CADTH

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

# Brigatinib (Alunbrig) for Non-Small Cell Lung Cancer

August 1, 2019

# 3 Feedback on pERC Initial Recommendation

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| Name of the Drug and Indication(s): | Brigatinib/ALK+ NSCLC |
| Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Group, Clinical Group): | Registered Clinician Feedback |
| Organization Providing Feedback | Cancer Care Ontario Lung DAC |

**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

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| *The CCO Lung DAC agrees with the initial recommendation as worded. The DAC agrees that there is uncertainty in the evidence. Further, the DAC is unsure that there is net clinical benefit compared to other currently available options. Brigatinib may be evaluated in the future pending the availability of new evidence.* |

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

☐ agrees ☐ agrees in part ☐ disagree

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| *n/a* |

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 |
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### 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.

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| ☒ | Support conversion to Final Recommendation.<br>Recommendation does not require reconsideration by pERC. | ☐ | Do not support conversion to Final Recommendation.<br>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 |
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# 3 Feedback on pERC Initial Recommendation

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| Name of the Drug and Indication(s): | **Brigatinib (Alunbrig) As a monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive metastatic non–small cell lung cancer (NSCLC) who have progressed on or who were intolerant to an ALK inhibitor (crizotinib).** |
| Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Group, Clinical Group): | **Registered clinician group** |
| Organization Providing Feedback | **Lung Cancer Canada** |

**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.*

## 3.2 Comments on the Initial Recommendation

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

☐ agrees ☐ agrees in part ☒ disagree

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| *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 rational. Please also highlight the applicable pERC deliberative quadrants for each point of disagreement. The points are to be numbered in order of significance.* |

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

☐ agrees ☐ agrees in part ☒ disagree

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| *Please explain why the* Stakeholder *agrees, agrees in part or disagrees with the provisional algorithm. Please note that comments should relate* ***only to the proposed place in therapy of the drug under review*** *in the provisional algorithm. If feedback includes New Information or about other therapies that are included in the provisional algorithm, the information will not be considered and will be redacted from the posted feedback. Substantive comments on the provisional algorithm will preclude early conversion of the initial recommendation to a final recommendation.* |

f) 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 |
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### 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 |
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| 1 | PERC Initial recommendation | | |

**This response made on behalf of the group was drafted by Dr Geoffrey Liu.**

It was the opinion of pERC there was too much uncertainty of degree of benefit because this submission was based on data from a Phase II trial. However, in comparison the sample size for each of the ALTA arms is 40-50% larger than the Phase III ALUR trial, and even its inferior 90 mg

arm had a PFS that was better than the best results of any alectinib second line arm. In fact, the ALK trials have demonstrated a constant improvement in PFS: first line crizotinib ~10-11 mos (6 trials), second or subsequent line ceritinib 5-6.5 months (4 trials), second or subsequent line alectinib 8.4-9.6 months (3 trials), and now brigatinib 180 mg second or subsequent line 15-16 months (2 trials, if you include the Phase I separately). It is reasonable to believe, based on the evidence that brigatinib is at least as efficacious as the other drugs available, and likely better.

There is also mounting data to suggest that brigatinib has a role post-alectinib as well (data released at the 2019 ASCO data showed a 40-50% RR post-second generation ALK TKI responses in brigatinib from the French group and ATOMIC study. I myself [Dr Geoffrey Liu] have two patients who had brigatinib for over 1.5 years each, and then each had responses of 6+ months on lorlatinib). So personally, I have little doubt about the space brigatinib falls into is second line after crizotinib, or second line after alectinib. ALTA-1L will only consolidate the idea that brigatinib has excellent activity, and it will be the HR and mPFS of ALTA-1L that will either convince me to move brigatinib to first-line OR leave it at second line.

PERC spoke about the lack of unmet need. However patient and physician choice should be available in lung cancer, the way it is in breast cancer and the way that it is available in so many cardiology, respirology, and gastroenterology drugs all listed as options by funders. Brigatinib is needed as it serves as an alternative choice for second line treatment of ALK positive lung cancer. Additionally, physicians believe that the brigatinib data offers reasonable proof to physicians that it is better than alectinib and ceritinib in the second line setting. Reimbursement of brigatinib at the same rate as ceritinib and alectinib allows patients to have an alternative - so the increased costs to the system are primarily the longer times a patient stays on the drug because of clinical benefit.

The reality was that at the time of development of brigatinib, it was no longer easily feasible to perform Phase III trials in the second and subsequent line setting. There were too many questions about the appropriate comparator, and every 6 months, the comparator arm was changing. To me, the lack of Phase III data had to do with the rapidly changing landscape; but that should not leave a good drug out of reach of patients simply because it was developed later. As mentioned before brigatinib is at least as good as the others, and we should let this be an alternative choice for patients and physicians who want to use it. It should not be penalized due to the changing landscape.

As clinicians we intimately understand the value of choice. In order to maintain these choices, we also understand the need for a sustainable system. Brigatinib offers a competitor to alectinib. Market place competition facilitates better pricing and thus sustainability. We understand PERC's dilemma with phase 2 data. We encourage PERC to reconsider this recommendation and allow for a conditional time limited positive recommendation upon further data collection. During this time, in acknowledgement of the data uncertainty, we also ask PERC to consider innovation pricing models of shared risk. Perhaps models where brigatinib can be priced at or under the current standard of care can be considered.

# 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 Submitter 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 Submitter 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.*