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Drug Utilization Study

Use of Cancer Therapies for Advanced Non–Small Cell Lung Cancer With an Oncogenic Driver Mutation

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Key Messages

In recent years, treatment strategies for non–small cell lung cancer (NSCLC) have expanded beyond standard chemotherapy.

Tumours with specific oncogenic driver mutations respond well to therapies that target the gene products of these mutations. These treatments are called targeted therapies.

However, it is unclear whether patients with advanced NSCLC with specific oncogenic mutations can benefit from treatments to augment their immune response, called immune checkpoint inhibitors (ICIs), after they have already received targeted therapies followed by chemotherapy.

This study aimed to understand the current treatment patterns for patients with advanced NSCLC with actionable driver mutations and to determine the feasibility of conducting a study to compare the effectiveness of ICIs and single-agent chemotherapy among patients who had received driver mutation-targeted therapies as their first treatment.

We used population-based data from Ontario, British Columbia, and Alberta from the Canadian Cancer Real-world Evaluation (CCRE) Platform, and additional data from patients captured in the Personalize My Treatment registry who were treated in Quebec, New Brunswick, and Nova Scotia.

To infer treatment sequence among patients with advanced NSCLC, we tracked up to 4 treatment exposures based on drug name. We found that targeted therapy was the most frequently used treatment in the second and third exposures for all included provinces, but that it decreased in the fourth exposure as the use of single-agent chemotherapy and ICIs increased.

The volume of patients who received ICIs for their third exposure was too small to support a comparative study examining the effectiveness of ICIs against other treatment options in this setting.

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Abbreviations

CCRE	Canadian Cancer Real-world Evaluation
DIN	drug identification number
ICD-O-3	International Classification of Diseases for Oncology, Third Edition
ICI	immune checkpoint inhibitor
IPCW	inverse-probability-of-censoring weighting
NSCLC	non–small cell lung cancer
PD-1	programmed cell death 1 protein
PD-L1	programmed cell death 1 ligand 1
PMT	Personalize My Treatment
SD	standard deviation

Introduction and Rationale

Background

Condition

Lung cancer is the most frequently diagnosed cancer in Canada and the leading cause of cancer-related deaths,[1] with more than 31,000 incident diagnoses (15,800 in females and 15,300 in males) and 20,600 disease-related deaths (9,800 in females and 10,800 in males) in 2023.[1] The adjusted 5-year net survival estimate in Canada for all forms of lung cancer is 22%,[1] and the overall 5-year survival for patients with NSCLC is approximately 25%. Survival decreases to 9% for patients with stage IV disease.[2] Smoking is an established risk factor for developing lung cancer and accounts for more than 72% of newly diagnosed cases in Canada.[1,3]

Tumour Mutations and Treatments

The treatment landscape for patients with advanced stage NSCLC has transformed in recent years through expansion of molecular testing and addition of targeted therapies and immunotherapy.

The expression of genome driver mutations in tumours is a root factor for tumour growth in some cancers. In recent years, several drug therapies have been developed to target these mutations. Predictive drivers identified in recent years include *EGFR* gene mutations, *ROS1* and *RET* fusions, *KRAS* G12C mutation, *ALK* fusions, and *BRAF* V600E mutation. Prevalence estimates from studies show that about 1% to 2% of NSCLC cases are *RET* fusion positive,[4] 1% are *ROS1* fusion positive,[5] 17% have activating mutations in the *EGFR* gene,[6] and 5% have an *ALK* positive rearrangement.[7,8] These mutations are typically mutually exclusive, and thus a single mutation is likely driving cancer progression.[9] Tumours bearing specific mutations respond well to treatment using targeted therapies; therefore, such treatments are widely recommended in the early settings for patients who have tumours bearing actionable driver mutations.

ICIs such as programmed cell death 1 protein (PD-1) or programmed cell death 1 ligand 1 (PD-L1) inhibitors act by promoting the immune response toward the tumour and have demonstrated benefit for the treatment of stage IV NSCLC in the first-line or second-line setting. Recent evidence suggests that treatment with ICIs may be less effective for tumours bearing certain *EGFR* mutations or *ALK*, *ROS1*, or *RET* rearrangement, while demonstrating efficacy in NSCLC harbouring *KRAS*, *MET* or *BRAF* mutations.[9-11] It is hypothesized that low immunogenicity and a low tumour mutation burden are associated with lower response to ICI therapy. These features have been associated with NSCLC harbouring genome driver mutations. As such, the role of ICIs in the treatment of NSCLC expressing genome driver mutations is controversial.

Purpose of This Report

The purpose of this report is to describe the real-world utilization and sequencing of treatment regimens for patients who received first-line driver mutation–targeted therapies and to determine the number of patients with advanced NSCLC bearing actionable driver mutations who receive ICI or single-agent chemotherapy in subsequent lines of therapy.

Policy Issue

Currently, ICI monotherapy using atezolizumab, nivolumab, or pembrolizumab is indicated for the treatment of advanced or metastatic NSCLC after chemotherapy, regardless of mutational status. Among patients with tumours bearing actionable mutations, ICI use must occur after treatment with targeted therapy and chemotherapy.[12-14] However, it is unclear whether treatment with ICIs in this setting (or beyond) affords any substantial benefits in this patient population. It is also uncertain as to how this treatment option compares with alternative treatment strategies such as single-agent chemotherapy using docetaxel or pemetrexed. Thus, jurisdictions seek to understand current treatment patterns for patients who have NSCLC with actionable driver mutations and, if possible, the comparative effectiveness of subsequent ICI therapy versus subsequent single-agent chemotherapy.

Policy Questions

1. How should ICI monotherapies following chemotherapy be funded in patients with advanced or metastatic NSCLC harbouring actionable driver mutations?
2. Should all chemotherapy options be exhausted before funding ICI monotherapy?

Research Question

What subsequent treatments are being used among patients with advanced NSCLC following receipt of first-line targeted therapy?

Objectives

The objectives of this study were to:

1. conduct a treatment pattern analysis for patients with advanced NSCLC who received first-line targeted therapy
2. use the results obtained from the treatment pattern analysis comprising objective 1 to determine the feasibility of a future observational study examining the comparative effectiveness of subsequent ICI therapy versus subsequent single-agent chemotherapy.

Main Take-Aways

ICI monotherapy is currently approved and funded for the treatment of advanced NSCLC with actionable driver mutations after patients have received targeted therapies as well as chemotherapy. However, it remains unclear if ICI monotherapy is beneficial in this setting. Our goal is to analyze real-world treatment patterns for patients with advanced NSCLC with actionable driver mutations and determine the feasibility of conducting a study to compare the effectiveness of subsequent ICI and subsequent single-agent chemotherapy in this population.

Methods

Population and Setting

We included adults aged 18 years and older who received first-line targeted therapy for the treatment of metastatic NSCLC in Ontario, Alberta, and British Columbia (CCRE Platform sites) and all adult participants from the Personalize My Treatment (PMT) registry in Quebec, New Brunswick, and Nova Scotia (Exactis Innovation sites). As detailed data on driver mutation status were unavailable for the majority of the study cohort, we used exposure to first-line targeted therapy as a proxy to define a cohort of patients with NSCLC who carried actionable driver mutations.

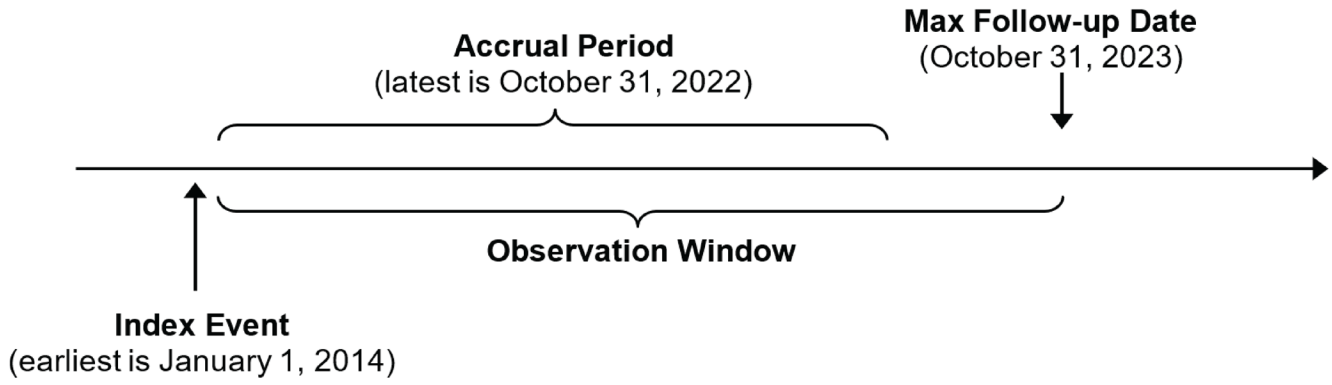
Study Design

We used a retrospective cohort design to conduct this study. Our study period differed between provinces due to differences in data availability and drug funding dates across Canadian jurisdictions. For each CCRE province, the accrual window extended from the earliest public funding date of driver mutation–targeted first-line therapy to the most recent available cancer registry data (Figure 1). Patients entered the cohort on the first dispensing date of driver mutation–targeted first-line therapy (afatinib, alectinib, brigatinib, ceritinib, crizotinib, entrectinib, erlotinib, gefitinib, or osimertinib); drug identification numbers (DINs) are available in Table 7. This date is defined as the index date, and patients were followed until death or censoring. Patients were censored if they were alive at the end of the observation period, or if they were diagnosed with a new primary cancer during the follow-up period. The accrual window was January 1, 2014, to October 31, 2022, for Ontario; January 1, 2014, to September 30, 2022, for Alberta; and October 1, 2010, to December 31, 2021, for British Columbia. The observation period extended to the most recent available drug dispensing data and mortality data (October 31, 2023, for Ontario; December 31, 2023, for Alberta; and September 30, 2023, for British Columbia).

We used a look-back period from the date of NSCLC diagnosis to index date, to apply exclusion criteria and define covariates for treatment history. In cases where patients had more than 1 recorded NSCLC cancer diagnosis, we used the last diagnosis before the patient's index date as the primary diagnosis.

We replicated this retrospective cohort study using patients in the PMT registry, accruing patients from April 1, 2011, to December 31, 2022, and observed each patient from the index date up to death or censoring (maximum follow-up date: December 31, 2023).

Figure 1: Study Design Diagrams for Ontario



Max = maximum.

Figure 2: Study Design Diagram for Alberta

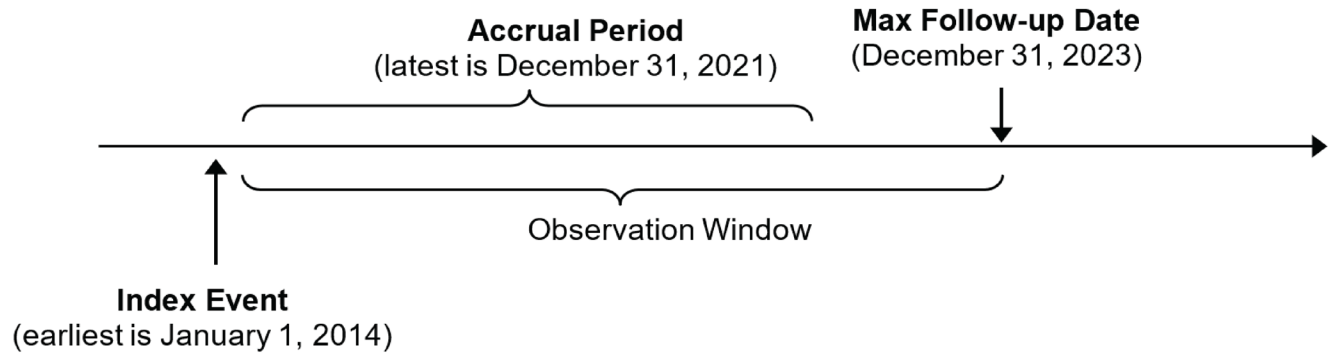


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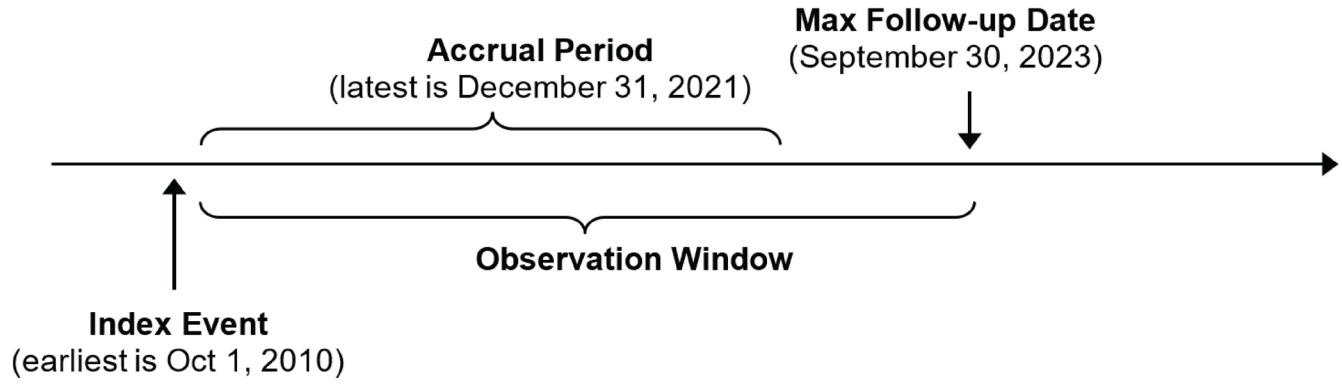
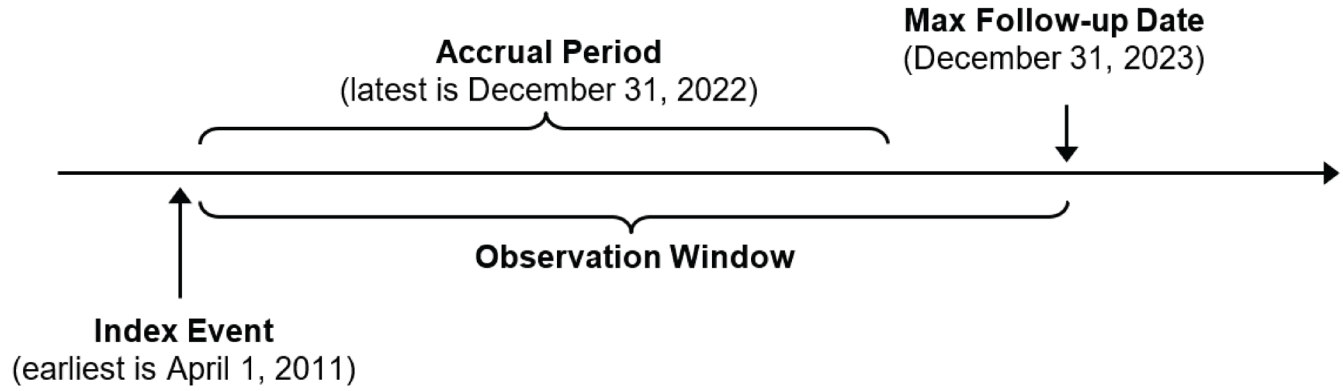
Figure 3: Study Design Diagram for British Columbia



Max = maximum.

Figure 4: Study Design Diagram for PMT Cohort (Quebec, Nova Scotia, New Brunswick)



Max = maximum.

Eligibility Criteria

Patients were included in the cohort if their first dispensing record for the targeted therapies of interest (afatinib, alectinib, brigatinib, ceritinib, crizotinib, entrectinib, erlotinib, gefitinib, or osimertinib) occurred during the accrual period, and if they had a previous diagnosis of lung cancer (defined as International Classification of Diseases for Oncology, Third Edition [ICD-O-3] site codes C34.0 to 34.9)

Patients were excluded based on the following criteria:

- Their primary lung cancer had a histology code unrelated to NSCLC (refer to Table 8) for histology codes included in the study.
- They were diagnosed with another primary cancer that is not lung cancer in the 5 years before their primary NSCLC diagnosis.

- Exception in Ontario: Patients with a brain cancer diagnosis within 30 days of their primary NSCLC diagnosis were not excluded. Consultation with clinical and data experts suggested these were likely brain metastases related to primary NSCLC.
- They were diagnosed with a new cancer between their primary NSCLC diagnosis and index date.
- They received systemic therapy for metastatic disease before their index date. In cases where treatment indication was not available from the data, we defined advanced disease as exposure to treatments **outside** of the following adjuvant therapies: vinorelbine, pemetrexed, or paclitaxel in combination with platinum doublet therapy (cisplatin or carboplatin), occurring within 120 days after primary lung excision or adjuvant radiation.
  - Adjuvant radiation is defined as radiation that lasts 4 or more weeks, or radiation given to patients with stage I to III disease.
- Their index date occurred before the jurisdictional public funding date for their initial targeted therapy agent.
- They were younger than 18 years of age at diagnosis.
- They had missing or invalid values for personal identification number, age, sex, and death date (i.e., death before index date).
- They were nonresidents at index date.
- British Columbia only: Their diagnosis date was before January 1, 2002. Diagnoses in British Columbia were limited to 2002 and beyond, due to major changes in surgery data structure and availability of records before 2002.

Data Sources

CCRE Platform sites (Ontario, Alberta, and British Columbia) used population-based administrative data to define the study cohort, obtain clinical and demographic characteristics, and define longitudinal drug utilization and mortality outcomes. Data sources included provincial cancer registries, systemic therapy dispensing records and/or claims, and other records of health services utilization, summarized in Table 9. The Ontario patient cohort consisted of those who received systemic therapy funded by the Ontario Drug Benefit provincial drug insurance program (individuals 65 years and older, those who live in long-term care facilities or receive home care, and those who have high medication costs relative to their income), as well as those who received systemic therapy through a regional cancer centre in Ontario or an outpatient clinic that receives funding through the Systemic Therapy – Quality Based Program. British Columbia and Alberta provide universal public coverage for systemic therapy drugs on their formularies. Dispensing records in those provinces include all publicly funded systemic therapy, regardless of route of administration (IV versus oral or take-home), location of care, or patient age. The Exactis Innovation sites used data from the PMT registry. This is an active registry developed and maintained by Exactis Innovation that includes clinical and molecular patient data for patients with cancer at 16 sites throughout Canada.[15]

CCRE's access to data in Ontario is governed under section 45 of the province's Personal Health Information Protection Act and is not subject to additional review by an ethics review board. Access to data in Alberta is

governed under the province's Health Information Act. The Alberta site of the CCRE Platform was approved by the Health Research Ethics Board of Alberta – Cancer Control. Data access was approved by the Alberta Data Stewards. The British Columbia site of the CCRE Platform was approved by the University of British Columbia – BC Cancer Research Ethics Board. Data access was approved by the British Columbia Cancer Data Stewards. Ethics approval for the PMT registry was provided by the Integrated University Health and Social Services Centres (CIUSSS) West-Central Montréal Research Ethics Board (Research Ethics Board number: MP-05-2016-321). Based on privacy policies to protect patient confidentiality set by each province, we only reported values greater than 5 in Ontario and British Columbia, and values greater than 9 in Alberta.

Key Study Measures

Exposure

The exposure of interest for this study was use of first-line driver mutation–targeted therapy. This was defined as the initial targeted therapy agent dispensed (afatinib, alectinib, brigatinib, ceritinib, crizotinib, entrectinib, erlotinib, gefitinib, or osimertinib).

Covariates of Interest

Covariates of interest included patient and disease characteristics, and treatment history. Patient characteristics included age at index date, sex, and neighbourhood income quintile (Ontario and Alberta only). Disease characteristics included stage at diagnosis, year of diagnosis, tumour histology (categorized as adenocarcinoma, large cell carcinoma, squamous cell carcinoma, or other), and time (in days) between diagnosis and index date. Prior treatments of interest included lung excision (Canadian Classification of Health Intervention codes in Table 10), prior adjuvant chemotherapy, radiotherapy to chest, and radiotherapy to brain.

Outcomes of Interest

The primary outcome of interest was receipt of systemic therapy after first-line driver mutation–targeted therapy. Information on disease progression or line of therapy was not available in the data; therefore, treatment exposure (constructed using systemic therapy dispensing records in each province) was used as proxy for line of therapy. The start of a new treatment exposure was defined as a change in treatment protocol, for the study sites where protocol identifiers (for example, a unique protocol code or name) were available in the data, or a change in dispensed systemic therapy agent if protocol identifiers were not available.

Treatment exposures were categorized by class of therapy (Table 1), and exposure sequence number, to a maximum of 4 separate exposures. We also constructed indicators for death or censoring following each treatment exposure.

Table 1: Definition of Treatment Classes

Class of therapy	Definition
Platinum doublet	Cisplatin or carboplatin **with** gemcitabine, vinorelbine, pemetrexed, paclitaxel, or docetaxel
ICIs	Atezolizumab, pembrolizumab, or nivolumab, with no concurrent therapy
Single-agent chemotherapy	Gemcitabine, vinorelbine, pemetrexed, paclitaxel, or docetaxel
Targeted therapy	Afatinib, alectinib, brigatinib, ceritinib, crizotinib, entrectinib, erlotinib, gefitinib, or osimertinib
Other	Any other treatment exposure not defined in this table, including clinical trials

ICI = immune checkpoint inhibitor.

We also examined incident utilization of ICI and single-agent chemotherapy, at any point following first-line targeted therapy. Variables included ICI agent (atezolizumab, pembrolizumab, or nivolumab), year of first ICI, time (in days) between index date and first dispensing date of ICI, single-agent chemotherapy (gemcitabine, vinorelbine, pemetrexed, paclitaxel, or docetaxel), year of first single-agent chemotherapy, time (in days) between index date and first dispensing date of single-agent chemotherapy, and indicators for use of prior platinum doublet between targeted therapy and ICI or chemotherapy. Among the patients who received ICI, we also created an indicator for prior single-agent chemotherapy, and vice versa.

Analyses

We summarized cohort characteristics and incident use of first-line targeted therapy agents using frequencies and proportions, by study site and for a combined total, and using mean and standard deviation for continuous variables.

The sequence of treatment exposures received by the study cohort was summarized graphically using Sankey diagrams. Treatment sequence and outcomes (death and censoring) were also summarized using frequency counts and percents, conditional on each new treatment exposure. To account for censoring, we calculated weighted frequency distributions, using inverse-probability-of-censoring weighting (IPCW) at the start of each new treatment exposure.[16]

We conducted 3 subgroup analyses in this study. First, we limited the cohort to patients receiving either ICI or single-agent chemotherapy at any point during the follow-up period. Characteristics of ICI or chemotherapy recipients were summarized in a table by study site and combined total. Additionally, we conducted a subgroup analysis to characterize the sequence of treatment exposures after publicly funded ICIs for NSCLC became available (contemporary era). The cohort was limited to patients whose index date was on or after the first public funding date for ICI in each study site (March 1, 2017, in Ontario; April 1, 2017, in Alberta; March 1, 2017, in British Columbia; and March 15, 2017, for the PMT cohort). We summarized treatment sequence and outcomes using frequency distributions and Sankey diagrams, with IPCW to account for censoring. Among this group of patients who started first-line targeted therapy in the contemporary era, we also examined the breakdown of targeted therapies by drug name for those who received these drugs in the second exposure to further understand potential drug switches due to toxicity. Given that we used treatment exposure as a proxy for lines of treatment, it is possible that some consecutive sequences of the same drug type (e.g., gefitinib to afatinib) may represent a therapy switch due to toxicity

rather than treatment progression. In this subgroup analysis, we reported first and second exposure to osimertinib separately from other *EGFR*-targeted treatments due to the higher expected volume of use for this drug in the contemporary era, as well as the fact that osimertinib is funded as a second-line treatment in Canada.

Results

Population Characteristics

Main Take-Aways

This study presents data from Ontario, British Columbia, and Alberta, as well as 3 provinces captured in the PMT registry (Quebec, New Brunswick, and Nova Scotia). The total cohort consists of 4,222 patients who received publicly funded targeted therapy as first-line treatment for NSCLC. On average, patients were in their mid-60s when starting targeted therapy, and the majority of patients were female.

This study examined patients who received first-line targeted therapy for the treatment of NSCLC. Our cohort included a total of 4,222 patients across 6 Canadian jurisdictions: 2,196 in Ontario, 474 in Alberta, 1,462 in BC, and 90 in the PMT registry (which captured patients in Quebec, New Brunswick, and Nova Scotia for this study). The mean age was 66.1 years (SD = 12.7) for the overall cohort, and the majority of patients of were female (n = 2,683 [63.5%] for females and n = 1,539 [36.5%] for males) (Table 3).

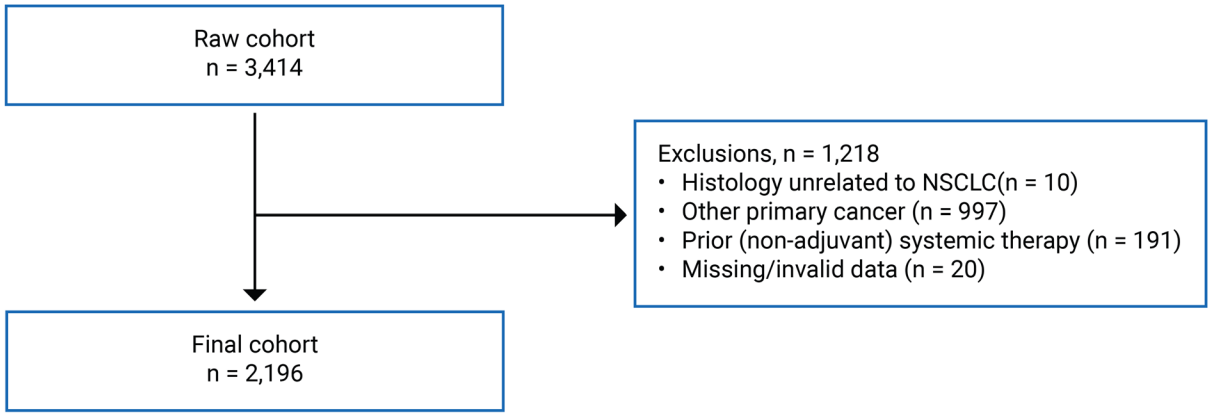
In Ontario, the mean age was 69.4 years (SD = 11.6) and almost two-thirds of the group were female (n = 1,393 [63.4%] for females and n = 803 [36.6%] for males). Income quintile was well distributed across the cohort, with approximately 20% of the cohort in each quintile. The mean time in days from diagnosis to the start of first-line targeted therapy was 189.2 (SD = 448.0), and the majority of patients were diagnosed at stage IV (n = 1,435; 65.4). Most patients had tumours identified as adenocarcinoma in histology (n = 1,826; 83.2%). In terms of prior treatments, 11.3% (n = 248) had a prior lung resection, 3.8% (n = 83) had adjuvant chemotherapy, 30.4% (n = 667) had prior radiotherapy to the chest, and 4.3% (n = 95) had prior radiotherapy to the brain. Gefitinib was the most commonly used first-line targeted therapy (n = 862; 39.2%), followed by osimertinib (n = 711; 32.2%).

In Alberta, the mean age of the population was 64.0 years (SD = 13.0), and more than half were female (n = 289 [61.0%] for females and n = 185 [39.0%] for males). On average, it took 259.0 days (SD = 643.0) for patients to receive first-line targeted therapy after diagnosis, and more than three-quarters of the cohort were diagnosed with stage IV disease (n = 360; 75.9%). Almost 90% of the group had a tumour histology of adenocarcinoma (n = 415; 87.5%). The results show that 14.1% (n = 67) of Alberta patients in this cohort had a prior lung resection, 61.1% (n = 29) had prior adjuvant chemotherapy, and 4.2% (n = 20) had prior radiotherapy to the chest. Afatinib was the most popular first-line targeted therapy in this cohort (n = 180; 38.0%), followed by osimertinib (n = 707; 32.2%).

In British Columbia, the cohort had a mean age of 67.9 years (SD = 12.2) and most were female (n = 946 [64.7%] for females and n = 516 [35.3%] for males). The average number of days between NSCLC diagnosis and start of targeted therapy was 184.7 days (SD = 363.7). Almost three-quarters of this cohort were diagnosed at stage IV (n = 1,071; 73.3%) and the majority of the group had a tumour histology of adenocarcinoma (n = 1,297; 88.7%). Among patients in British Columbia, prior lung resection occurred in 11.4% (n = 166), prior adjuvant chemotherapy in 4.9% (n = 72), prior radiotherapy to the chest in 20.7% (n = 302), and prior radiotherapy to the brain in 11.7% (n = 171). More than half of the group started targeted therapy using gefitinib (n = 739; 50.6%), followed by afatinib (n = 273; 18.7%) and osimertinib (n = 264; 18.1%).

In the PMT cohort consisting of patients from Quebec, New Brunswick, and Nova Scotia, the mean age was 63.0 years (SD = 14.0) and more than half of the group were female (n = 55 [61.0%] for females and n = 35 [38.9%] for males). The average time between diagnosis and start of first-line targeted therapy was 271.0 days (SD = 604.0), and just under two-thirds of the PMT cohort were diagnosed with stage IV NSCLC (n = 58; 64.5%). Almost one-quarter of the PMT cohort had a prior lung resection (n = 22; 24.5%), 7.7% (n = 7) had prior adjuvant chemotherapy, 24.5% (n = 22) had prior radiotherapy to the chest, and 10.0% (n = 9) had prior radiotherapy to the brain. Osimertinib was the most commonly used targeted therapy in the first line for this cohort (n = 46; 51.1%), followed by afatinib (n = 16; 17.8%).

Figure 5: Cohort Creation and Exclusion Criteria for Ontario



NSCLC = non–small cell lung cancer.

Figure 6: Cohort Creation and Exclusion Criteria for British Columbia

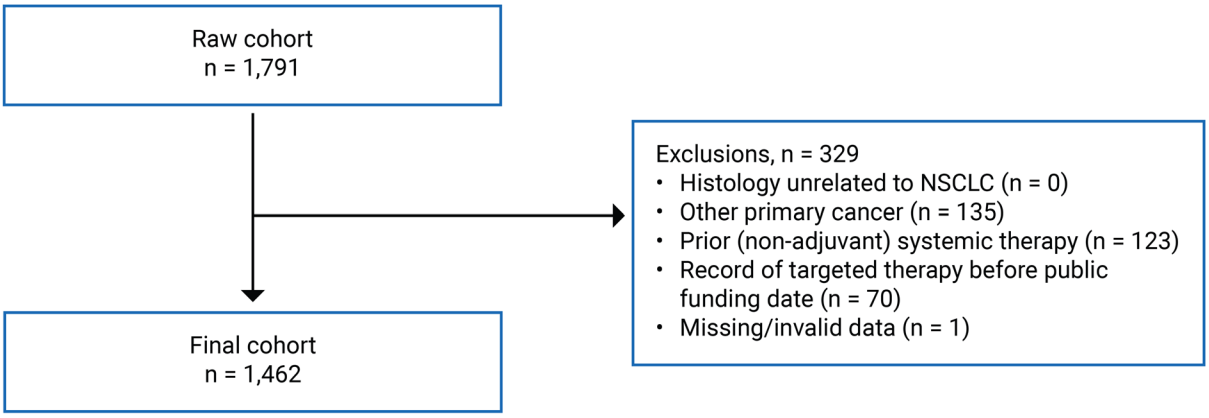


Figure 7: Cohort Creation and Exclusion Criteria for Alberta

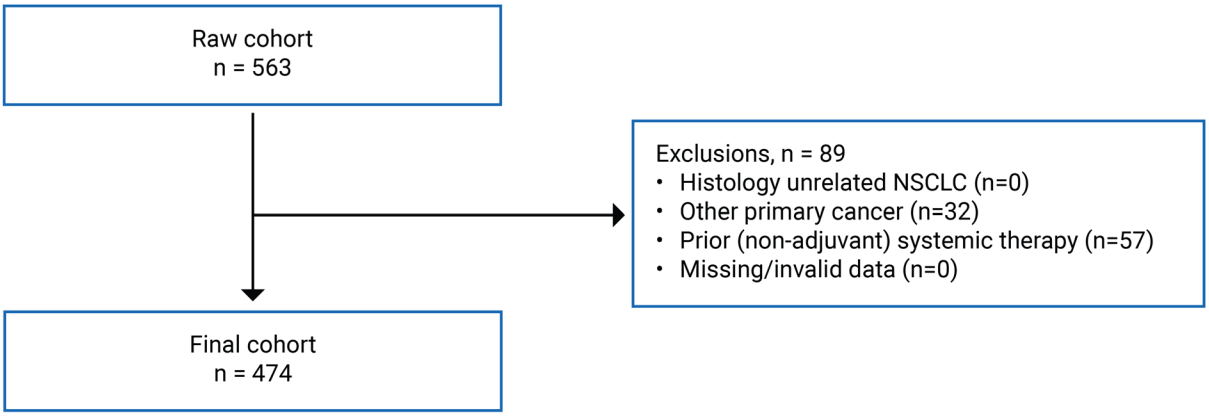


Figure 8: Cohort Creation and Exclusion Criteria for the PMT Registry

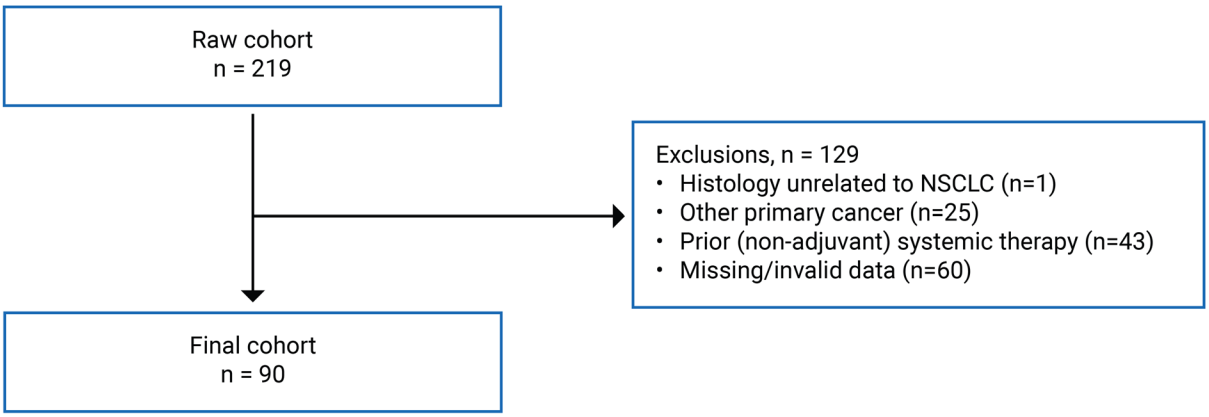


Table 2: Cohort Characteristics at Index Date by Study Site

Baseline characteristics	Total n = 4,222	Ontario n = 2,196	Alberta n = 474	BC n = 1,462	PMT cohort n = 90
Age, mean ± SD	66.1 ± 12.7	69.4 ± 11.6	64.0 ± 13.0	67.9 ± 12.2	63.0 ± 14.0
Female sex, n (%)	2,683 (63.5)	1,393 (63.4)	289 (61.0)	946 (64.7)	55 (61.1)
Male sex, n (%)	1,539 (36.5)	803 (36.6)	185 (39.0)	516 (35.3)	35 (38.9)
Income quintile, n (%)					
1 – lowest	559 (13.2)	461 (21.0)	98 (20.6)	NA	NA
2	537 (12.7)	460 (21.0)	77 (16.2)	NA	NA
3	525 (12.4)	428 (19.5)	97 (20.4)	NA	NA
4	529 (12.5)	428 (19.5)	101 (21.3)	NA	NA
5 – highest	514 (12.2)	417 (19.0)	97 (20.4)	NA	NA
Missing	8 to 10	< 6	< 10	NA	NA
Year of NSCLC diagnosis, n (%)					
2014 or earlier	689 (16.3)	303 (13.8)	25 (5.2)	352 (24.1)	9 (10.0)
2015	348 (8.2)	199 (9.1)	23 (4.9)	124 (8.5)	2 (2.2)
2016	452 (10.7)	231 (10.5)	56 (11.8)	161 (11.0)	4 (4.4)
2017	450 (10.7)	226 (10.5)	49 (10.3)	169 (11.6)	6 (6.7)
2018	447 (10.6)	193 (8.8)	59 (12.4)	186 (12.7)	9 (10.0)
2019	516 (12.2)	261 (11.9)	61 (12.9)	174 (11.9)	20 (22.2)
2020	551 (13.1)	281 (12.8)	92 (19.4)	165 (11.3)	13 (14.4)
2021	563 (13.3)	308 (14.0)	109 (23.0)	131 (9.0)	15 (16.7)
2022	206 (4.9)	194 (8.8)	NA	NA	12 (13.3)
Time in days from diagnosis to index date, mean ± SD	226.0 ± 527.0	189.2 ± 448.0	259.0 ± 643.0	184.7 ± 363.6	271.0 ± 604.0
Stage at diagnosis, n (%)					
I to II	429 (10.2)	217 (9.9)	52 (11.0)	150 (10.3)	10 (11.1)
III	430 (10.2)	184 (8.4)	52 (11.0)	172 (11.8)	22 (24.5)
IV	2,924 (69.3)	1,435 (65.4)	360 (75.9)	1,071 (73.3)	58 (64.5)
Missing	439 (10.4)	360 (16.4)	10 (2.1)	69 (4.7)	0
Tumour histology, n (%)					
Adenocarcinoma	3,632 (85.7)	1,826 (83.2)	415 (87.6)	1,297 (88.7)	80 (88.9)
Large cell carcinoma	12 to 18	7 (0.3)	< 10	< 6	0
Squamous cell carcinoma	35 to 40	28 (1.3)	< 10	15 to 20	1 (1.1)
Other	542 (12.8)	335 (15.3)	53 (11.2)	145 (9.9)	9 (10.0)
Prior lung resection, n (%)	508 (12.0)	248 (11.3)	67 (14.1)	166 (11.4)	22 (24.5)

Baseline characteristics	Total n = 4,222	Ontario n = 2,196	Alberta n = 474	BC n = 1,462	PMT cohort n = 90
Prior adjuvant chemotherapy, n (%)	191 (4.5)	83 (3.8)	29 (6.1)	72 (4.9)	7 (7.7)
Prior radiotherapy – chest, n (%)	1,011 (23.9)	667 (30.4)	20 (4.2)	302 (20.7)	22 (24.5)
Prior radiotherapy – brain, n (%)	275 (6.5)	95 (4.3)	NA	171 (11.7)	9 (10.0)
First-line targeted therapy, n (%)					
***EGFR*-targeted**					
Afatinib	865 (20.3)	387 (17.6)	180 (38.0)	273 (18.7)	16 (17.8)
Erlotinib	< 10	NA	< 10	NA	NA
Gefitinib	1,608 to 1,613	862 (39.2)	< 10	739 (50.6)	6 (4.7)
Osimertinib	1,182 (28.0)	707 (32.2)	165 (34.8)	264 (18.1)	46 (51.1)
***ALK*-targeted**					
Alectinib	266 (6.3)	139 (6.3)	45 (9.5)	69 (4.7)	13 (14.4)
Brigatinib	< 6	< 6	0	NA	0
Ceritinib	< 10	0	< 10	0	0
Crizotinib[a]	287 (6.8)	98 (4.5)	64 (13.5)	117 (8.0)	8 (8.9)
***ROS1*-targeted**					
Entrectinib	1 (0.02)	0	0	NA	1 (1.1)
Index year					
2014 or earlier	483 to 493	174 (7.9)	< 10	303 (20.7)	5 (5.6)
2015	320 (7.6)	202 (9.1)	13 (2.7)	103 (7.1)	2 (2.2)
2016	445 to 450	235 (10.7)	50 (10.5)	156 (10.7)	3 (3.3)
2017	440 to 445	231 (10.5)	51 (10.8)	155 (10.6)	2 (2.2)
2018	429 (10.1)	192 (8.7)	48 (10.1)	179 (12.2)	7 (7.8)
2019	518 (12.2)	254 (11.6)	64 (13.5)	185 (12.7)	15 (16.7)
2020	630 (14.9)	307 (14.0)	108 (22.8)	195 (13.3)	18 (20.0)
2021	66 (15.7)	344 (15.7)	115 (24.3)	186 (12.7)	20 (22.2)
2022	300 (7.1)	257 (11.7)	23 (4.9)	N/A	18 (20.0)

BC = British Columbia; NA = not applicable; NSCLC = non–small cell lung cancer; PMT = Personalize My Treatment; SD = standard deviation.

[a]Crizotinib is also indicated for *ROS1* mutations.

Main Findings

Main Take-Aways

The study followed patients for a maximum of 4 treatment exposures. We found that targeted therapy was the most frequently used treatment during the second and third exposures in all participating provinces. However, in the fourth exposure, there was an increase in the use of both single-agent chemotherapy and ICIs. The cohort sizes in each province were too small to conduct a comparative effectiveness analysis.

We reported the sequence of systemic treatment exposures for patients in each study site as proportions in Table 3 and as a visual representation via Sankey diagrams in Figure 9. The most frequent second exposure treatment type was driver mutation–targeted therapy. We conducted an ad hoc analysis to examine the distribution of second exposure targeted therapies and found that osimertinib was the most common second targeted therapy. In Ontario, 65.8% of those receiving a second exposure targeted therapy received osimertinib, while 44.0% received this drug as a second exposure in Alberta, 58.5% in British Columbia, and 51.1% in the PMT cohort. The second most common treatment after first-line targeted therapy in all jurisdictions was platinum-doublet chemotherapy (36.6% in Ontario, 18.7% in Alberta, 42.0% in British Columbia, and 27.7% in the PMT cohort), followed by a small proportion of individuals who received ICIs, single-agent chemotherapy, or other treatments. In the third exposure, the breakdown of type of treatment was more evenly distributed in British Columbia and the PMT cohort (22.1% on targeted therapy and 33.6% on platinum double chemotherapy in British Columbia; 37.5% on targeted therapy and 29.2% on platinum-doublet chemotherapy in the PMT cohort); however, targeted therapy remained the most common exposure for Ontario and Alberta (53.4% in Ontario and 40.2% in Alberta). With the exception of the PMT cohort, in which targeted therapy remained the most common treatment type in the fourth exposure (38.5%), the proportion of single-agent chemotherapy and ICI use increased in Ontario, Alberta, and British Columbia in the fourth exposure.

In a subgroup analysis, we observed 1,552 patients in Ontario, 402 patients in British Columbia, 878 patients in Alberta, and 80 patients in the PMT cohort who initiated first-line targeted therapy after ICIs became publicly funded in early 2017 (Table 4, Figure 13). Targeted therapy remained the most frequent class of therapy for second treatment exposure, with relative frequency ranging from 56.5% in British Columbia to 76.8% in Alberta. Among patients in this group who received second exposure targeted therapy, osimertinib was the most common drug in all 3 CCRE provinces (Table 5). Patients who received second exposure targeted therapy typically received a different drug targeting the same mutation, likely indicating a switch in treatment due to toxicity. The treatment distributions for third treatment exposure varied between sites: among patients who received a third treatment exposure, platinum-doublet chemotherapy was most frequent in British Columbia (42.5%), targeted therapy was most frequent in Alberta (37.8%), single-agent chemotherapy was most frequent in Ontario (35.0%), and use of targeted therapy and platinum-doublet chemotherapy were tied in the PMT cohort (both 29.4%). Among patients receiving a fourth treatment exposure, single-agent chemotherapy was the most commonly used class of therapy in Alberta (37.5%),

Ontario (56.8%), and the PMT cohort (37.5%), while single-agent ICI was the most frequently used class of therapy in British Columbia (36.5%).

In addition to identifying the sequence of treatments experienced by this patient population, we sought to identify the number of patients in each jurisdiction who were treated with single-agent ICI or chemotherapy at any point after first-line targeted therapy (Table 6). In Ontario, we found that 83 patients received ICIs and 235 patients received single-agent chemotherapy during the follow-up period. There were 26 patients in Alberta who received subsequent-line ICIs and 39 who received subsequent-line single-agent chemotherapy, and in British Columbia, there were 77 patients on subsequent-line ICIs and 130 patients on subsequent-line single-agent chemotherapy. The number of patients who received these treatments in the PMT cohort was substantially smaller, with 6 patients receiving ICIs and 5 patients receiving single-agent chemotherapy.

We conducted a power analysis for the comparison of 2 survival curves to determine whether the observed patient numbers for subsequent ICI use may be feasible for a comparative effectiveness analysis. We used reference estimates from seminal clinical trials comparing ICIs and single-agent chemotherapy.[17,18] Based on a 1-year overall survival of 50%, with a reference hazard ratio of 0.6 to 0.73[17,18] and a 2-year follow-up, each exposure group would require 428 to 1,025 patients to achieve 80% power. Given that our current cohort remains at 192 patients using subsequent ICIs after combining all study sites, a comparative analysis is currently not feasible.

Table 3: Summary of Subsequent Treatment Exposures, After First-Line Targeted Therapy

Exposure	Ontario		Alberta		BC		PMT cohort	
	Crude	IPCW	Crude	IPCW	Crude	IPCW	Crude	IPCW
	n = 2,196	n = 2,196	n = 474	n = 474	n = 1,462	n = 1,462	n = 90	n = 90
Outcome following first treatment exposure,[a] n (%)								
Died	802 (36.5)	1,068.0 (48.7)	155 (32.7)	211.7 (44.7)	651 (44.5)	747.7 (51.1)	9 (10.0)	14.5 (16.1)
Censored	548 (25.0)	NA	127 (26.8)	NA	189 (12.9)	NA	34 (37.8)	NA
Received second treatment exposure[a]	846 (38.5)	1,126.6 (51.3)	192 (40.5)	262.2 (55.3)	622 (42.5)	714.4 (48.9)	47 (52.2)	75.5 (83.9)
Class of second treatment exposure,[b] n (%)								
Targeted therapy	524 (61.9)	697.8 (61.9)	152 (79.2)	207.6 (79.2)	287 (46.1)	329.6 (46.1)	32 (68.1)	51.4 (68.1)
Platinum doublet	287 (33.9)	382.2 (33.9)	36 (18.8)	49.1 (18.7)	261 (42.0)	299.8 (42.0)	8 to 14	20.9 (27.7)
Single-agent ICI	< 6	6.7 (0.6)	< 10	< 10	9 (1.5)	10.3 (1.5)	0	0
Single-agent chemotherapy	20 to 25	32.0 (2.8)	< 10	< 10	31 (5.0)	35.6 (5.0)	0	0
Other	6	8.0 (0.7)	< 10	< 10	34 (5.5)	39.05 (5.5)	< 6	< 6
Outcome following second treatment exposure,[b] n (%)								
Died	238 (28.1)	352.7 (31.3)	70 (36.5)	120.7 (46.0)	285 (45.8)	384.9 (53.9)	12 (25.5)	25.2 (33.3)
Censored	86 (10.2)	NA	40 (20.8)	NA	93 (15.0)	NA	11 (23.4)	NA
Received third treatment exposure[b]	522 (61.7)	773.6 (68.7)	82 (42.7)	141.4 (53.9)	244 (39.2)	329.5 (46.1)	24 (51.1)	50.4 (66.7)
Class of third treatment exposure,[c] n (%)								
Targeted therapy	305 (58.4)	452.0 (58.4)	33 (40.2)	56.9 (40.2)	54 (22.1)	72.9 (22.1)	9 (37.5)	18.9 (37.5)
Platinum doublet	57 (10.9)	84.5 (10.9)	22 (26.8)	37.9 (26.8)	82 (33.6)	110.7 (33.6)	7 (29.2)	14.7 (29.2)
Single-agent ICI	21 (4.0)	31.1 (4.0)	< 10	< 10	32 (13.1)	43.2 (13.1)	< 6	8.4 (16.7)

Exposure	Ontario		Alberta		BC		PMT cohort	
	Crude	IPCW	Crude	IPCW	Crude	IPCW	Crude	IPCW
	n = 2,196	n = 2,196	n = 474	n = 474	n = 1,462	n = 1,462	n = 90	n = 90
Single-agent chemotherapy	131 (25.1)	194.1 (25.1)	21 (25.6)	36.2 (25.6)	59 (24.2)	79.7 (24.2)	< 6	< 6
Other	8 (1.5)	11.9 (1.5)	< 10	< 10	17 (7.0)	23.0 (7.0)	< 6	< 6
Outcome following third treatment exposure,[c] n (%)								
Died	210 (40.1)	389.2 (50.1)	33 (40.2)	65.7 (46.5)	125 (51.2)	188.9 (57.3)	5 to 10	14.0 (27.8)
Censored	105 (20.0)	NA	11 (13.4)	NA	26 (10.7)	NA	5 to 10	NA
Received fourth treatment exposure[c]	209 (40.0)	387.4 (49.9)	38 (46.3)	75.7 (53.5)	93 (38.1)	140.6 (42.7)	13 (54.2)	36.4 (72.2)
Class of fourth treatment exposure,[d] n (%)								
Targeted therapy	56 (26.8)	103.8 (26.8)	< 10	17.9 (23.6)	14 (15.1)	21.2 (15.1)	< 6	14.0 (38.5)
Platinum doublet	55 to 60	101.9 (26.3)	< 10	13.9 (18.4)	15 (16.1)	22.7 (16.1)	< 6	8.4 (23.1)
Single-agent ICI	30 (14.4)	55.6 (14.4)	< 10	15.9 (21.0)	26 (28.0)	39.3 (28.0)	< 6	< 6
Single-agent chemotherapy	63 (30.1)	116.8 (30.1)	12	23.9 (31.6)	32 (34.4)	48.4 (34.4)	< 6	8.4 (23.1)
Other	< 6	9.3 (2.4)	< 10	< 10	6 (6.5)	9.1 (6.5)	< 6	< 6
Outcome following fourth treatment exposure,[d] n (%)								
Died	88 (42.1)	189.4 (48.9)	10	14.2 (18.8)	63 (67.7)	106.7 (75.9)	< 6	20.2 (55.6)
Censored	29 (13.9)	NA	< 10	NA	10 (10.8)	NA	< 6	NA

BC = British Columbia; ICI = immune checkpoint inhibitor; IPCW = inverse-probability-of-censoring weighting; NA = not applicable; PMT = Personalize My Treatment.

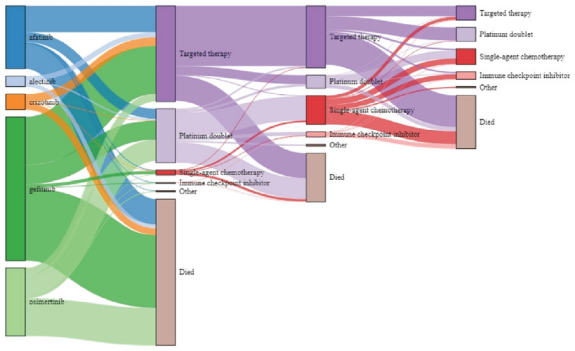
[a]Denominator for Ontario: N = 2,196 (unweighted), N = 2,196 (weighted); denominator for Alberta: N = 474 (unweighted), N = 474 (weighted); denominator for BC: N = 1,462 (unweighted), N = 1,462 (weighted); denominator for PMT cohort: N = 90 (unweighted), N = 90 (weighted).

[b]Denominator for Ontario: N = 846 (unweighted), N = 1,126.6 (weighted); denominator for Alberta: N = 192 (unweighted), N = 262.1 (weighted); denominator for BC: N = 622 (unweighted), N = 714.4 (weighted); denominator for PMT cohort: N = 47 (unweighted), N = 75.6 (weighted).

[c]Denominator for Ontario: N = 522 (unweighted), N = 773.6 (weighted); denominator for Alberta: N = 82 (unweighted), N = 141.7 (weighted); denominator for BC: N = 244 (unweighted), N = 329.6 (weighted); denominator for PMT cohort: N = 24 (unweighted), N = 50.4 (weighted).

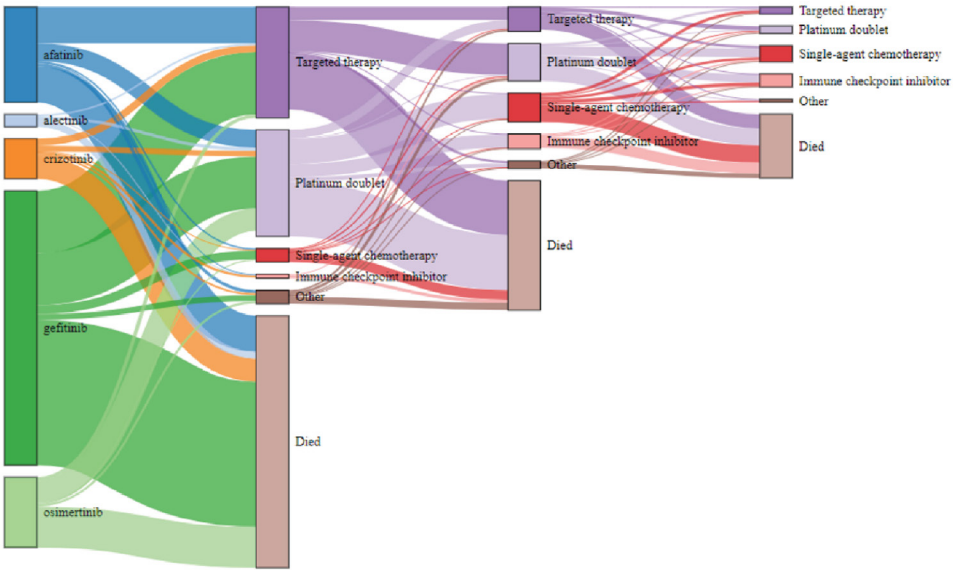
[d]Denominator for Ontario: N = 209 (unweighted), N = 387.2 (weighted); denominator for Alberta: N = 38 (unweighted), N = 75.5 (weighted); denominator for BC: N = 93 (unweighted), N = 140.6 (weighted); denominator for PMT cohort: N = 13 (unweighted), N = 36.3 (weighted).

Figure 9: Sankey Diagram of Subsequent Treatment Exposure in Ontario



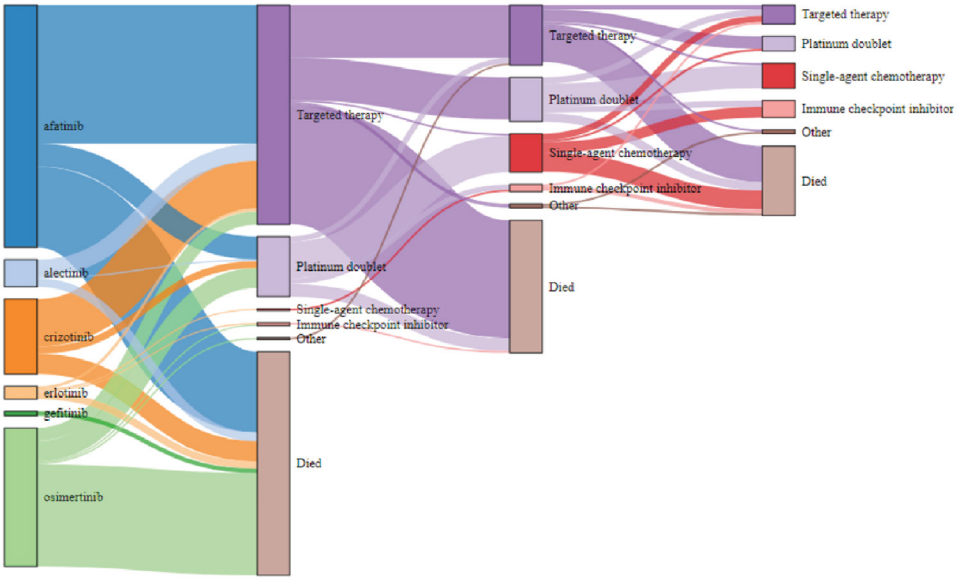
IPCW = inverse-probability-of-censoring weighting.

Figure 10: Sankey Diagram of Subsequent Treatment Exposure in British Columbia



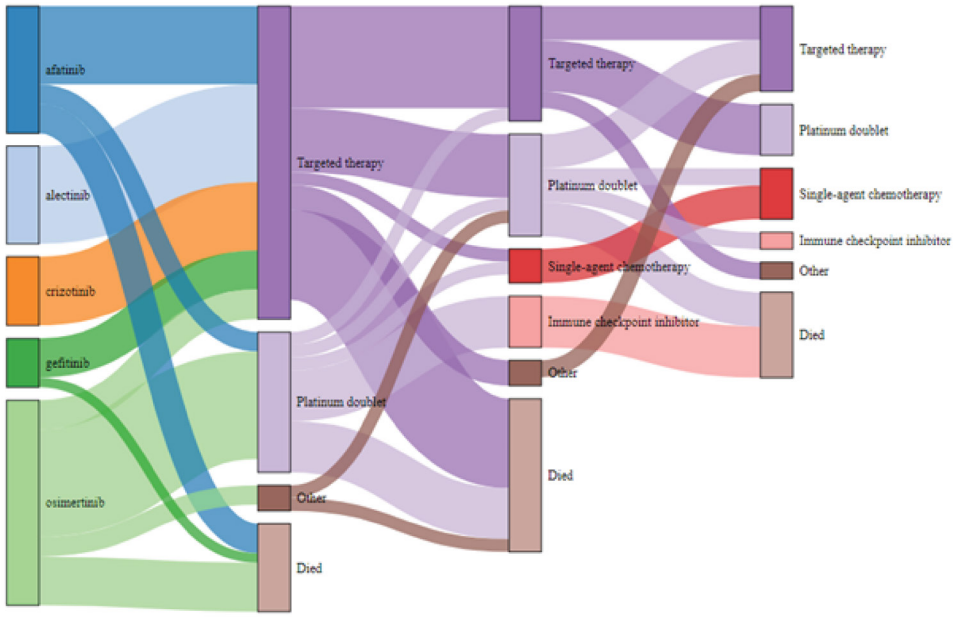
IPCW = inverse-probability-of-censoring weighting.

Figure 11: Sankey Diagram of Subsequent Treatment Exposure in Alberta



IPCW = inverse-probability-of-censoring weighting.

Figure 12: Sankey Diagram of Subsequent Treatment Exposure in the PMT Registry Cohort



IPCW = inverse-probability-of-censoring weighting; PMT = Personalize My Treatment.

Table 4: Summary of Subsequent Treatment Exposures Among Patients Receiving First-Line Targeted Therapy After Public Funding of ICIs

Exposure	Ontario		Alberta		BC		PMT cohort	
	Crude	IPCW	Crude	IPCW	Crude	IPCW	Crude	IPCW
	n = 1,552	n = 1,552	n = 402	n = 402	n = 878	n = 878	n = 80	n = 80
Outcome following first treatment exposure,[a] n (%)								
Died	480 (30.9)	703.5 (45.4)	134 (33.3)	193.7 (48.0)	349 (39.8)	427.4 (48.7)	9 (11.3)	15.7 (19.6)
Censored	494 (31.8)	NA	124 (30.8)	NA	161 (18.3)	NA	34 (42.5)	NA
Received second treatment exposure[a]	578 (37.2)	847.1 (54.6)	144 (42.0)	208.2 (51.8)	378 (41.9)	450.6 (51.3)	37 (46.3)	64.4 (80.4)
Class of second treatment exposure,[b] n (%)								
Targeted therapy	369 (63.8)	540.8 (63.8)	111 (77.0)	160.5 (76.8)	208 (56.5)	254.7 (56.5)	22 (59.5)	38.3 (59.5)
Platinum doublet	192 (33.2)	281.4 (33.2)	29 (20.1)	41.9 (20.1)	130 (35.3)	159.2 (35.3)	12 to 17	22.6 (35.1)
Single-agent ICI	< 6	< 6	< 10	< 10	9 (2.5)	11.0 (2.5)	0	0
Single-agent chemotherapy	6 to 10	10 to 15	< 10	< 10	6 (1.6)	7.4 (1.6)	0	0
Other	6	8.8 (1.0)	< 10	< 10	15 (4.1)	18.4 (4.1)	2 (5.4)	3.5 (5.4)
Outcome following second treatment exposure,[b] n (%)								
Died	159 (27.5)	267.1 (31.6)	54 (37.5)	100.4 (48.2)	154 (41.9)	236.9 (52.6)	12 (32.4)	26.6 (41.4)
Censored	74 (12.8)	NA	32 (22.2)	NA	75 (20.4)	NA	8 (21.6)	NA
Received third treatment exposure[b]	345 (59.7)	579.6 (68.5)	58 (40.3)	107.8 (51.7)	139 (37.8)	213.8 (47.4)	17 (46.0)	37.7 (58.6)
Class of third treatment exposure,[c] n (%)								
Targeted therapy	212 (61.4)	356.1 (61.4)	22 (37.9)	40.9 (37.8)	36 (25.9)	55.4 (25.9)	5 (29.4)	11.1 (29.4)
Platinum doublet	36 (10.4)	60.5 (10.4)	15 (25.8)	27.8 (25.7)	59 (42.5)	90.7 (42.5)	5 (29.4)	11.1 (29.4)
Single-agent ICI	13 (3.8)	21.8 (3.8)	< 10	< 10	20 (14.4)	30.8 (14.4)	4 (23.5)	8.8 (23.5)

Exposure	Ontario		Alberta		BC		PMT cohort	
	Crude	IPCW	Crude	IPCW	Crude	IPCW	Crude	IPCW
	n = 1,552	n = 1,552	n = 402	n = 402	n = 878	n = 878	n = 80	n = 80
Single-agent chemotherapy	76 (22.0)	127.7 (22.0)	16 (27.5)	29.7 (27.5)	18 (13.0)	27.7 (13.0)	2 (11.8)	4.4 (11.8)
Other	8 (2.3)	13.4 (2.3)	< 10	< 10	6 (4.3)	9.2 (4.3)	1 (5.9)	2.2 (5.9)
Outcome following third treatment exposure,[c] n (%)								
Died	133 (38.3)	289.3 (49.6)	26 (44.8)	56.0 (51.9)	67 (48.2)	120.4 (56.3)	4 (23.5)	12.6 (33.3)
Censored	79 (22.8)	NA	8	NA	20 (14.4)	NA	5 (29.4)	NA
Received fourth treatment exposure[c]	135 (38.9)	293.6 (50.4)	24 (41.4)	51.7 (47.9)	52 (37.4)	93.4 (43.7)	8 (47.1)	25.2 (66.7)
Class of fourth treatment exposure,[d] n (%)								
Targeted therapy	38 (28.2)	82.7 (28.2)	< 10	10.7 (20.6)	4 to 7	12.6 (13.5)	1 (12.5)	3.1 (12.5)
Platinum doublet	37 (27.4)	80.5 (27.4)	< 10	< 10	8 (15.4)	14.4 (15.4)	2 (25.0)	6.3 (25.0)
Single-agent ICI	10 to 15	26.1 (8.9)	< 10	10.7 (20.6)	19 (36.5)	34.1 (36.5)	1 (12.5)	3.1 (12.5)
Single-agent chemotherapy	43 (31.9)	93.5 (31.9)	< 10	19.4 (37.5)	17 (32.7)	30 to 35	3 (37.5)	9.4 (37.5)
Other	< 6	10.9 (3.7)	< 10	< 10	< 6	< 6	1 (12.5)	3.1 (12.5)
Outcome following fourth treatment exposure,[d] n (%)								
Died	44 (59.5)	134.5 (45.8)	< 10	15.5 (29.9)	33 (63.5)	71.7 (76.7)	3 (37.5)	12.1 (60.0)
Censored	6 (8.1)	NA	< 10	NA	9 (17.3)	NA	3 (37.5)	NA

BC = British Columbia; ICI = immune checkpoint inhibitor; IPCW = inverse-probability-of-censoring weighting; NA = not applicable; PMT = Personalize My Treatment.

[a]Denominator for Ontario: N = 1,552 (unweighted), N = 1,552 (weighted); denominator for Alberta: N = 402 (unweighted), N = 402 (weighted); denominator for BC: N = 878 (unweighted), N = 878 (weighted); denominator for PMT cohort: N = 80 (unweighted), N = 80 (weighted).

[b]Denominator for Ontario: N = 578 (unweighted), N = 847.1 (weighted); denominator for Alberta: N = 144 (unweighted), N = 208.2 (weighted); denominator for BC: N = 378 (unweighted), N = 450.7 (weighted); denominator for PMT cohort: N = 37 (unweighted), N = 30.1 (weighted).

[c]Denominator for Ontario: N = 345 (unweighted), N = 579.6 (weighted); denominator for Alberta: N = 58 (unweighted), N = 107.7 (weighted); denominator for BC: N = 139 (unweighted), N = 213.8 (weighted); denominator for PMT cohort: N = 17 (unweighted), N = 37.8 (weighted).

[d]Denominator for Ontario: N = 135 (unweighted), N = 293.6 (weighted); denominator for Alberta: N = 24 (unweighted), N = 51.8(weighted); denominator for BC: N = 52 (unweighted), N = 93.5 (weighted); denominator for PMT cohort: N = 8 (unweighted), N = 25.2 (weighted).

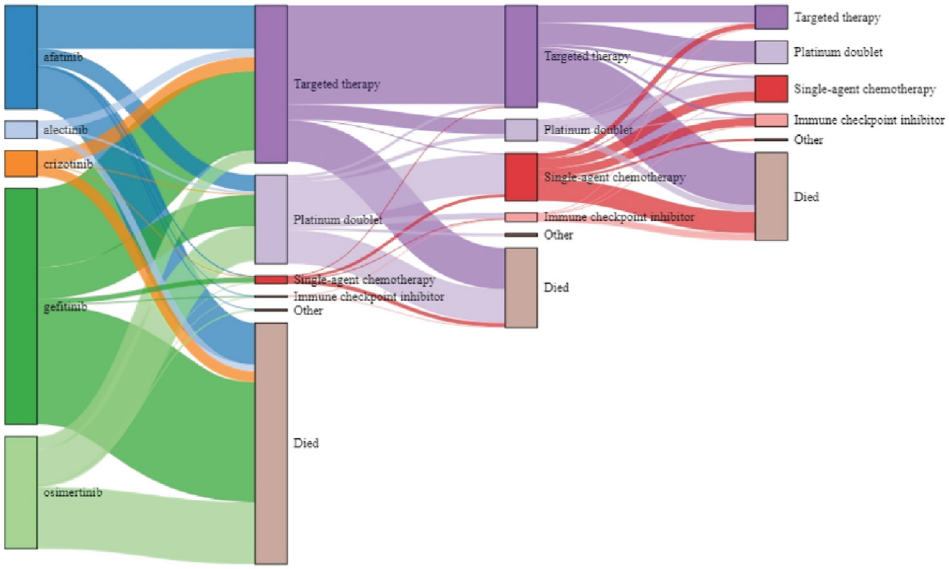
Table 5: Breakdown of the Number of Patients Who Received Various Targeted Therapies Received in Second Exposure Among Patients Who Started First-Line Targeted Therapy After Public Funding of Immune Checkpoint Inhibitors, in CCRE Provinces (Ontario, Alberta, and British Columbia)

First exposure		Second exposure				
			EGFR-targeted			
Therapy type		*ALK*-targeted	Osimertinib	Others (afatinib, gefitinib, erlotinib)	*ROS1*-targeted	*RET*-targeted
ALK-targeted		95	< 6	0	< 6	0
EGFR-targeted	Osimertinib	0	0	52	0	< 6
	Others (afatinib, gefitinib, erlotinib)	9	410	120	0	0

CCRE = Canadian Cancer Real-world Evaluation.

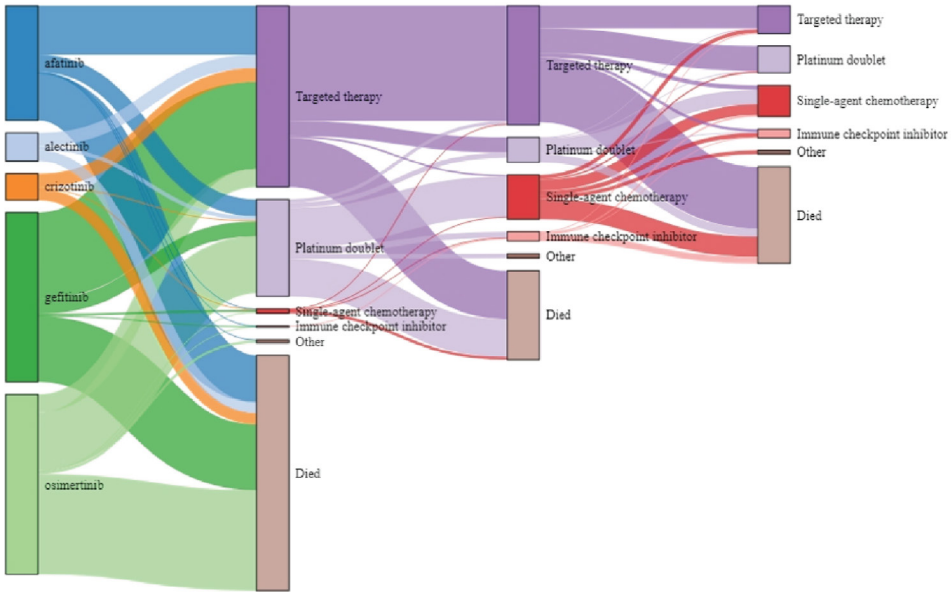
Note: This table only includes patients who received targeted therapy in the second exposure, therefore only 6 different targeted therapies were identified in the first exposure. There may be patients who initiated first-line targeted therapies using drugs outside of the 6 listed in this table, however those patients did not continue to have second exposure targeted therapy.

Figure 13: Sankey Diagram of Subsequent Treatment Exposure in the Contemporary Era in Ontario



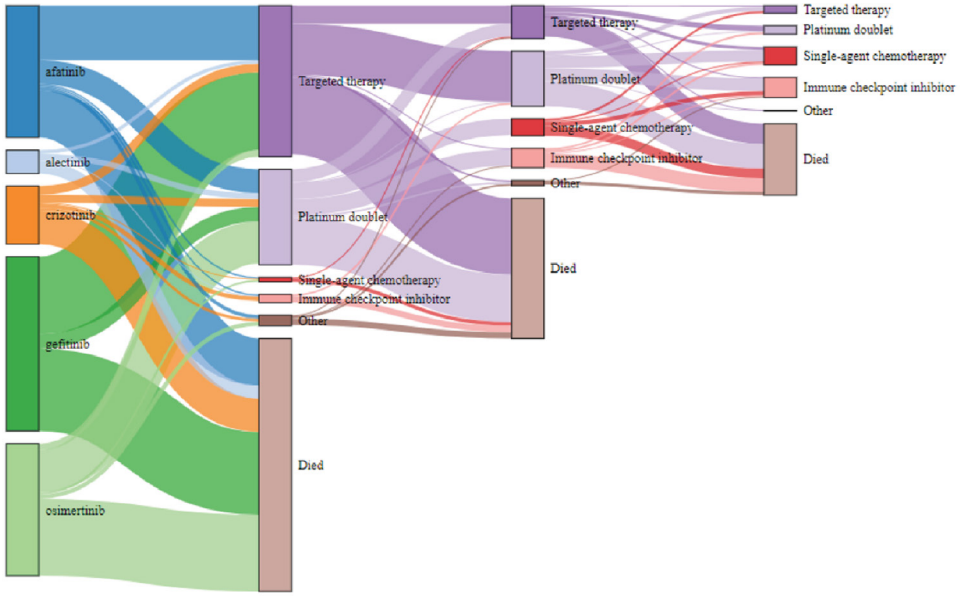
ICI = immune checkpoint inhibitor; IPCW = inverse-probability-of-censoring weighting.

Figure 14: Sankey Diagram of Subsequent Treatment Exposure in the Contemporary Era in British Columbia



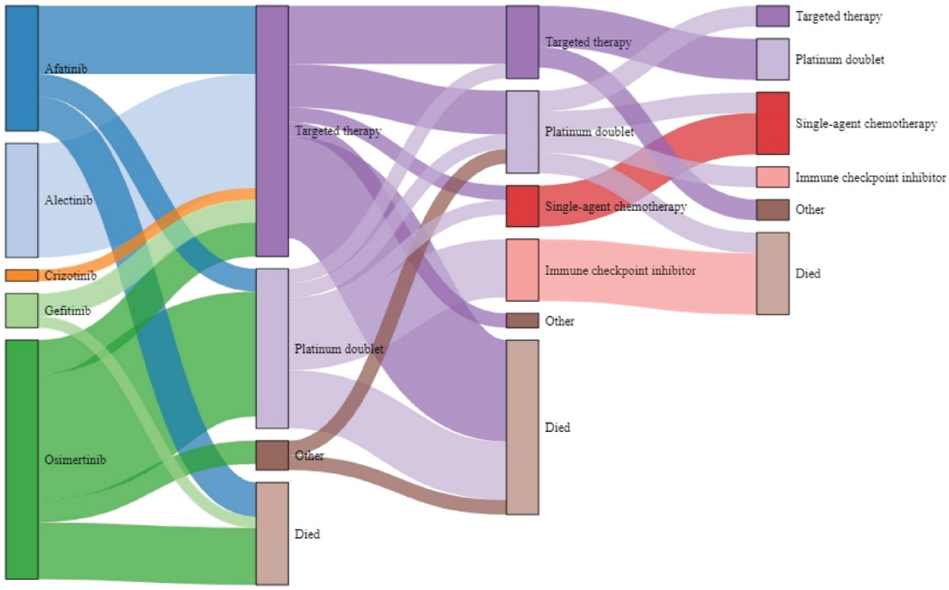
ICI = immune checkpoint inhibitor; IPCW = inverse-probability-of-censoring weighting.

Figure 15: Sankey Diagram of Subsequent Treatment Exposure in the Contemporary Era in Alberta



ICI = immune checkpoint inhibitor; IPCW = inverse-probability-of-censoring weighting.

Figure 16: Sankey Diagram of Subsequent Treatment Exposure in the Contemporary Era in the PMT Registry Cohort



ICI = immune checkpoint inhibitor; IPCW = inverse-probability-of-censoring weighting; PMT = Personalize My Treatment.

Table 6: Characteristics of Patients Receiving Subsequent ICIs or Single-Agent Chemotherapy at Any Time After First-Line Targeted Therapy

Characteristics at start of subsequent ICI or single-agent chemotherapy	Total		Ontario		Alberta		BC		PMT cohort	
	ICI n = 192	Chemotherapy n = 409	ICI n = 83	Chemotherapy n = 235	ICI n = 26	Chemotherapy n = 39	ICI n = 77	Chemotherapy n = 130	ICI n = 6	Chemotherapy n = 5
Age, mean ± SD	63.3 ± 11.2	60.4 ± 11.1	65.5 ± 12.2	66.0 ± 10.7	56 ± 12	59 ± 12	66.2 ± 11.3	64.5 ± 11.4	65.5 ± 8.8	52.2 ± 10.1
Female sex, n (%)	110 (57.3)	258 (63.1)	48 (57.8)	141 (60.0)	14 (53.8)	22 (56.4)	44 (57.1)	93 (71.5)	4 (66.7)	2 (40.0)
Male sex, n (%)	82 (74.5)	151 (36.9)	35 (42.2)	94 (40.0)	12 (46.2)	17 (43.6)	33 (42.9)	37 (28.5)	2 (33.3)	3 (60.0)
Income quintile, n (%)										
1 – lowest	24 to 28 (22.0 to 25.7)	58 (21.2)	17 (20.5)	48 (20.4)	< 10	10 (25.6)	NA	NA	NA	NA
2	20 (18.3)	59 (21.5)	19 (22.9)	54 (23.0)	< 10	< 10	NA	NA	NA	NA
3	25 (22.9)	58 (21.2)	21 (25.3)	52 (22.1)	< 10	< 10	NA	NA	NA	NA
4	17 to 21 (15.6 to 19.3)	52 (19)	11 (13.3)	42 (17.8)	< 10	10 (25.6)	NA	NA	NA	NA
5 – highest	19 (17.4)	47 (17.2)	15 (18.1)	39 (16.6)	< 10	< 10	NA	NA	NA	NA
Missing			0	0	0	0	NA	NA	NA	NA
Year of NSCLC diagnosis, n (%)										
2014 or earlier	27 (14.1)	108 (26.4)	16 (19.3)	45 (19.2)	< 10	< 10	8 (10.4)	59 (45.3)	1 (16.7)	1 (20.0)

Characteristics at start of subsequent ICI or single-agent chemotherapy	Total		Ontario		Alberta		BC		PMT cohort	
	ICI n = 192	Chemotherapy n = 409	ICI n = 83	Chemotherapy n = 235	ICI n = 26	Chemotherapy n = 39	ICI n = 77	Chemotherapy n = 130	ICI n = 6	Chemotherapy n = 5
2015	26 (13.5)	45 (11)	18 (21.7)	28 (11.9)	< 10	< 10	7 (9.1)	13 (10.0)	0	1 (20.0)
2016	29 (15.1)	41 (10)	10 (12.1)	23 (9.8)	< 10	< 10	12 (15.6)	12 (9.2)	0	0
2017	33 (17.2)	43 (10.5)	11 (13.3)	28 (11.9)	< 10	< 10	16 (20.8)	10 (7.7)	0	0
2018	23 (12)	44 (10.8)	8 (9.6)	27 (11.5)	< 10	< 10	11 (14.3)	10 (7.7)	0	1 (20.0)
2019	23 (12)	41 (10)	8 (9.6)	26 (11.1)	< 10	< 10	10 (13.0)	6 to 11	2 (33.3)	0
2020	13 (6.8)	46 (11.2)	< 6	27 (11.5)	< 10	< 10	7 (9.1)	12 (9.2)	0	1 (20.0)
2021	15 (7.8)	35 (8.6)	6 (7.2)	26 (11.1)	< 10	< 10	6 (7.8)	< 6	2 (33.3)	0
2022	3 (1.6)	6 (1.5)	< 6	< 6	NA	NA	NA	NA	1 (16.7)	1 (20.0)
Time in days from diagnosis to subsequent ICI or chemo, mean ± SD	844.4 ± 654.7	888.5 ± 743.2	853.1 ± 579.9	909.1 ± 722.1	835.9 ± 492.8	649.7 ± 368.7	863.1 ± 550.1	790.7 ± 525.4	985.5 ± 912.5	1,204.5 ± 985.5
Stage at diagnosis, n (%)										
I to II	17 (8.9)	25 (6.1)	8 (9.6)	12 (5.1)	< 10	< 10	8 (10.4)	11 (8.5)	0	0
III	17 (8.9)	28 (6.8)	< 6	14 (6.0)	< 10	< 10	11 (14.3)	11 (8.5)	0	0
IV	139 (72.4)	319 (78)	57 (68.7)	181 (77.0)	22 (84.6)	31 (79.4)	54 (70.1)	102 (78.5)	6 (100.0)	5 (100.0)
Missing	1 (0.5)	3 (0.7)	14 (16.9)	28 (11.9)	< 10	< 10	< 6	6 (4.6)	0	0

Characteristics at start of subsequent ICI or single-agent chemotherapy	Total		Ontario		Alberta		BC		PMT cohort	
	ICI n = 192	Chemotherapy n = 409	ICI n = 83	Chemotherapy n = 235	ICI n = 26	Chemotherapy n = 39	ICI n = 77	Chemotherapy n = 130	ICI n = 6	Chemotherapy n = 5
Tumour histology, n (%)										
Adenocarcinoma	163 (84.9)	363 (88.8)	69 (83.1)	211 (89.8)	21 (80.8)	31 (79.4)	68 (88.3)	116 (89.2)	5 (83.3)	5 (100.0)
Large cell carcinoma	0 to 4	< 6	0	0	0	< 10	0	< 6	0	0
Squamous cell carcinoma	4 to 8	< 6	< 6	< 6	< 10	< 10	< 6	< 6	0	0
Other	16 (8.3)	40 (9.8)	10 to 15	20 to 25	< 10	< 10	6 to 10	11 (8.5)	1 (16.7)	0
Prior lung resection, n (%)	28 (14.6)	35 (8.6)	10 (12.1)	14 (6.0)	< 10	< 10	16 (20.8)	16 (12.3)	0	1 (20.0)
Prior radiotherapy – chest, n (%)	42 (21.9)	88 (21.5)	21 (25.3)	64 (27.2)	< 10	< 10	18 (23.4)	20 (15.4)	2 (33.3)	1 (20.0)
Prior radiotherapy – brain, n (%)	8 (4.2)	22 (5.4)	< 6	7 (3.0)	NA	NA	< 6	14 (10.8)	0	1 (20.0)
ICI, n (%)										
Atezolizumab	10 (5.2)	NA	< 6	NA	0	NA	7 (9.1)	NA	0	NA
Pembrolizumab	57 (29.7)	NA	17 to 22	NA	< 10	NA	29 (37.7)	NA	3 (50.0)	NA
Nivolumab	125 (65.1)	NA	61 (73.5)	NA	20 (76.9)	NA	41 (53.3)	NA	3 (50.0)	NA
Chemotherapy agent, n (%)										
Pemetrexed	NA	244 (59.7)	NA	160 (68.1)	NA	32 (82.1)	NA	51 (39.2)	NA	1 (20.0)
Docetaxel	NA	123 (30.1)	NA	52 to 56 (22.1 to 23.8)	NA	< 10	NA	64 (49.2)	NA	4 (80.0)

Characteristics at start of subsequent ICI or single-agent chemotherapy	Total		Ontario		Alberta		BC		PMT cohort	
	ICI n = 192	Chemotherapy n = 409	ICI n = 83	Chemotherapy n = 235	ICI n = 26	Chemotherapy n = 39	ICI n = 77	Chemotherapy n = 130	ICI n = 6	Chemotherapy n = 5
Paclitaxel	NA	7 (1.7)	NA	6 to 11 (2.6 to 4.7)	NA	0	NA	< 6	NA	0
Vinorelbine	NA	20 (4.9)	NA	4 to 8 (1.7 to 3.4)	NA	< 10	NA	9 (6.9)	NA	0
Gemcitabine	NA	15 (3.7)	NA	10 (4.3)	NA	< 10	NA	< 6	NA	0
Year of subsequent therapy, n (%)										
2014 or earlier	0 to 4	38 to 42	NA	< 6	NA	NA	NA	35 (26.9)	0	0
2015	< 6	32 (7.8)	< 6	22 (9.4)	0	NA	NA	10 (7.7)	0	0
2016	7 (3.6)	31 (7.6)	7 (8.4)	10 to 15	0	< 10	NA	14 (10.8)	0	0
2017	27 (14.1)	29 (7.1)	19 (22.9)	22 (9.4)	< 10	< 10	7 (9.1)	6 to 10 (4.6 to 7.7)	0	0
2018	25 (13)	27 (6.6)	12 (14.5)	18 (7.7)	< 10	< 10	12 (15.6)	< 6	0	0
2019	22 (11.5)	32 (7.8)	7 (8.4)	17 (7.2)	< 10	< 10	8 (10.4)	6 to 10	0	1 (20.0)
2020	33 (17.2)	47 (11.5)	10 (12.1)	29 (12.3)	10 (38.5)	< 10	13 (16.9)	11 (8.5)	0	1 (20.0)
2021	36 (18.8)	58 (14.2)	12 (14.5)	31 (13.2)	< 10	< 10	17 (22.1)	19 (14.6)	0	0
2022	26 (13.5)	66 (16.1)	10 (12.1)	42 (17.9)	NA	12 (30.8)	11 (14.3)	11 (8.5)	5 (83.3)	1 (20.0)
2023	13 (6.8)	45 to 49	< 6	35 (14.9)	NA	NA	9 (11.7)	10 (7.7)	1 (16.7)	2 (40.0)
First-line targeted therapy, n (%)										
***EGFR*-targeted**										

Characteristics at start of subsequent ICI or single-agent chemotherapy	Total		Ontario		Alberta		BC		PMT cohort	
	ICI n = 192	Chemotherapy n = 409	ICI n = 83	Chemotherapy n = 235	ICI n = 26	Chemotherapy n = 39	ICI n = 77	Chemotherapy n = 130	ICI n = 6	Chemotherapy n = 5
Afatinib	—	—	25 (30.12)	57 (24.26)	17 (65.3)	20 (51.2)	26 (33.8)	29 (22.3)	2 (33.3)	1 (20)
Erlotinib	< 10	< 10	NA	NA	< 10	< 10	NA	NA	NA	NA
Gefitinib	—	—	43 (51.81)	108 (45.96)	0	0	27 (35.1)	80 (61.5)	0	0
Osimertinib	—	—	12 (14.46)	62 (26.38)	< 10	11 (28.2)	10 (13.0)	16 (12.3)	3 (50)	2 (40)
***ALK*-targeted**										
Alectinib	—	—	1 (1.2)	4 (1.7)	< 10	< 10	< 6	< 6	0	0
Brigatinib	—	—	0	0	0	0	0	0	0	0
Ceritinib	—	—	0	0	0	0	0	0	0	0
Crizotinib[a]	—	—	2 (2.41)	4 (1.7)	< 10	< 10	12 (15.6)	< 6	1 (16.7)	2 (40)
***ROS1*-targeted**										
entrectinib	—	—	0	0	0	0	0	0	0	0
Prior platinum doublet therapy, n (%)	360 (187.5)	296 (72.4)	70 (84.3)	169 (71.9)	24 (92.3)	37 (94.9)	61 (79.2)	87 (66.9)	5 (83.3)	3 (60.0)
Prior single-agent chemotherapy, n (%)	42 (21.9)	NA	30 (36.1)	NA	12 (46.2)	NA	25 (32.5)	NA	0	NA
Prior ICI, n (%)	NA	67 (16.4)	NA	< 6	NA	10 to 14	NA	25 (19.2)	NA	0

BC = British Columbia; ICI = immune checkpoint inhibitor; NA = not applicable; NSCLC = non–small cell lung cancer; PMT = Personalize My Treatment; SD = standard deviation.

[a]Crizotinib is also indicated for *ROS1* mutations.

Strengths and Limitations

The main strength of this study is that we used a population-based cohort in Ontario, Alberta, and British Columbia. Our data in Alberta and British Columbia captured all publicly funded NSCLC treatments in these provinces, and therefore the cohorts were not subject to selection bias. In Ontario, a portion of the cohort was captured based on the receipt of therapies that were funded through the Ontario Drug Benefit program. Although it remains that our results are generalizable to patients in Ontario who are a part of the public drug program (and to patients in other jurisdictions with similar programs), we are unable to capture all patients under 65 years of age who may have paid for treatment out of pocket or through private insurance. However, given that our baseline characteristics and general trends in treatment sequencing are broadly consistent across all jurisdictions, it is possible that the use of an Ontario Drug Benefit–based cohort in Ontario only minimally limited the generalizability of our results. The PMT cohort represents patients who have enrolled in a registry, which is not representative of the jurisdictions included (Quebec, New Brunswick, and Nova Scotia). We observed slightly different outcomes in the PMT cohort, such as no deaths among patients who started first-line alectinib and crizotinib. This may be due to multiple factors, including the fact that the PMT cohort is more recent than other sites, with more than 60% of patients starting first-line targeted therapy between 2020 and 2022; the Exactis network comprises academic centres, which may contribute to more favourable outcomes; some patient vital status data may be missing and result in underestimation of deaths; and the small sample size may contribute to observed differences. Additionally, ICIs were introduced to the Canadian treatment landscape in the recent past. It is possible that uptake could continue to increase; therefore, we applied IPCW to a restricted subcohort of patients who initiated therapy in 2017 or later to mitigate this potential underestimation of use. This year was chosen because ICIs were funded through public drug programs across Canada starting in 2017. Finally, we were unable to identify patient biomarker status in Ontario, Alberta, and British Columbia. However, the primary objective of this study was to describe sequential treatments among individuals who started first-line targeted therapy. We used the exposure to targeted therapy as a proxy for mutation status.

Conclusions and Implications for Decision- or Policy-Making

Main Take-Aways

We found that only a small proportion of patients with NSCLC received ICI treatment after their first-line targeted therapy. Therefore, it is not currently feasible to conduct a comparative analysis on the safety and effectiveness of using ICI in this context. For patients who receive further treatments after first-line targeted therapy, the most common options for subsequent treatments are different targeted therapies and platinum-doublet chemotherapy.

In this treatment pattern analysis examining the sequence of NSCLC treatments among patients who received first-line targeted therapy, we summarized the treatment trajectory for 2,196 patients in Ontario, 474 patients in Alberta, 1,462 patients in British Columbia, and 90 patients in the PMT registry. Targeted therapy

was the most common treatment in the second and third exposures for all jurisdictions, but decreased in the fourth exposure as use of single-agent chemotherapy and ICIs increased. The proportions of differing treatments in second exposures and beyond were similar across all 4 jurisdictions. Over the course of the study period, we found that a small proportion of patients were treated with subsequent-line ICI and/or single-agent chemotherapy.

In Ontario, Alberta, and British Columbia, the most common targeted therapy that patients start treatment on is the one that was funded first in each province (gefitinib for Ontario and British Columbia, afatinib for Alberta). However, after restricting to patients who started treatment in the “contemporary era” (2017 or later) when public drug programs began funding ICIs, we found that these older targeted therapies were no longer the most frequently used. In the contemporary era, the distribution of first exposure targeted therapies is more balanced and the proportion of osimertinib use has increased. This was not the same in the PMT cohort, where more than half of the patients initiated treatment with osimertinib in the first exposure in both the overall and contemporary eras. This was likely due to the fact that the majority of patients in the PMT cohort started treatment during the contemporary era, during which time osimertinib became available through public funding. In both study eras, we found that targeted therapy was the most common second exposure across Canada. Although this may be evidence of some patients switching to another targeted therapy due to potential toxicity, the majority of second exposure targeted therapies in all study jurisdictions was a switch from a non-osimertinib targeted therapy to osimertinib. This may indicate an advancement in the treatment sequence, as osimertinib is among the publicly funded second-line treatments in Canada.

Currently, the use of ICIs among patients who have tumours bearing actionable mutations is only indicated after a course of targeted therapy followed by chemotherapy. However, we observed a small portion of patients in each study jurisdiction who received ICI in the second exposure directly after first-line targeted therapy (< 6 in Ontario, < 10 in Alberta, 1.5% in British Columbia, and 0 in the PMT cohort). Although this remains a small portion of the cohort, it may be useful to examine the effectiveness of such a sequence of treatments.

Implications for Future Research

Although we found that the proportion of patients who received ICI treatment subsequent to first-line targeted therapy was low and that a comparative analysis on the safety and effectiveness of its use is not currently feasible, it is possible that patient numbers may grow in future years and lead to a feasible comparative analysis. A descriptive survival analysis of patients who continue on to subsequent ICI or single-agent chemotherapy could be considered in the interim, but with significant limitations in the interpretability of the results. It is important to understand how (and if) ICI treatment in later lines of therapy may benefit patients who have exhausted other treatment options in the Canadian setting. This may be of use for both policy-makers and clinicians.

Conclusion

The current treatment patterns analysis shows that subsequent-line ICI and single-agent chemotherapy is used in a small proportion of patients who receive first-line targeted therapy for the treatment of NSCLC. For

patients who continue to receive subsequent treatments after first-line targeted therapy, additional targeted therapies and platinum-doublet chemotherapy are the most common options.

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Authors

Clinical Review

Qi Guan led the conceptualization, design analysis, interpretation of results, and drafting of the report.

Suriya J Aktar provided substantial contributions to the conception and design acquisition of data analysis and interpretation of the study results, including the key messages and conclusions, and contributed to the report draft and revisions.

Reka E Pataky contributed to the development of the study protocol, acquired and analyzed the data for British Columbia, drafted sections of the final report, and critically reviewed the final report.

Mariet Mathew Stephen contributed to analyzing data and generating reports specific to the Alberta site, as per the study protocol, and reviewed multiple iterations of both the study protocol and report.

Maud Marques reviewed the protocol and provided information regarding the specific contribution of Exactis, identified patients, quality-checked the data and performed all analyses, reviewed the report, and provided the specific information for Exactis.

Karen Gambaro participated in the conception and feasibility assessment of the study, with a focus on the PMT cohort; participated in the acquisition of data, quality control, and conducting analysis of the PMT cohort data; participated in interpreting the results both from the PMT cohort and in the context of overall study findings; and participated in drafting and revising the report.

Kahina Rachedi contributed to writing the protocol and provided accurate medical guidelines, reviewed and verified all data related to the study, and assured data quality.

Katharina Forster supported the drafting and review of the proposal and protocol for the study, contributed to review and interpretation of data, and participated in writing and reviewing the report.

Samara Strub contributed to conception, drafting key messages, revising the report for content, and reviewing for consistency.

Nicola Bai analyzed administrative data and contributed to the final report.

Tamer Jareda contributed to writing, reviewing, and editing of the report; methodology; data curation; and conceptualization.

Christie Farrer contributed to Alberta data acquisition, reviewing and revising the report, and Alberta project management.

Scott Gavura contributed to conception and design, and drafting and reviewing the report, including key messages and conclusions.

Winson Y Cheung contributed as the Alberta lead by overseeing the analysis and interpretation, and reviewing and revising the report.

Stuart Peacock contributed to conceptualization, study design, data and results interpretation, and drafting of the report.

Mina Tadrous contributed to design development and revising the report.

Cheryl Ho contributed to the concept, interpretation of data, and drafting of the report, and approved the final version.

Vishal Navani contributed to the conception, design, drafting, and editing of the report.

Kelvin KW Chan contributed to all aspects of the research, including study design, analysis, and interpretation of results, and drafting and revising the entire report.

Content Experts

This individual kindly provided comments on this report:

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Louis de Léséleuc and **David Stock** reviewed the drafts and final report. Emily Farrell provided knowledge mobilization support. Brandy Appleby provided project management support.

Conflicts of Interest

Mina Tadrous disclosed the following:

Consulting Fees:

- Health Canada – Drug shortages

Payment as Advisor or Consultant:

- Green Shield Canada – Data analytics

Cheryl Ho disclosed the following:

Educational Lectures:

- Amgen – NSCLC
- Astra Zeneca – NSCLC
- Bayer – Thyroid
- Pfizer – NSCLC
- Sanofi – NSCLC

Speaking Engagement:

- Precision Rx Dx – Thyroid biomarker testing

Payment as Advisor or Consultant:

- AstraZeneca – Durvalumab, osimertinib
- Bayer – Larotrectinib
- BMS – Nivolumab, ipilimumab
- Eisai – Lenvatinib
- EMD Serono – Tepotinib
- Janssen – Amivantamab
- Jass – Lurbinectedin
- Merck – Pembrolizumab
- Novartis – Capmatinib, dabrafenib, trametinib
- Roche – Atezo, entrectinib, foundation 1 testing
- Sanofi – Cemiplimab
- Sterimax – Tedopi

Research Funding or Grants:

- AstraZeneca – Durvalumab, osimertinib
- EMD Serono - Tepotinib
- Roche – Atezo, entrectinib, foundation 1 testing

Other:

- Abbvie – Drug access
- Pfizer – Lorlatinib
- Takeda – Brigatinib

Scott Gavura disclosed the following:

- Chair, Pharmaceutical Advisory Committee (2023 to 2024)
- Lead, CCRE (2023 to 2024)

- Director, Provincial Drug Reimbursement Programs, Ontario Health (2023 to 2024)

Vishal Navani disclosed the following:

Travelling Funding or Payment:

- EMD Serono 2023
- Sanofi 2023
- Pfizer 2023

Speaking Engagement:

- Ipsen 2023

Educational Lectures:

- Janssen 2023 – Amivantamab Lung

Writing Articles or Editorials:

- AstraZeneca 2023 – Real World Data Lung
- Ipsen 2022

Other:

- AstraZeneca 2023 – Durvalumab, Lung

Payment as Advisor or Consultant – Advisory Boards:

- EMD Serano 2023 – Avelumab, bladder
- Pfizer 2022 – Lorlatinib, lung
- Sanofi – Lung 2023
- AstraZeneca 2023 – Durvalumab, lung
- BMS 2023 – Nivolumab, lung

No other conflicts of interest were declared.

Appendix 1: Large Tables and Figures

Note that this appendix has not been copy-edited.

Table 7: Cohort DIN List

Description	DIN
Afatinib	02415666, 02415674, 02415682
Alectinib	02458136
Brigatinib	02479206, 02479214, 02479222, 02479230
Ceritinib	02436779
Crizotinib	02384256, 02384264
Entrectinib	02495015
Erlotinib	02461862, 02461870, 02461889, 02483912, 02483920, 02483939, 02454386, 02454394, 02269007, 02269015, 02269023, 02377691, 02377705, 02377713
Gefitinib	02468050, 02248676, 02500663, 02491796, 02487748
Lorlatinib	02485966, 02485974
Osimertinib	02456222, 02456214
Atezolizumab	0246299, 0249239
Pembrolizumab	0244115, 0245686
Nivolumab	0244662, 0244663, 0254141

DIN = drug identification number.

Table 8: Histology Codes

NSCLC histology types	Codes used
Squamous cell carcinoma	8051 to 8052, 8070 to 8076, 8078, 8083 to 8084, 8090, 8094, 8123
Adenocarcinoma	8015, 8050, 8140 to 8141, 8143 to 8145, 8147, 8190, 8201, 8211, 8250 to 8255, 8260, 8290, 8310, 8320, 8323, 8333, 8401, 8440, 8470 to 8471, 8480 to 8481, 8490, 8503, 8507, 8550, 8570 to 8572, 8574, 8576
Large cell carcinoma	8012 to 8014, 8021, 8034, 8082
Other	8046, 8003 to 8004, 8022, 8030, 8031 to 8033, 8035, 8120, 8200, 8240 to 8241, 8243 to 8246, 8249, 8430, 8525, 8560, 8562, 85

NSCLC = non-small cell lung cancer.

Table 9: Summary of Data Sources by Site

Site	Data sources
Ontario	**Cohort creation (accrual period)** • **Ontario Drug Benefits database:** all records of publicly funded medications in Ontario • **Activity Level Reporting database:** records of visits to oncology centres in Ontario

Site	Data sources
	• **Ontario Cancer Registry:** records of cancer diagnoses • **Registered Persons Database:** demographics data
	Clinical and demographic characteristics (at index date or in look-back period) • **CIHI-Discharge Abstract Database:** all records of procedures and diagnoses that occur in an inpatient setting • **CIHI-Same Day Surgery:** records of same day surgeries • **Ontario Health Insurance Plan:** all records of procedures and diagnoses that occur in an outpatient setting • **New Drug Funding Program:** all records of new and expensive injectable cancer drugs administered in hospital settings in Ontario • **Ontario Cancer Registry** • **Ontario Drug Benefits database** • **Activity Level Reporting database** • **Registered Persons Database**
	Outcomes (observation window) • Activity Level Reporting database • New Drug Funding Program • Ontario Drug Benefit • Registered Persons Database
Alberta	**Cohort creation** • **PIN database:** all records of prescription medications dispensed in Alberta for all payers
	Clinical or demographic characteristics (on index date or during look-back period) and outcomes (during observation window) • **Alberta Cancer Registry:** records of patient demographics, cancer diagnosis and mortality https://www.cihi.ca/en/discharge-abstract-database-dad-metadata • **Discharge Abstract Database:** National Ambulatory Care Reporting System
BC	**Cohort creation (accrual period), and clinical or demographic characteristics (on index date or during look-back period)** • **BC Provincial Systemic Therapy Program:** pharmacy dispensing records for all publicly funded systemic therapies • **BC Cancer Registry:** records of patient demographics, cancer diagnosis, and mortality • **BC Cancer Radiotherapy treatment data:** records of radiotherapy treatment (planning and delivery) in BC • **BC Cancer Surgery database:** records of all surgical procedures received by cancer patients, from 6-months before diagnosis onward
	Outcomes (during observation window) • BC Provincial Systemic Therapy Program • BC Cancer Registry
PMT cohort	**Cohort creation clinical or demographic characteristics and outcomes** • **PMT registry, Exactis Innovation:** Data collected in the PMT registry are abstracted from electronic medical records of patient enrolled in the PMT initiative, in Quebec, New Brunswick, and Nova Scotia

BC = British Columbia; CIHI- = Canadian Institute for Health Information; PIN = Pharmaceutical Information Network; PMT = Personalize My Treatment.

Table 10: Canadian Classification of Health Intervention Codes for Prior Lung Resection

Code	Long description	Length of stay category
1GJ87LA	Excision partial, trachea open approach [e.g., transcervical, collar incision] with simple apposition [anastomosis]	Lung - Other
1GJ87LANR	Excision partial, trachea open approach with stent implant with simple apposition [anastomosis]	Lung - Other
1GJ87LANRA	Excision partial, trachea open approach with stent implant using autograft	Lung - Other
1GJ87LANRE	Excision partial, trachea open approach and stent implant using local flap (e.g., omental wrap, pericardial patch)	Lung - Other
1GJ87LAXXA	Excision partial, trachea open approach [e.g., transcervical, collar incision] using autograft	Lung - Other
1GJ87LAXXE	Excision partial, trachea open approach [e.g., transcervical, collar incision] using local flap (e.g., omental wrap, pericardial patch)	Lung - Other
1GJ87QB	Excision partial, trachea open thoracic approach [e.g., mediastinal, posterolateral thoracotomy] with simple apposition [anastomosis]	Lung - Other
1GJ87QBNR	Excision partial, trachea open thoracic approach with stent implant with simple apposition [anastomosis]	Lung - Other
1GJ87QBNRA	Excision partial, trachea open thoracic approach with stent implant using autograft	Lung - Other
1GJ87QBNRE	Excision partial, trachea open thoracic approach with stent implant using local flap (e.g., omental wrap, pericardial patch)	Lung - Other
1GJ87QBXXA	Excision partial, trachea open thoracic approach [e.g., mediastinal, posterolateral thoracotomy] using autograft	Lung - Other
1GJ87QBXXE	Excision partial, trachea open thoracic approach [e.g., mediastinal, posterolateral thoracotomy] using local flap (e.g., omental wrap, pericardial patch)	Lung - Other
1GM87DA	Excision partial, bronchus NEC using endoscopic (percutaneous) approach	Lung - Other
1GM87LA	Excision partial, bronchus NEC using open approach	Lung - Other
1GR87DA	Excision partial, lobe of lung using endoscopic approach [VATS]	Lung - Other
1GR87NW	Excision partial, lobe of lung using intrapericardial [transpericardial] approach	Lung - Other
1GR87QB	Excision partial, lobe of lung using open thoracic approach	Lung - Other
1GT87DA	Excision partial, lung NEC using endoscopic approach [VATS]	Lung – Other
1GT87NW	Excision partial, lung NEC using intrapericardial [transpericardial] approach	Lung – Other
1GT87QB	Excision partial, lung NEC using open thoracic approach	Lung – Other
1GV87DA	Excision partial, pleura using endoscopic approach [VATS]	Lung – Other
1GV87LA	Excision partial, pleura using open approach	Lung – Other
1ME87DA	Excision partial, lymph node(s), mediastinal using endoscopic approach	Lung – Other
1ME87LA	Excision partial, lymph node(s), mediastinal using open approach	Lung – Other
1MF87DA	Excision partial, lymph node(s), intrathoracic NEC using endoscopic approach	Lung – Other

Code	Long description	Length of stay category
1MF87LA	Excision partial, lymph node(s), intrathoracic NEC using open approach	Lung – Other
1MN87DA	Excision partial, lymphatic vessels of thoracic region no tissue used Endoscopic approach	Lung – Other
1GN92LA	Excision radical with reconstruction, carina using open approach	Lung –– Other
1GR91NW	Excision radical, lobe of lung open intrapericardial [transpericardial] approach with simple closure	Lobectomy
1GR91NWXXA	Excision radical, lobe of lung open intrapericardial [transpericardial] approach using autograft [pericardium]	Lobectomy
1GR91NWXXF	Excision radical, lobe of lung open intrapericardial [transpericardial] approach using free flap	Lobectomy
1GR91NWXXG	Excision radical, lobe of lung open intrapericardial [transpericardial] approach using distant pedicled flap	Lobectomy
1GR91NWXXL	Excision radical, lobe of lung open intrapericardial [transpericardial] approach using xenograft	Lobectomy
1GR91NWXXN	Excision radical, lobe of lung open intrapericardial [transpericardial] approach using synthetic material	Lobectomy
1GR91NWXXQ	Excision radical, lobe of lung open intrapericardial [transpericardial] approach using combined sources of tissue	Lobectomy
1GR91QB	Excision radical, lobe of lung open thoracic approach with simple closure	Lobectomy
1GR91QBXXA	Excision radical, lobe of lung open thoracic approach using autograft [pericardium]	Lobectomy
1GR91QBXXF	Excision radical, lobe of lung open thoracic approach using free flap	Lobectomy
1GR91QBXXG	Excision radical, lobe of lung open thoracic approach using distant pedicled flap	Lobectomy
1GR91QBXXN	Excision radical, lobe of lung open thoracic approach using synthetic material	Lobectomy
1GR91QBXXQ	Excision radical, lobe of lung open thoracic approach using combined sources of tissue	Lobectomy
1GT91NW	Excision radical, lung NEC using simple closure open intrapericardial [transpericardial] approach	Pneumonectomy
1GT91NWXXF	Excision radical, lung NEC using free flap open intrapericardial [transpericardial] approach	Pneumonectomy
1GT91NWXXG	Excision radical, lung NEC using distant pedicled flap open intrapericardial [transpericardial] approach	Pneumonectomy
1GT91NWXXN	Excision radical, lung NEC using synthetic material open intrapericardial [transpericardial] approach	Pneumonectomy
1GT91NWXXQ	Excision radical, lung NEC using combined sources of tissue open intrapericardial [transpericardial] approach	Pneumonectomy
1GT91QB	Excision radical, lung NEC with simple closure open thoracic approach	Pneumonectomy
1GT91QBXXF	Excision radical, lung NEC using free flap open thoracic approach	Pneumonectomy

Code	Long description	Length of stay category
1GT91QBXXG	Excision radical, lung NEC using distant pedicled flap open thoracic approach	Pneumonectomy
1GT91QBXXN	Excision radical, lung NEC using synthetic material open thoracic approach	Pneumonectomy
1GT91QBXXQ	Excision radical, lung NEC using combined sources of tissue open thoracic approach	Pneumonectomy
1GR89DA	Excision total, lobe of lung using endoscopic approach [VATS]	Lobectomy
1GR89NW	Excision total, lobe of lung using intrapericardial [transpericardial] approach	Lobectomy
1GR89QB	Excision total, lobe of lung using open thoracic approach	Lobectomy
1GT89DA	Excision total, lung NEC using endoscopic approach [VATS]	Pneumonectomy
1GT89NW	Excision total, lung NEC using intrapericardial [transpericardial] approach	Pneumonectomy
1GT89QB	Excision total, lung NEC using open thoracic approach	Pneumonectomy
1GV89DA	Excision total, pleura using endoscopic approach [VATS]	Lung – Other
1GV89LA	Excision total, pleura using open approach	Lung – Other
1ME89DA	Excision total, lymph node(s), mediastinal using endoscopic approach	Lung – Other
1ME89LA	Excision total, lymph node(s), mediastinal using open approach	Lung – Other

NEC = not elsewhere classified; VATS = video-assisted thoracoscopic lobectomy.

For more information on CoLab and its work, visit colab.cda-amc.ca.

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CoLab is a pan-Canadian network of experts in applied research, scientific methods, and data analysis. CoLab members work with the Post-Market Drug Evaluation Program to produce credible and timely evidence on postmarket drug safety and effectiveness.