CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

CEMIPLIMAB (Libtayo)

(Sanofi-Aventis Canada Inc.)

Indication: Cemiplimab in combination with platinum-based chemotherapy for the first-line treatment of adult patients with non-small cell lung cancer (NSCLC) whose tumors have no epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK) or c-ROS oncogene 1 (ROS1) aberrations and is locally advanced where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic NSCLC.

October 10, 2023

Stakeholder Input

Disclaimer: The views expressed in each submission are those of the submitting organization or individual and not necessarily the views of CADTH or of other organizations. As such, they are independent of CADTH and do not necessarily represent or reflect the views of CADTH. No endorsement by CADTH is intended or should be inferred.

By filing with CADTH, the submitting organization or individual agrees to the full disclosure of the information. CADTH does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no identifying personal information or personal health information is included in the submission. The name of the submitting organization or individual and all conflict of interest information are included in the submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

CADTH is committed to treating people with disabilities in a way that respects their dignity and independence, supports them in accessing material in a timely manner, and provides a robust feedback process to support continuous improvement. All materials prepared by CADTH are available in an accessible format. If materials provided to CADTH by a submitting organization or individual are not available in an accessible format, CADTH will provide a summary document upon request. More details can be found within CADTH's accessibility policies.

Patient Input #1

Lung Health Foundation

CADTH Reimbursement Review
Patient Input Template

Name of the Drug and Indication	**Libtayo (cemiplimab for injection): in combination with platinum based chemotherapy for the first line treatment of adult patients with NSCLC whose tumours have no EGFR, ALK or ROS1 aberrations and is:- locally advanced where patients are not candidates for surgical resection or definitive chemoradiation, or - metastatic NSCLC.**
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

Describe the purpose of your organization. Include a link to your website.

The Ontario Lung Association (now named Lung Health Foundation) is registered with the CADTH and pCODR (www.lunghealth.ca). The Lung Health Foundation (Ontario Lung Association) is a registered charity that assists and empowers people living with or caring for others with lung disease. It is a recognized leader, voice and primary resource in the prevention and control of respiratory illness, tobacco cessation and prevention, and its effects on lung health. The Foundation provides programs and services to patients and health-care providers, invests in lung research and advocates for improved policies in lung health. It is run by a board of directors and has approximately 46 employees, supported by thousands of dedicated volunteers.

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include when the data were gathered; if data were gathered in Canada or elsewhere; demographics of the respondents; and how many patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

The information provided from the Lung Health Foundation in this submission was obtained from an online survey completed by 15 patients living with lung cancer and one caregiver. Information on age, gender and geographical location was not collected from any of the 15 online respondents. All of the online respondents completed the survey between January 2021 and October 2023 . Input from a Registered Nurse was obtained for this submission. This individual reviewed sections related to disease experience, experiences with available treatments and outcomes based on information received from monthly patient support groups and phone consultations.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

The respondents had varying experiences with their lung cancer diagnosis. Symptoms and challenges these patients experienced as a result of their lung cancer were shortness of breath (80%), fatigue (60%), depression (25%), cough (30%), difficulty fighting infection (21%) and chest tightness (14%). Weight loss, diminished appetite, low mood and challenges with physical and emotional intimacy were also noted by a few 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
- Participate in leisure activities and hobbies
- Use stairs

- Participate in sports and physical activities
- Go shopping
- Travel
- Go out for a daytrips

Patients also described having a challenging time maintaining relationships with families and friends. They felt short tempered and impatient and this made them feel isolated. Patients also described withdrawing from social activities because of the stigma attached to a lung cancer diagnosis. To quote one of the respondents, "I did not want anyone to know I had lung cancer, I wanted people to still have empathy for my children."

Family members and caregivers of those living with lung cancer share the same psychosocial burdens as the patients and have the added responsibility of providing care. Being a caregiver affects their ability to work, relationships with family and friends and their emotional well-being. As well, their independence and ability to travel and socialize are often impacted. Having to take time off work to drive those they are caring for to get groceries, run errands or attend medical appointments can be problematic for caregivers and feelings of fatigue and emotional exhaustion are not uncommon.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers. Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

The treatments tried by the respondents included surgery, radiation, chemotherapy, targeted therapy and immunotherapy. The medications tried included Maxolone, Memantine, Cisplatin, Docetaxel, Gefitinib, Entrectnib, Alectinib, Brigatinib, Tagrisso, Nivolumab and Ipilimumab. 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. Although these benefits were noted, most patients struggled 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 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. One of the respondents reported that while on chemotherapy, because of the hair loss and side effects, he was visibly ill which severely impacted his self-esteem.

When asked about challenges with access to treatment, the respondents reported that they struggled to navigate the healthcare system and in some cases, they were not clear where to go for information and support. One respondent stated, "anybody who has chronic conditions like mine needs a secretary - someone to navigate the bureaucracy that is suddenly everywhere in one's life, someone to keep track of the appointments and the things said".

Patients also struggled with the amount of time spent attending medical appointments and the cost associated with travel. Patient also reported that they struggled with the high cost associated with some medications.

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Key treatment outcomes for this group of lung cancer patients included stopping or slowing the progression of the disease with minimal side effects. 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.

Patients state that if treatments were more effective in treating lung cancer at any stage, then a diagnosis would not feel like a "death sentence".

Side effects are also a great source of distress for patients. Some reported that they had no symptoms from the actual cancer but struggled with the side effects from treatment more. Patients would like treatments with minimal side effects so that they can carry on with regular activities while on treatment. The importance of maintaining some quality of life cannot be overstated.

Caregivers report having to make decisions about treatment options. Seeing patients suffer through side effects is particularly challenging and they report often feeling conflicted as they want the patient to receive treatment but do not want them to suffer through side effects.

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 a guarantee that the medication would stop or slow down the progression of lung cancer.

Patients have also expressed frustration with the speed at which treatments are approved in Canada, compared to other countries. Patients and caregivers perceive that there are fewer treatment options available to them and that the drug approval process is a barrier to quick access. A caregiver stated that, "Health Canada is too slow and HTAs are too slow in Canada. Patients are missing out.".

5. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

No

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- **Access to testing: for example, proximity to testing facility, availability of appointment.**
- **Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?**
- **Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?**
- **How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.**

The majority 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.

6. Anything Else?

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

Not applicable

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
Sanofi				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/Ontario Lung Association
Date: 6 October, 2023

Patient Input #2

Lung Cancer Canada

Name of Drug: cemiplimab (Libtayo)
Indication: Libtayo (cemiplimab for injection): in combination with platinum based chemotherapy for the first line treatment of adult patients with NSCLC whose tumours have no EGFR, ALK or ROS1 aberrations and is:- locally advanced where patients are not candidates for surgical resection or definitive chemoradiation, or - metastatic NSCLC.
Name of Patient Group: Lung Cancer Canada - Patient Group
Author of Submission: Winky Yau, Coordinator, Medical Affairs, Lung Cancer Canada

1. About Your Patient Group

Lung Cancer Canada is a national charity, focusing our efforts on increasing awareness of lung cancer, providing support and education to persons living with lung cancer, their care partners and loves ones, and to support research and advocate for access to the best practices and care for all those living with lung cancer across Canada. LCC is a member of the Global Lung Cancer Coalition and the only 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 basis of this submission is on the recent EMPOWER-Lung-3 clinical trial for cemiplimab-rwlc, in combination with platinum-based chemotherapy. It was recently approved in the US and Canada, though there are no Canadian trial sites. As a result, it was difficult to source patients with experience on this treatment in line with the indication. Lung Cancer Canada spoke to 1 individual living with lung cancer in Canada on this treatment indication, in addition to gathering other patient experiences listed below via environmental scans. All information was gathered in September/October 2023.

Patient Name	Age	Year of diagnosis	Diagnosis	Location	Contact method
LR	73	2021	Stage 4 NSCLC	Canada (SK)	Phone interview
FI	60	2014	NSCLC	United Kingdom	Environmental scan

PD	Unknown	Unknown	Squamous cell carcinoma	USA	Environmental scan
KM	Unknown	Unknown	Stage 4B cervical cancer	Unknown	Environmental scan

3. Disease Experience

73-year-old LR had always lived a relatively healthy lifestyle, playing sports and running on the treadmill nearly every day. In 2002, he had just retired from a 30-year career with an agricultural manufacturing company, where he was living a busy lifestyle balancing work and looking after his wife. Looking forward to the extra time he would have to enjoy retirement, LR started to make plans for travel and exploring new hobbies. However, only a year later in 2003, LR was diagnosed with colon cancer, a journey he was not prepared to battle. As treatment options then were limited, he endured 6 gruesome months of chemotherapy prior to surgery to remove the tumour, at which point he was declared cancer-free. He continued to be NED for 18 years until a routine CT scan in 2021 highlighted a tumour in his lung, ribs and two lymph nodes. He was officially diagnosed with stage 4 non-small cell lung cancer, albeit this diagnosis was even more shocking to LR and his family as he had no symptoms of cancer and did not feel unwell at all. It was tough to hear he had cancer again and to wrap his head around the diagnosis. LR recalls if her had not gone for the CT scan, his cancer would not have been found, even though it was already at such an advanced stage. Unfortunately, this is the reality for many lung cancer patients alike because of delayed diagnosis and treatment, and LR highlights his case was just one of the “lucky ones that were found earlier than others”.

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer and occurs in 80-85% of all lung cancer cases. Among those with NSCLC, about 69% of these patients are diagnosed with locally advanced or metastatic disease (stage 3 or 4), in which five-year net survival rates are at a mere 14% and 3% respectively (Canadian Cancer Statistics, 2020). There has been much improvement in these statistics, albeit there is still room for more, especially with the recent developments of new therapies, screening, and earlier detection programs across the country. Biomarker testing is a key step in the patient pathway during diagnosis and staging to determine best treatment options, those with mutation-positive tumours are able to access targeted therapies specific to their disease. However, these do not carry forward with mutation-negative patients, leaving systemic treatments such as immunotherapy and chemotherapy to be the standard of care for first line treatment.

Cemiplimab is an immunotherapy treatment approved for advanced NSCLC patients who have a PDL-1 level <50% without ALK, ROS1, or EGFR mutations. It is indicated for first line treatment, and results from the EMPOWER-Lung 3 and previous EMPOWER-Lung 1 clinical trials as a monotherapy have shown very promising results in its efficacy and safety profiles, including the management of adverse effects.

A key advantage cemiplimab brings is the flat-dosing option that is available for patients, without the need for a weight-based option. This carries significant benefits and cost-saving potential as it allows for treatment administration at smaller community hospitals closer to home, in turn bringing better patient compliance, easier access to care, shorter travel times, better patient outcomes, and lessening the gap in barriers to treatment. Currently available treatments like pembrolizumab utilize weight-based dosing, and though this allows for the fine-tuning of dosages that cater specifically to each individual patient, it also comes with drawbacks in accessibility of treatment. Patients may need to travel to larger hospitals for infusions, which carries financial, emotional, and mental barriers that inhibit ease of access.

Overall, cemiplimab brings a treatment alternative to the current standard of care, which is needed to allow for the diversification of options available to patients. The reality is that systemic and geographical barriers impede timely access to diagnosis, treatment, and care that makes all the difference for lung cancer patients. Advanced NSCLC

already has a very low five-year survival rate, and so the need for additional therapeutic options for these patients is clear.

References:

Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics: A 2020 special report on lung cancer. Toronto, ON: Canadian Cancer Society; 2020. Available at: cancer.ca/Canadian-Cancer-Statistics-2020-EN (accessed October 5, 2023).

4. Experiences With Currently Available Treatments

20 years prior, LR had been diagnosed with colon cancer in 2003 when chemotherapy was the standard of treatment then, which he endured 6 months of. He was incredibly sick and side effects from the chemotherapy were almost intolerable. He was constantly nauseous, struggled with self-image after losing his hair, and could hardly finish a meal without feeling ill. He then had surgery to remove the tumour and was cancer-free for nearly 20 years until being diagnosed with stage 4 lung cancer in 2021. When asked about his experience with chemotherapy in comparison to his current treatment with cemiplimab, he states “it is like night and day”. Since being diagnosed with lung cancer, cemiplimab is the first treatment he has had for the cancer, and he is still doing very well on it to this day.

The current first line standard of care for those with locally advanced or metastatic NSCLC without actionable mutations, such as EGFR, ALK or ROS1, is immunotherapy in combination with chemotherapy, namely pembrolizumab. Pembrolizumab, as highlighted in Lung Cancer Canada’s previous submissions, has been on the market for a number of years and has proven to be effective at treating disease and maintaining a clear survival advantage with the combination of platinum doublet chemotherapy.

Overall, cemiplimab will act as an alternative to the current standard of care for the first-line treatment of the aforementioned population. Based on the scientific research, both pembrolizumab and cemiplimab’s efficacy rates, tolerability, and list of common adverse events are similar, and thus, comparable to each other. Patients deserve additional treatment options that extend beyond the current standard of care, as the question of accessibility, equity, and other socioeconomic factors, influence one’s decision in their cancer care. There is a large gap in unmet needs for those in rural and remote geographical regions, and having a treatment option closer to home will lessen the gaps in accessibility barriers.

5. Improved Outcomes

Patients all across the cancer paradigm have arguably very similar wishes in desired outcomes when choosing a therapy that is best for them. Although there may be differences based on prognosis and type of treatments available to them, lung cancer patients simply just want treatments that will:

- Have manageable side effects and improve their NSCLC symptoms
- Allow them to have a full and worthwhile quality of life
- Maintain their independence and functionality to minimize the burden on their caregivers and loved ones
- Delay disease progression and ultimately, settle patients into long-term remission for improved survivorship
- In this case, as there is a comparable funded immunotherapy, patients expect cemiplimab to be as equally effective, if not better, than the current standard of care

6. Experience With Drug Under Review

Patient Name	Cemiplimab treatment type (i.e., monotherapy or chemo combo)	Cemiplimab access method	Line of therapy with cemiplimab	Period on cemiplimab	Duration on cemiplimab
LR	Cemiplimab/chemo combo	Clinical trial	1L	May 2023 - present	5 months
FI	Cemiplimab/chemo combo	Clinical trial	1L	Oct 2020 - Jan 2022	1 year 3 months
PD	Monotherapy	unknown	unknown	June 2020 – March 2021	9 months
KM	Monotherapy	unknown	2L	October 2022 - June 2023	8 months

Patients' tumours have responded well to treatment.

When LR was diagnosed in 2021 from a routine CT scan, he was shocked to hear he had an 18.9cm mass in his lung alongside nodules in his rib and 2 lymph nodes. As his first line treatment, LR was hopeful that this therapy would help resolve his disease. Since he started combination cemiplimab and chemotherapy about 5 months ago, his most recent scan from September 2023 has shown his primary tumour had shrunk from 18.9cm to 8.7cm and the two lymph nodes are now classified as "normal", a response his oncologist was very pleased with. They are unsure whether his rib nodule has also responded to treatment, but LR is doing very well and continuing to receive the treatment every 3 weeks.

FI started treatment with cemiplimab in combination with chemotherapy on October 14, 2020, after previous treatment plans changed since new scans confirmed they were no longer candidates for radiotherapy. Their first scan in late November showed that although their chest nodules and the primary tumour in the lung had grown slightly after two treatments, their oncologist was nonetheless optimistic as this was still well within the "stable" range, thus continuing the treatment. By February 2021, FI had received some great news that their lung tumour had shrunk considerably in size after 5 rounds of immunotherapy, though the chest nodes remained stable. FI continued to remain stable on cemiplimab and chemotherapy combo for another 11 months until having to stop treatment in January 2022 due to complications from radiotherapy.

Cemiplimab has also been approved for use in Canada in other disease areas, and these patients have also seen very similar positive results on cemiplimab. PD lives with squamous cell carcinoma and has been very fortunate to have seen very positive success on cemiplimab. Their 11 cm metastasized squamous cell tumor on the psoas muscle has shrunk "significantly" to approximately 3cm at her 6-month scan. An additional tumor in their right axillary has essentially disappeared as well.

KM lives with stage 4B cervical cancer and was on cemiplimab for 8 months between October 2022 and June 2023. As her 2nd+ line of treatment, cemiplimab helped keep her tumours stable for 8 months until progression, a feat she hadn't seen with any of her previous treatments.

Patients have seen a noticeable difference in their disease symptoms and other comorbidities.

LR has had arthritis in his right knee for years since even before being diagnosed with lung cancer. He used to enjoy playing basketball and other sports up until about 20 years ago when he developed arthritis and could no longer continue without pain. However, since starting treatment with cemiplimab, the pain in his knee has completely resolved and is “completely normal now”, a sensation he admits he hadn’t felt in over a decade. When LR spoke to Lung Cancer Canada, he stated, “I’ve had no pain in my right knee at all anymore – it’s completely normal and I never thought I’d ever have a day without it bothering me. The treatment has truly been a miracle drug in ways that extend even beyond treating my lung cancer!”

Quality of life on treatment is very good, allowing patients to maintain their functionality and independence.

During LR’s first experience with cancer 20 years ago, he recalls his experience with chemotherapy treatments during that time were “a complete 180” from what he had experienced now with cemiplimab. Albeit cancer treatments and research has progressed quite significantly since then, it is ultimately the burden on the patient’s quality of life that is often feared when diagnosed with cancer for the first time, which is what LR recalled when speaking to LCC. LR has always had some trouble walking for long periods of time due to his arthritic knee, but since starting the cemiplimab/chemotherapy treatment, his pain has resolved near completely, a feat he never expected he’d experience. He has been able to continue doing activities of daily living as normal, drives himself to medical appointments, complete chores around the house, grocery shopping, and mow the lawn. Being able to maintain this functionality and independence has allowed LR to focus on more important things, like caring for his wife and family.

Less than 2 weeks after FI started treatment with cemiplimab/chemo, her second grandson was born, and she felt incredibly blessed to say the least. She felt well, had no more symptoms of disease, and was actively running errands as usual. She continued to live a fulfilling life with few disease symptoms and is extremely grateful to have been able to live long enough to see the birth of her grandson. Although she had to stop treatment with cemiplimab due to complications with other treatments, she has since been on other clinical trials and had even returned to work briefly in early 2022 after stopping cemiplimab. She mentions cemiplimab has been able to help her maintain quality of life to a manageable level that even allowed her to return to work, something she didn’t anticipate would happen.

Independence is a key factor in patients’ wishes for treatment outcomes, and with cemiplimab, patients like LR and FI have been able to see these changes first-hand. In the current appropriate climate of focusing on equity and access, being able to deliver an efficacious treatment combination much closer to home is a priority. This would save travel time, fuel, parking costs, time off work and loss of income for patients and caregivers, and in itself would support approval of this regimen.

Patients reported very manageable and minimal side effects with cemiplimab.

According to the EMPOWER-Lung 3 clinical trial, the most common side effects seen with cemiplimab in combination with chemotherapy were anemia, alopecia, nausea, and decreased appetite, all of which are relatively manageable. Treatment discontinuation due to toxicity was only recorded in 6% of study participants in the treatment group, a relatively low percentage (Makharadze T, Gogishvili M, Melkadze T, Baramidze A, Giorgadze D, Penkov K, Laktionov K, Nemsadze G, Nechaeva M, Rozhkova I, Kalinka E. Cemiplimab plus chemotherapy versus chemotherapy alone in advanced NSCLC: 2-year follow-up from the phase 3 EMPOWER-Lung 3 part 2 trial. Journal of Thoracic Oncology. 2023 Jun 1;18(6):755-68).

This was similarly reflected in the patient experiences gathered for this submission, all of whom have each noted very minimal side effects, if any, with their treatment on cemiplimab in combination with chemotherapy. LR said he has no noticeable side effects at all in his 5 months of treatment, alongside no symptoms of disease. FI mentioned only having mild side effects, including itchy skin, fatigue, and mild joint pain in her shoulders. However, she said being on the

treatment and the benefits it brings is completely worth it, for the small price to pay for the mild side effects. They do not impede their lives in any way and are still able to go about day-to-day tasks while on treatment.

Cemiplimab's flat dose administration allowed patients to stay close to home for treatment and minimizes barriers to treatment access.

As noted previously in Section 3, cemiplimab utilizes a flat dosing administration method, which carries significant advantages over other immunotherapy treatments available for these patients, including pembrolizumab. Perhaps the key advantage is the ability for cemiplimab to be administered in more hospitals and community clinics across the country as vial sharing is not required, thus allowing patients to receive treatment close to home and subsequently carrying fewer barriers to access.

LR and his wife seldomly travel outside his hometown as travel is difficult for them. LR's wife uses a wheelchair for mobility, so although he wishes to be able to travel and explore the world with his family, he admits travelling is out of the question. Because his oncologist is 3 hours away in the nearest major city, his initial scans and tests at diagnosis were all completed there, which took a major toll on him having to drive far distances every few weeks. However, his treatments with cemiplimab have allowed him to receive treatments only a few blocks away at the hospital in town, which he continues to drive himself to, giving him back the time to spend with family and friends, and doing things that matter most to him.

In Lung Cancer Canada's previous patient submission for cemiplimab monotherapy, our survey highlighted 91% of respondents would choose to receive the treatment option closer to home compared to one at a large cancer center at least one hour away, if given the option between two equally as efficacious treatment options. This same question was posed to LR in his interview with LCC, who also stated he would choose the option closer to home rather than one a few hours away. This sets the case with cemiplimab and pembrolizumab, the current immunotherapy standard of care, as both treatments are virtually equally as efficacious and are comparable to each other. The fixed dose model that cemiplimab offers will allow for infusions to be done at local community hospitals across the country and will fill the gap in accessibility and variety of treatment options for patients across Canada. There needs to be equity in healthcare that can allow patients to access the care they need, without having to sacrifice or compromise on important variables such as efficacy of treatment, financial implications, and quality of life. Having cemiplimab accessible in smaller, rural, community hospitals scattered around the country will ultimately bring ease of access and equity to cancer care.

7. Companion Diagnostic Test

There is no additional companion diagnostic test associated with cemiplimab-rwlc, as PDL-1 levels, and oncogenic driver mutations (EGFR, ALK, ROS1) is currently tested in all provinces and is standard of care.

8. Anything Else?

Lung Cancer Canada thanks CADTH for the opportunity to submit and their commitment to honouring and considering the patient voice in these files, and hopes pERC receive, review, and thoroughly consider these important points made throughout this submission. Cemiplimab will act as an alternative to the current pembrolizumab combination, an equally efficacious treatment for this indication in NSCLC. Having a secondary option that will be closer to home for patients thanks to fixed dosing will only positively benefit the current barriers and gaps in treatment access in cancer care. Additionally, the introduction of a second molecule in this space allows for marketplace competition to keep costs reasonable. The sustainability of our healthcare system is a social responsibility; options mean patients are given a choice and can make informed decisions based on their individual situations. For these reasons, Lung Cancer Canada urges CADTH to make a positive funding recommendation for this submission.

Appendix: Patient Group Conflict of Interest Declaration

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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
Sanofi Pharmaceuticals				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: October 10, 2023

Patient Input #3

Canadian Cancer Survival Network

Name of Drug: Cemiplimab
Indication: in combination with platinum based chemotherapy for the first line treatment of adult patients with NSCLC whose tumours have no EGFR, ALK or ROS1 aberrations and is:- locally advanced where patients are not candidates for surgical resection or definitive chemoradiation, or - metastatic NSCLC.
Name of Patient Group: Canadian Cancer Survivor Network
Author of Submission: Lindsay Timm

1. About Your Patient Group

Describe the purpose of your organization. Include a link to your website.

The Canadian Cancer Survivor Network (CCSN) is a national network of patients, families, survivors, friends, community partners, funders, and sponsors who have come together to take action to promote the very best standard of care, whether it be it be early diagnosis, timely treatment and follow-up care, support for cancer patients, or issues related to survivorship or quality of end-of-life care. https://survivornet.ca/

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

The Canadian Cancer Survivor Network utilized SurveyMonkey to create and collect all data for the survey on Cemiplimab. We then utilized our newsletter as well as our social media platforms to disseminate the survey to collect responses. The survey was conducted from September 18, 2023, to October 5, 2023, to obtain responses. All of the survey respondents are from Canada. Nine of the ten (9 of 10) respondents to the survey are patients and one is a caregiver. Seven of the ten (7 of 10) respondents to the survey are female and three of the ten (3 of 10) are male. When the survey data was analyzed, it was clear that two of the nine patients (2 of 9) had experience with Cemiplimab, and seven of nine patients (7 of 9) do not have experience with Cemiplimab.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

When asked what stage of prostate cancer they had been diagnosed with, the following responses were received from the respondents:

- Just diagnosed: 2

- Early Stage (1): 1
- Middle Stage (2 or 3): 1
- Late Stage (4),
- Metastatic: 6

Current treatments that were identified include:

- Radiation: 4
- Surgical therapy: 3
- Targeted therapy: 3
- Immunotherapy: 1
- Clinical trials: 2
- Chemotherapy: 2
- Other: 3 (1 I am free of cancer thanks to getting checked out as soon as I noticed the blood, 1 Lenvatinib, 1 None)

When asked if there was an aspect of their disease that is most important to them to control, seven respondents replied:

- “Emotions.”
- “I had stopped smoking 30 years before I came down with cancer.”
- “Weight loss would be my concern. When you lose too much weight your body cannot tolerate any treatments and it also brings on other problems like no energy, shortness of breath, etc.”
- “Tumour.”
- “Survival.”
- “Shortness of breath.”
- “The anxiety of my own mind taking over in the land of imagination and my future.”

Respondents were asked if they have had any issues accessing any therapies. The following issues were highlighted by their responses:

- Limited availability in my community: 1
- Travel costs associated with accessing therapy/treatment: 1
- I haven’t had any issues accessing therapy: 4
- Other: 4 (1 Long wait, 1 Treatments that work are not available, 1 Initially as stage 3 NSCLC patient I was considered not a candidate for surgery and following chemo and radiation had to

advocate for surgery. I also had no gene biomarker testing or PD-L1, 1 Just starting biopsy see what mutations are I guess)

When asked if there was anything that they would like to share about their cancer journey, six respondents shared these comments:

- “It's a rollercoaster ride and always having that fear of the unknown between waiting for results and waiting for it to be explained and discussed, and the next steps if there are any.”
- “Get to a doctor as soon as you notice any symptoms.”
- “Thankful for my oncologist and PMH.”
- “It sucks to get cancer.”
- “Early screening for lung cancer would detect cancer at earlier stages when curative. Also doing extensive gene biomarker testing would enable patients to revive precision medicine that targets the genes driving their cancer.”
- “I’m a fighter.”

We asked what the issues are that they have encountered as a caregiver for someone with lung cancer. The caregiver selected these issues:

- Fatigue
- Emotional drain
- Anxiety/Worrying
- Management of side effects
- Hours spent in medical appointments
- Monetary concerns (absence from work, driving expenses, etc.)
- Lifestyle changes
- Inability to plan ahead
- Anger
- Feelings of ‘doom’ due to challenging prognosis
- Feelings of helplessness

When asked how caring for someone with lung cancer has affected their daily routine or lifestyle, the caregiver had these thoughts to share:

- “Depressing and high anxiety watching someone die.”

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

With the use of currently available treatments, patients reported that the following symptoms affected their quality of life and day-to-day living:

- A persistent cough that can get worse over time: 1
- Coughing up blood: 2
- Chest pain or discomfort: 3
- Trouble breathing: 1
- Wheezing: 4
- Hoarseness: 1
- Loss of appetite: 2
- Unexplained weight loss: 3
- Fatigue: 4
- Trouble swallowing: 2
- Loss of quality of life: 2
- Other: 5 (1 Depressed and mood changes, 1 I only coughed up a very little speck of blood every two days, 1 Heart problems, 1 Ting of blood in cough up mucus but not every time, 1 None at the moment)

When asked if any needs in their current therapy are not yet being met, eight respondents said no. Of the respondent's who replied yes, the first replied, "Liquid biopsy to determine reoccurrence and gene biomarkers." The second respondent replied, "Had radiation to spine cancer two spots and now called in for a CT scan needle biopsy for lung."

Respondents were asked to select what adverse effects they are currently dealing with while on their treatments. Eight respondents selected the following:

- Fatigue: 8
- Breathing problems: 2
- Infection: 2
- Bleeding: 1
- Nausea: 4

- Vomiting: 1
- Constipation: 3
- Changes in appearance, including hair loss: 2
- Pain: 2
- Changes in sexual functioning: 1
- Other: 1 (1 Little pain randomly on spine but bearable)

When asked if their adverse effects were tolerated, two said no, and six said yes with these responses on how they did:

- “Slept.”
- “Muscle spasms and cramps.”
- “With medication, radiation pain management, exercise.”
- “Meditation.”
- “Exercise and diet.”
- “Sennakot and rest.”

We asked respondents to respond with how they are managing on their current treatment as if they were talking to a friend and what they would tell them. These are their responses:

- “I would say I am in a steady state.”
- “I'm doing well with Targeted Therapy, just fatigued most of the time.”
- “No more treatment. Get checked out as soon as you notice any symptoms.”
- “I'm on Pembrolizumab/Keytruda. I'm doing the best I can. Pushing myself to eat and exercise. Side effects are slowly tolerable.”
- “Lenvatinib.”
- “Waiting to see if I have progression on my next scan. Very anxious.”

We asked what the caregivers find are the most challenging adverse effects of their loved one’s current therapy or treatments. The caregiver responded with this comment:

- “Them losing so much weight, and muscles mass.”

We also asked the caregivers to rate how they feel current treatments are addressing the needs of lung cancer patients. On a four-point rating scale ranging from excellent to very poor, the caregiver rated the current treatments as ‘Good’ in addressing the needs of lung cancer patients.

5. Improved Outcomes

CADTH is interested in patients’ views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily

life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

When asked about the following issues that they would hope to see a new drug address to manage their disease, eight respondents answered as follows:

- Maintain quality of life: 8
- Delay onset of symptoms: 5
- Access to a new option for treatment: 6
- Reduce side effects from current medications or treatments: 4
- Ease of use: 4
- Prolong life: 8
- Provide a cure: 6

Patients were asked to describe how much of an improvement would be needed from the new drug to make it better than the current treatment:

- "Easier and faster access to supports."
- "Minimal or no side effects. In pill form would be great."
- "Stop progressing."
- "Waiting for a scan to see if there is a progression is my current treatment. If there is a progression- a cure, new treatment since I cannot have any more radiation all would improve the quality of my life."

We then followed up with the question of how might their quality of life be different with those improvements:

- "Less anxiety."
- "I would be able to do daily things without fatigue, legs weakness. The pill form is better than having an IV each transfusion, quicker simpler."
- "Peace of mind."
- "If there was a cure or prevent progression, I would be happy to live my life stress and cancer free."
- "Can live on my own more independently."

We asked what considerations patients make when it comes to balancing the advantages and disadvantages of a treatment. Four respondents all commented that they consider how it will affect their quality of life, one respondent shared that their doctor makes all the decisions, and another respondent shared this reply, "Is it going to work? Will it make me worse? If no quality of life I'm better off considering a treatment."

When the caregivers were asked what they would like to see out of a new treatment for lung caner patients, the caregiver responded with, “Less side effects.”

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

Respondents were asked to select what adverse effects they experienced while taking Cemiplimab. The two respondents highlighted these key areas as being affected:

- Anemia: 1
- Fatigue: 2
- Hyperglycemia: 1
- Diarrhea: 1
- Nausea: 1
- Constipation: 1

We asked respondents to rate on a scale of 1-5 how likely they would be to recommend that Cemiplimab be available to all patients who qualify for it. One of the respondents responded with a ‘3’ on the scale and the other respondent replied with a ‘5’.

When asked in comparison to other therapies how was their treatment experience with Cemiplimab in treating their lung cancer, the respondents rated the following areas on a scale of much better, little or no difference, and much worse:

- Symptom management: Much better (2), Little or no difference (1)
- Side effects: Much better (2), Little or no difference (1)
- Ease of use: Much better (2), Little or no difference (1)
- Disease progression: Much better (1), Little or no difference (2)

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

N/A

8. Anything Else?

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

CCSN is aware of the limitations of this submission given the small number of respondents and with only two patients on Cemiplimab. However, it is clear from some of the responses given in the survey that there is a desire from patients for a change when it comes to the treatment of their lung cancer. Almost all respondents to our survey responded that they are looking for a treatment that can maintain their quality of life. Patients are looking for treatments that not only treat their disease but also support their lifestyle. There was also the desire highlighted for access to a new option for treatment. Patients want choice and hope and with lung cancer still being the most lethal there is room for us to allow them to have that option of choice.

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 2 years AND who may have direct or indirect interest in the drug under review.

Table: 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
Sanofi-2022			X	
Sanofi-2023			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: Lindsay Timm
Position: Community Engagement Manager
Patient Group: Canadian Cancer Survivor Network
Date: **October 6, 2023**

Clinician Input #1

Lung Cancer Canada (LCC)

Name of Drug: cemiplimab (Libtayo)
Indication: Libtayo (cemiplimab for injection): in combination with platinum based chemotherapy for the first line treatment of adult patients with NSCLC whose tumours have no EGFR, ALK or ROS1 aberrations and is:- locally advanced where patients are not candidates for surgical resection or definitive chemoradiation, or - metastatic NSCLC.
Name of Clinician Group: Lung Cancer Canada – Medical Advisory Committee
Author of Submission: Dr. Paul Wheatley-Price (lead), Dr. Michela Febbraro, Dr. Geoffrey Liu, Dr. Ron Burkes, Dr. Shaqil Kassam, Dr. Biniam Kidane, Dr. Barbara Melosky, Dr. Jeffrey Rothenstein, Dr. Rosalyn Juergens, Dr. Quincy Chu, Dr. Sunil Yadav, Dr. Mahmoud Abdelsalam

1. About Your Clinician Group

Lung Cancer Canada (LCC) is a national charity with the purpose of increasing awareness about lung cancer, providing support and education to lung cancer patients and their families, to support research and to advocate for access to the best care for all lung cancer patients in all provinces and territories.

Through the LCC Medical Advisory Committee (MAC), we have been providing clinician input for submissions of new lung cancer drugs to the HTA process for many years. The LCC MAC is made up of clinicians and key opinion leaders in the field of lung cancer across the country.

www.lungcancercanada.ca

2. Information Gathering

Information is from publicly available sources, primarily published manuscripts and conference presentations, together with experience of the members of the clinician group. This submission is entirely independent of the manufacturer (Sanofi Genzyme).

3. Current Treatments and Treatment Goals

The current first line standard of care for patients with advanced non-small cell lung cancer (NSCLC) with a PDL1 level <50%, who do not harbor an activating oncogenic driver mutation such as EGFR, ALK or ROS1, is combination chemotherapy and immunotherapy. The most widely used regimens include 4 cycles of platinum doublet chemotherapy in combination with pembrolizumab. This is based on 2 landmark clinical trials: Keynote-189 (Gandhi et al. N Engl J Med. 2018 May 31;378(22):2078-2092) and Keynote-407 (Paz-Ares et al. N Engl J Med. 2018 Nov 22;379(21):2040-2051) that demonstrated a clear survival advantage from the addition of pembrolizumab, which can be continued for up to a total of 2 years as a maintenance therapy. Depending on the choice of platinum doublet, maintenance chemotherapy with pemetrexed (generally in non-squamous NSCLC) is also a standard of care.

The reimbursement of pembrolizumab does impact how it is used in parts of Canada, most notably in Ontario. Most pembrolizumab clinical trials use a flat dose of 200mg, however the earlier clinical trials had established the dose of 2mg/kg as an efficacious option, and therefore some jurisdictions reimburse based on this weight-based dosing. As the drug is only manufactured in 100mg vials, only patients weighing 50kg or 100kg+ will have weight-based dose that does not involve any drug wastage from a vial. To avoid

wastage many centres have strategies of vial sharing, which requires patients to all be treated in a single infusion centre, or on specific days. In large geographic regions with more remote or rural populations, this poses an equity challenge as many patients will have to travel long distances with associated time and fuel costs, or time off work for carers, to allow the patients to receive pembrolizumab in a larger centre whereby wastage can be avoided.

More recently the Checkmate 9LA clinical trial was approved by Health Canada, CADTH and is publicly reimbursed. The 9LA trial employs a slightly different strategy, with just 2 cycles of chemotherapy in combination with the dual immune checkpoint blockage from ipilimumab and nivolumab (Paz-Ares et al. Lancet Oncol. 2021 Feb;22(2):198-211). This has become an option for patients based on the superiority to chemotherapy, although has not been compared directly with the platinum doublet + pembrolizumab regimens.

For patients not eligible for immunotherapy due to co-morbidities and other contraindications, platinum doublet chemotherapy remains a longstanding option.

For patients with poor performance status or those who choose not to receive systemic therapy, best supportive care with early palliative care involvement is also adopted.

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 Empower-Lung 3 clinical trial (Gogishvili et al. Nat Med. 2022 Nov;28(11):2374-2380) that provides the data for this submission, offers a valuable option for patients and clinicians treating advanced or metastatic NSCLC with a PDL1 level <50%.

While not a novel clinical trial, in its design it largely mirrors the approach of Keynote-189 and Keynote-407, the demonstrated efficacy and safety is completely in line with the benefits expected from the addition of a PD1 monoclonal antibody immune checkpoint inhibitor to chemotherapy. The results are also in line with the aforementioned Keynote studies and the Checkmate 9LA trial.

The potential advantages of cemiplimab are twofold. From a safety perspective, the rates of adverse events were favourable, and the side effects and management of these adverse events are well known.

Secondly, cemiplimab is prescribed as a flat dose of 350mg, without a weight-based option. This has significant advantages over pembrolizumab, particularly in the cost-effective ability to deliver treatment closer to home for many lung cancer patients because vial sharing will not be required. Cemiplimab has already been approved by CADTH as monotherapy in advanced or metastatic NSCLC with PDL1 >=50% (https://www.cadth.ca/sites/default/files/DRR/2022/PC0262%20Libtayo%20NSCLC%20%20–%20CADTH%20Final%20Rec.pdf), on the basis of the EMPower-Lung 1 clinical trial. This recommendation would have given patients and clinicians the option for cemiplimab monotherapy as an alternative to pembrolizumab, although unfortunately negotiations with the pan-Canadian Pharmaceutical Alliance failed to conclude with an agreement (https://www.pcpacanada.ca/negotiation/21898).

Nevertheless, CADTH has a strong track record of supporting efficacious options, and the efficacy and tolerability data from EMPower-Lung 3 clearly establishes cemiplimab and platinum doublet chemotherapy as a reasonable first line option in advanced NSCLC, with the potential advantages for patients of access.

5. Place in Therapy

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

EMPower-Lung 3 clearly establishes cemiplimab and platinum chemotherapy as a valid first-line option that would serve as an alternative to the Keynote-189, Keynote-407 and Checkmate-9LA regimens. It would not serve as an additional line of therapy, but rather as an alternative first line option. Patients would not be anticipated to have received any other therapy in the metastatic setting prior to this combination.

The platinum doublet combination therapy can be varied, as seen in the trial, with the use of cisplatin or carboplatin, together with either pemetrexed or paclitaxel which is in line with current practice.

For patients who have had reactions to pembrolizumab, this could also reasonably be considered as a substitute.

This does not represent a shift in the treatment paradigm, but rather simply an alternative option (analogous to the CADTH approvals of first line ALK drugs for ALK+ NSCLC [alectinib, brigatinib, lorlatinib]).

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?

The combination of cemiplimab and platinum chemotherapy would be used as first-line option in patients with advanced NSCLC with a PDL1 <50%. The response rate was 43% and the disease control rate was 82%, so the majority of patients can anticipate benefit. The clinical trial allowed patients with a PDL1 >50% to be enrolled. As seen across NSCLC immunotherapy trials, the response rate increased with increasing PDL1 level, but benefit was seen across subgroups, with the exception of a small number of patients with pre-existing brain metastases. However this was a small number (just 31 patients) with a wide confidence interval.

There are no additional issues with this regimen related to diagnosis, diagnostic tools or companion diagnostics. The mechanisms for pathological diagnosis of NSCLC, determination of PDL1 level, and exclusion of oncogenic driver mutations (EGFR, ALK, ROS1) are well established as standards of care.

In our opinion the patients who may benefit in particular from this option are those who live in rural communities that are served by infusion clinics, but who have been unable to receive pembrolizumab due to the vial sharing issues related to weight-based dosing that have previously been discussed. In the current appropriate climate of focusing on equity and access, being able to deliver an equally efficacious combination much closer to home is a priority (https://www.partnershipagainstcancer.ca/topics/lung-cancer-equity/). This would save travel time, fuel and parking costs, time off work and loss of income for patients and carers, and in itself would support approval of this regimen.

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?

There are well established practices for assessing response to treatment that are widely known and adopted. Briefly, patients should have baseline imaging (usually CT scan) within approximately 1 month of initiating treatment, and then repeat CT scans are used to assess response. Typically these are requested at intervals of 6-12 weeks, based on patient and clinician factors and discussions.

Palliative treatments in advanced cancer have the dual goals of helping patients to a) live longer and b) feel better. Both of these are met by adding cemiplimab to chemotherapy in this patient population.

Clinically meaningful responses are generally assessed by tumor response (complete or partial response) or stable disease with symptomatic improvement. Further efficacy is established by prolonged disease control and survival. When compared to chemotherapy alone, the addition of cemiplimab led to an increase in response rate from 23% to 43%, a prolongation of median progression free survival (PFS) from 5.0 to 8.2 months, and an improvement in overall survival from 13.0 to 21.9 months. All of these are statistically significant and clinically both substantial and relevant.

There were clear improvements in patient reported outcomes in the EMPower-Lung-3 trial, based on the widely accepted and validated EORTC QLQ-C30 measures.

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

Treatment generally would continue until one of the following conditions is met:

1. Toxicity requiring permanent discontinuation of therapy
2. Patient wishes
3. Concurrent medical condition(s) that will jeopardize the safety of cemiplimab (such as uncontrolled immune related adverse events
4. Unequivocal radiological disease progression
5. Completion of the entire course of treatment (36 cycles / 108 weeks)

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]?

Treatment generally should only be prescribed by a certified medical oncologist with expertise in the management of thoracic malignancies. In many jurisdictions across Canada, particularly in more remote or rural communities, medical oncologists work in partnership with General Practitioners in Oncology (GPOs) to co-manage patients.

As cemiplimab has the potential to be easier to deliver in rural communities, the infusions could occur in cancer centres or in smaller affiliated and licensed infusion clinics.

6. Additional Information

CADTH, and formerly pCODR, have a track record of approving new therapies as alternatives to existing available options. An example is the approval of atezolizumab, pembrolizumab and nivolumab all as second line immunotherapy options in patients with advanced NSCLC who previously have received platinum-based therapy. Another example is the recent approval of lorlatinib and brigatinib as first line treatment for advanced ALK+ NSCLC, as an alternative to either crizotinib or alectinib.

Indeed, CADTH approved cemiplimab as monotherapy as a first-line option for advanced NSCLC with PDL1 expression >50%.

This file is a similar scenario, whereby patient and/or clinician preference and ease of dosing (standard 350mg dose, not weight based), will make this a clear option in many scenarios

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 each clinician 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. 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: 02-OCT-2023

☒ **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**
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 2

Name: Dr. Geoffrey Liu
Position: Medical Oncologist, Princess Margaret Cancer Centre
Date: October 2, 2023

☒ 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
Takeda Canada	Advisory Board, Health Technology Assessment Submission Advice, Speaker's Bureau, past 10 years	☐	☐	☒	☐
Takeda Canada	(To institution, not individual) Observational Study funding, past 10 years	☐	☐	☐	☒
Hoffman La Roche	Advisory Board, Health Technology Assessment Submission Advice, past 10 years	☐	☐	☒	☐
Pfizer	Advisory Board, Health Technology Assessment Submission Advice, part 10 years	☐	☐	☒	☐
AstraZeneca	Advisory Board, Health Technology Assessment Submission Advice, Speaker's Bureau, past 10 years,	☐	☐	☒	☐
AstraZeneca	(To institution, not individual) Observational Study funding, past 10 years	☐	☐	☐	☒
Bristol Myers Squibb	Advisory Board	☒	☐	☐	☐
Boehringer Ingerheim	(To institution, not individual) Observational Study funding, past 10 years	☐	☐	☒	☐
Abbvie	Advisory Board, past 10 years	☐	☒	☐	☐

Merck	Advisory Board, Health Technology Assessment Submission Advice, past 10 years	☐	☒	☐	☐
EMD Serono	Speaker's Bureau, past 10 years	☒	☐	☐	☐
Novartis	Advisory Board,past 10 years	☐	☐	☒	☐
Glaxo Smith Kline	Advisory Board, past 10 years	☐	☒	☐	☐

Declaration for Clinician 3

Name: Dr. Ronald Burkes
Position: Medical oncologist, Mount Sinai Health
Date: October 10, 2023

☒ 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**

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

Declaration for Clinician 4

Name: Dr. Shaqil Kassam
Position: Medical Oncologist, Southlake Regional Hospital
Date: October 10, 2023

☒ 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**	**$10,001 to $50,000**	**In excess of $50,000**

		$10,000		
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 5

Name: Dr. Barb Melosky
Position: Medical Oncologist, BC Cancer
Date: October 10, 2023

☒ 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

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	☒	☐	☐	☐

Declaration for Clinician 6

Name: Dr Jeffrey Rothenstein
Position: Medical Oncologist, Lakeridge Health
Date: October 10, 2023

☒ 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 6: 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			

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

Declaration for Clinician 7

Name: Dr. Rosalyn Juergens
Position: Chair, LCC Medical Advisory Committee; Medical Oncologist, Juravinski Cancer Center
Date: October 10, 2023

☒ 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 7: Conflict of Interest Declaration for Clinician 7

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bristol Myers Squibb	x			
Astra Zeneca		x		
Merck Sharp and Dohme	x			
Roche	x			

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

Declaration for Clinician 8

Name: Dr. Quincy Chu
Position: Medical Oncologist, Cross Cancer Institute
Date: October 10, 2023

☒ 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 8

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
Abbvie	Advisory Board and Honoraria	☒	☐	☐	☐
Amgen	Advisory Board and Honoraria	☒	☐	☐	☐
Astra Zeneca	Advisory Board and Honoraria	☐	☐	☒	☐
Boehringer Ingeiheim	Advisory Board and Honoraria	☐	☒	☐	☐
Bristol-Myers Squibb	Advisory Board and Honoraria	☐	☒	☐	☐
Eisai	Advisory Board and Honoraria	☒	☐	☐	☐
Merck	Advisory Board and Honoraria	☐	☐	☒	☐
Novartis	Advisory Board and Honoraria	☐	☒	☐	☐
Pfizer	Advisory Board and Honoraria	☐	☒	☐	☐
Roche	Advisory Board and Honoraria	☐	☒	☐	☐
Astra Zeneca	Research Funding	☐	☐	☐	☒
Bristol-Myers Squibb	Educational Grant	☒	☐	☐	☐

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

Declaration for Clinician 9

Name: Dr Sunil Yadav
Position: Medical Oncologist, Saskatoon Cancer Centre
Date: October 10, 2023

☒ 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 9

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 10

Name: Dr. Mahmoud Abdelsalam
Position: Medical Oncologist, Horizon Health Network
Date: October 10, 2023

☒ 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 10: Conflict of Interest Declaration for Clinician 10

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 11

Name: Dr. Biniam Kidane
Position: Associate Professor, Dept of Surgery, University of Manitoba
Date: October 10, 2023

☒ 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 11: Conflict of Interest Declaration for Clinician 11

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	☒	☐	☐	☐

Declaration for Clinician 12

Name: Dr. Michela Febbraro
Position: Medical Oncologist - Algoma District Cancer Program
Date: October 10, 2023

☒ 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 12

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**

None	☐	☐	☐	☐

Clinician Input #2

OH-CCO Lung Cancer Drug Advisory Committee

CADTH Project Number: PC0331
Generic Drug Name (Brand Name): Cemiplimab (Libtayo)
Indication: <in combination with platinum based chemotherapy for the first line treatment of adult patients with NSCLC whose tumours have no EGFR, ALK or ROS1 aberrations and is: - locally advanced where patients are not candidates for surgical resection or definitive chemoradiation, or - metastatic NSCLC.
Name of Clinician Group: OH-CCO Lung Cancer Drug Advisory Committee
Author of Submission: Dr. Donna Maziak, Dr. Peter Ellis, Dr. Andrew Robinson

1. About Your Clinician Group

OH-CCO's 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 through videoconferencing.

3. Current Treatments and Treatment Goals

The current treatments that are available include: chemotherapy with pembrolizumab, chemotherapy with ipilimumab and nivolumab, or pembrolizumab alone in patients with a PDL1 status >50%. Another option can be platinum based chemotherapy.

The treatment goals include tumor shrinkage, improvement of symptoms and quality of life, and prolongation of survival.

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.

Cemiplimab is comparable to pembrolizumab and can be used in the same place of therapy as pembrolizumab. However, cemiplimab can be given at a fixed dose in full vials whereas pembrolizumab is dosed on a mg/kg basis. This may mean that there can be more wastage seen with pembrolizumab than with cemiplimab. Specific to Ontario, certain regions may give preference to cemiplimab to reduce wastage and the costs associated with this.

Cemiplimab may have more infusion reactions than pembrolizumab which may require premedications.

5. Place in Therapy

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

Cemiplimab in combination with platinum based chemotherapy would be given as a first line treatment and this is an alternative therapy to combination pembrolizumab plus chemotherapy, and to 2 cycles of platinum doublet plus ipilimumab/nivolumab.

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 with stage 4 NSCLC considering 1st line therapy would be best suited for treatment.

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?

Clinical assessment of symptoms and imaging such as CT scans and chest xrays are used to determine response. Treatment response should be assessed every 3 months.

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

Disease progression or intolerable side effects are factors to consider when deciding to discontinue treatment.

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]?

Cemiplimab should be administered in an outpatient cancer clinic with experience in managing systemic cancer treatments.

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.

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: 18-09-2023

☒ **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: 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				

* 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: 18-09-2023

☒ 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: 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**
Add company name				

* 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: 18-09-2023

☒ 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: 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**
Sanofi	X			
Add company name				

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