CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

durvalumab (Imfinzi)

(AstraZeneca Canada Inc.)

Indication: Imfinzi (durvalumab) in combination with chemotherapy as neoadjuvant treatment, followed by durvalumab as monotherapy after surgery, is indicated for the treatment of patients with resectable (tumours 4 cm and/or node positive) non-small cell lung cancer (NSCLC) and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.

July 19, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings.

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. 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 received.

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 group and all conflicts of interest information from individuals who contributed to the content are included in the posted submission.

Patient Group Input

Name of Drug: Durvalumab

Indication: Durvalumab in combination with chemotherapy as neoadjuvant treatment, followed by durvalumab as monotherapy after surgery, is indicated for the treatment of patients with resectable (tumours ≥ 4 cm and/or node positive) non-small cell lung cancer (NSCLC) and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.

Name of Patient Group: Joint submission by Canadian Cancer Survivor Network, Lung Cancer Canada, and Lung Health Foundation

Author of Submission: Lindsay Timm - Canadian Cancer Survivor Network, Winky Yau - Lung Cancer Canada, Riley Sanders - Lung Health Foundation

1. About Your Patient Group

This patient input submission is jointly submitted by the Canadian Cancer Survivor Network (CCSN), Lung Cancer Canada (LCC), and the Lung Health Foundation (LHF).

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 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/

Lung Cancer Canada is a registered national charitable organization that serves as Canada's leading resource for lung cancer education, patient support, research and advocacy. Lung Cancer Canada is a member of the Global Lung Cancer Coalition and is the only national organization in Canada focused exclusively on lung cancer. Lung Cancer Canada is registered with CADTH. https://www.lungcancercanada.ca/

The Lung Health Foundation (previously named the Ontario Lung Association) is registered with the CADTH and pCODR. 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. www.lunghealth.ca

2. Information Gathering

The Canadian Cancer Survivor Network utilized SurveyMonkey to create and collect all data for the survey on Durvalumab. The survey was reviewed by both Lung Cancer Canada (LCC) and the Lung Health Foundation (LHF). The survey was disseminated through all of the organizations' social media platforms, CCSN's newsletter list, an e-blast from LCC, as well as reaching out to the lead clinicians. CCSN also reached out to other Canadian lung cancer organizations as well as international organizations to broaden the scope of response. The survey was conducted from June 11, 2024, to July 17, 2024, to obtain responses. All of the respondents to the survey are from Canada. All respondents identified as patients. Four of the five respondents to the survey identify as female and one identifies as male. When the survey data was analyzed, it was identified that there were three (3) patients who were either taking or had taken Durvalumab, and there were two (2) patients who had not taken Durvalumab.

3. Disease Experience

Respondents were asked to identify the stage of their lung cancer. All respondents answered with the following levels of disease:

- Stage 4a: 2
- Stage 4b: 1
- Other: 2 (1 stage 4 but only spread to brain, 1 stage 4 metastatic NSCLC)

Respondents were asked to identify the symptoms or problems that they experience with lung cancer that affect their quality of life. The following issues were highlighted by the individual's responses:

- Pain in the chest, shoulder, back, or arms: 3
- Recurrent lung infection (pneumonia or bronchitis): 1
- Fatigue: 5
- Shortness of breath: 2
- Loss of quality of life: 1
- Other: 2 (1 more susceptible to infections, 1 loss of appetite, weight loss, hair loss, teeth loss)

Current treatments that were identified include:

- Radiation: 2
- Surgical Therapy: 1
- Targeted Therapy: 2
- Immunotherapy: 3
- Chemotherapy: 4
- Other: 1 (I was on a clinical trial)

When asked if there was an aspect of their disease that is most important to them to control, three of the respondents gave these responses:

- "I want to keep the tumours and nodules from growing."
- "Shortness of breath."
- "Managing pain and side effects from current chemo."
- "Tough question. All aspects are important, greater understanding and support would help."

Respondents were asked if there were any needs in their current therapy that were not yet being met. One respondent shared that they felt that there was a need for better mental health support.

Respondents were asked if they have had any issues accessing any therapies. One respondent mentioned having issues in regard to being able to acquire counseling. Another respondent mentioned that the travel costs associated with accessing therapy/treatment was an issue for them.

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

- "I would like to see immunotherapy on the market but would also like to see radiation controlled so that it can remove the tumour. I would like to see all people get CT or X-rays to see if they have lung cancer."
- "Make sure more money is going into lung cancer research."
- "I've had good care. I think it's important to feel comfortable with your doctors. Patients need to advocate for themselves."
- "My cancer journey and treatments have been tolerable except for the past two months. I am concerned that there will be no more options for me if the current chemo (Vinorelbine) does not work."
- "Connecting with experts and organizations, like Lung Cancer Canada, and other lung cancer patients is key. Knowledge, understanding, and knowing where to go for supports is key.

4. Experiences With Currently Available Treatments

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

- Fatigue: 3
- Neuropathy: 2
- Anemia: 1
- Nausea: 1
- Diarrhea: 3
- Vomiting: 1
- Constipation: 1
- Weight loss: 2
- Joint and muscle pain: 4
- Other: 2 (1 I am not on a treatment at the moment, 1 Migraines, change in vision and hearing, forgetfulness)

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

- “Taking acetaminophen daily.”

We asked respondents to respond with how they are managing their current treatment as if they were talking to a friend and what they would tell them. One respondent commented on how they recovered well with surgery but needed time and support for left upper lobectomy. In regard to radiation therapy, one respondent said that they have had hair loss but no other symptoms. For chemotherapy, one individual said that she had some nausea but that she does generally well. Another respondent said that they managed ok until the CT scan showed that the tumours were getting bigger. One respondent shared that while they were on immunotherapy (Keytruda) that they managed well with the treatment. Another respondent on immunotherapy stated that the body responded well with minimal side effects.

When asked if their needs were being met while on their current treatment, one respondent replied that they wished they could have stayed on the immunotherapy longer than one year and that it was available longer. Another respondent commented that there is a need for mental health support.

5. Improved Outcomes

When asked about the following issues that they would hope to see a new drug address to manage their disease, the respondents rated the issues on a scale of 1 to 7 with 1 being the most important and 7 being the least important:

- Maintain quality of life: Rated 1 by 4 respondents, rated 7 by 1 respondent
- Delay onset of symptoms: Rated 1 by 2 respondents, rated 2 by 1 respondent, rated 3 by 1 respondent, rated 7 by 1 respondent
- 14 Access to a new option for treatment: Rated 1 by 2 respondents, rated 2 by 1 respondent, rated 7 by 2 respondents
- Reduce side effects from current medications or treatments: Rated 1 by 2 respondents, rated 3 by 1 respondent, rated 5 by 1 respondent, rated 7 by one respondent
- Ease of use: Rated 1 by 3 respondents, rated 5 by 1 respondent, rated 7 by 1 respondent
- Prolong life: Rated 1 by 4 respondents, rated 7 by 1 respondent
- Provide a cure: Rated 1 by 4 respondents, rated 7 by 1 respondent

Respondents were asked to rate what level of side effects they would be willing to tolerate in order to extend survival by two months after having been told there is no other available treatment. The side effects would be things such as nausea, fatigue, vomiting and diarrhea. The scale would represent 1 being no side effects and 10 being significant effects. One respondent was willing to accept a level two on the scale, two respondents were willing to accept a level three, and one respondent was willing to accept a level seven.

Respondents were asked to rate what level of side effects they would be willing to tolerate in order to extend survival by six months after having been told there is no other available treatment. The side effects would be things such as nausea, fatigue, vomiting and diarrhea. The scale would represent 1 being no side effects and 10 being significant effects. One respondent would accept a level two on the scale, one respondent would accept a level three on the scale, another would accept a level six on the scale, and the last respondent would accept a level ten on the scale to extend survival by six months.

Respondents were asked to rate what level of side effects they would be willing to tolerate in order to extend survival by one year after having been told there is no other available treatment. The side effects would be things such as nausea, fatigue, vomiting and diarrhea. The scale would represent 1 being no side effects and 10 being significant effects. Two of the respondents were willing to accept a level two on the scale, one respondent was willing to accept a level seven, and another was willing to accept a level ten on the scale to extend survival by one year.

We asked what considerations patients make when it comes to balancing the advantages and disadvantages of a treatment. Two respondents shared these thoughts:

- “How much I want to live and if it will possibly help others.”
- “To allow me to be comfortable and not in too much pain. Hopefully keep the tumours stable with no new growth.”
- “Quality of life and time with family is key. However, will consider side effects to extend life for family and self. Also recognizing each day alive there may be new treatments/opportunities.”

6. Experience With Drug Under Review

The main adverse effect reported by the respondents was fatigue. One of the respondents stated that they developed hives during the third year.

When asked to describe the advantages and disadvantages of Durvalumab and how it made an impact on their life, the respondents replied:

- “I felt normal on durvalumab and it kept my tumour quiet. Have to remember I was on chemo and on other immunotherapy at first. I was taken off chemo as I was ending up in emergency too often. The durvalumab helped my body notice the cancerous growths.”
- “Tumour shrinking a little.”
- “I am currently stable and am healthy.”

We asked respondents to rate on a scale of 1-5 with 1 being ‘absolutely not’ and 5 being ‘yes, immediately' how likely they would be to recommend that Durvalumab be available to all patients who qualify for it. One respondent rated their recommendation level four and two respondents rated their recommendation a level five.

When asked in comparison to other therapies how was their treatment experience with Durvalumab 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: 2 Much better, 1 Little or no difference
- Side effects: 3 Little or no difference
- Ease of use: 2 Little or no difference
- Disease progression: 1 Much better, 2 Little or no difference

7. Companion Diagnostic Test

N/A

8. Anything Else?

CCSN, LCC, and LHF are aware of the limitations of this submission given the small number of respondents. As you have seen through this submission, from the responses of the participants, there is a real fear of not having another choice available to them should the line of treatment they are on stop working. There is also frustration of some treatments only being available or an option for a short period of time depending on how they gain access to the treatment. Patients are willing to endure a considerable level of side effects should they gain a significant amount of time in return (six months or greater). From the information that we gathered, the patients experienced less adverse effects on Durvalumab and felt better versus their previous lines of care. With lung cancer still being the cancer with the highest mortality rate and patients looking to have options there is an unmet need for these patients to have a comfortable and higher quality of life during their treatment.

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 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
AstraZeneca - 2023 (CCSN)				X
AstraZeneca - 2024 (CCSN)				X
AstraZeneca – 2023 (LHF)				X
AstraZeneca – 2024 (LHF)				X
AstraZeneca – 2023 (LCC)				X
AstraZeneca – 2024 (LCC)			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: July 18, 2024

Clinician Group Input

CADTH Project Number: PC0372-000

Generic Drug Name (Brand Name): Durvalumab (Imfinzi)

Indication: Imfinzi (durvalumab) in combination with chemotherapy as neoadjuvant treatment, followed by durvalumab as monotherapy after surgery, is indicated for the treatment of patients with resectable (tumours ≥ 4 cm and/or node positive) non-small cell lung cancer (NSCLC) and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.

Name of Clinician Group: Lung Cancer Canada – Medical Advisory Committee

Author of Submission: Dr. Quincy Chu (lead), Dr. David Stewart, Dr. Mahmoud Abdelsalam, Dr. Biniam Kidane, Dr. Silvana Spadafora, Dr. Kevin Jao, Dr. Barb Melosky, Dr. Ron Burkes, Dr. Rosalyn Juergens, Dr Paul Wheatley-Price, Dr. Michela Febbraro, Dr. Normand Blais, Dr. Catherine Labbé, Dr. Alison Wallace, Dr. Vishal Navani, Dr. Susanna Cheng, Dr. Nathalie Daaboul, Dr. Sunil Yadav, Dr. Randeep Sangha, Dr. Geoffrey Liu

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 provide clinician input for submissions of new lung cancer drugs to the HTA process for many years. The LCC MAC consists of clinicians and key opinion leaders in the field of lung cancer across the countries.

www.lungcancercanada.ca

2. Information Gathering

The information provided in this submission is from publicly available sources, primarily published manuscripts and conference presentations, together with clinical experience of members from the MAC. This Submission is entirely independent of the manufacturer (Janssen).

3. Current Treatments and Treatment Goals

According to the Canadian Cancer Society annual report, lung cancer is the most commonly diagnosed cancer and the most common cause of cancer death in Canada. In 2024, 32,100 Canadians will be diagnosed and 20,700 will die from lung cancer [1]. About 80-85% are non-small cell lung cancer (NSCLC with only 20-30% are deemed to have early-staged, namely stage I-IIIA [2,3],which are potentially resectable. But only a portion of these patients will be considered as operable due to comorbidity, lung function and patient wishes.

The goals of any treatment in the early-stage resectable patients are:

1. Reduction of the chance of recurrence measured by disease-free survival (DFS): with surgery alone, the 5-year DFS for stages IB, II and III according to AJCC 7th and 8th edition were 62%, 50% and 34%, respectively. Almost all the patients who have disease recurrence will be deemed incurable. Thus, prevention of recurrence of NSCLC is key to improve their overall survival [Rajaram et al. Thoracic Oncology 2024;165(5):1260-1370]. West et al. [Lung Cancer 2023;24(3):260-268] reported the use of adjuvant

chemotherapy and outcome in this patient population using the SEER database. Forty-one percent of patients received adjuvant chemotherapy among those patients with stage IB (>4cm)-IIIA by AJCC 7th edition and specifically, only 21.6% in stage IB, 42.6% in stage II and 53% in stage III. The median DFS in the overall population was a sobering 24.8 months and the 5-year DFS rate was 29.3%. The corresponding median DFS and 5-year DFS for stage IB, stage II and stage IIIA were 40.9 months and 38.9%, 24.4 months and 29.1% and 13.8 months and 21.5%, respectively.

2. Increase in chance of cure measured by overall survival (OS) post resection: West et al. also reported the median OS and 5-year OS for the entire population being 76.6 months and 57.5%, respectively. The median OS and 5-years OS by stage were correspondingly 97.9 months and 66% in stage IB, 75.5 months and 55.6% in stage II, and 66.2 months and 54% in stage IIIA.

3. As surgery is still considered as the most important treatment in early-stage NSCLC, there is no increase in the risk for patients not able to undergo surgery and the risk of surgical complications who undergo neoadjuvant and perioperative systemic therapy.

4. Toxicity and quality-of-life

Therefore, there is significant room for further improvement.

Recently, with the adaptation of precision medicine, the current Canadian treatment algorithm for patients with resectable Stage IB-IIIA NSCLC, the standard of care will be determined by the presence or absence of actionable mutation, PDL-1 status and stage.

1. For those with EGFR mutation, the standard of care is based on the results of ADAURA [4, 5] demonstrating 3 years of adjuvant osimertinib statistically and clinically improvement the median DFS (NR versus 28.1 months; HR= 0.20, p<0.001) and median OS (HR=0.49, p=0.001) over placebo, regardless of stage and prior cisplatin-based adjuvant chemotherapy. The 2-year DFS in those who had received osimertinib and placebo were 89%, 87%, 91%, 88% and 53%, 73%, 56% and 32% for all patients, stage IB, stage II and Stage IIIA patients, respectively. The 5-year OS for osimertinib-arm and placebo were 88%, 94%, 85%, 85% and 78%, 88%, 78%, 67% for all patients, stage IB, stage II and stage IIIA patients, respectively. The treatment will include:

a. An anatomical resection such as a lobectomy, bi-lobectomy, and pneumonectomy, and systemic therapy according to stage of disease:

i. For those who have stage IB (3-4 cm) by AJCC 7th edition, patients will receive 3 years of adjuvant Osimertinib.

ii. For those who have stage IIA (4-5 cm) by AJCC 7th edition, patients may receive 4 cycles of adjuvant cisplatin-based chemotherapy and will have 3 years of adjuvant Osimertinib.

iii. For those who have Stage IIB-IIIA by AJCC 7th edition, patients will receive 4 cycles of adjuvant cisplatin-based chemotherapy and 3 years of adjuvant Osimertinib.

2. For those with ALK translocation, the standard of care is based on the results of ALINA [6], demonstrating a statistically and clinically important improvement in median DFS (NR versus 44.4 months; HR=0.24, p<0.0001) over 4 cycles of cisplatin-based adjuvant chemotherapy, regardless of stage. The corresponding 2-year DFS for all patients, stage IB, stage II and stage IIIA for alectinib-treated and chemotherapy-treated patients were 93.6% ,92.3%, 95.6%, 92.7% and 63.7%, 71.6%, 66.3%, 60.7%, respectively. There have not been enough events for the overall survival analysis. The treatment will include:

a. An anatomical resection such as lobectomy, bi-lobectomy, and pneumonectomy and systemic therapy of alectinib for 2 years in those with stage IB (≥4 cm)-Stage IIIA by AJCC 7th edition. The value of 4 cycles of adjuvant chemotherapy prior to alectinib has not been established.

3. For those with no EGFR and ALK gene aberration, the standard of care includes

a. An anatomical resection such as a lobectomy, bi-lobectomy, and pneumonectomy and

i. For those with stage IB (<4 cm) by AJCC 6th edition, no adjuvant platinum-based adjuvant chemotherapy [7].

ii. For those with Stage IB > 4 cm by AJCC 6th edition, adjuvant platinum-based chemotherapy can be offered with an absolute improvement of 5-year OS rate of 5% (HR=0.92) [7].

iii. For those with stage IIA-IIIA by AJCC 6th edition, adjuvant platinum-based chemotherapy will be offered with an absolute improvement of 5-year OS rate of 10% (HR=0.83) [7].

Based on the results of

1. IMPOWER 010, there was a statistically and clinically important improvement in the median DFS for stage II-IIIA patients by AJCC 7th edition with PDL-1 $\geq$1% and any PDL-1 after adjuvant atezolizumab (NR versus 35.3 months; HR=0.66, p=0.0039 and 42.3 months versus 35.3 months; HR=0.79, p=0.02, respectively) across all major subgroups. Specifically, the HR were 0.71 and 0.68, 0.77 and 0.88, 0.62 and 0.81 for those with stage IIA, IIB and IIIA disease with PDL-1 $\geq$1 and any PDL-1, respectively. The OS is still immature with a HR of 0.77 and 0.99 for those of stage II-IIIA and PDL-1 $\geq$ 1% and any PDL-1, respectively, favouring atezolizumab. Currently, only those patients with stage II-IIIA by AJCC 7th edition and PDL-1 $\geq$ 50% who have received at least 1 cycle of cisplatin-based adjuvant chemotherapy, based on subgroup analysis, the median DFS was improved with HR=0.43 (NR versus 35.7%), atezolizumab at 1200 mg every 3 weeks for 17 cycles after adjuvant chemotherapy is considered the standard of care [6].

2. KEYNOTE091/PEARL, stage IB >4 cm to stage IIIA by AJCC 7th edition patients of any PDL-1 level treatment with pembrolizumab at 200 mg every 3 weeks for 1 year had improvement of median DFS (53.6 months versus 42 months; HR 0.74, p=0.0014) while for those with PDL-1 $\geq$50%, the median DFS was not reached in either arm with HR 0.82 (p=0.14) and the overall survival for all patients is immature with a HR 0.87 (p=0.17). While there was no benefit of pembrolizumab in those patients received no prior adjuvant chemotherapy with a HR of 1.25, benefit of pembrolizumab was observed in those who had prior adjuvant chemotherapy with HR 0.73. The benefit was observed regardless of stage (HR=0.76 in stage IB, HR=0.70 in stage II and HR=0.92 in stage III). Thus, current Health Canada indication and available Patient Access Program allows only stage IB-IIIA patients who have received at least 1 cycle of cisplatin-based adjuvant chemotherapy at any PDL-1 level to receive 1 year of pembrolizumab at 200 mg every 3 weeks. Reimbursement is currently being considered in patients with stage IB >4cm-stage IIIA and PDL-1 <50% in resected stage IB > 4cm to stage IIIA by AJCC 7th edition who have at least 1 cycle of adjuvant cisplatin-based chemotherapy.

The rationale for neoadjuvant immunotherapy was based on that the presence of tumour during neoadjuvant therapy, there may be a stronger antitumour T-cell response due to increased tumour burden and antigen presentation [Uprety D et al. J Thorac oncol 2020;15:1281-97 and Liu et al. Cancer Discov 2016;6:1382-99; Cascone Cancer Res 2018;78:1719]. The addition of chemotherapy to immunotherapy, may further stimulate the immune system by inducing immunogenic tumour cell death and increase antigen presentation to dendritic cells, directly stimulating T-cell response and inhibiting immunosuppressive mechanisms [Chaft J et al. Nat Rev Clinic Oncol 2021;18:547-57; bracci et al. Cell Death Differ 2014; 21:15-25; Wang Z et al. Oncoimmunology 2017;6:e1331807]. Thus, neoadjuvant chemotherapy and PD(L)1 inhibitors will improve the outcome of early-staged NSCLC.

b. One alternative is neoadjuvant platinum-based chemotherapy and nivolumab at 360 mg every 3 weeks in resectable stage IB (>4cm)-IIIA NSCLC by AJCC 7th edition of 3 cycles, followed by anatomical resection with an optional cycle of adjuvant platinum-based chemotherapy based on CHECKMATE 816 study. The initial results showed a statistically significant improvement in the pathological complete response (pCR) of 24% versus 2.2% (OR=13.94, p<0.0001) and median event-free survival (EFS) at 31.6 months as compared to 20.8 months (HR=0.63, p=0.0052) and all subgroups including stage, PDL-1 level, and histology benefited with the combination. Specifically, there was an improvement of median EFS in stage IB-II (NR versus NR; HR=0.87) and stage IIIA (32 months versus 16 months; HR=0.54). The overall survival was still immature and there was an improvement for the combination with HR=0.57 (p=0.0079), though not statistically significant yet. In 2024, the 4-year follow-up data continued to show an improvement of median EFS (43.8 months versus 18.4 months, HR=0.66) with 4-year EFS at 49% versus 38% and a trend towards improvement in median OS (HR=0.71, p=0.0451) and a 4-years OS of 71% versus 58%.

c. Another alternative is neoadjuvant platinum-based chemotherapy and durvalumab at 1500 mg every 3 weeks for 4 cycles, followed by anatomical resection and adjuvant durvalumab at 1500 mg every 4 weeks for 12 cycles as perioperative therapy in AEGEAN trial. The study demonstrated an improvement in EFS (HR=0.53, p=0.004), a 2-year EFS (63.3% versus 52.4%) and pCR rate (17.2 % versus 4.3%, p<0.001) in resectable stage IIA-IIIB with N2 nodes by AJCC 8th edition with no EGFR and ALK gene aberrations, regardless of prespecified subgroups including age, stage, and PDL-1 status. Specially by stage, the median EFS was NR versus 31.1 months (HR=0.76), NR versus 19.5 months (HR=0.57) and 31.9 months versus 18.9 months (HR=0.83) for stage II, stage IIIA and stage IIIB, respectively.

At this time, it is still unclear if adjuvant chemotherapy, followed by adjuvant immunotherapy or neoadjuvant chemotherapy or immunotherapy or perioperative chemotherapy and immunotherapy is superior. This will be answered in ongoing and future clinical trials.

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.

As stated above, there is no direct comparison in DFS/EFS of adjuvant chemotherapy followed by immunotherapy, neoadjuvant chemotherapy and immunotherapy and perioperative chemotherapy and immunotherapy, followed by immunotherapy.

Related to this submission, the most appropriate comparator will be neoadjuvant chemotherapy and nivolumab as per CHECKMATE816 as both studies included similar early-staged NSCLC patients as compared to the patients enrolled in IMPOWER 010 and KEYNOTE091/PEARL trials. The most significant treatment gaps are the role of adjuvant immunotherapy after neoadjuvant therapy and if there is a role who are the patients to get the adjuvant immunotherapy after initial neoadjuvant chemotherapy and immunotherapy. The gap in knowledge is especially clinically relevant in those with no pCR. It is not uncommon that such cases are being brought to Multidisciplinary Rounds (MDT).

The 2-year EFS reported for neoadjuvant chemotherapy and nivolumab or chemotherapy and durvalumab were similar at 64% and 62.4%, respectively. In the exploratory analysis of CHECKMATE 816, the median EFS in patients who did not have pCR, the outcome in patients treated with neoadjuvant chemotherapy and nivolumab was comparable to those with neoadjuvant chemotherapy (26.6 months versus 18.4 months).

Similar exploratory analysis was performed in KEYNOTE671, perioperative chemotherapy and pembrolizumab followed by pembrolizumab versus perioperative chemotherapy/placebo, followed by placebo study in this setting, those with neoadjuvant chemotherapy and pembrolizumab and adjuvant pembrolizumab and with or without pCR, may have better outcome than chemotherapy/placebo (HR=0.39 and 95% CI 0.09-1.22 and HR 0.69 and 95% CI 0.55-0.85).

No such data is reported in AEGEAN to date.

Having the perioperative option as in AEGEAN, it will allow patients and clinicians to discuss whether continuing with durvalumab by balancing the EFS results from the exploratory analysis with the toxicity associated with durvalumab in the adjuvant setting.

Urban et al. presented the toxicity reported in chemotherapy/placebo arm and chemotherapy/durvalumab arm during the neoadjuvant, post-operative and adjuvant periods. The incidences of all grades and at least grade 3 toxicity associated with treatment was 82.3% versus 78.6% and 29.9% versus 32.7% during the neoadjuvant period, 25.5% versus 11% and 4.6% versus 0.9% during the post-operative period and 48.1% versus 29.1% and 7.9% versus 3.9% during the adjuvant period. Overall, there was a trend towards high incidence of all grade and grade 3 or higher treatment-related toxicity in the chemotherapy/durvalumab arm during the post-operative and adjuvant periods, though incidences of grade 5 toxicity in either arm at any time during treatment were similar.

5. Place in Therapy

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

Based on the discussion in Section 3 and 4, perioperative platinum-based chemotherapy and durvalumab should be available as the alternative option to neoadjuvant chemotherapy and nivolumab as in CHECKMATE 816 for early-staged, stage IIA-IIIB by AJCC 8th edition, resectable NSCLC patients who are candidates for neoadjuvant therapy.

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 NSCLC patients who are best suited for AEGEAN are those with

1. Stage II-IIIB with N2 disease after radiological staging by CT chest/abdomen +/- pelvis, PET scan and MR as well as mediastinal staging by PET and EBUS/mediastinoscopy according to AJCC 8th edition

2. Deemed a surgical candidate with adequate lung function before and after surgical resection and with no significant comorbidity that will increase the surgical morbidity and mortality

3. Deemed by thoracic surgeons to be a candidate for a complete or R0 resection except pneumonectomy prior to neoadjuvant therapy, but pneumonectomy can be done at the time of surgery if deems appropriate for an R0 resection

4. No contraindication to platinum-based chemotherapy and immunotherapy

5. No EGFR, ALK and possibly ROS1 mutation by molecular testing, regardless of the PDL-1 status. Of note, reimbursement of molecular testing for EGFR, ALK and PDL-1 in this setting is still not universal across the country. Additional funding may be needed for those provinces that does not have provincial reimbursement yet.

Province	Funding (Yes/No)
Newfoundland	
Nova Scotia	
New Brunswick	
Prince Edward Island	
Quebec	
Ontario	
Manitoba	
Saskatchewan	
Alberta/Northwest Territory	No, but can be done upon request by oncologists.
British Columbia/Yukon	

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?

During the pre-operative period, the response evaluation by CT scan chest/abdomen +/- pelvis after 2 cycles and 4 cycles of neoadjuvant therapy as in the AEGEAN study. PET scan may be done as per the oncology team discretion. Scan will be reviewed by thoracic surgeons to ensure resectability.

During the adjuvant period, a post-operative CT scan chest/abdomen +/- pelvis can be done as a baseline, followed by CT scan every 3-4 cycles during treatment to determine if patients have recurrence of disease.

During the post-treatment period, CT scan surveillance will continue as per provincial guidelines.

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

During the pre-operative period, treatment will discontinue if there is clinical or radiological evidence of progression, clinically important chemotherapy and/or immune-related toxicity that are deemed unsafe to continue and patient wishes.

During the adjuvant period, treatment will discontinue if there is clinical or radiological evidence of recurrence, clinically important immune-related toxicity that are deemed unsafe to continue, patient wishes and a total of 16 cycles of durvalumab is given.

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]?

Chemotherapy and durvalumab as per AEGEAN trial can be deliver in the outpatient setting in both the academic and non-academic oncology clinics under the supervision of medical oncologists.

The diagnosis of NSCLC is done through pulmonary physicians/respirologists/thoracic surgeons via EBUS biopsy or radiologist via percutaneous CT guided biopsy.

The histological and molecular diagnostics are done through accredited pathology services in each hospital.

The surgery will be performed by thoracic surgeons associated with the cancer centres.

6. Additional Information

N/A

7. Conflict of Interest Declarations

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

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

   No

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

   No

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

Declaration for Clinician 1

Name: Quincy Chu

Position: Medical Oncologist, Cross Cancer Institute, Edmonton, AB

Date: July 19, 2024

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

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie	X			
Amgen	X			
AnHeart	X			
Astellas	X			
Astra Zeneca		X		
Boehringer Ingelheim	X			
BMS	X			
Daichii Sankyo	X			
Eli Lilly	X			
GSK	X			
Janssen	X			
Meck	X			
Novartis	X			
Ocellaris	X			
Pfizer	X			
Roche		X		
Takeda	X			

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

Declaration for Clinician 2

Name: Dr. Mahmoud Abdelsalam
Position: Medical Oncologist, Horizon Health Network
Date: July 19, 2024

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

Table 5: Conflict of Interest Declaration for Clinician 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
BMS	Advisory role, Honoraria and travel grants	☐	☒	☐	☐

1.1.1.1 Declaration for Clinician 3

Name: Susanna Cheng

Position: Medical Oncologist, Sunnybrook Hospital; Associate Professor, University of Toronto

Date: July 19, 2024

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

Table 1: Conflict of Interest Declaration for Clinician 3

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

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

New or Updated Declaration for Clinician 4	
Name	Michela Febbraro
Position	Medical Oncologist, Algoma District Cancer Program
Date	July 19, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

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

New or Updated Declaration for Clinician 5	
Name	*Biniam Kidane*
Position	*Associate Professor, Dept of Surgery, University of Manitoba*
Date	July 19, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

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

AstraZeneca	☐	☐	☒	☐
Merck	☒	☐	☐	☐
Roche	☐	☒	☐	☐
Bristol Myers Squibb	☒	☐	☐	☐
Medtronic	☒	☐	☐	☐

1.1.1.2

New or Updated Declaration for Clinician 6	
Name	*Dr. Alison Wallace*
Position	*Assistant Professor Department of Surgery, Division of Thoracic Surgery and Department of Pathology, Dalhousie University. Thoracic Surgeon QEII HSC, Halifax. NS.*
Date	July 19, 2024
-☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Confli-ct of Interest Declaration

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

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

Declaration for Clinician 7

Name: NATHALIE DAABOUL

Position: Hematologist-Oncologist, Université de Sherbrooke

Date: July 19, 2024

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

Table 1: Conflict of Interest Declaration for Clinician 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**
Amgen	x			
AstraZeneca	x			
BMS	x			
Eisai	x			
Jazz	x			
Merck	x			
Novartis	x			
Pfizer	x			
Sanofi	x			
Takeda	x			
Taiho	x			

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

New or Updated Declaration for Clinician 8	
Name	*Ronald Burkes*
Position	*Medical Oncologist Mount Sinai Hospital*
Date	July 19, 2024

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

Conflict of Interest Declaration

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

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

Declaration for Clinician 9

Name: Silvana Spadafora
Position: Medical Oncologist, Algoma District Cancer Program
Date: July 19, 2024

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

Table 2: Conflict of Interest Declaration for Clinician 9

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

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

Conflict of Interest Declaration for Clinician 10

Name: Dr. Kevin Jao
Position: Medical Oncologist, Hôpital Sacré-Cœur, Montreal
Date: July 19, 2024

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

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
Bristol-Myers Squibb	Advisory Role	☒	☐	☐	☐

Declaration for Clinician 11

Name: Dr Catherine Labbé
Position: Head of Respiratory Medicine Service, Université de Laval
Date: July 19, 2024

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

Table 13: Conflict of Interest Declaration for Clinician 11

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

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

Declaration for Clinician 12

Name: Dr. Rosalyn Juergens
Position: Chair, LCC Medical Advisory Committee; Medical Oncologist, Juravinski Cancer Center
Date: July 19, 2024

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

Table 3: Conflict of Interest Declaration for Clinician 12

	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			

Declaration for Clinician 13

Name: Dr. Paul Wheatley-Price
Position: Medical Oncologist, The Ottawa Hospital. Associate Professor, Department of Medicine, University of Ottawa
Date July 19, 2024

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

Table 2: Conflict of Interest Declaration for Clinician 13

	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			
Astra Zeneca	X			
Jazz Pharmaceuticals	X			
Amgen	X			
Janssen	X			
Novartis	X			
Merck	X			
BMS	X			
Roche	X			
EMD Serono	X			
Pfizer	X			
Bayer	X			
Novartis	X			

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

New or Updated Declaration for Clinician 14	
Name	*Vishal Navani*
Position	*Medical Oncologist, University of Calgary*
Date	July 19, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Janssen	☐	☐	☒	☐
Consulting - Novotech Pty, Pfizer, Sanofi, Astra Zeneca, EMD Serono, Oncology Education, Sanofi, Janssen, Roche, MSD, Bristol Meyers Squibb, Takeda	☐	☐	☒	☐
Speaking – Ipsen, Astra Zeneca, MSD, Bristol Meyers Squibb	☐	☐	☒	☐
Research – Astra Zeneca (Inst), Janssen (Inst)			X	
Travel – EMD Serono, Pfizer, Sanofi			X	

Declaration for Clinician 15

Name: Normand Blais
Position: Medical Oncologist, CHUM Cancer Center, Montreal
Date: July 19, 2024

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

Table 1: Conflict of Interest Declaration for Clinician 15

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	☒	☐	☐	☐
Beigene	Advisory Board and Honoraria	☒	☐	☐	☐
Bristol-Myers Squibb	Advisory Board and Honoraria	☒	☐	☐	☐
EMD Serono	Advisory Board and Honoraria	☒	☐	☐	☐
Merck	Advisory Board and Honoraria	☒	☐	☐	☐
Novartis	Advisory Board and Honoraria	☒	☐	☐	☐
Pfizer	Advisory Board and Honoraria	☒	☐	☐	☐
Roche	Advisory Board and Honoraria	☒	☐	☐	☐
Sanofi	Advisory Board and Honoraria	☒	☐	☐	☐
Astra Zeneca	Research Funding to institution	☐	☐	☐	☒

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

Declaration for Clinician 16

Name: Dr Randeep Sangha
Position: Medical Oncologist, Cross Cancer Institute
Date: July 19, 2024

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

Table 9: Conflict of Interest Declaration for Clinician 16

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

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

Declaration for Clinician 17

Name: Dr Sunil Yadav
Position: Medical Oncologist, Saskatoon Cancer Centre
Date: July 19, 2024

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

Table 12: Conflict of Interest Declaration for Clinician 17

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 18

Name: Dr. Barb Melosky
Position: Medical Oncologist, BC Cancer
Date: July 19, 2024

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

Table 5: Conflict of Interest Declaration for Clinician 18

Company		Check Appropriate Dollar Range

	Nature or description of activities or interests	$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	☒	☐	☐	☐

New or Updated Declaration for Clinician 19	
Name	*David J. Stewart*
Position	Professor of Medicine, University of Ottawa and The Ottawa Hospital
Date	*July 19, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Merck Canada 2021, 2023	☒	☐	☐	☐
AstraZeneca Canada 2021, 2023	☒	☐	☐	☐
Abbvie Canada 2021, 2022, 2023	☒	☐	☐	☐
Canadian Agency for Drugs and Technologies in Health 2021	x			
Amgen Canada 2022	x			

New or Updated Declaration for Clinician 20	
Name	*Dr. Geoffrey Liu*
Position	*Medical Oncologist*
Date	*July 19, 2024*

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

Conflict of Interest Declaration

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

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

CADTH Project Number: PC0372-000

Generic Drug Name (Brand Name): durvalumab

Indication: Imfinzi (durvalumab) in combination with chemotherapy as neoadjuvant treatment, followed by durvalumab as monotherapy after surgery, is indicated for the treatment of patients with resectable (tumours ≥ 4 cm and/or node positive) non-small cell lung cancer (NSCLC) and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.

Name of Clinician Group: OH (CCO) Lung Cancer Drug Advisory Committee

Author of Submission: Dr. Donna Maziak

1. About Your Clinician Group

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

2. Information Gathering

Information was gathered by a videocall and finalized through email.

3. Current Treatments and Treatment Goals

Current treatment options include neoadjuvant nivolumab for 3 cycles with chemotherapy (currently reimbursed). Another treatment option is to give adjuvant 4 cycles of platinum-based chemotherapy with the option of adding 1 year of immunotherapy which is currently not funded.

In stage II/III NSCLC, for patient with a high PDL-1 status, they can receive adjuvant chemotherapy followed by atezolizumab.

The treatment goal is to cure and improve overall 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.

There is currently no access to immunotherapy in the adjuvant setting in patients who received neoadjuvant chemoimmunotherapy. Neoadjuvant chemoimmunotherapy and neoadjuvant plus adjuvant (perioperative) approaches have both demonstrated improvements in event free survival. There are no data comparing neoadjuvant IO strategies to perioperative IO strategies. Therefore, there is uncertainty whether there is additional survival benefit from the addition of adjuvant IO to neoadjuvant chemo immunotherapy. However, perioperative immunotherapy could offer patients improved therapy.

Currently, immunotherapy in the adjuvant setting is only available to those with PDL-1>50%.

5. Place in Therapy

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

Perioperative chemoimmunotherapy with durvalumab would represent an alternative treatment approach to neoadjuvant chemoimmunotherapy with 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 resectable stage II/III disease (8th edition TNM) and no contraindication to immunotherapy. As well as patients with no EGFR or ALK mutations.

There is no clear indication as to who would be more suitable to this treatment than 3 cycles of neoadjuvant immunotherapy.

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?

These are patients who have undergone curative resection for stage II/III (8th edition TNM) NSCLC. The standard is to have a CT chest scan performed within 2 months prior to surgery. Standard of care follow up post surgical resection would be CT imaging 3-6 months post surgery, then every 6 months for 2 years, then yearly thereafter. For patients receiving adjuvant immunotherapy, patients should be imaged every 3-6 months in the initial year on therapy.

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

Severe adverse events, disease recurrence or completion of therapy.

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]?

Patients should be treated in an outpatient setting under the supervision of a medical oncologist, or pulmonologist experienced in the management of thoracic malignancies.

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.

4. 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.

5. 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.

6. 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: Donna Maziak

Position: Lead, OH (CCO) Lung Cancer Drug Advisory Committee

Date: 15-07-2024

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

Table 1: Conflict of Interest Declaration for Clinician 1

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

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

Declaration for Clinician 2

Name: Dr. Andrew Robinson

Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee

Date: 18-06-2024

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

Table 2: Conflict of Interest Declaration for Clinician 2

Company	**Check appropriate dollar range***

	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca	X			
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 3

Name: Dr. Stephanie Brule

Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee

Date: 18-06-2024

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

Table 3: Conflict of Interest Declaration for Clinician 3

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

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

Declaration for Clinician 4

Name: Dr. Peter Ellis

Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee

Date: 12-07-2024

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

Table 4: Conflict of Interest Declaration for Clinician 4

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		X		
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 5

Name: Dr. Natash Leighl

Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee

Date: 18-06-2024

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

Table 5: Conflict of Interest Declaration for Clinician 5

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

Add or remove rows as required				

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