CADTH

pan-Canadian Oncology Drug Review

Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation

Atezolizumab (Tecentriq) for Small Cell Lung Cancer

Ontario Lung Association

December 5, 2019

Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Atezolizumab (Tecentriq) / Small Cell Lung Cancer
Eligible Stakeholder Role in Review (Sponsor and/or Manufacturer, Patient Group, Clinical Organization Providing Feedback	Patient Group Ontario Lung Association

**The pCODR program may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by the pCODR program.*

3.1 Comments on the Initial Recommendation

a) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the Initial Recommendation:

☐ agrees ☐ agrees in part ☒ disagree

Patients would like greater treatment options to consider and choose from, and most would be willing to try additional and / or combination treatments if the adverse effects were no worse than what they were currently experiencing. Quality of life is of utmost importance to the patients we work with – they would like to be well enough to enjoy time with family and friends for whatever time they may have left.

Cost of medications has been an ongoing theme that continually comes up in our discussion with patients about possible treatments. Many are on limited incomes and would like available treatments to be less expensive or at no cost to theme. Another ongoing theme has been the desire for more treatment options so there needs to be movement in our health care system towards increasing available and affordable options for treating patients living with lung cancer.

b) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the provisional algorithm:

☐ agrees ☐ agrees in part ☒ disagree

The Ontario Lung Association disagrees with the provisional algorithm. The pERC recommendation acknowledges the unmet need for effective treatments but highlights the OS and PFS during this trial. What is not taken into consideration is the aggressive nature of extensive stage small-cell lung cancer.

There is a desire for more respiratory and lung cancer specialists and a better coordinated health system. Patients would like the ability to do treatments at home, so it would

remove the need for the patient or the caregiver to take time off of work. This would also lead to less disruption of the daily routine. Quality of life, not just extension of life, is a theme that continually came through from patients.

c) Please provide editorial feedback on the Initial Recommendation to aid in clarity. Is the Initial Recommendation or are the components of the recommendation (e.g., clinical and economic evidence or provisional algorithm) clearly worded? Is the intent clear? Are the reasons clear?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
			Editorially, the Initial Recommendation is clear.

3.2 Comments Related to Eligible Stakeholder Provided Information

Notwithstanding the feedback provided in part a) above, please indicate if the Stakeholder would support this Initial Recommendation proceeding to Final pERC Recommendation ("early conversion"), which would occur two (2) Business Days after the end of the feedback deadline date.

☐	Support conversion to Final Recommendation. Recommendation does not require reconsideration by pERC.	☒	Do not support conversion to Final Recommendation. Recommendation should be reconsidered by pERC.

If the eligible stakeholder does not support conversion to a Final Recommendation, please provide feedback on any issues not adequately addressed in the Initial Recommendation based on any information provided by the Stakeholder in the submission or as additional information during the review.

Please note that new evidence will be not considered at this part of the review process, however, it may be eligible for a Resubmission. If you are unclear as to whether the information you are providing is eligible for a Resubmission, please contact the pCODR program.

Additionally, if the eligible stakeholder supports early conversion to a Final Recommendation; however, the stakeholder has included substantive comments that requires further interpretation of the evidence, including the provisional algorithm, the criteria for early conversion will be deemed to have not been met and the Initial Recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting.

Page Number	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information
1	pERC Recommendation	Pgh 2 Line 5-9	SCLC has been an area with a great unmet need for advancements in treatment options. Patients are willing to try new

			combinations but many have acknowledged cost as a significant barrier due to low income. We received feedback from one patient who stressed the importance of both new and affordable treatment options for SCLC patient.

1 About Stakeholder Feedback

pCODR invites eligible stakeholders to provide feedback and comments on the Initial Recommendation made by the pCODR Expert Review Committee (pERC), including the provisional algorithm. (See www.cadth.ca/pcodr for information regarding review status and feedback deadlines.)

As part of the pCODR review process, pERC makes an Initial Recommendation based on its review of the clinical benefit, patient values, economic evaluation and adoption feasibility for a drug. (See www.cadth.ca/pcodr for a description of the pCODR process.) The Initial Recommendation is then posted for feedback from eligible stakeholders. All eligible stakeholders have 10 (ten) business days within which to provide their feedback on the initial recommendation. It should be noted that the Initial Recommendation, including the provisional algorithm may or may not change following a review of the feedback from stakeholders.

pERC welcomes comments and feedback from all eligible stakeholders with the expectation that even the most critical feedback be delivered respectfully and with civility.

A. Application of Early Conversion

The Stakeholder Feedback document poses two key questions:

1. **Does the stakeholder agree, agree in part, or disagree with the Initial Recommendation?**

   All eligible stakeholders are requested to indicate whether they agree, agree in part or disagrees with the Initial Recommendation, and to provide a rational for their response.

   Please note that if a stakeholder agrees, agrees in part or disagrees with the Initial Recommendation, the stakeholder can still support the recommendation proceeding to a Final Recommendation (i.e. early conversion).

2. **Does the stakeholder support the recommendation proceeding to a Final Recommendation ("early conversion")?**

   An efficient review process is one of pCODR's key guiding principles. If all eligible stakeholders support the Initial Recommendation proceeding to a Final Recommendation and that the criteria for early conversion as set out in the *pCODR Procedures* are met, the Final Recommendation will be posted on the CADTH website two (2) Business Days after the end of the feedback deadline date. This is called an "early conversion" of an Initial Recommendation to a Final Recommendation.

   For stakeholders who support early conversion, please note that if there are substantive comments on any of the key quadrants of the deliberative framework (e.g., differences in the interpretation of the evidence), including the provisional algorithm as part of the feasibility of adoption into the health system, the criteria for early conversion will be deemed to have **not** been met and the Initial Recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting. If the substantive comments relate specifically to the provisional algorithm, it will be shared with PAG for a reconsideration. Please note that if any one of the eligible stakeholders does not support the Initial Recommendation proceeding to a Final pERC Recommendation, pERC will review all feedback and comments received at a subsequent pERC meeting and reconsider the Initial Recommendation. Please also note that substantive comments on the provisional algorithm will preclude early conversion of the initial recommendation to a final recommendation.

B. Guidance on Scope of Feedback for Early Conversion

Information that is within scope of feedback for early conversion includes the identification of errors in the reporting or a lack of clarity in the information provided in the review documents. Based on the feedback received, pERC will consider revising the recommendation document, as appropriate and to provide clarity.

If a lack of clarity is noted, please provide suggestions to improve the clarity of the information in the Initial Recommendation. If the feedback can be addressed editorially this will done by the CADTH staff, in consultation with the pERC chair and pERC members, and may not require reconsideration at a subsequent pERC meeting. Similarly if the feedback relates specifically to the provisional algorithm and can be addressed editorially, CADTH staff will consult with the PAG chair and PAG members.

The Final pERC Recommendation will be made available to the participating federal, provincial and territorial ministries of health and provincial cancer agencies for their use in guiding their funding decisions and will also be made publicly available once it has been finalized.

2 Instructions for Providing Feedback

a) The following stakeholders are eligible to submit Feedback on the Initial Recommendation:
   - The Sponsor making the pCODR Submission, or the Manufacturer of the drug under review;
   - Patient groups who have provided input on the drug submission;
   - Registered clinician(s) who have provided input on the drug submission; and
   - The Provincial Advisory Group (PAG)

b) The following stakeholders are eligible to submit Feedback on the provisional algorithm:
   - The Sponsor making the pCODR Submission, or the Manufacturer of the drug under review;
   - Patient groups who have provided input on the drug submission;
   - Registered clinician(s) who have provided input on the drug submission; and
   - The Board of Directors of the Canadian Provincial Cancer Agencies

c) Feedback or comments must be based on the evidence that was considered by pERC in making the Initial Recommendation. No new evidence will be considered at this part of the review process, however, it may be eligible for a Resubmission.

d) The template for providing *Stakeholder Feedback on pERC Initial Recommendation* can be downloaded from the pCODR section of the CADTH website. (See www.cadth.ca/pcodr for a description of the pCODR process and supporting materials and templates.)

e) At this time, the template must be completed in English. The Stakeholder should complete those sections of the template where they have substantive comments and should not feel obligated to complete every section, if that section does not apply.

f) Feedback on the pERC Initial Recommendation should not exceed three (3) pages in length, using a minimum 11 point font on 8 ½" by 11" paper. If comments submitted exceed three pages, only the first three pages of feedback will be provided to the pERC for their consideration.

g) Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the

recommendation document under discussion (i.e., page number, section title, and paragraph). Opinions from experts and testimonials should not be provided. Comments should be restricted to the content of the Initial Recommendation, and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.

h) References to support comments may be provided separately; however, these cannot be related to new evidence. New evidence is not considered at this part of the review process, however, it may be eligible for a Resubmission. If you are unclear as to whether the information you are considering to provide is eligible for a Resubmission, please contact the pCODR program.

i) The comments must be submitted via a Microsoft Word (not PDF) document to pCODR by the posted deadline date.

j) If you have any questions about the feedback process, please e-mail pcodrsubmissions@cadth.ca

Note: CADTH is committed to providing an open and transparent cancer drug review process and to the need to be accountable for its recommendations to patients and the public. Submitted feedback will be posted on the CADTH website (www.cadth.ca/pcodr). The submitted information in the feedback template will be made fully disclosable.

CADTH

pan-Canadian Oncology Drug Review Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation (Patient Advocacy Group)

Atezolizumab (Tecentriq) for Small Cell Lung Cancer

Lung Cancer Canada

December 5, 2019

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Atezolizumab (Tecentriq). In combination with a platinum-based chemotherapy and etoposide for the first-line treatment of patients with extensive stage small cell lung cancer.
Eligible Stakeholder Role in Review (Sponsor and/or Manufacturer, Patient Group, Clinical Organization Providing Feedback	Patient Group Lung Cancer Canada

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3.1 Comments on the Initial Recommendation

a) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the Initial Recommendation:

Lung Cancer Canada
DISAGREES

Lung Cancer Canada disagrees with this initial recommendation as we feel that PERC has not fully considered all the relevant factors in making this decision.

Lung cancer is the leading cause of cancer deaths in Canada. Small cell lung cancer (SCLC) which makes up about 10 – 15% of lung cancer cases is a more aggressive form of lung cancer. It has a significant disease burden and with the current available treatment, a median survival of 10.3 months. There is a high unmet need for these group of patients as there are currently few treatment options with the current standard of care being chemotherapy.

1. The unmet need in SCLC is higher than other forms of lung cancer. SCLC makes up 10 – 15% of lung cancer cases and is a more aggressive form of lung cancer. According to the 2019 Canadian Cancer Statistics, extensive stage SCLC has a median survival of 9- 11 months.
2. There have been no new treatments for SCLC since the current standard of care was approved in the 1980's. This does not mean that there has not been trials. Trials have not generated positive results and this is the first new treatment to be approved in decades. This indicates that SCLC is very difficult to treat.

3. Recognizing that SCLC is difficult to treat places the 2 month mOS in a new more significant light. LCC also believes that PERC has not fully considered the 12 and 18 month follow-up data where the overall survival rate was 52.7% and 34% in the atezolizumab/chemo arm compared with 38.2% and 21% in the chemo only arm. This data is consistent with the recent CASPIAN data released at the World Conference in Lung Cancer. This study examined durvalumab (another IO) in combination with chemotherapy vs chemotherapy alone in SCLC. The results are very consistent with IMPOWER133, adding additional certainty to the current data submission. All factors combined, this indicates that the benefit observed in the IMPOWER 133 study is clinically meaningful and represents progress in a disease with a high unmet need.
4. PERC also noted that there will be additional data from this study that will be released in March 2020 at which time there could be a resubmission. LCC asked the manufacturer to confirm the data release. They have indicated that there will be NO NEW DATA coming from the IMPOWER133 trial. This means that SCLC patients will not be able to get a chance at this therapy if PERC does not reconsider its decision.
5. This treatment option according to pERC aligns with patient values because it maintains QoL, has manageable side effects, and provides a needed an additional treatment choice, so why should these group of patient be denied the opportunity to live longer. PERC has previously approved other immunotherapy treatments similar or lower HR, so why should this case be any different? Given the high mortality and difficulty in treating this group of patients, SCLC patients cannot wait for other treatments.
6. PERC should also note that INESSS has recently recognized the clinical benefit of this treatment https://www.inesss.qc.ca/index.php?id=72&no_cache=1&L=1&DemandePluginController%5Buid%5D=4866&DemandePluginController%5Bonglet%5D=2&DemandePluginController%5BbackUrl%5D=%252Findex.php%253Fid%253D42%2526no_cache%253D1%2526L%253D1%2526DemandePluginController%25255Bterme%25255D%253Dtecentriq%2526DemandePluginController%25255Bliste%25255D%253D0%2526DemandePluginController%25255Bfabricant%25255D%253D0%2526DemandePluginController%25255Bonglet%25255D%253D2%2526DemandePluginController%25255BEVALUES_pointer%25255D%253D0&cHash=78e62c03b76837ff0cadcdb7b15a45b3. They suggested the following funding criteria if a listing agreement is established:

- *In combination with platinum and etoposide-based chemotherapy, as first-line therapy for extensive small-cell lung cancer in individuals:*
    - *whose central nervous system metastases, if present, are treated or asymptomatic; and*
    - *whose ECOG performance score is 0 or 1.*
    - *The maximum duration of each authorization is 4 months. When requesting the continuation of treatment, the physician must provide evidence of a beneficial clinical effect, established by the absence of disease progression, according to RECIST criteria, and confirmed by imaging.*

They also felt that the clinical benefit was modest but relevant and clinically significant given the therapy is for SCLC. INESSS noted that the treatment was not cost effective and recommended a price reduction be negotiated before it is listed in Quebec.

Lung Cancer Canada hopes that PCODR will align the final recommendation with INESSS and deliver a positive funding recommendation contingent on acceptable pricing. This will

allow this treatment to proceed to PCPA and negotiations to proceed between the provinces and the manufacturer with a the goal of an affordable price that can be supported by the system. LCC encourages the manufacturer and PCPA to negotiate with the need of these patients in mind.

When the initial recommendation was released, Lung Cancer Canada received a note from a caregiver of someone living with extensive stage SCLC. His feedback is below:

"It looks like they will not recommend Tecentriq for the funding of SCLC based on documents posted on Oct 3. However, review status is "Open for Feedback". Would you please send my feedback to people who are going to make final decision on Tecentriq, scheduled for Oct 18?

CADTH is basing its decision on 13 months of data for Tecentriq. However, recently there was a follow up of nearly 2 years. According to updated results from the phase III IMpower133 trial, at 18 months, **34% of patients were alive in the atezolizumab-CP/ET arm compared with 21% in the placebo-CP/ET arm.** And this is a statistically significant data.

I am asking decision makers to approve Tecentriq immunotherapy for SCLC. After 50 failed clinical trials for SCLC, this is the first immunotherapy that succeeded."

b) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the provisional algorithm:

☐ agrees ☐ agrees in part ☒ disagree

The current chemo only treatment algorithm has not resulted in any improvement in the 9 – 11 month overall survival rate. Adding the combination of atezolizumab plus chemotherapy to the algorithm as a first line treatment allows patients a chance to live longer.

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The typical treatment for SCLC patient is chemotherapy. Studies have shown that the addition of atezolizumab to chemotherapy in the first-line treatment of extensive-stage small-cell lung cancer resulted in a longer overall survival and progression-free survival than chemotherapy alone.

pERC provided a negative recommendation becase it was unable to conclude that there is a meaningful clinical benefit with atezolizumab (Tecentriq) in combination with a platinum-based chemotherapy and etoposide compared with platinum-based chemotherapy and etoposide in this patient population. The benefit is well demonstrated in the results of the IMPOWER133 as well as patient input.

LCC asks pERC to reconsider their recommendation for this group of patients as it offers them the chance to live longer, spend more time with their loved ones and this aligns with patient values.

Page Number	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information

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