PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

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

Colorectal Cancer Association of Canada

Regorafenib (Stivarga) for Metastatic Colorectal Carcinoma

November 15, 2013

1 Feedback on pERC Initial Recommendation

Name of the drug indication(s): Regorafenib (Stivarga®) for mCRC

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

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.

Third and fourth line patients are very much in need of an additional therapeutic option to help manage their metastatic colorectal cancer (mCRC), help maintain QoL and prolong overall survival (OS). The CORRECT Study has demonstrated Regorafenib's ability to increase OS and progression free survival (PFS). The expert committee focused and based their recommendation on the CORRECT trial concluding that the magnitude of the absolute benefit in median OS and PFS was modest for Regorafenib compared to placebo. Narrowing the study conducted and results down to simply looking at median difference may be problematic. The median only represents one patient on each Kaplan-Meier curve and is hardly able to capture the benefit experienced by the entire study population. An examination of the Hazard Ratio (HR) may prove more helpful and serve as a better parameter. The OS HR of 0.77 denotes a 23% reduction in death events with Regorafenib which is clinically meaningful. The PFS results suggest a poor performance of the median, but the HR is very strong at 0.49, translating into a 51% reduction of risk of progression while on Regorafenib. This too is clinically meaningful and indicated a significant advantage for patients with late stage disease.

Of particular note is the fact that the study completed its accrual within 10 months, rather than 26 months as was originally projected, demonstrating that there is a significant unmet need for patients. Finally, it is quite possible that adverse effects may have been disease-related rather than treatment-induced. Therefore, it may be appropriate to give less weight to the absolute percentage of events while on Regorafenib and focus on the delta between the arms.

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.	__X__ Do not support conversion to final recommendation.
Recommendation does not require reconsideration by pERC.	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
2	Summary of pERC Deliberations	3; 5	- An examination and review of the delta between the arms would be more meaningful. - Some of the side effects may have been disease-related vs. treatment-induced. - QoL may also be improved by avoiding clinic and hospital visits associated with infusional therapies and infusion-related adverse events. There is a great unmet need for patients at this stage.
2	Summary of pERC Deliberations	2; 6-7	An examination and review of HRs for endpoints would be more significant.

1.2 Comments Related to Patient Advocacy Group Input

Please provide feedback on any issues not adequately addressed in the initial recommendation based on patient advocacy group input provided at the outset of the review on outcomes or issues important to patients that were identified in the submitted patient input. Please note that new evidence will be 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 providing is eligible for a Resubmission, please contact the pCODR Secretariat.

Examples of issues to consider include: what are the impacts of the condition on patients' daily living? Are the needs of patients being met by existing therapies? Are there unmet needs? Will the agents included in this recommendation affect the lives of patients? Do they have any disadvantages? Stakeholders may also consider other factors not listed here.

Page Number	Section Title	Paragraph, Line Number	Comments related to initial patient advocacy group input
2	Summary of pERC Deliberations	3;6	Our MAB survey clearly demonstrates that Regorafenib's potential benefits outweigh the risks, as long as patients are closely monitored.
4	Evidence in Brief: Quality of Life	2; 1-5	Since Regorafenib is an oral agent, able to be administered in the comfort of the patient's home, clinic and hospital visits may ultimately be decreased, allowing for an improvement in the patient's QoL

1.3 Additional Comments About the Initial Recommendation Document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
5	**Patient Based Values**	**2;6**	**The number of patients who were alive and able to complete the questionnaire was significantly higher when compared to the placebo arm throughout the study. Please see attachment.** **The attachment clearly demonstrates that a significantly higher percentage of patients are still living and able to complete the questionnaire forms (compared to placebo group) at any given time throughout the study. This is clinically meaningful.**
4	**Evidence in Brief**	**1;4**	**A modest clinical benefit is nevertheless considered to be a benefit to treatment-refractory mCRC patients. In the metastatic setting, long term health is relative and is viewed by patients in small increments, which includes "modest benefits". As noted in our submission, any extension in life is considered an extension in long term health by mCRC patients and caregivers.**

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.