CADTH | pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

# pan-Canadian Oncology Drug Review

# Registered Clinician Feedback on a pCODR Expert Review Committee Initial Recommendation

# Alectinib (Alecensaro) for Non-small Cell Lung Cancer

**May 4, 2017**

# Feedback on pERC Initial Recommendation

Name of the drug indication(s): __Alectinib_____

Name of registered clinician(s): __ Dr. Quincy Chu, oncologist, AB and Dr. Jeff Rothenstein, oncologist, ON;

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

### 3.1 Comments on the Initial Recommendation

a) Please indicate if the registered clinician(s) agrees or disagrees with the initial recommendation:

____ agrees ____ agrees in part __X__ disagree

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|---|
| *See Below* |

b) Notwithstanding the feedback provided in part a) above, please indicate if the registered clinician(s) 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.

| | |
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| ____ Support conversion to final recommendation. | __X__ Do not support conversion to final recommendation. |
| Recommendation does not require reconsideration by pERC. | Recommendation should be reconsidered by pERC. |

c) Please provide feedback on the initial recommendation. 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 |
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| Pg. 6 | **Overall Clinical Benefit** | **Studies Included**<br><br>…evaluating the safety and efficacy of alectinib in patients with ALK positive NSCLC who | The highlighted phrase is the key and Lung Cancer Canada reminds the committee of the reason for this submission and the chance that alectinib offers for patients that have progressed beyond crizotinib.<br><br>"There is no comparison, (alectinib) has allowed me to live." – CZ, patient |

| Page Number | Section Title | Paragraph, Line Number | Comments and Suggested Changes to Improve Clarity |
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| | | progressed on or were intolerant to treatment with crizotinib. | "I want to get on (alectinib) as soon as possible…the suffering has been out of the stratosphere." – S, patient.<br><br>Excerpted from pg. 13 of original submission.<br><br>We feel that the committee has not adequately weighted the voices of patients like CZ or S and our response brings us back to the reason and need for alectinib. |
| Pg. 3 | **Summary of pERC Deliberations** | Para 3:<br><br>pERC noted that tere appears to be anti-tumour activity with alectinib and was confident that there was tumour response with alectinib; however, the magnitude of effect compared with available treatments is unknown, given the lack of comparative data… | To recognize that ceritinib has anti-tumour activity but then to conclude that there is not enough evidence does not recognize both the uniqueness of targeted therapy and the high unmet need. In this case waiting for phase 3 denies life to those that are in need of it now.<br><br>On Dec. 11, 2015 the FDA and in Oct 2016 Health Canada, both granted alectinib breakthrough therapy designation based on preliminary evidence of clinical activity in patients with metastatic ALK-positive NSCLC previously treated with crizotinib. The approval of alectinib was based on the results of two, single-arm clinical trial, the same two that pCODR used for its consideration.<br><br>The FDA and Health Canada approvals stand in stark contrast to the arguments used by pERC vis a vis safety, strength of evidence and the need for randomized trials<br><br>In fact, Phase 3 data may not be required in this case. As argued by Stewart and Kurzrock, and more particularly Stewart and Batist: "Common cancers may arise from several different mutations, and each causative mutation may require different treatment approaches. There are also several mechanisms by which malignancies may become resistant to therapy, and each mechanism will also require a different therapeutic strategy. Hence, the paradigm of devising therapies based on tumor type is suboptimal. Each common malignancy may now be regarded as a collection of morphologically similar but molecularly |

| Page Number | Section Title | Paragraph, Line Number | Comments and Suggested Changes to Improve Clarity |
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| | | | distinct orphan diseases, each requiring unique approaches. Current strategies that employ randomized clinical trials (RCTs) in unselected patients carry a high risk of misleading results. Available data suggest that it is reasonable to grant marketing approval for new anticancer agents based solely on high single-agent response rates in small phase I-II studies involving molecularly-defined patient groups where benefit from other therapies is unlikely." |
| Pg. 8 | **Need:**<br><br>pERC agreed with the CGP…there is a significant need for effective treatments…with CNS metastases. | | Alectinib has demonstrated efficacy in patients with brain metastases. This is a highly significant finding that the committee has not given enough consideration to. Studies suggest that lung cancer has a higher incidence of brain metastases as compared to other cancers and those with brain metastases have a outlook on lower survival [A Ali et al., Survival of patients with non-small cell lung cancer after a diagnosis of brain metastases. Curr Oncol. 2013 Aug; 20(4): e300–e306]<br><br>"I was so weak I could barely get out of bed. 16 weeks later, my CT scans were summarized as: 'No CT evidence of residual or recurrent disease.' A complete response!" – patient<br><br>This is highly meaningful and data suggests that she is more typical.<br>This meets a huge unmet need in lung cancer. To the patient, brain metastases represents despair and a loss of function. Patients on alectinib remain highly functional.<br><br>If the high unmet need is recognized, why then have two ALK+ therapies for NSCLC been rejected? |
| Pg. 1 | **pERC Recommendation** | Unable to determine how alectinib compares to other treatments including best supportive care, | This statement ignores two of the key elements presented in the patient group submission: Time and quality of life filled with hope. |

| Page Number | Section Title | Paragraph, Line Number | Comments and Suggested Changes to Improve Clarity |
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| | | radiation and chemotherapy. | |
| Pgs 6/7 | **Overall Clinical Benefit** | Key Efficacy Results:<br><br>Because a percentage of patients in each trial – 21% (n=18) in trial NP28761 and 12% (n=16) in trial NP26673 – were deemed not to have measurable disease… | Chemotherapy does not have the same response rates. |

### 3.2 Comments Related to the Registered Clinician(s) Input

Please provide feedback on any issues not adequately addressed in the initial recommendation based on registered clinician(s) input provided at the outset of the review on outcomes or issues important that were identified in the submitted clinician input. Please note that new evidence will be not considered during 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.

Examples of issues to consider include: Are there therapy gaps? Does the drug under review have any disadvantages? Stakeholders may also consider other factors not listed here.

| Page Number | Section Title | Paragraph, Line Number | Comments related to initial registered clinician input |
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### 3.3 Additional comments about the initial recommendation document

Please provide any additional comments:

| Page Number | Section Title | Paragraph, Line Number | Additional Comments |
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| | | | ALK+ patients in Canada currently have one line of publically funded targeted therapy. People living with other cancers for example |

| Page Number | Section Title | Paragraph, Line Number | Additional Comments |
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| | | | breast, have more than one line of publically funded targeted therapy.<br><br>The FDA has awarded alectinib breakthrough status – recognizing its efficacy. Health Canada has also provided approval. Lung cancer already falls behind other cancers in terms of other cancers. We ask the pCODR panel to give lung cancer patients a chance… a chance to have standards of care similar to other cancers - life-extending therapies that will help increase the four month median survival for stage 4 lung cancer patients. In this case, the data sufficiently demonstrates efficacy. The patients that need alectinib now cannot wait until 2018. Help bring efficacious choice to lung cancer patients, similar to other cancers and other countries. Please reconsider the funding decision. Do not take away the "real hope" that alectinib represents for these patients. |

## About Completing This Template

- The following template form should be used by the registered clinician(s) to submit input at the beginning of a drug review. Please note that there is a separate template for providing feedback on an initial recommendation.

- The clinician(s) **must be registered with the pCODR program** to provide input. (See https://www.cadth.ca/pcodr/registration for information on eligibility and registration.)

- The registered clinician(s) must also complete the *pCODR Clinician Conflict of Interest Declarations Template* when providing input at the beginning of a drug review (see Appendix A of this document). While CADTH encourages collaboration among registered clinicians and that feedback submitted for a specific drug or indication be made jointly, each registered clinician must complete their own separate *pCODR Clinician Conflict of Interest Declarations Template*.

- Please ensure that the input is in English, and that it is succinct and clear. Please use a minimum 11-point font and do not exceed six (6) typed, 8 ½" by 11" pages. If a submission exceeds six pages, only the first six will be considered.

- The registered clinician(s) 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. Similarly, the registered clinician(s) should not feel restricted by the space allotted on the form and can expand the tables in the template as required. The categories and questions outlined are only examples, to guide identification of relevant clinical factors for pERC's consideration. Please note that comments may be attributed to a specific individual clinician and that registered clinicians who submit input will be identified as a contributor to the specific input. CADTH's pCODR program maintains the discretion to remove any information that may be out of scope of the review.

- It is important to note that scientific published references are not required, as pCODR has access to current scientific literature through the manufacturer's submission, tumour groups, and a rigorous, independent literature search.

- The registered clinician(s) must be submitted by the **deadline date** for this drug, posted on the pCODR section of the CADTH website under *Find a Review* so that it can be available in time to be fully used in the pCODR review process. If more than one submission is made by the same registered clinician(s), only the first submission will be considered.

- In addition to its use in the pCODR process, the information provided in this submission may be shared with the provincial and territorial ministries of health and Provincial cancer agencies that participate in pCODR, to use in their decision-making.

Should you have any questions about completing this form, please email submissions@pcodr.ca