pan-Canadian Oncology Drug Review

Patient Advocacy Group Feedback on a pCODR Expert Review Committee Initial Recommendation

Ceritinib (Zykadia) for Metastatic Non-Small Cell Lung Cancer

Lung Cancer Canada

December 3, 2015

Feedback on pERC Initial Recommendation

Name of the drug indication(s): Ceritinib

Name of registered patient advocacy group: Lung Cancer Canada

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

1.1 Comments on the Initial Recommendation

a) Please indicate if the patient advocacy group agrees or disagrees with the initial recommendation:

____ agrees ____ agrees in part ___X_ disagree

Please explain why the patient advocacy group agrees, agrees in part or disagrees with the initial recommendation.
This submission does not consider the huge unmet need in lung cancer and the uniqueness of molecular targeted therapy. It does not adequately consider ceritinib's efficacy in brain-metastases. It also places Canadian lung cancer patients at a disadvantage in comparison to other cancers and other countries. Ceritinib meets a need we have now. These patients do not have the time to wait until 2018.

b) Notwithstanding the feedback provided in part a) above, please indicate if the patient advocacy group would support this initial recommendation proceeding to final pERC recommendation ("early conversion"), which would occur within 2(two) business days of the end of the consultation period.

____ Support conversion to final recommendation.
Recommendation does not require reconsideration by pERC.

__X__ Do not support conversion to final recommendation.
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

1.2 Comments Related to Patient Advocacy Group Input

Page Number	Section Title	Paragraph, Line Number	Comments related to initial patient advocacy group input
	Overall clinical benefit. Studies included.	1 …evaluating the safety and efficacy of ceritinib in patients with ALK positive NSCLC who had disease progression despite previous treatment with crizotinib.	The highlighted phrase is the key and Lung Cancer Canada reminds the committee of the reason for this submission and the chance that ceritinib offers for patients that have progressed beyond crizotinib. "These patients just ask for the chance to continue to fight. A, an ALK+ patient who was in her 60's before she passed away, was on chemotherapy and was having a very difficult time. She persevered and her reasons to summed up the thoughts of many patients and involved three parts: Time to spend with her grandchildren and husband. Hope to beat the disease and, promise of a better treatment (more effective and more tolerable) on the horizon. Ceritinib represents that treatment." Excerpted from pg. 8 of original submission. We feel that the committee has not adequately weighted the voices of patients like A and our response brings us back to the reason and need for ceritinib.
2	Key results and interpretation – interpretation and guidance	Paragraph 1 And Paragraph 6	These paragraphs are in contradiction. 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.
On March 6, 2013, FDA granted ceritinib breakthrough therapy designation based on preliminary evidence of clinical activity in patients with metastatic ALK-positive NSCLC previously treated with crizotinib. The approval of ceritinib was based on the results of a multicenter, single-arm, open-label clinical trial enrolling a total of 163 patients with metastatic, ALK-positive, NSCLC who had progressed on or were intolerant to crizotinib. All patients received ceritinib at a dose of 750 mg once daily. This was essentially a phase I/II combined study. The FDA and Health Canada approval stands in stark contrast to the arguments used by pERC vis a vis safety, strength of evidence and the need for randomized trials In fact, Phase 3 data may not be required in this case. As argued by Stewart and			

Kurzrock, and more particularly Stewart and Batist (papers attached): "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 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."			
2, 3	Guidance in Brief	Interpretation and Guidance paragraph 2 and Conclusions paragraph 2	The committee has not provided enough consideration to brain metastases. There are only two brief mentions in the guidance in brief. Ceritinib 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]
Remember M from our submission: *"M had 10 small tumours in her brain. She started on ceritinib and 6 – 8 weeks later, all the tumours had disappeared. Toda*y she is living with no evidence of disease." This is highly meaningful and data suggests that she is not a ceritinib outlier. In ASCEND-1, patients who presented with brain metastases (n=124) at study entry had an overall response rate (ORR) of 51%. In ASCEND 2, patients who presented with brain metastases (n=100) at study entry had an overall response rate (ORR) of 33%. This finding meets a huge unmet need in lung cancer. To the patient, brain metastases represents despair and a loss of function. Patients on ceritinib remain highly functional. As A says, *"I feel great, and I look great. I just hope that [when I go for my check-up] my insides will match my outside!"*			
1	**PERC Recommendation "Unable to determine how ceritinib compares to other treatments including best supportive care and chemotherapy."**		This statement ignores two of the key elements presented in the patient group submission: Time and quality of life filled with hope.
Ceritinib meant a continuation of "real hope". In contrast all those on ceritinib agreed			

that if they were on chemotherapy as opposed to ceritinib, it would mean a loss of hope.
"[Certinib] made me stop wondering if this is my last Christmas."
- *Patient living with stage 4 lung cancer and on ceritinib –*

The concept of time is extremely important. Crizotinib gives almost 11 months of progression free survival. Data suggested that second line ceritinib would provide 6 – 8 month of PFS. This is highly significant in a disease where data suggests that 4 month median survival for stage 4 lung cancer patients and a 17% 5-year survival rate. The concept of time was clearly outlined in our submission. In reminder,
"Its amazing to have the drug. It's unbelievable. I am not working anymore but it allows me to be almost bored! I go to the gym several times a week. It's amazing!" states one patient. "There is no comparison – it is a life saving drug and gives you a life. I take care of my grandchildren and enjoy time with my family", says M.

Like crizotinib, after the side effects were managed, all felt that they could "function normally". "Sometimes I forget I have cancer – Its bizarre!" says one patient.
They continue to be parents and patients continue to go to work. "Day to day, I continue to feel good", says J. He's able to come back home at night and "roll around with their baby" on the floor. "I don't feel like I have lost anything."

Psychologically, continuing on an oral targeted therapy really helped all the patients feel better and believe in treatment, and the possibility of a future. For many, progression on crizotinib differed from progression after chemotherapy as many did not feel "sick" when they found out that crizotinib was no longer working. "Going back on chemotherapy would be devastating."

Chemotherapy carries a high management burden on the caregiver. Chemotherapy often left caregivers feeling helpless as the side effects carried a high level of unpredictability. Everyone spoke to the challenge of constantly "trying this, or that" to make the patient more comfortable. "I was running a short order kitchen", said B. "Constantly we would be trying something and then she would have one bite and throw up," said B. Ceritinib has allowed them to continue to spend quality time together as a couple.

1.3 Additional Comments About the Initial Recommendation Document

ALK+ patients in Canada currently have one line of publically funded targeted therapy. People living with other cancers for example breast, have more than one line of publically funded targeted therapy.

The FDA has awarded ceritinib 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 ceritinib 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 ceritinib represents for these patients.

About Completing This Template

pCODR invites those registered patient advocacy groups that provided input on the drug under review **prior** to deliberation by the pCODR Expert Review Committee (pERC), to also provide feedback and comments on the initial recommendation made by pERC. (See www.cadth.ca/pcodr for information regarding review status and feedback deadlines.)

As part of the pCODR review process, the pCODR Expert Review Committee makes an initial recommendation based on its review of the clinical, economic and patient evidence for a drug. (See www.cadth.ca/pcodr for a description of the pCODR process.) The initial recommendation is then posted for feedback and comments from various stakeholders. The pCODR Expert Review Committee welcomes comments and feedback that will help the members understand why the patient advocacy groups agree or disagree with the initial recommendation. In addition, the members of pERC would like to know if there is any lack of clarity in the document and if so, what could be done to improve the clarity of the information in the initial recommendation. Other comments are welcome as well.

All stakeholders have 10 (ten) business days within which to provide their feedback on the initial recommendation and rationale. If all invited stakeholders, including registered patient advocacy groups, agree with the recommended clinical population described in the initial recommendation, it will proceed to a final pERC recommendation by 2 (two) business days after the end of the consultation (feedback) period. This is called an "early conversion" of an initial recommendation to a final recommendation.

If any one of the invited stakeholders does not support the initial recommendation proceeding to final pERC recommendation, pERC will review all feedback and comments received at the next possible pERC meeting. Based on the feedback received, pERC will consider revising the recommendation document as appropriate. It should be noted that the initial recommendation and rationale for it may or may not change following consultation with stakeholders.

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

Instructions for Providing Feedback

a) Only registered patient advocacy groups that provided input at the beginning of the review of the drug can provide feedback on the initial recommendation.

- Please note that only one submission per patient advocacy group is permitted. This applies to those groups with both national and provincial / territorial offices; only one submission for the entire patient advocacy group will be accepted. If more than one submission is made, only the first submission will be considered.
- Individual patients should contact a patient advocacy group that is representative of their condition to have their input added to that of the group. If there is no patient advocacy group for the particular tumour, patients should contact pCODR for direction at www.cadth.ca/pcodr.

b) 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 during this part of the review process; however, it may be eligible for a Resubmission.

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

d) At this time, the template must be completed in English. Patient advocacy groups 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 to their group. Similarly, groups should not feel restricted by the space allotted on the form and can expand the tables in the template as required.

e) Feedback on the initial pERC recommendations **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 forwarded to the pERC.

f) 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.

g) References to support comments may be provided separately; however, these cannot be new references. New evidence is 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 considering to provide is eligible for a Resubmission, please contact the pCODR Secretariat.

h) The comments must be submitted via a Microsoft Word (not PDF) document by logging into www.cadth.ca/pcodr and selecting "Submit Feedback" by the posted deadline date.

i) Patient advocacy group feedback must be submitted to pCODR by **5 P.M. Eastern Time** on the day of the posted deadline.

j) If you have any questions about the feedback process, please e-mail pcodrinfo@cadth.ca. For more information regarding patient input into the pCODR drug review process, see the *pCODR Patient Engagement Guide*. Should you have any questions about completing this form, please email pcodrinfo@cadth.ca

Note: Submitted feedback is publicly posted and also may be used in other documents available to the public. The confidentiality of any submitted information at this stage of the review cannot be guaranteed.