PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

Submitter or Manufacturer Feedback on a pCODR Expert Review Committee Initial Recommendation

Nivolumab (Opdivo) for Squamous Cell Cancer of the Head and Neck

August 31, 2017

FEEDBACK ON PERC INITIAL RECOMMENDATION

Name of the Drug and Indication:	OPDIVO (nivolumab) for the treatment of recurrent or metastatic squamous cell cancer of the head and neck (SCCHN) after platinum-based therapy in adults
Role in Review:	Manufacturer and Submitter
Organization Providing Feedback:	Bristol-Myers Squibb Canada
Contact Person:	Amir Tahami
Title:	Director, Market Access & Health Technology Assessment
Phone:	514.333.4203
Email:	amir.tahami@bms.com

1. COMMENTS ON THE INITIAL RECOMMENDATION

a) Indicate if the Submitter (or the Manufacturer of the drug under review, if not the Submitter) agrees or disagrees with the initial recommendation:

____ agrees ___X___ agrees in part __ __ disagree

BMS Canada agrees that nivolumab should be recommended for the treatment of recurrent or metastatic SCCHN cancer. However, the proposed coverage criteria do not correspond wholly to the approved Health Canada indication. Contrary to expert opinion in the pCODR Clinical Guidance Report, the pERC initial recommendation unduly restricts nivolumab to a subpopulation of patients progressing within 6 months of the previous therapy.

b) Indicate if the Submitter (or the Manufacturer of the drug under review, if not the Submitter) 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.

__X__ Do not support conversion to final recommendation. Recommendation should be reconsidered by pERC.

c) Please provide feedback on the initial recommendation.

Page number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
1	pERC recommend-dation	1st paragraph	BMS Canada suggests the following two options to clarify pERC initial recommendation: (1) *"for the treatment of patients with SCCHN who have a recurrence of potentially curative therapy or after receiving platinum-based therapy in a non-curative setting, and who have a good performance status";* (2) *"for the treatment of recurrent or metastatic squamous cell cancer of the head and neck (SCCHN) progressing on or after platinum-based therapy"*. The latter corroborates with Health Canada indication. This is also consistent with pCODR Clinical Guidance Report, which explicitly states that this time frame was not critical in this patient population and should not be used as a requirement for eligibility to receive nivolumab.

2. COMMENTS RELATED TO MANUFACTURER-PROVIDED INFORMATION

Page number	Section Title	Paragraph, Line Number	Comments related to Submitter or Manufacturer-Provided Information
4	Summary of pERC deliberations	3rd and 4th paragraphs	BMS Canada disagrees with pERC and CADTH reviewers that cetuximab is not used after platinum-based therapy in Canada. The chart reviews[1,2] have shown that there is a potentially significant use of cetuximab in that setting, especially in the locally advanced patient population, as it is indicated by Health Canada in this setting, and reimbursed in several institutions in Canada. In addition, cetuximab is recommended as a systemic therapy for the treatment of SCCHN by Cancer Care Ontario.[3]
8	Economic evaluation	6th and 7th paragraphs	BMS Canada disagrees with a conclusion that nivoluamb is not cost-effective compared with chemotherapy. The conclusion is based on the Reviewers' suggestion that the new base case ICER should be at $159,092 $ / QALY. The new base case is based on the upper range of three assumptions as follows: (1) three year model horizon; (2) reduced utilities by 10%; (3) Time to treatment discontinuation curve replaces PFS curve to estimate the cost of nivolumab. 1. A short model horizon of 3 years may not adequately capture the natural course of the disease. Five year model horizon is more appropriate. 2. BMS Canada disagrees with reducing utilities by 10% to estimate the upper range of ICER. This is an arbitrary number, and it is not supported by the evidence. BMS Canada suggests using either treatment specific or overall utilities estimated from HRQoL data in a CA209141 trial. 3. BMS Canada disagrees about changing nivolumab's duration of treatment estimates from PFS curve to the Time_to_Discontinuation curve in the economic model. Some patients on nivolumab were treated beyond progression in a CA209141 trial. However, pERC recommends duration of treatment to be limited to 'until unacceptable toxicity or disease progression." Should the latter wording prevail in the final recommendation, then a duration of nivolumab treatment should be estimated from the PFS curve. Provided that the final recommendation allows for treatment on nivolumab to continue as long as the clinical benefit is observed or until treatment is no longer tolerated by the patient, then 'time to treatment discontinuation' curve is a valid assumption for a base case. Consequently, the upper range for ICER for a comparison vs. docetaxel and vs. methotrexate would be 75,996 $ / QALY and $98,239 $ / QALY, respectively.

3. ADDITIONAL COMMENTS ABOUT THE INITIAL RECOMMENDATION DOCUMENT

Page number	Section Title	Paragraph, Line Number	Additional Comments
1	pERC recommend-dation	1st paragraph	BMS acknowledges that the enrollment of patients that had progressed on or within six-months of platinum-based therapy. This was carried out in order to establish a reasonably homogenous population within the controlled environment of the clinical trial. Clinical guidelines differentiate SCCHN treatment by potentially curative and non-curative intent. However, the choice of subsequent therapy is highly individualized, and the clinical guidelines do not differentiate subsequent therapy choice by progression within or outside of 6 months. As the pCODR Clinical Guidance Report stated, tumor progression within this time frame is not routinely used to make treatment decisions and might be difficult to ascertain in real world practice, and requiring this for nivolumab eligibility may impose a burden of additional CT scanning on patients. The coverage criteria as stated in the pERC initial recommendation may create an equity gap in coverage particularly for patients with recurrence of SCCHN immediately after 6 months following a potentially curative therapy and those who do not tolerate platinum-based therapy. As a result, such patients would receive either docetaxel or methotrexate treatment, which were found to be inferior in clinical benefit and improvement of patient's quality of life as compared to nivolumab by the pERC committee. They would also not be eligible for cetuximab, as CADTH reviewers indicated that cetuximab is not used in this setting, despite the fact that the chart reviews show some use in this setting. BMS Canada suggests that the final recommendation mirrors the approved label by Health Canada without having a '6-month' limitation.

[1] Head and neck Cancer treatment patterns and outcomes research study in Canada. Final report CA 209551. Unpublished. 2016.

[2] Byrne K et al. Real-world treatment patterns among patients with squamous cell carcinoma of the head and neck (SCCHN) in Canada. Poster presentation at the ISPOR 22nd Annual International Meeting, May 22-24, 2017 Boston, MA, USA.

[3] Winquist et al., Systemic Therapy in the Curative Treatment of Head and Neck Squamous Cell. Guidelien 5-11. August 10, 2016. Accessed at https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=364309 on July 12, 2017.