PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

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

Obinutuzumab (Gazyva) for Chronic Lymphocytic Leukemia

January 27, 2015

3 Feedback on pERC Initial Recommendation

Name of the drug indication(s): Obinutuzumab (Gazyva) for CLL

Endorsed by: Provincial Advisory Group Chair

Feedback was provided by all nine 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:

__X___ Agrees ____ Agrees in part ____ Disagree

Most members providing feedback agree with the recommendation. One member agrees in part because it was felt that bendamustine is the more appropriate clinical and cost effectiveness comparator. PAG requests clarification from pERC around their conclusion of the most relevant comparator.

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.

__X__ 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.

Most PAG members support conversion of the initial recommendation to final. One member does not support conversion to final and would like pERC to reconsider the cost effectiveness of obinutuzumab + chlorambucil compared to bendamustine. In the absence of direct or indirect comparative cost-effectiveness, this PAG member considers that cost-effectiveness has not been sufficiently addressed.

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 and through out	pERC Recommendation	Line 1	Suggest "obinutuzumab plus chlorambucil" be added to first sentence in pERC Recommendation and consistently used throughout the document clearly state that the review is obinutuzumab plus chlorambucil and not obinutuzumab monotherapy or obinutuzumab in combination with other agents.
2	Summary of pERC Deliberations	Paragraph #2, page 11	Spelling error: "creatinine clearance"
3		Paragraph #5, line 11	Could wording acknowledge that Bendamustine would be a reasonable comparator.

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

3.3 Additional comments about the initial recommendation document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
4	Patient populations: Older patients with comorbidities, considered ineligible for fludarabine	Paragraph #6	The pERC comments regarding "adequate renal function" are too ambiguous. The CLL11 trial was designed to include patients who were not considered fit for fludarabine-based therapy. One way of identifying such patients was a CIRS score greater than 6. A second way was through a reduction of renal function with a creatinine clearance of 30 to 60. Presumably, this reduction in GFR made these patients unsuitable for fludarabine-based treatment, but it doesn't address the minimum GFR for safe administration of obinutuzumab. Practitioners may reasonably expect clearer guidance than simply stating "adequate renal function". To further address the renal problem, eligibility required a Creatinine Clearance of <70. As indicated above, this is a range which makes Fludarabine based regimens more toxic. Patients <30cc/min seem to not be eligible. Also, although CIRS >6 was needed, the median score was 8 so the vast majority of the patients were not very sick with scores of 7, 8 or 9.

5	Key efficacy results: Clinically significant improvement in overall survival and progression-free survival	Paragraph #2	Suggest to highlight that the primary end point of the study was progression-free survival
			Could pERC address the time limited need for patients who have started treatment with chlorambucil monotherapy but have not yet progressed and would be eligible for obinutuzumab/chlorambucil?
8	Considerations for implementation and budget impact: Comparative efficacy with other treatment options unknown	Paragraph #3	Clarification around dosing was requested, e.g., the recommendation states that "…patients require one dose per week for 28 days." Which implies 4 weekly doses. Obinutuzumab is dosed on Days 1, 8 and 15 in the first 28 day cycle, therefore, it may be more appropriate to note as: "...patients require three doses within the 28 days."
			PAG is requesting whether further follow up should be requested, looking at the survival advantage of obinutuzumab + clorambucil vs rituxumab + chlorambucil, given the rituxumab is expected to become genericized shortly.

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.pcodr.ca 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.pcodr.ca 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.pcodr.ca 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.