CADTH

pan-Canadian Oncology Drug Review
Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation
(Registered Clinician)

Trifluridine-Tipiracil (Lonsurf) for Metastatic Colorectal Cancer Resubmission

August 29, 2019

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Lonsurf – metastatic colorectal cancer
Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Group, Clinical Group):	Clinician – Medical Oncologist
Organization Providing Feedback	Sunnybrook Odette Cancer Centre

**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 the pCODR program.*

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 ☐ agrees in part ☒ disagree

This feedback is submitted on behalf of Drs. Petr Kavan(Quebec), Ralph Wong (Manitoba), Sharlene Gill and Howard Lim (British Columbia), Patricia Tang (Alberta), Ron Burkes, Mark Vincent (Ontario), Mahmoud Abdelsalam (New Brunswick)

Net Clinical Benefit

- We strongly disagree with the current pERC recommendation and are deeply disappointed in the negative recommendation for funding.
- In Canada, there are no currently funded treatment options following chemotherapy. Lonsurf provides an important additional line of therapy for patients.
- The median OS (2.0mos) gain is modest but clinically meaningful in the chemo-refractory mCRC setting. Ko et al. 2019 (Curr Oncol. 2019 April;26(2):e255-e259)
- The AE and tolerability profile of Lonsurf show manageable toxicities and maintenance of performance status (0,1) vs BSC. Lonsurf is very well-tolerated in clinical practice. We also feel that the quality of life data that was prospectively collected in the TAGS Gastric study should be generalizable to the colorectal population given that the dose and schedule of Lonsurf used in the study.
- We agree with the CGP that the totality of evidence supports an overall net clinical benefit associated with Lonsurf. We feel that the experience and real-world opinion of the Clinical Guidance Panel and clinician feedback from those who use Lonsurf and treat mCRC has been minimized.

- The province of Quebec has reviewed the same evidence and concluded that Lonsurf has a net overall clinical benefit. Quebec patients and those with private insurance, including those who work for the government will have access to Lonsurf compared to the rest of Canada, which creates a significant inequity in for mCRC patients.
- The company has submitted real-world evidence of Lonsurf in a post-marketing Canadian setting. These results should be examined in the totality of evidence to support funding.

Furthermore,

Patients in clinical practice may derive a greater survival advantage than patients in the trials because they will not have had all the therapies that the trial patients woul have had, although there were no conclusive data on this

The National Institute for Health Care and Excellence (NICE) review determined that Lonsurf represents a well-tolerated treatment that would help extend life by even a relatively short time, while maintaining a reasonably good quality of life at a late stage in the treatment pathway when there are no further options left, and that Lonsurf met the criterion for extending life. Having concluded that Lonsurf meets th end-of-life criteria for the third-line treatment of metastatic colorectal cancer, and that the most plausible ICER was £49,392 per QALY gained, the committee concluded that it could recommend Lonsurf as a cost-effective use of NHS resources for adults who have had previous treatment with available therapies including fluoropyrimidine-oxaliplatin- or irinotecan-based chemotherapies, anti-vascular endothelial growth factor (VEGF) agents and anti-epidermal growth factor receptor (EGFR) agents, or when these therapies are not suitable, and only when the company provides Lonsurf with the discount agreed in the patient access scheme.

b) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the provisional algorithm:

☒ agrees ☐ agrees in part ☐ disagree

- Patients should be eligible for Lonsurf after failure on FOLFOX/FOLFIRI, bevacizumab, EGFR(if eligible) in chemo-refractory setting. Good performance status (0, 1)

c) 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 or provisional algorithm) clearly worded? Is the intent clear? Are the reasons clear?

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

3-5	Summary of pERC deliberations		Considering the weight of all evidence available, there is a net clinical benefit to Lonsurf over BSC. Lonsurf demonstrates clinically meaningful benefit in OS and the observed benefit from the study should be considered significant in the chemo-refractory setting. Given the patient and clinician input, quality of life appears comparable to BSC. Lonsurf should be available as an additional option following chemotherapy in mCRC.

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.

☐ 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.

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, including the provisional algorithm, 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

1 About Stakeholder Feedback

pCODR invites eligible stakeholders to provide feedback and comments on the Initial Recommendation made by the pCODR Expert Review Committee (pERC), including the provisional algorithm. (See www.cadth.ca/pcodr for information regarding review status and feedback deadlines.)

As part of the pCODR review process, pERC makes an Initial Recommendation based on its review of the clinical benefit, patient values, economic evaluation and adoption feasibility for a drug. (See www.cadth.ca/pcodr for a description of the pCODR process.) The Initial Recommendation is then posted for feedback from eligible stakeholders. All eligible stakeholders have 10 (ten) business days within which to provide their feedback on the initial recommendation. It should be noted that the Initial Recommendation, including the provisional algorithm may or may not change following a review of the feedback from stakeholders.

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), including the provisional algorithm as part of the feasibility of adoption into the health system, 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. If the substantive comments relate specifically to the provisional algorithm, it will be shared with PAG for a reconsideration. 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. Please also note that

substantive comments on the provisional algorithm will preclude early conversion of the initial recommendation to a final 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.

If a lack of clarity is noted, please provide suggestions to improve the clarity of the information in the Initial Recommendation. If the feedback can be addressed editorially this will done by the CADTH staff, in consultation with the pERC chair and pERC members, and may not require reconsideration at a subsequent pERC meeting. Similarly if the feedback relates specifically to the provisional algorithm and can be addressed editorially, CADTH staff will consult with the PAG chair and PAG members.

The Final pERC Recommendation will be made available to the participating federal, provincial and territorial ministries of health and provincial cancer agencies for their use in guiding their funding decisions and will also be made publicly available once it has been finalized.

2 Instructions for Providing Feedback

b) The following stakeholders are eligible to submit Feedback on the Initial Recommendation:

- The Submitter making the pCODR Submission, or the Manufacturer of the drug under review;
- 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)

c) The following stakeholders are eligible to submit Feedback on the provisional algorithm:

- The Submitter making the pCODR Submission, or the Manufacturer of the drug under review;
- Patient groups who have provided input on the drug submission;
- Registered clinician(s) who have provided input on the drug submission; and
- The Board of Directors of the Canadian Provincial Cancer Agencies

d) 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.

e) 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.)

f) 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.

g) 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 provided to the pERC for their consideration.

h) 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, and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.

i) 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 program.

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

k) If you have any questions about the feedback process, please e-mail pcodrsubmissions@cadth.ca

Note: CADTH is committed to providing an open and transparent cancer drug review process and to the need to be accountable for its recommendations to patients and the public. Submitted feedback will be posted on the CADTH website (www.cadth.ca/pcodr). The submitted information in the feedback template will be made fully disclosable.