CADTH

CADTH Reimbursement Review

Patient Input

PEMBROLIZUMAB (Keytruda)

(Merck Canada Inc.)

Indication: Esophageal carcinoma, gastroesophageal junction adenocarcinoma

CADTH received patient input from:
Colorectal Cancer Canada/Gastrointestinal Society/My Gut Feeling - Stomach Cancer Foundation of Canada

June 4, 2021

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Pembrolizumab for the first-line treatment of locally advanced unresectable or metastatic, carcinoma of the esophagus or HER-2 negative gastroesophageal junction adenocarcinoma in combination with platinum and fluoropyrimidine based chemotherapy, in adult patients**
Name of the Patient Group	**Colorectal Cancer Canada, Gastrointestinal Society, and My Gut Feeling - Stomach Cancer Foundation of Canada**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

Colorectal Cancer Canada (CCC) is a charitable not-for-profit organization dedicated to colorectal cancer awareness and education, supporting patients and caregivers, and advocacy on their behalf. Colorectal Cancer Canada is registered with CADTH. We aspire to reduce the incidence and mortality of colorectal cancer in Canada while improving the quality of life of patients, their families and their caregivers. We aspire to reduce the incidence and mortality of colorectal cancer in Canada while improving the quality of life of patients, their families and their caregivers.

www.colorectalcancercanada.com

As the Canadian leader in providing trusted, evidence-based information on all areas of the gastrointestinal tract, the GI (Gastrointestinal) Society is committed to improving the lives of people with GI and liver condition, supporting research, advocating for appropriate patient access to healthcare, and promoting gastrointestinal and liver health. The Gastrointestinal Society is registered with CADTH.

www.badgut.org | www.mauxdeventre.org

My Gut Feeling – Stomach Cancer Foundation of Canada is the first and only non-profit organization in Canada, founded by two survivors, that is dedicated to provide support, awareness, education, information and advocacy to stomach cancer patients, survivors and caregivers. Our goals are to dispel misconceptions about stomach cancer, to provide information on the day to day journey of being diagnosed, living with and surviving stomach cancer, and to improve the quality of life, give a voice to patients and caregivers, and provide peer mentorship based on personal experience with stomach cancer.

https://mygutfeeling.ca

2. Information Gathering

To help capture the patient perspective on this cancer therapy under review, Colorectal Cancer Canada (CCC), Gastrointestinal Society, and My Gut Feeling - Stomach Cancer Foundation of Canada co-created and launched an online patient/caregiver survey from April 23, 2021 to May 16, 2021. Twenty-five patients (75.8%) and eight caregivers provided detailed and high quality responses to our questions. Specifically, of the responses collected, 36.36% are patients previously treated, 30.3% are patients in remission, 24.24% are patients undergoing treatment, 18.18% are caregivers on behalf of a patient previously treated, and 6.06% are caregivers on behalf of a patient undergoing treatment. A total of two patients (Patient 2 and 6) have experience with the drug under review: one patient with Stage III esophageal cancer was previously treated with the drug, and another patient with Stage IV esophageal cancer is currently undergoing treatment with the drug. One patient (Patient 19) is currently on another immunotherapy drug, Nivolumab. Patients' ages at cancer diagnoses ranged from 20-29 years (6.06%) to 70-79 years (3.03%) with the highest percentage of patients aging 50-59 years (39.39%). Of those patients, 62.5% of patients were male. Data was gathered from patients across the United Kingdom of Great Britain and Northern Ireland (45.45%), United States (36.36%), Canada (9.09%), New Zealand (3.03%), Ireland (3.03%), and Belgium (3.03%).

The survey link was posted on CCC's social media platforms (Facebook, Instagram and Twitter). The CCC team also reached out to an independent patient advocate for esophageal-gastric cancer patients who was able to share the survey in a patient group he leads in the UK.
The Gastrointestinal Society posted the survey link on their Facebook and Twitter platforms.
The Stomach Cancer Foundation of Canada shared the survey link on their Facebook page and also shared it in private online groups for patients with Esophageal Cancer, Lynch Syndrome and Stomach Cancer.

3. Disease Experience

Most patients (77.42%) were diagnosed with adenocarcinoma, followed by 12.9% diagnosed with squamous cell carcinoma. 38.71% of patients were diagnosed with Stage III esophageal cancer, 25.81% with Stage IV, 22.58% with Stage II, and 3.23% with Stage I. Of those who had their cancer spread beyond their initial diagnoses, metastases occurred mostly in the lymph nodes (37.93%), liver (20.69%), lung (17.24%), and stomach (14.29%).

Patients and caregivers were asked if any esophageal cancer-induced symptoms were experienced prior to diagnosis. All except one patient had experienced symptoms with the most common symptoms reported being: trouble swallowing (80.7%), heartburn (35.5%), weight loss (32.3%), fatigue (29.0%), worsening indigestion (25.8%), frequent choking on food (22.6%), hiccups (19.4%), and indigestion (19.4%).

4. Experiences With Currently Available Treatments

Treatments received by patients while not using the drug under review include chemotherapy (96.7%), surgery (66.7%), radiation therapy (50.0%), endoscopic therapy (16.7%), and other targeted therapies (10.0%). Of these patients and caregivers, 58.62% said that these therapies were effective at controlling the symptoms of esophageal cancer. The most common side effects from therapies reported by patients and caregivers included: fatigue (88.89%), nausea (62.96%), loss of appetite (62.96%), and low white blood cell count (51.85%).
While the majority of patients and caregivers (75.86%) believe that most of their needs are being met by the current drugs available, 24.14% patients/caregivers believe otherwise. Unmet needs include the short survival rate (Caregiver 2), *"[ability of the cancer] to continue to spread"* (Patient 6), the lack of *"metabolism of food"* (Patient 12), the *"inability to eat enough to constitute a healthy diet"* (Patient 18), and the fact that "*it is not possible for [current drugs] to stop the growth, only prolong life"* (Caregiver 7).

Caregiver 8 expresses that: *"the chemotherapy was tolerable but did not improve quality of life as the side effects in addition to the side effects from the surgery and need for a feeding tube really impacted my brother in laws ability to go out, eat, carry on a conversation or enjoy his family."*

5. Improved Outcomes

In two questions, patients and caregivers were presented with trade-offs when choosing a new therapy such as improved quality of life and severity of side effects. Almost all patients and caregivers (92%) expressed a common reaction on the willingness to take a drug that has been proven to better quality of life even if it does not extend overall survival. On a scale of 1-10 (no side effects to severe side effects), patients and caregivers rated an average of 5 for the severity of side effects in order to extend survival by 2 months, 6 months, and 1 year. Caregiver 2 and Patient 25 would be willing to tolerate significant side effects in order to extend survival by only 2 months. However, Patient 10 and Patient 16 are not willing to tolerate any side effects even if it extends survival by 1 year.

When questioned how important it is for patients along with their physicians to have a choice in deciding which drug to take on a scale of 1-10 (not important to very important), the average of all respondents was as high as 8 (very important).

6. Experience With Drug Under Review

Two (6.25%) patients/caregivers had access to the drug under review (Patient 2 and Patient 6). Both patients were informed of immunotherapy as a potential treatment option at the start of their discussion with their oncologists. Patient 2 had cryotherapy, radiation, and targeted therapy included in the treatment with Pembrolizumab. Patient 6 accessed the drug via clinical trial (T cell therapy at NIH) with no other therapy included.

While on Pembrolizumab, Patient 2 experienced side effects such as abdominal pain, diarrhea, rash, shortness of breath, and constipation. Patient 6 experienced fatigue, itching and some allergic reactions. Both patients mentioned that there is no particular gap or unmet patient need with current therapies that the drug can help alleviate. However, both patients believe that Pembrolizumab will change their long-term health and well-being for the better. Patient 6 remains hopeful as *"for some people it has worked".* Patients were questioned what effect they expect, or hope, that Pembrolizumab will have on the cancer and their prognoses, both patients (100%) reported "increase overall survival". Patient 2 additionally mentioned effects such as "delay the need of chemotherapy" and the "ease of use". Patient 2 mentioned few symptoms that Pembrolizumab manages less effectively than the existing therapies including: coughing, back pain, hoarseness, and vomiting. However both Patients 1 and 6 reported that the drug under review does manage certain symptoms better than existing therapies. Patient 2 reported symptoms that were managed better were: pain behind the breastbone or in the throat, black stool, and weight loss. Patient 6 reported symptoms that are managed better were fatigue and vomiting.

While Patient 6 faced no difficult aspects while taking this drug, Patient 2 notes that the most difficult aspects included social issues, lifestyle changes, and anxiety. Given the severity of the symptoms, improved quality of life is an important outcome to consider for esophageal patients. Both patients rate their overall experience with Pembrolizumab as a 6 on a scale of 1-10 (much worse – much better) compared to other treatments.

Given the poor and short survival rate for most patients, it is necessary for patients to have access to new effective therapies that can help patients have a good quality of life and have a longer overall survival. Patients and caregivers were asked on the importance of access to Pembrolizumab and other future immunotherapies. They expressed their thoughts:

"Any treatment that helps someone with esophageal cancer is a chance" (Caregiver 1)
"Many people have had a very successful story with Keytruda" (Patient 6)
"I would like access to anything that would extend my life" (Patient 18)
"My child with cancer passed away but for other patients there should be hope" (Caregiver 7).
"Given the lack of good quality of life and in light of this new immunotherapy, it would have been much better to try that than to have put him through the surgery and from the combined side effects of surgery and chemo" (Caregiver 8).

7. Companion Diagnostic Test

We did not ask questions related to companion diagnostic testing.

8. Biosimilar

N/A

9. Anything Else?

In our short time-span survey, the thirty-three patients/caregivers provided ample confirmation that a new drug is necessary to prolong the overall survival of esophageal cancer patients, improve their quality of life, and reduce their cancer symptoms with tolerable side effects from the drug. Specifically for this cancer type, there is significant unmet need for new effective therapies that can prolong overall survival rate and reduce severity of symptoms. It is also as necessary to highlight the importance of having this drug as first-line treatment as most patients have a poor prognosis at time of progression and are often unable to last till future therapy choices. The drug under review, Pembrolizumab, serves as an example of precision oncology practice that can improve the lives of cancer patients.

Patients and caregivers provided heartfelt and compelling comments on why new treatments should be accessible to anyone with the specific biomarker.

"I was one of the lucky ones to survive so I know how important access to new treatments are to all patients" (Patient 25).

"Immunotherapy was not an option. We consulted the world's leading scientist at the world's greatest cancer hospital. They did not give us any hope, just prepare for the worst. If I know as much as I know today, I would have taken a different course. I am investing with PMH in what is a biobank in the hope for early detection" (Caregiver 7).

"A good quality of life is essential for esophageal patients. Even if overall survival is not dramatically improved, the quality of life improvement from this drug can bring significant advantages enabling them to spend more time with their families with the side effects of existing treatments" (Caregiver 8).

Based on the objective research carried out as represented herein, Colorectal Cancer Canada, Gastrointestinal Society, and My Gut Feeling - Stomach Cancer Foundation of Canada strongly urge that a positive funding recommendation be issued for Pembrolizumab for the first-line treatment of locally advanced unresectable or metastatic, carcinoma of the esophagus or HER-2 negative gastroesophageal junction adenocarcinoma in combination with platinum and fluoropyrimidine based chemotherapy, in adult patients. We believe it is essential to provide these patients equitable access of effective drugs that improves their quality of life and outcomes as well as the impact on their families, unaccompanied by any financial restrictions. Providing molecularly targeted therapies that are easily administered with minimal side effects, and permit patients to carry on normal lives is fundamental for basic and high quality care in Canada.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

Yes, this submission was drafted by Colorectal Cancer Canada and was reviewed by other patient groups: Gastrointestinal Society and My Gut Feeling - Stomach Cancer Foundation of Canada prior to its submission to CADTH.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

Colorectal Cancer Canada, Gastrointestinal Society, and My Gut Feeling - Stomach Cancer Foundation of Canada co-created the survey and collected data by posting the survey link on their respective social media platforms (Facebook, Instagram, and Twitter). The Stomach Cancer Foundation of Canada also shared the survey link in private online groups for Esophageal Cancer, Lynch Syndrome, and Stomach Cancer. Colorectal Cancer Canada collected data from a private patient group in the UK.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Colorectal Cancer Canada:

Company	Check Appropriate Dollar Range

	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbvie Corp			X	
Amgen Canada				X
AstraZeneca Canada				X
Bayer Inc				X
Boehringer Ingelheim Ltd			X	
Bristol Myers Squibb Canada				X
Celgene Corporation			X	
Eli Lilly Canada			X	
GlaxoSmithKline				X
Hoffman-La Roche				X
Janssen Inc			X	
Merck Canada Inc.			X	
Novartis Pharma Canada			X	
Pfizer Canada				X
Taiho Pharma Canada				X

My Gut Feeling - Stomach Cancer Foundation of Canada:

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Eli Lilly Canada Inc.				X
Taiho Pharma Canada Inc.			X	
Bristol Myers Squibb			X	

Gastrointestinal Society

Company	Check Appropriate Dollar Range

	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Merck Canada			X	

Name: Barry D. Stein
Position: President
Patient Group: Colorectal Cancer Canada, Gastrointestinal Society, My Gut Feeling - Stomach Cancer Foundation of Canada
Date: May 30, 2021