pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

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

Aflibercept (Zaltrap) for Metastatic Colorectal Cancer

September 5, 2014

Feedback on pERC Initial Recommendation

Name of the drug indication(s): Aflibercept + Folfiri in 2nd Line Treatment of mCRC

Name of registered patient advocacy: Colorectal Cancer Association of Canada (CCAC)

**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.

- While pERC considered the addition of Aflibercept to Folfiri to confer only a modest overall clinical benefit with significant toxicities and unknown impact on Quality of Life (QoL), patients surveyed have repeatedly reported how important it would be to access additional treatments whose benefits might only be short term **despite treatment adverse effects**. Patients surveyed would not refuse taking a cancer therapy based on a severe toxicity profile. Furthermore, as stipulated in our submission, the CCAC QoL survey demonstrated that part of maintaining QoL for patients is linked to **providing greater access to therapies that treat mCRC**. As noted in our submission, in the metastatic setting long term health is relative and is viewed by patients in small increments. Any extension in life is considered an extension in long term health by mCRC patients and caregivers.
- For patients facing provincial reimbursement restrictions (in respect of Bevacizumab), access to another anti-VEGF therapy (especially one that has the theoretical advantage of more effective angiogenic suppression) such as Aflibercept in combination with Folfiri in 2nd line therapy following Bevacizumab + Folfox may ensure patients continue to respond optimally.
- Based on the above-noted points, the pERC recommendation does not align with our patient values.

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
3	Summary of pERC …..	2; 5-7	While Bevacizumab may be available across provinces, it is not widely available in **both** 1st and 2nd line therapy for treatment of mCRC.
3	Overall Clinical Benefit	8; 8-9	A "modest" clinical benefit is, nevertheless, found to be statistically significant in the VELOUR study and highly sought after by mCRC patients surveyed. Clinical utility cannot be ignored.
4	Overall Clinical Benefit	2; 2-5	While QoL data would have been helpful, our patient survey results indicate that an improvement in QoL does not trump an extension in overall survival (O.S.) or progression free survival (P.F.S.) which patients admit may be accompanied with severe toxicities.
4	Overall Clinical Benefit	3; 9-11	Ibid
6	Adoption Feasibility	4; 11-13	The funding of Aflibercept in the interim would not detract from the funding of any future therapies deemed to be more effective at providing improved patient outcomes. This is in keeping with patients' desire (together with their treating oncologist) to be afforded the opportunity to have choice in the selection of the best therapeutic option in the treatment of their mCRC.

1.2 Comments Related to Patient Advocacy Group Input

Page Number	Section Title	Paragraph, Line Number	Comments related to initial patient advocacy group input
5	Patient Values	3; 1-3	The unmet patient needs relate specifically to those patients who access Bevacizumab in 1st line therapy and are unable to access it in 2nd line due to provincial funding restrictions.
5	Patient Values	3; 5-8	Every effort was made to contact Canadian and U.S.- based patients who had received Aflibercept therapy. Efforts are currently underway to expand access globally.
4	Safety: Increased	3; 9-11	While our surveyed oncologists did report that Aflibercept is associated with an increase in

	Grade 3 and 4….		adverse events, they did **not** report any Aflibercept-related hospital admissions and did conclude that side effects were manageable.
4	Need: therapies that meaningfully..	5; 4-5	Both patient surveys and anecdotal evidence do not reflect this practice pattern. Folfox + Bevacizumab appears to be quite popular in 1st line especially when metastatic disease is confined to the liver.

1.3 Additional Comments About the Initial Recommendation Document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
3	Evidence In Brief	8; 8-9	pERC considered Aflibercept's clinical benefit to be "modest". How was the magnitude measured and according to whose definition of the word "modest"? pERC provided no threshold for the basis of the "modest" determination.
3	Studies Included: one randomized ….	6; 5-8	In terms of the drug's toxicity profile, the VELOUR study was the only reference study utilized for review. Perhaps other studies may have been reviewed such as the Cartwright or Mitchell Study.
4	Quality of Life	2; 3-5	While VELOUR did not examine QoL, the increased Response Rate demonstrated that Aflibercept conferred a greater benefit on a subset of the population with liver-only disease; a benefit which may ultimately lead to highly sought-after liver resections. This conferred benefit speaks to the personalization of patient care.
4	Need: therapies that meaningfully…..	5; 10-12	While Bevacizumab may indeed be the most relevant comparator to Aflibercept in the 2nd line setting, Aflibercept has the theoretical ability to target a broader set of proangiogenic growth factors when compared to Bevacizumab, thereby producing more effective angiogenic suppression and potentially capable overcoming Bevacizumab resistance in certain patients.

pCODR Patient Advocacy Group Feedback on a pERC Initial Recommendation

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.pcodr.ca 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.pcodr.ca 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 info@pcodr.ca.

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.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. 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.pcodr.ca 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 info@pocr.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 info@pcodr.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.