pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation

(Manufacturer)

Brentuximab (Adcetris) for Hodgkin Lymphoma - Resubmission

March 7, 2019

Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	ADCETRIS for the treatment of adult patients (≥ 18 years) with Hodgkin lymphoma (HL) after failure of at least two multi-agent chemotherapy regimens in patients who are not autologous stem cell transplant (ASCT) candidates.
Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Group, Clinical Organization Providing Feedback	Manufacturer Seattle Genetics Inc.

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

DELIBERATIVE FRAMEWORK QUADRANT: CLINICAL BENEFIT.

ADCETRIS fills an important unmet medical need for HL patients not eligible for ASCT. The net clinical benefit of ADCETRIS in this indication was acknowledged on page 22.

"The Clinical Guidance Panel concluded that there is a net clinical benefit to brentuximab vedotin, compared with chemotherapy, for the treatment of HL patients after failure of at least two multi-agent chemotherapy regimens in patients who are not ASCT candidates. From the results of the phase IV trial presented by the submitter, although limited by the non-comparative design and the misalignment of the trial population with the reimbursement criteria, it appears that the response rates and PFS are acceptable evidence of efficacy, compared to the paucity of data with other agents or regimens available, such as single agent gemcitabine, miniBEAM or other chemotherapy options. Available options have comparable or less efficacy, with significantly larger toxicity profiles and resource use for inpatient admissions, transfusion, and growth factor support. Brentuximab vedotin was able to bridge patients, both directly and subsequently to ASCT transforming their prognosis from incurable to a possible chance at longer survival. From larger phase II and III trials post-ASCT, we know the drug has a high degree of efficacy with durable responses and acceptable and predictable toxicity in HL patients. Brentuximab vedotin represents an important addition to the limited therapy options, which also lack substantial data, available for these young HL patients who are considered incurable at this disease time point. More effective and less toxic therapies which lead to a clinical response and potentially improved survival rates are urgently required in this population."

The unmet need with current available standards of care and the place in therapy of ADCETRIS was also clearly articulated by physicians having experience with ADCETRIS as outlined in Section 5 (page 38-39) of the CGR:

"Both clinicians stated that there is currently a large unmet need for patients with HL who are ASCT ineligible. One of the clinicians stated that the inclusion/exclusion criteria from trial C25007 seem reasonable. Both clinicians also stated that while brentuximab vedotin

is appropriate as a third-line therapy, it may also be appropriate in the second-line.

One of the clinicians stated that patients with relapsed or refractory HL are potentially curable, and that therapies used as current standards of care were defined by usually small, phase 2 clinical trials or institutional studies.

One clinician noted that while there are currently no prospective clinical trials employing large datasets in the ASCT ineligible disease setting, there are data available to highlight the favorable outcomes of brentuximab vedotin. These results are further supported by accumulated clinical experience in this setting. Given improved efficacy and favourable toxicity, brentuximab vedotin was stated to be the preferred option over alternatives, such as systemic single- or multi-agent chemotherapies.

Seattle Genetics agrees with the clinicians' perspectives that:

- **Due to the rarity of transplant ineligible patients, the study required 20 countries to enroll 60 patients. Therefore, studies with large datasets or comparative therapies in the ASCT ineligible setting are not feasible. There is data available to highlight the favorable outcomes of ADCETRIS and these results are further supported by accumulated clinical experience in this setting. It was on this basis that Health Canada approved ADCETRIS in this patient segment with great unmet medical need.**
- **There are also no studies available demonstrating the efficacy of the comparator chemotherapies and QOL in transplant ineligible patients. Funding of the comparators has been made available based on clinical experience.**

Other jurisdictions (Australia and the UK) have made positive funding decisions for ADCETRIS on the basis of similar clinical evidence submitted to pCODR as well as real world evidence (references available if requested).

Current access to ADCETRIS is clearly inequitable given some provinces fund ADCETRIS in this indication. Seattle Genetics is aware that physicians have made requests for funding of ADCETRIS in this patient population and this may contribute to the reason that PAG requested that the Seattle Genetics, Inc. make a resubmission and approved the Resubmission Eligibility Form outlining the available evidence to support the file.

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

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.

Page Number	Section Title	Paragraph, Line	Comments related to Stakeholder Information
Page 3	Summary of pERC Deliberations *pERCs Deliberative Framework: Patient-Based Values.*	P3, L1	Seattle Genetics requests that the sentence "pERC noted that the impact of brentuximab vedotin on patients QoL is unknown" be adjusted to read "the impact of brentuximab vedotin on the QoL in the ASCT ineligible population is unknown…." The impact of brentuximab vedotin on QoL was measured in previous trials including AETHERA (N=329) in the post-ASCT consolidation setting. This was acknowledged in the January 18, 2018 recommendation in which pERC concluded that "the AETHERA data did not show a negative effect of brentuximab vedotin consolidation therapy on QoL compared with placebo, which pERC considered reasonable in the setting of consolidation treatment." Seattle Genetics believes it is important from a patient perspective that ADCETRIS is unlikely to negatively impact QoL especially as the only other option in this setting is chemotherapy.
Page 3	Summary of pERC Deliberations *pERCs Deliberative Framework: Adoption Feasibility*	P2, L10 P3, L5	Seattle Genetics believes the statement that "the requested reimbursement criteria included patients who were ASCT ineligible because of: 1) lack of response to salvage prior to ASCT or 2) advanced age or comorbidities" is misleading and implies a larger population of patients would be eligible for ADCETRIS in this setting. The requested reimbursement criteria was for "patients with HL after failure of at least two-multi-agent chemotherapy regimens in patients who are not ASCT candidates" and it is aligned with the Health Canada approved indication for ADCETRIS. Seattle Genetics wants to strongly re-iterate that the request was not for ADCETRIS to be reimbursed as a second-line agent for older patients or patients with comorbidities as proposed on page 9 under Registered clinician input. Seattle Genetics therefore requests for clarity the words "requested reimbursement criteria" be adjusted to read as submitted.

About Completing This Template

pCODR invites the Provincial Advisory Group (PAG) to provide feedback and comments on the initial recommendation made by the pCODR Expert Review Committee. (See www.cadth.ca/pcodr for information regarding review status and feedback deadlines.)

As part of the pCODR re view 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 pERC 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 PAG, either as individual PAG members and/or as a group, agrees or disagrees with the pERC 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 pERC 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 agree with the recommended clinical population described in the initial recommendation, it will proceed to a pERC final 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 a pERC final 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 pERC final 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 members of the PAG can provide feedback on the pERC initial recommendation; delegates must work through the PAG representative to whom they report.
    a. Please note that only one submission is permitted for the PAG. Thus, the feedback should include both individual PAG members and/or group feedback.

b) Feedback or comments must be based on the evidence that was considered by pERC in making the pERC 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 *Provincial Advisory Group (PAG) 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. PAG 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. Similarly, PAG 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 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 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 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 Secretariat.

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

i) If you have any questions about the feedback process, please e-mail submissions@pcodr.ca.

Note: Submitted feedback may be used in documents available to the public. The confidentiality of any submitted information cannot be protected.