# pan-Canadian Oncology Drug Review Patient Advocacy Group Feedback on a pERC Initial Recommendation

## Venetoclax (Venclexta) for Chronic Lymphocytic Leukemia

## CLL Patient Advocacy Group and Lymphoma Canada

**March 2, 2018**

# 1 Feedback on pERC Initial Recommendation

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| Name of the drug indication(s): | Venetoclax as mono-therapy for treatment of chronic lymphocytic leukemia (CLL) who have received at least one prior therapy and who have failed a B-cell receptor inhibitor (BCRi) |
| Name of registered patient group: | CLL Patient Advocacy Group and Lymphoma Canada |

**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 group agrees or disagrees with the initial recommendation:

____ agrees ____ agrees in part **X** disagree

*Please explain why the patient group agrees, agrees in part or disagrees with the initial recommendation.*

Venclexta should have been recommended for funding, subject to an acceptable price negotiation, given that there is a positive clinical guidance report, supportive registered clinician and patient advocacy input and that pERC itself concludes that results are promising and there is a need for effective treatment options for this subset of patients.

Waiting for more mature OS data, when a clear OS benefit has already been demonstrated, means an unacceptable delay for patients who have no reasonable treatment options remaining.

The provided data was sufficient to obtain approval for use and reimbursement in Finland, France, Norway, Denmark, Germany, Israel, Italy, Scotland, Belgium, Austria, Netherlands, Slovakia, Luxembourg and the UK. Why does pERC disagree not only with local experts (the clinical guidance panel and clinicians) but also their counterparts in other countries?

It is unacceptable to risk patients' lives by suggesting an RCT when the clinicians who treat this population believe it would be unethical, as up to 50% of patients would receive an ineffective treatment. For patients, enrolling in such an RCT would be tantamount to flipping a coin to determine whether they die or receive a treatment that can lead to meaningful survival and, for some, the possibility of proceeding to an allo-transplant (a potentially curative therapy). Why is pERC willing to expose patients to ineffective, toxic therapies?

There is a disconnect between pERC's assessment of the evidence and their recommendation. pERC agrees that 1) there is a need for effective treatment options in this patient population; 2) there is a net clinical benefit of venetoclax compared with comparators (i.e. rituximab and rituximab plus HDMP); and 3) the comparators are ineffective treatment options (with all of which we agree). pERC then states venetoclax could not be considered cost effective compared with available therapies, yet pERC already stated there are no other effective therapy options for this population. Is pERC suggesting patients be treated with an ineffective treatment because it is cheaper?

b) Notwithstanding the feedback provided in part a) above, please indicate if the patient group 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.

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| ____ | 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 | 2, 6 | pERC was not satisfied that there was a net overall benefit to patients, yet peer-reviewed, interim results of the M14-032 study (at a median follow-up of 14 months) estimated 12-month PFS for all patients was 80%, and neither median PFS or OS had yet been achieved. This is a significantly better outcome than the < 6 months survival for this heavily pre-treated patient population that pERC acknowledges in paragraph 1 of the same section. |
| 2 | Summary of pERC Deliberations | 3, 6 | Regarding QoL data, the report notes that there is no data comparing venetoclax with available options. Given that the report concludes that treatment options for this sub-group of patients are especially poor and most people die within months, in addition to the clearly established well tolerated nature of venetoclax, we question what value further QoL data would bring to the discussion. |
| 2 | Summary of pERC Deliberations | 3, 10 | After TLS was seen in early trials, the dosing schedule was changed to reduce the likelihood of TLS, and patients are pre-tested for tumour burden to determine who is at high risk of developing TLS, so they can be better managed. With the adoption of the ramp-up schedule, the risk of TLS is managed well before clinical symptoms develop. Why is TLS a concern for pERC when clinicians state they can effectively manage the risk of its development? |
| 2 | Summary of pERC Deliberations | 4, 5 | Why is pERC willing to risk patients' lives by suggesting an RCT is feasible when the clinicians who treat this population believe it would be unethical, as up to 50% of patients would receive an ineffective treatment. Why is pERC willing to expose patients to ineffective, toxic therapies? |

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| 3 | Overall Clinical Benefit | 1, 7 | Regarding low rates of CR, CR is not often seen in this patient population with available therapies and the results achieved with venetoclax are in fact better than other therapies. Why the focus on CR rather than the prolonged PFS, OS, and favourable side effect profile compared to historical outcomes with chemotherapy in these poor risk patients? |
| 9 | Adoption Feasibility | 1, 4 | Management of TLS has been cited to cause an increase in costs of treatment yet, with the concomitant prophylaxis prior to and during the venetoclax ramp-up period, clinical TLS does not typically occur. Registered clinical input indicates the cost will not be greater than management of side effects of other treatments. |

### 1.2 Comments Related to Patient Group Input

| Page Number | Section Title | Paragraph, Line Number | Comments related to initial patient group input |
|---|---|---|---|
| 3 | Overall Clinical Benefit | 3, 6 | 80% of patients on the venetoclax trials were alive at 12 months and median PFS and OS had not been reached. pERC acknowledges that this patient population usually has a PFS of less than 6 months with currently available therapies and the clinicians estimate this patient group has a 3-month life expectancy. We would argue a longer remission and being alive (i.e. not dead) completely aligns with patient values. |
| 8 | Patient-Based Values | 3, 5 | 80% of patients on the venetoclax trials were alive at 12 months and median PFS and OS had not been reached. pERC acknowledges that this patient population usually has a median PFS of less than 6 months with currently available therapy and the clinicians estimate this patient group has a 3-month life expectancy. We would argue a longer remission and being alive completely aligns with patient values, especially when considered alongside the data in the patient input submission—provided by patients with venetoclax experience—who reported manageable side effects while taking the medication. |

# pCODR Patient Group Feedback on a pERC Initial Recommendation

## About Completing This Template

pCODR invites those registered patient 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. (Seehttp:// 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 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 groups, agree with the recommended clinical population described in the initial recommendation, it will proceed to a final pERC recommendation 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.

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 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 group is permitted. This applies to those groups with both national and provincial / territorial offices; only one submission for the entire patient group will be accepted. If more than one submission is made, only the first submission will be considered.
- Individual patients should contact a patient group that is representative of their condition to have their input added to that of the group. If there is no patient group for the particular tumour, patients should contact pCODR for direction at pcodrinfo@cadth.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 Group Feedback on a pERC Initial Recommendation* can be downloaded from the pCODR website. (See http://www.pcodr.ca/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 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 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.*