# pan-Canadian Oncology Drug Review

# Provincial Advisory Group (PAG) Feedback on a pCODR Expert Review Committee Initial Recommendation

# Nivolumab (Opdivo) for Non-Small Cell Lung Cancer

**June 3, 2016**

# 3 Feedback on pERC Initial Recommendation

Name of the drug indication(s): Nivolumab (Opdivo) for Non-Small Cell Lung Cancer

Endorsed by: Provincial Advisory Group Chair

Feedback was provided by all provinces (Ministries of Health and/or provincial cancer agencies) participating in pCODR.

## 3.1 Comments on the Initial Recommendation

a) Please indicate if the PAG (either as individual PAG members and/or as a group) agrees or disagrees with the initial recommendation:

_____ Agrees ___x___ Agrees in part ____ Disagree

All PAG members providing feedback agree in part with the pERC initial recommendation

b) Notwithstanding the feedback provided in part a) above, please indicate if the PAG 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.

PAG is seeking clarity on the patient population and definition of pseudoprogression to address adoption feasibility.

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 | pERC Recommendation | Paragraph 1 | Suggest revising "who progressed on or after chemotherapy" to be consistent with the trial criteria: "who progressed on or after platinum-based chemotherapy". |

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| | | | Patients who have received first-line oral targeted therapy may be interpreted as having received "chemotherapy" and being eligible for nivolumab at progression.<br><br>Patients unfit for platinum-based chemotherapy may be treated with single agent chemotherapy and would not have been included in the clinical trial. |
| 1 | pERC Recommendation | Paragraph 1 | PAG is seeking clarity on the number of previous therapies: In the trial with non-squamous cell histology, majority of the patients had received only one or two prior lines of therapy. The recommendation does not specify the number of previous therapies and thus, patients could be treated with nivolumab in the third or fourth-line setting. |
| 1 | pERC Recommendation | Paragraph 1 | To facilitate adoption feasibility, PAG is seeking clarity on whether the recommendation includes<br><br>• ALK positive mutations and EGFR positive mutations<br>• both non-squamous and squamous cell histologies are included<br>• patients with CNS metastasis |
| 1 | pERC Recommendation | Performance Status | The clinical trials included performance status of 0 to 1. The recommendation allows for patients with performance status of 2 or greater to be allowed to receive this drug. However, PAG agrees with "good performance status" given that the limitation of PS to 0-1 in the trial was due to the docetaxel and patients with PS-2 will be able to tolerate the much milder toxicity profile of nivolumab. |
| 2 | Time Limited Need | Last sentence | The Checkmate studies accepted patients with ECOG PS of 0 or 1 only. PAG suggests revising to "for patients who remain in good performance status".<br><br>Time limited funding may need to be considered for patients who had platinum-based therapy in the past but are currently on single agent treatment. |

### 3.2 Comments related to PAG input

Please provide feedback on any issues not adequately addressed in the initial recommendation based on the PAG input provided at the outset of the review on potential impacts and feasibility issues of adopting the drug within the health system.

| Page Number | Section Title | Paragraph, Line Number | Comments related to initial PAG input |
|---|---|---|---|
| | | | Definition of "patients who progressed on or after chemotherapy" should be specific as in the trials.<br>PAG noted potential for indication creep into other lines of treatment or patient population such as patients who<br>• have progressed on oral targeted therapies<br>• have not received platinum-based doublet chemotherapy<br>• received three or more previous treatments<br>• are not previously treated (i.e. first-line treatment with nivolumab) |
| | | | If this is within the scope of the review, it would be ideal if information be provided on how nivolumab compares to other PD-L1 inhibitors, or alternatively, which patients nivolumab may be better suited for compared to other PD-L1 inhibitors. |
| | | | PAG has also asked pERC to comment on sequencing of the currently available treatments. |

### 3.3 Additional comments about the initial recommendation document

Please provide any additional comments:

| Page Number | Section Title | Paragraph, Line Number | Additional Comments |
|---|---|---|---|
| 9 | | Last paragraph | PAG noted that the definition of true disease progression vs pseudoprogression and thus, discontinuation criteria, could be interpreted differently amongst the jurisdictions. PAG would appreciated any guidance from the CGP on how to define pseudo-progression vs. true disease progression for consistent adoption across the jurisdictions. |
| 4 and 9 | | Paragraph 3 | For the statement "it is important to prospectively collect such data", PAG suggests additional statement(s) that treatment duration should be reassessed in the event that new evidence emerges on how long treatment should be given. |

## About Completing This Template

pCODR invites the Provincial Advisory Group (PAG) to provide feedback and comments on the initial recommendation made by the pCODR Expert Review Committee. (See www.cadth.ca/pcodr for information regarding review status and feedback deadlines.)

As part of the pCODR re view 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 pERC 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 PAG, either as individual PAG members and/or as a group, agrees or disagrees with the pERC 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 pERC 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 agree with the recommended clinical population described in the initial recommendation, it will proceed to a pERC final 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 a pERC final 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 pERC final 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 members of the PAG can provide feedback on the pERC initial recommendation; delegates must work through the PAG representative to whom they report.
    a. Please note that only one submission is permitted for the PAG. Thus, the feedback should include both individual PAG members and/or group feedback.

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

c) The template for providing *Provincial Advisory Group (PAG) 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. PAG 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, PAG 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 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 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 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 Secretariat.

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

i) If you have any questions about the feedback process, please e-mail submissions@pcodr.ca.

*Note: Submitted feedback may be used in documents available to the public. The confidentiality of any submitted information cannot be protected.*