is drug intolerance/severe complications. In the ALINA trial, less than 4% of patients discontinued due to adverse events.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

This oral medication is suitable in all oncology settings (i.e. academic and community settings). It is specifically appropriate for patients being followed in medical oncology outpatient clinics.

6. Additional Information

N/A

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   No

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for <u>each clinician</u> who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Kevin Jao
Position: Medical Oncologist, Hôpital du Sacré-Cœur
Date: April 30th, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Bristol-Myers Squibb – Advisory Role	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Barb Melosky
Position: Medical Oncologist, BC Cancer
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis	Advisory Board	☒	☐	☐	☐
Roche	Advisory Board	☒	☐	☐	☐
Merck	Advisory Board	☒	☐	☐	☐
BMS	Advisory Board	x			
AstraZeneca	Advisory Board	x			
Pfizer	Advisory Board	x			
GSK	Advisory Board	x			
Bayer	Advisory Board	x			
Amgen	Advisory Board	x			
Jazz	Advisory Board	x			

New or Updated Declaration for Clinician 3	
Name	*David J. Stewart*
Position	Professor of Medicine, University of Ottawa and The Ottawa Hospital
Date	April 30, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Merck Canada 2021, 2023	☒	☐	☐	☐
AstraZeneca Canada 2021, 2023	☒	☐	☐	☐
Abbvie Canada 2021, 2022, 2023	☒	☐	☐	☐
Canadian Agency for Drugs and Technologies in Health 2021	x			
Amgen Canada 2022	x			

Declaration for Clinician 4

Name: Dorothy Lo
Position: Medical oncologist
Date: April 30, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Merck	X			
BMS	x			
Sanofi	x			
Novartis	x			
astellas		x		
Eisai	x			
Astra Zeneca	x			

* Place an X in the appropriate dollar range cells for each company.

New or Updated Declaration for Clinician 5	
Name	*Dr. Geoffrey Liu*
Position	*Medical Oncologist*
Date	April 30, 2024

☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Pfizer	☐	☒	☐	☐
Novartis	☒	☐	☐	☐
Anheart	☒	☐	☐	☐
Takeda	X			
AstraZeneca		X		
Jazz	X			
Roche	X			
Johnson & Johnson	X			
EMD Seron	X			
Merck	X			

Declaration for Clinician 6

Name: NATHALIE DAABOUL
Position: Hematologist-Oncologist, Université de Sherbrooke
Date: April 30, 2024

X **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Amgen	x			
AstraZeneca	x			

BMS	x			
Eisai	x			
Jazz	x			
Merck	x			
Novartis	x			
Pfizer	x			
Sanofi	x			
Takeda	x			
Taiho	x			

* Place an X in the appropriate dollar range cells for each company.

New or Updated Declaration for Clinician 7	
Name	*Dr. Alison Wallace*
Position	*Assistant Professor Department of Surgery, Division of Thoracic Surgery and Department of Pathology, Dalhousie University. Thoracic Surgeon QEII HSC, Halifax. NS.*
Date	April 30, 2024
-☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Confli-ct of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Merck	☒	☐	☐	☐
Bristol Myers Squibb	☒	☐	☐	☐
AstraZeneca	☒	☐	☐	☐

New or Updated Declaration for Clinician 8	
Name	*Rosalyn A. Juergens*
Position	*Associate Professor of Oncology – McMaster University*
Date	April 30, 2024

☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Amgen	☐	☒	☐	☐
AstraZeneca	☐	☐	☒	☐
Bayer	☐	☐	☒	☐
BMS	☐	☐	☒	☐
Johnson and Johnson	☐	☒	☐	☐
Lilly	☒	☐	☐	☐
Jazz	☐	☒	☐	☐
Merck	☐	☒	☐	☐
Novartis	☐	☒	☐	☐
Pfizer	☒	☐	☐	☐
Roche	☐	☐	☒	☐
Sanofi	☐	☒	☐	☐
Takeda	☐	☒	☐	☐

New or Updated Declaration for Clinician 9

Name	*Quincy Chu*
Position	*Medical Oncologist, Cross Cancer Institute*
Date	April 30, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Abbvie	☒	☐	☐	☐

Amgen	X			
Astra Zeneca	☒	☒	☐	☐
AnHeart	☒	☐	☐	☐
BMS	☒	☐	☐	☐
Boehringer Ingelehim	☒	☐	☐	☐
Eli Lilly	☒	☐	☐	☐
Jazz	☒	☐	☐	☐
Johnson and Johnson	☐	☒	☐	☐
Merck	☒	☐	☐	☐
Pfizer	X			
Novartis	☒	☐	☐	☐
Roche	☒	☒	☐	☐
Sanofi	☒	☐	☐	☐
Takeda	☒	☐	☐	☐

Declaration for Clinician 10

Name: Stephanie Snow
Position: Professor Dalhousie University, Medical Oncologist QEII Health Sciences Centre, Halifax, NS
Date: April 30, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 10

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
AstraZeneca			X	
Astellas	X			
BMS		X		
Taiho	X			
Roche			X	
Merck		X		
GSK	X			
Janssen	X			
Pfizer	X			

Sanofi	X			
Knight	X			
Lilly	X			
Takeda	X			

* Place an X in the appropriate dollar range cells for each company.

New or Updated Declaration for Clinician 11	
Name	*Dr. Susanna Cheng*
Position	*Medical Oncologist, Associate Professor, Sunnybrook Health Sciences Centre, University of Toronto*
Date	April 30, 2024
X	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Merck	X	☐	☐	☐
BMS	X	☐	☐	☐
Janssen	X	☐	☐	☐
Roche	X			

New or Updated Declaration for Clinician 12	
Name	*Biniam Kidane*
Position	*Associate Professor, Dept of Surgery, University of Manitoba*
Date	April 30, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
AstraZeneca	☐	☐	☒	☐
Merck	☒	☐	☐	☐

Roche	☐	☒	☐	☐
Bristol Myers Squibb	☒	☐	☐	☐
Medtronic	☒	☐	☐	☐

New or Updated Declaration for Clinician 13	
Name	Michela Febbraro
Position	Medical Oncologist, Algoma District Cancer Program
Date	April 30, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
AstraZeneca	☐	☒	☐	☐

New or Updated Declaration for Clinician 14	
Name	*Dr. Ronald Burkes*
Position	*Medical Oncologist, Mount Sinai Hospital*
Date	April 30, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
AZ / Pfizer	☒	☐	☐	☐
Merck / Taiho / Takeda / Amgen	☒	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Declaration for Clinician 15

Name: Dr. Shaqil Kassam
Position: Medical Oncologist, Southlake Regional Hospital
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 15

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Roche	x			
Merck	x			
BMS	x			
Takeda	x			
Novartis	x			
Ipsen	x			
Sanofi	x			
Pfizer	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 16

Name: Dr Sunil Yadav
Position: Medical Oncologist, Saskatoon Cancer Centre
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 12: Conflict of Interest Declaration for Clinician 16

Bristol-Myers Squibb	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	
Bristol-Myers Squibb	Advisory Board	☒	☐	☐	
Astra Zeneca	Advisory Board and Speaking	☒	☐	☐	☐
Merck	Advisory Board and Speaking	☐	☐	☒	☐
Roche	Advisory Board and Speaking	☐	☒	☐	☐

Takeda	Advisory Board and Speaking	☒	☐	☐	☐

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 17

Name: Dr. Zhaolin Xu
Position: Pathologist, QEII Health Sciences Centre
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 17

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
AstraZeneca	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 18

Name: Dr Nicole Bouchard
Position: Respirologist, Sherbrooke University Hospital
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 18

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Astra Zeneca	Advisory Role/Conference	☒	☐	☐	☐
Bristol-Myers Squibb	Advisory Role/Research	☒	☐	☐	☐
Merck	Advisory Role /Research/Conference	☒	☐	☐	☐
Bayer	Advisory Role	☒	☐	☐	☐
Pfizer	Conference/Research	☒	☐	☐	☐
Roche	Advisory Role	☒	☐	☐	☐

Declaration for Clinician 19

Name: Dr Randeep Sangha
Position: Medical Oncologist, Cross Cancer Institute
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 9: Conflict of Interest Declaration for Clinician 19

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 20

Name: Dr. Mark Vincent
Position: Medical Oncologist, London Regional Cancer Centre
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 20

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
			☐	☐	☐

Declaration for Clinician 21

Name: Dr. Mahmoud Abdelsalam
Position: Medical Oncologist, Horizon Health Network
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 21

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
BMS	Advisory role, Honoraria and travel grants	☐	☒	☐	☐

Declaration for Clinician 22

Name: Dr. David Dawe
Position: Medical Oncologist, CancerCare Manitoba
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 8: Conflict of Interest Declaration for Clinician 22

Name of Organization	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AstraZeneca	Advisory boards	☒	☐	☐	☐
Merck	Advisory Boards	☒	☐	☐	☐
AstraZeneca	Research Grant	☐	☐	☒	☐
Boehringer-Ingelheim	Honoraria	☒	☐	☐	☐

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 23

Name: Dr Catherine Labbé
Position: Head of Respiratory Medicine Service, Université de Laval
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 13: Conflict of Interest Declaration for Clinician 23

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Amgen	X			
Astra Zeneca		X		
Brystol-Myers Squibb	X			
Jazz Pharmaceuticals	X			
LEO Pharma	X			
Merck	X			
Pfizer	X			
Roche	X			
Sanofi Genzyme	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 24

Name: Silvana Spadafora
Position: Medical Oncologist, Algoma District Cancer Program
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 24

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Astra Zeneca		X		
Merck		X		
Novartis		X		

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 25

Name: Normand Blais
Position: Medical Oncologist, CHUM Cancer Center, Montreal
Date: April 30, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 25

Bristol-Myers Squibb	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen	Advisory Board and Honoraria	☒	☐	☐	☐
Astra Zeneca	Advisory Board and Honoraria	☒	☐	☐	☐
Beigene	Advisory Board and Honoraria	☒	☐	☐	☐
Bayer	Advisory Board and Honoraria				
Bristol-Myers Squibb	Advisory Board and Honoraria	☒	☐	☐	☐
EMD Serono	Advisory Board and Honoraria	☒	☐	☐	☐
Eli Lilly	Advisory Board and Honoraria				
Ipsen	Advisory Board and Honoraria				
Janssen	Advisory Board and Honoraria				
Merck	Advisory Board and Honoraria	☒	☐	☐	☐
Novartis	Advisory Board and Honoraria	☒	☐	☐	☐
Pfizer	Advisory Board and Honoraria	☒	☐	☐	☐
Roche	Advisory Board and Honoraria	☒	☐	☐	☐
Sanofi	Advisory Board and Honoraria	☒	☐	☐	☐
Servier	Advisory Board and Honoraria				
Astra Zeneca	Research Funding to institution	☐	☐	☐	☒

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 26

Name: Dr Jeffrey Rothenstein
Position: Medical Oncologist, Lakeridge Health
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 26

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Roche	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 27

Name: Dr. Paul Wheatley-Price
Position: Associate Professor, Department of Medicine, University of Ottawa; Staff Medical Oncologist at The Ottawa Hospital; Immediate Past President and Medical Advisory Committee Member of Lung Cancer Canada
Date: April 30, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 27

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Astra Zeneca		X		
Abbvie	X			
GSK	X			
Amgen	X			
Merck	X			
Roche	X			
BMS	X			
Lilly	X			
Novartis	X			
Sanofi	X			
Janssen	X			
Jazz Pharmaceuticals	X			
Guardant	X			
Bayer	X			

Takeda	X			

Declaration for Clinician 28

Name: Dr. Callista Phillips
Position: Medical Oncologist, Hamilton Health Sciences Center
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 28

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Astra Zeneca	Advisory Board Stage 3 NSCLC	☒	☐	☐	☐
Bayer	National Consultancy meeting and Train the Trainer- Larotrectenib in NTRK fusion positive cancers	☒	☐	☐	☐
Roche	Lung regional Consultancy meeting	☒	☐	☐	☐

Declaration for Clinician 29

Name: Dr. Cheryl Ho
Position: Medical Oncologist, BC Cancer
Date: April 30, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 29

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Bayer	Advisory role	☒	☐	☐	☐
Roche	Advisory role, travel, research grants	☐	☐	☐	☒

Declaration for Clinician 30

Name: Lacey Pitre

Position: Medical Oncologist, Systemic Therapy Lead - Northeast Region, CCO/Ontario Health
Date: April 30, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician30

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis Ribbon Program 2018	X			
MERCK Oncology Speaker's honoraria 2017	X			
EMD Serono Speaker's honoraria 2018	X			
MERCK Oncology Speaker's honoraria 2021	X			
Astra Zeneca Speaker's honoraria 2021	X			
Astra Zeneca Speaker's honoraria 2022	X			
Fuse Health Advisory Board 2017	X			
Novartis Advisory Board 2018	X			
Astella's Oncology Advisory Board 2016	X			

* Place an X in the appropriate dollar range cells for each company.