CADTH | pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

Registered Clinician Feedback on a pCODR Expert Review Committee Initial Recommendation

Regorafenib (Stivarga) for Hepatocellular Carcinoma

April 18, 2018

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Regorafenib for Hepatocellular Carcinoma
Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Group, Clinical Organization Providing Feedback	Registered Clinician who previously provided input Dr. Vincent Tam

**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 pCODR.*

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 __X__ agrees in part ____ disagree

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.*

1. **Agree with overall recommendation to fund regorafenib for HCC patients previously treated with sorafenib given the potential clinically relevant survival benefit and lack of other treatment options for these patients**
2. **Agree that cost-effectiveness could be improved.**
3. **I disagree with limiting reimbursement strictly to the RESORCE trial eligible population. In my professional opinion there are certain patients in clinical practice with Childs Pugh B7 liver function (just low albumin and no ascites) and relatively well ECOG 2 who may benefit from regorafenib.**
4. **Regarding the implementation of a first assessment at 6 weeks, this is doable, but also very reasonable to scan at 8 weeks. Current standard imaging interval for the HCC patients I treat is 8 to 12 weeks depending on clinical status of the patient, tolerability of the drug and AFP trend (if elevated at start).**

b) 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) clearly worded? Is the intent clear? Are the reasons clear? **Yes, wording, intent and reasons are clear.**

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity

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.

__X__	Support conversion to Final Recommendation.	____	Do not support conversion to Final Recommendation.
	Recommendation does not require reconsideration by pERC.		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, 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

About Stakeholder Feedback

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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), 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. 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.

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.

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   - 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) 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.

c) 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.)

d) 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.

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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.

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Name of the Drug and Indication(s):	Regorafenib/HCC
Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Organization Providing Feedback	Tumour Group Cancer Care Ontario Gastrointestinal DAC
Contact Person*:	Dr. Erin Kennedy
Title:	GI Disease Site Ontario Cancer Lead
Phone:	_____
Email:	Erin.Kennedy@sinaihealthsystem.ca

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The DAC agrees that the dosing schedule of regorafenib may be challenging for some patients and that toxicities and AEs may require additional resources to monitor and manage. In practice, regorafenib, like sorafenib, is commonly dosed lower than labeled dose to avoid toxicity.

Regarding radiographic assessment of progression, the DAC feels that having a mandated CT earlier than every 3 months (suggested 6-8 weeks) is wise for patients with refractory HCC. Every 8 weeks allows the CT to be timed for a patient's week off during their 2nd cycle. The DAC recognizes that it may be difficult for patients to get scans exactly when needed, and therefore recommends including flexibility in this portion of the recommendation.

It should also be noted that a mRECIST criteria was used in the RESORCE trial (mRECIST allows small volume disease under 1cm not to be progression.

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