CADTH

pan-Canadian Oncology Drug Review Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation (Registered Clinician)

Dabrafenib (Tafinlar) in Combination with Trametinib (Mekinist) for Non-Small Cell Lung Cancer with a BRAF V600 Mutation

Lung Cancer Canada

May 28, 2021

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Tafinlar and Mekinist (Dabrafenib and Trametinib) For the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with a BRAF V600 mutation and who have not received any prior anti-cancer therapy for metastatic disease.
Eligible Stakeholder Role	Clinician Group
Organization Providing Feedback	Lung Cancer Canada

3.1 Comments on the Initial Recommendation

a) Please indicate if the stakeholder agrees, agrees in part, or disagrees with the initial recommendation:

☒ Agrees ☐ Agrees in part ☐ Disagrees

"Thank you for your excellent review. We agree with this review and support conversion to final recommendation. We appreciate that PAG has also considered eligible patients who are currently treated with other therapies. (Appendix 1 pg 13). We suggest that the current wording and placement of the "first line" phrase may be confusing. We suggest the following wording:

"At the time of implementing a reimbursement recommendation for dabrafenib plus trametinib, jurisdictions may consider addressing the time-limited need of dabrafenib plus trametinib for patients with BRAF-mutated positive NSCLC who are currently receiving first-line chemotherapy or immunotherapy +/- chemotherapy and for patients who have previously been treated with other therapies (e.g., chemotherapy, PD-1 inhibitors). pERC noted that this time-limited access should be for patients who would otherwise meet the reimbursement criteria."

b) 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) clearly worded? Is the intent clear? Are the reasons clear?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity

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 recommendation ("early conversion"), which would occur two 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 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.

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, 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

Template for Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation

1 About Stakeholder Feedback

CADTH invites eligible stakeholders to provide feedback and comments on the pan-Canadian Oncology Drug Review Expert Review Committee (pERC) initial recommendation.

As part of the CADTH's pan-Canadian Oncology Drug Review (pCODR) process, pERC makes an initial recommendation based on its review of the clinical benefit, patient values, economic evaluation and adoption feasibility for a drug. The initial recommendation is then posted for feedback from eligible stakeholders. All eligible stakeholders have 10 business days within which to provide their feedback on the initial recommendation. It should be noted that the initial recommendation may or may not change following a review of the feedback from stakeholders.

CADTH 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 disagree with the initial recommendation, and to provide a rationale for their response. Please note that if a stakeholder agrees, agrees in part or disagrees with the initial recommendation, they 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 the key guiding principles for CADTH's pCODR process. 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 *Procedures for the CADTH Pan-Canadian Oncology Drug Review* are met, the final recommendation will be posted on the CADTH website two 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), 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. Please note that if any one of the eligible stakeholders does not support the initial recommendation proceeding to a final recommendation, pERC will review all feedback and comments received at a subsequent pERC meeting and reconsider the initial 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 pERC, and may not require reconsideration at a subsequent pERC meeting.

The final 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

- The following stakeholders are eligible to submit feedback on the initial recommendation:
    - The sponsor and/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
    - CADTH's Provincial Advisory Group (PAG)
- 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.
- The template for providing stakeholder is located in section 3 of this document.
- 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.
- Feedback on the initial recommendation should not exceed three 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.
- 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.
- References may be provided separately; however, these cannot be related to new evidence.
- 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 must be disclosable and will be posted on the CADTH website.
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CADTH

pan-Canadian Oncology Drug Review Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation (Registered Clinician)

Dabrafenib (Tafinlar) in Combination with Trametinib (Mekinist) for Non-Small Cell Lung Cancer with a BRAF V600 Mutation

Ontario Health (Cancer Care Ontario) Lung Cancer Drug Advisory Committee

May 28, 2021

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Dabrafenib-Trametinib/Non-Small Cell Lung Cancer (NSCLC) BRAF V600 mutation
Eligible Stakeholder Role	Registered clinicians
Organization Providing Feedback	Ontario Health (Cancer Care Ontario) Lung Cancer Drug Advisory Committee

3.1 Comments on the Initial Recommendation

a) Please indicate if the stakeholder agrees, agrees in part, or disagrees with the initial recommendation:

☐ Agrees ☒ Agrees in part ☐ Disagrees

Please explain why the stakeholder agrees, agrees in part or disagrees with the initial recommendation. If the stakeholder agrees in part or disagrees with the initial recommendation, please provide specific text from the recommendation and rationale. Please also highlight the applicable pERC deliberative quadrants for each point of disagreement. The points are to be numbered in order of significance.

The Response Rate is not different in subsequent lines. Dab/Tram should be funded as a line of therapy, whether first, second, or third.

The CCO/ASCO joint guidelines recommend dab/tram as a "may use" option for first line (there's no evidence it's any better than standard chemo or chemo/IO), and as a "may use" option for second line if not previously used. Funding ideally would reflect this.

Reference: Hanna NH, Schneider BJ, Temin S, et al. Therapy for Stage IV Non-Small-Cell Lung Cancer Without Driver Alterations: ASCO and OH (CCO) Joint Guideline Update. J Clin Oncol. 2020;38(14):1608-1632. doi:10.1200/JCO.19.03022

For patients with stage IV NSCLC and driver alterations with BRAF V600E mutation

* In the first-line setting, dabrafenib/trametinib may be offered (Type: informal consensus; Evidence quality: low; Strength of recommendation: moderate) or standard first-line treatment based on the ASCO/OH nondriver mutation guideline may be offered (Type: informal consensus; Evidence quality: low; Strength of recommendation: moderate).

Recommendations 8.1, 8.2, 8.3, and 8.4.

For patients with stage IV NSCLC and driver alterations with BRAF V600E mutation

* In the second-line setting, if previous BRAF/MEK-targeted therapy (dabrafenib/trametinib) was given in the first-line setting, standard treatment based on the ASCO/OH nondriver mutation guideline should be offered (Type: informal consensus; Evidence quality: low; Strength of recommendation: moderate).

* In the second-line setting, if BRAF-targeted therapy was not given in the first-line setting, dabrafenib/trametinib may be offered (Type: informal consensus; Evidence quality: low;

Strength of recommendation: moderate) or dabrafenib or vemurafenib alone may be offered (Type: informal consensus; Evidence quality: low; Strength of recommendation: weak).

b) 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) clearly worded? Is the intent clear? Are the reasons clear?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
13	Eligible patient population	re: BRAF V600 patients currently on first-line chemotherapy or immunotherapy and who have not progressed may need to be addressed on a time-limited basis and seeks advice on switching these patients to dabrafenib plus trametinib.	Re: about existing patients on chemotherapy, or chemo-IO and a time limited need for these patients to switch to dabrafenib-trametinib. This is not entirely appropriate. If a patient switches from one effective therapy without disease progression, then they may be losing potential benefit, particularly if they would not have access to that therapy again. There is also a time limited need for patients who are already on therapy to have access to dabrafenib and trametinib when they progress. This is consistent with other pCODR recommendations including crizotinib for ROS1 NSCLC. It is essential that there is consistency across recommendations.

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