pan-Canadian Oncology Drug Review Patient Advocacy Group Input on a Drug Review

Trifluridine-Tipiracil (Lonsurf) metastatic Colorectal Cancer

Colorectal Cancer Canada

July 6, 2018

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	**Trifluridine and Tipiracil (Lonsurf®) for Metastatic Colorectal Cancer (mCRC)**
Eligible Stakeholder Role in Review (Submitter and/or Manufacturer,	**Patient Group**
Organization Providing Feedback	**Colorectal Cancer Canada**

**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 ☐ 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.*

- For patients with refractory mCRC, limited therapeutic options exist to treat their disease, regardless of RAS mutational status. There are currently **NO** treatment options available in Canada for the metastatic population who exhaust standard of care therapies. Regorafenib is **not** publicly funded in any of the provincial or territorial jurisdictions. An additional therapeutic option is clearly required for this group of mCRC patients.
- Lonsurf could help address this **unmet medical need** by providing patients with a new therapeutic option that has:
  - an acceptable toxicity profile (surveyed and interviewed patients, as well as caregivers maintain Lonsurf has manageable side effects)
  - ease of oral administration
  - the ability to provide disease control.
- Quality of Life (QoL) can be maintained while on the therapy according to surveyed and interviewed patients. Patients who were interviewed (in detail) and whose therapy-related experiences were captured entirely in TABLE 1 (previously submitted) were quite supportive of the therapy under review and made every effort to relay the benefits of the therapy including a QoL score (which ranged between 7 and 10 out of a possible 10) and reported a personal survival benefit.
- Based on the above noted points, pERC's recommendation does not align with our patients' values.

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?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
2	Summary of pERC Deliberations	1;21-24	According to our patient population, regorafenib is not widely available through private drug insurance. Access to regorafenib is, therefore, cost prohibitive since it is not reimbursed in any of the provinces or territories in Canada. Also, pERC acknowledges that regorafenib was not used as a formal comparator in the assessment of Lonsurf. Yet, the pCODR review of regorafenib provided contextual information that contributed and negatively impacted the funding recommendation in respect of Lonsurf.
2	Summary of pERC Deliberations	2;18-20	"*…the benefits seen in clinical trials often do not translate into clinical practice*;…" The opposite may also hold true. At times, the benefits observed in clinical trials can be surpassed in clinical practice, which was the case with our surveyed and interviewed patients. Our patients responded well to Lonsurf, having achieved disease regression or disease stability.
2	Summary of pERC Deliberations	2;24-27	While QoL measurements were not captured in the three studies provided, Lonsurf's toxicity profile was thoroughly explored and reported in all three studies. Toxicity does contribute to QoL and is an important element of QoL. The most commonly reported Lonsurf-induced side effect from our interviewed and surveyed patients was low blood counts, which were quite manageable. The hematologic toxicities reported in the studies were also quite manageable. If toxicities are manageable, QoL can often be maintained. Issuing a negative funding recommendation based on no QoL measurements is not reasonable under these circumstances, which is why we are respectfully requesting a reversal in the decision to not recommend the funding of Lonsurf.
3	Summary of pERC Deliberations	1;4-8	We are not in agreement with the finding of "*No net overall clinical benefit*" for the following reasons: 1. There **is** a statistically significant survival benefit observed in both phase III studies 2. The moderate toxicity profile has been deemed to be manageable which can positively impact a patient's QoL
3	Summary of pERC Deliberations	2;9-12	Funding Lonsurf completely aligns with our patients' values for the following reasons: • Provides a treatment that offers ease of oral administration • Provides a treatment whose toxicity profile is manageable • Can offer metastatic patients disease control once standard of care therapies have been exhausted
4	Overall Clinical Benefit	4;1-8	The network meta-analysis (NMA), provided by pCODR, compared Lonsurf to regorafenib. While there may not have been any significant differences in efficacy between the two therapies, regorafenib was associated with greater toxicity. This implies that Lonsurf had a superior toxicity profile and,

			therefore, QoL maintenance. As stated in the NMA: *"Regorafenib was associated with more significant toxicity of any grade 3 to 5 toxicities. Regorafenib was associated with higher HFS (all grade and grade 3-5) and grade 3 to 5 fatigue when compared with TAS-102".*
5	Patient-reported outcomes: Not measured; therefore, impact uncertain	5;6-9	PS at treatment discontinuation may not be a validated or formally recognized surrogate for QoL. But it does reflect an improved toxicity profile for Lonsurf. And since toxicity contributes to and is an important element of QoL for patients, PS at treatment discontinuation could serve as an indicator for QoL in the two post hoc analyses.

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.

Page Number	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information
6	Patient Values on Treatment: Management of Toxicities and Disease Control	4;6-8	Based on patient input, treatment aligns well with our patients' values because in addition to providing a therapeutic option which offers ease of oral administration, it also: • provides a therapy whose toxicities are manageable • provides disease control and • provides a therapeutic option that currently does not exist for the metastatic population who has exhausted all other standard treatment options.
6	Patient Values on Treatment: Management of Toxicities and Disease Control	4;6-8	A "***modest***" clinical benefit is subject to interpretation and may be subjective. What pERC considers to be "modest" may be interpreted as "robust" on the part of a metastatic colorectal cancer patient. Patients are happy to be provided with any survival benefit especially if the toxicities are deemed to be manageable, which they appear to be in the case of Lonsurf. Every incremental survival benefit will increase a patient's total overall survival. We are, therefore, respectfully requesting a reversal in the funding recommendation issued in respect of Lonsurf so that an unmet medical need for the metastatic colorectal cancer population in Canada may finally be met.

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.cadth.ca/pcodr 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.cadth.ca/pcodr 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 www.cadth.ca/pcodr.

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.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. 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.cadth.ca/pcodr 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 pcodrinfo@cadth.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 pcodrinfo@cadth.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.