Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

nivolumab and ipilimumab (Opdivo and Yervoy)

(Bristol Myers Squibb Canada Co.)

Indication: Opdivo (nivolumab), in combination with ipilimumab, is indicated for the first-line treatment of adult patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer.

April 7, 2025

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Nivolumab and ipilimumab
Indication: Nivolumab is indicated for the first-line treatment of adult patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer, when used in combination with ipilimumab.
Name of Patient Group: Colorectal Cancer Canada
Author of Submission: Iris Karry

1. About Your Patient Group

Colorectal Cancer Canada is the nation's not for profit colorectal cancer patient organization dedicated to colorectal cancer awareness and education, supporting patients and their caregivers and advocating on their behalf. Colorectal Cancer Canada is registered with CDA. www.colorectalcancercanada.com

2. Information Gathering

Between August 2024 and April 2025, Colorectal Cancer Canada gathered patient and caregiver perspectives regarding nivolumab and ipilimumab through an online survey conducted using the Survey Monkey platform and semi-structured interviews that were conducted through Zoom. Data were collected from individuals residing in Canada, the USA, Australia, England. 4 online interviews were conducted, and 12 survey responses were collected. Recruitment was conducted through social media platforms, Colorectal Cancer Canada's support groups, as well as online patient forums. Recruitment materials are attached in **Appendix 2.**

Table 1: Demographics of Patients and Caregiver Surveyed

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Country and Region	Florida, USA	New South Wales, Australia	Alabama, USA	Pennsylvania, USA	Manitoba, Canada	California, USA
Gender, Age at Dx	Female, 61-70 years	Male, 61-70 years	Female, 41-50 years	Female, 61-70 years	Female, 61-70 years	Male, 51-60 years
Stage at start of Tx with drug under review	IV	IV	IV	IV	IV	IV
	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Caregiver 1
Country and Region	Alberta, Canada	Ontario, Canada	Massachusetts, USA	Washington, USA	Georgia, USA	Leeds, England
Gender, Age at Dx	Female, 51-60 years	Female, 41-50 years	Female, 31-40 years	Male, 41-50 years	Female, 51-60 years	Female, 41-50 years
Stage at start of Tx with drug under review	IV	IV	IV	IV	IV	IV

Table 2: Demographics of Patients Interviewed

	Patient 12	Patient 13	Patient 14	Patient 15
Country and Region	Quebec, Canada	Toronto, Canada	Washington, USA	Alberta, Canada
Gender, Age at Dx	Male, 41-50 years	Female, 61-70 years	Male, 41-50 years	Female, 41-50 years
Stage at start of Tx with drug under review	IV	IV	IV	IV

3. Disease Experience

Colorectal Cancer Canada is in the process of updating how we collect patient experience data regarding disease experience, experiences with currently available treatments, and improved outcomes. For this submission, we will refer to survey data submitted in 2024 for a previous CDA patient input submission. This data is summarized in the PDF attached, entitled: "Summary graphs – Disease Experience".

Patients and caregivers were asked about which symptoms of colorectal cancer (CRC) they experienced (Q9). 90.5% of respondents experienced CRC symptoms, with bloody stools, fatigue/weakness, abdominal cramping/gas/feeling bloated cited as the most common symptoms. When asked what the top CRC symptoms were the most important to control (Q10), respondents selected abdominal cramping/gas/feeling bloated, abdominal pain, fatigue/weakness and diarrhea. 22 out of 23 patients/caregivers indicated that CRC symptoms limited their quality of life. Respondents were asked to select the three most important ways the CRC symptoms they experienced impacted their quality of life (Q11), with ability to work, ability to participate in social activities, and ability to exercise cited as the most important. Respondents added the following open-ended responses:

- "*I no longer work, I have to be careful not to overdo it*"
- *"Not able to work, not able to volunteer, can't travel"*
- *"Can't really fulfill any part of life, family, exercise, work, etc*"

When asked about the psychological impact of CRC (Q12), patients cited feeling consistently worried, nervous or uneasy and persistent fear of [the] cancer getting worse or recurring (coming back) as the most common impacts.

Caregivers were uniquely questioned on the difficulties they faced while caring for the individual living with CRC (Q36-39). The one caregiver who responded to the survey indicated that the main difficulties they faced included being unable to work outside the home, loss of income/financial strain, the time spent at medical appointments, and the feelings of helplessness or inadequacy. The respondent added the following open-ended response: *"Physically draining. More home duties. My inability to help make it better makes me feel helpless*." They indicated that an average of 11-25 hours were dedicated per week to managing the patient's side effects, and an average of 11-25 hours a week were dedicated to managing the patient's treatment including taking them to appointments, administration of medication, and hospital/clinic visits.

4. Experiences With Currently Available Treatments

Colorectal Cancer Canada is in the process of updating how we collect patient experience data regarding disease experience, experiences with currently available treatments, and improved outcomes. For this submission, we will refer to survey data submitted in 2024 for a previous CDA patient input submission. This data is summarized in the PDF attached, entitled: "Summary graphs – Experiences with Currently Available Treatments".

Patients and caregivers were asked to indicate which drug therapies they have accessed to treat their CRC (Q17). FOLFOX, FOLFIRI, capecitabine, and bevacizumab were cited most frequently. Fatigue, brain fog, diarrhea, loss of appetite, hair loss and nausea were cited as the most common side effects experienced with drug therapies (Q21), while the most difficult side effects to tolerate were diarrhea, Hand and Foot syndrome, and fatigue (Q23). When asked whether these drug therapies have been effective

at controlling the symptoms of the cancer, such as pain (Q18), 11% of patients/caregivers said “no”, 37% said “somewhat”, and 53% said “yes”.

When asked whether these drug therapies have been effective at controlling the progression of the disease, 5% said “no”, 45% said “somewhat”, and 50% said “yes”.

One patient stated that they received a “*left hemicolectomy removed tumour. Underwent 6 months of FOLFOX. Have been in remission for 1 year so far, but long-term side effects from chemo continue to affect my quality of life*”.

Another patient stated that “*panitumumab worked well at first, but then my cancer [grew] aggressively*”.

Respondents also indicated (Q20) that they accessed other therapies such surgery and radiation therapy to treat their cancer. When patients/caregivers were asked whether they believed their needs are not being met by current drugs available to treat their cancer (Q35), 30% replied “yes”, with the following open-ended responses:

- *“Yes, while existing drugs have a certain efficacy in prolonging life, the challenge is still what can I do to shrink the tumour to make surgery possible [and] be cured”*
- *“while I am hoping I’m in remission, there may be microscopic cancer cells floating around. Obviously, fighting cancer is the priority. That being said, there was not a choice. I was told Folfox was the treatment. I was not informed about long-term neuropathy & muscle pain caused by these drugs prior to treatment. Microscopic cancer cells are a mystery. Did I need Folfox or not? It was what I was prescribed. So I trusted. But not it seems there is no support for my long-term effects of chemo”.*
- *“studies are not moving fast enough”*

5. Improved Outcomes

Colorectal Cancer Canada is in the process of updating how we collect patient experience data regarding disease experience, experiences with currently available treatments, and improved outcomes. For this submission, we will refer to survey data submitted in 2024 for a previous CDA patient input submission. This data is summarized in the PDF attached, entitled: “Summary graphs – Improved Outcomes”.

Patients/caregivers were asked to rate how important it is to them for a new therapy to bring about improvement to their physical condition and quality of life (Q40 and Q41). 89% of respondents replied that it is very important for a new therapy to bring about improvement to their physical condition (e.g. tumour shrinkage, tumour stability, reduction of pain) and 72% indicated that it was very important for a new therapy to bring about improvement in their quality of life. 83% of patients/caregivers indicated that they would be willing to take a drug that has been proven to provide better quality of life even if it does not extend overall survival (Q42).

6. Experience With Drug Under Review

Survey results on patient and caregiver experiences with nivolumab and ipilimumab can be found in the PDF attached, entitled: “Nivolumab and ipilimumab survey results April 2025”.

Access to the combination therapy

Three patients (Patients 1, 2 & 4) accessed the combination therapy through a Special Access Program. One Canadian patient (Patient 7) accessed the combination therapy off-label through self-pay with 20% reimbursement through a Special Access Program, which resulted in approximately CA$100,000 in out-of-pocket fees.

Five patients (Patients 3, 6, 9, 10, 11), all residents of the USA, were prescribed the combination therapy and received coverage from their private health insurance plan. Patient 14, a U.S. resident, was prescribed the combination therapy while it was still in phase 2 trials. Initially, his insurance provider denied coverage. However, after significant advocacy by his oncologist, full coverage for nivolumab and ipilimumab was eventually approved.

Three respondents (Patients 5, 8; Caregiver 1), indicated that they accessed the combination therapy through their public healthcare plan. However, since this combination treatment is not currently covered under public healthcare in Canada, it is assumed that Patients 5 and 8 who are residents of Canada accessed the combination through a Special Access Program.

One Canadian patient (Patient 12) accessed the combination therapy off-label in the USA and was able to get the drug costs reimbursed through a Patient Assistance Program. However, this patient paid for travel, lodging, and food to receive monthly treatments in San Diego out of pocket, amounting to a total cost of approximately CA$150,000.

Another Canadian patient (Patient 13) accessed the combination therapy through a clinical trial, which covered all drug-related costs.

Patient 15, also a resident of Canada, was prescribed the combination treatment after genetic testing confirmed that she could benefit from immunotherapy, however, she had to pay for all costs out-of-pocket. She was scheduled to pay $108,000 for the combination therapy, after 20% of costs were covered by the manufacturer through a Special Access Program. She strongly advocated for reimbursement through her provincial health authority and eventually $48,000 of the total $108,000 were waived.

Benefits and disadvantages

11 of 12 survey respondents indicated that nivolumab plus ipilimumab was able to shrink and control their cancer and its spread to other organs.

Patient 5 had exhausted all other treatment options and "*…was given 3 months to live if this treatment didn't work*" and was able to control the cancer and reach stable disease with the combination therapy.

Patient 7 was diagnosed with stage IV colon cancer and she experienced a complete response with the combination treatment, and has remained no evidence of disease for the past 5 years.

Patient 9 began receiving the combination therapy following cancer recurrence to various organs after surgery and chemotherapy. After about two years of treatment, she had no evidence of disease and has since then remained in surveillance.

Patient 12 had received various lines of chemotherapy, targeted therapy, and immunotherapy (pembrolizumab) to treat refractory stage IV colorectal cancer. After developing extensive metastases throughout his body including to his bones which severely limited his mobility, he began treatment with nivolumab and ipilimumab. Within 6 weeks he could walk again with a cane, and within a few more weeks experienced "*massive reductions in the tumours throughout [his] body*". Patient 12 underwent a dramatic change to what he was able to do, going from being "*immobile and close to death*" to regaining his strength and a sense of normalcy in his life again. He still faced many challenges with respect to side effects while receiving this treatment, but he was able to see a very rapid improvement to his condition within weeks.

Patient 13 received the combination therapy through a clinical trial for 2 years to treat metastatic colorectal cancer. The combination immunotherapy was able to stabilize her tumours with no new growth. Lesions decreased in density and size. She was eventually unable to continue the drug combination because the clinical trial only offered the drugs for a maximum of two years. Her oncologist advised that she could continue but would have to pay out-of-pocket, which was not feasible for her.

Patient 14 experienced a blockage in his small intestine due to an unresectable colorectal cancer metastasis. As a result of the blockage, he was put on total parenteral nutrition (TPN). He began treatment with nivolumab and ipilimumab, and within 2-3 months he was able to drink some liquids again and within 3 months was on a full liquid diet. By 6 months, the tumour that was blocking his small intestine had shrunk enough to be able to eat normally again. Patient 14 was able to regain the weight he had lost and was able to achieve a healthy weight. After treatment with nivolumab and ipilimumab, he was able to get out of the house and return to a "*normalish*" life. Patient 14 indicated that while he was less mobile and active while receiving nivolumab and ipilimumab, his daily activities were "*close to normal after 6 months, participating in about 80% of [his] normal activities*". After he stopped receiving ipilimumab following the fourth dose, he noted that side effects were "*really insignificant*" when he was receiving nivolumab alone. At that time, he still had an ileostomy, which he described as having a greater impact on his quality of life than his treatment with nivolumab.

Patient 15 was initially prescribed FOLFOX chemotherapy following a stage IIIc colon cancer diagnosis. Despite treatment, the cancer spread to her uterus and ovary, leading to a hysterectomy. With limited treatment options, she began exploring alternatives through her own research, including immunotherapy. Given her prior history of breast cancer (diagnosed 13 years prior to her colon cancer diagnosis), she underwent genetic testing, which revealed MLH1 and PMS2 mutations, suggesting she could benefit from immunotherapy. Although her oncologist initially discouraged this due to lack of public coverage in Canada, Patient 15 received a second opinion that supported the use of immunotherapy for her cancer, and she insisted on pursuing this treatment option despite having to pay out-of-pocket. She initially had a reaction to the infusion but received a pre-medication treatment which extended her total infusion time at each visit but resolved the issue and allowed her to continue receiving treatment. For Patient 15, compared to chemotherapy, the treatment was far more tolerable—milder fatigue, no nausea or hair loss, and she was able to participate in many more daily activities. After a few months of treatment, she had a significant reduction in peritoneal metastases (approximately 50% reduction) and eventually had no evidence of disease within one year of starting treatment. She finished treatment in April 2020 and remains free of colon cancer to this day.

50% of survey respondents experienced no difficulties receiving the combination therapy, while 3 respondents indicated that they experienced some difficulty with their port/accessing veins. Anxiety/worrying (50%), fatigue (50%), and management of side effects (42%) were cited by survey respondents as the most difficult aspects of receiving nivolumab plus ipilimumab. When asked to rate their quality of life while receiving nivolumab and ipilimumab on a scale of 1-10, with 1 being “low, severely impacted” and 10 being “high/normal living”, one respondent rated their quality of life a 1, and 42% of respondents rated their quality of life as less than or equal to 5. Two respondents rated their quality of life a 10, and 58% of respondents rated their quality of life as greater than 5.

64% of survey respondents indicated that they were able to continue their daily activities or work while undergoing treatment with nivolumab plus ipilimumab. Patient 7 indicated that the combination therapy “*allowed [her] to continue working and be a productive member of society. Gave [her] more time with [her] loved ones*”.

Side effects of the treatment under review

Several patients indicated that the side effects of the combination therapy were easier to manage than those associated with chemotherapy. Patient 3 noted that “*it was a lot easier to deal with than chemo and I wish it had been available when I was first diagnosed*”, while Patient 6 indicated that they experienced a “*more normal life than on chemo*”.

The top five side effects of nivolumab and ipilimumab as indicated by the survey respondents were fatigue and weakness (92%), skin rash (67%), skin itchiness (67%), joint stiffness (50%), and vomiting and diarrhea (33%). When asked to rate the side effects of the combination therapy on a scale of 1-10, with 1 being “no side effects at all” and 10 being “debilitating side effects that impact daily living”, 67% of respondents rated their side effects as less than or equal to 5. 33% of respondents rated their side effects as greater than 5, with 17% of respondents rating their side effects as 10.

While on nivolumab plus ipilimumab, Patient 12 experienced a range of side effects including fatigue and an itchy rash, but “*not as bad as with other drugs [he] had taken previously*”. He was prescribed cortisone and antihistamines to control the rash. He described side effects as generally tolerable compared to the severe nausea he experienced from chemotherapy. The combination therapy exacerbated digestive issues he already had, but cannabis helped to manage these side effects. He eventually experienced a more serious side effect, adrenal failure, that built up for a long time before it was diagnosed. He eventually had to stop treatment with nivolumab plus ipilimumab due to this side effect.

Patient 13 indicated in the interview that side effects on nivolumab plus ipilimumab were mild compared to side effects she experienced on previous lines of treatment which included various chemotherapy regimens, bevacizumab and regorafenib. She experienced significant side effects from both FOLFIRI and FOLFOX, including “*severe fatigue, lack of appetite, and always feeling nauseous and unwell*”. After a cancer recurrence she was put on regorafenib, which “*caused many side effects including high blood pressure, vomiting, skin peeling on hands, diarrhea, nausea, and generally feeling very sick*”. During the first cycle of nivolumab and ipilimumab, she experienced symptoms similar to an allergic reaction, for which the trial staff provided Benadryl. Patient 13 eventually had to stop the combination treatment early after breaking out in a sudden rash from head to toe, due what her doctor suspected was most certainly an adverse drug interaction with the antibiotic amoxycillin, which she was taking for a sinus infection.

Patient 15 indicated that she tolerated the combination therapy well, with the most common side effect being fatigue, which she cited as being “*manageable*”. Unlike her experience with FOLFOX chemotherapy, she did not experience nausea, hair loss, or neuropathy

and was able to maintain functional independence and work capacity. Peripheral neuropathy in her fingertips while receiving chemotherapy severely impacted her fine motor skills, which had a major impact on her ability to work as a piano teacher. While receiving nivolumab and ipilimumab, Patient 15 could return to work as a piano teacher, with small modifications to her schedule to help her manage her fatigue. Furthermore, while receiving FOLFOX chemotherapy, Patient 15 used a portable infusion pump over multiple days per cycle, which caused significant discomfort sleep disruption. With nivolumab and ipilimumab, she experienced far fewer disruptions to her day-to-day quality of life.

75% of survey respondents were able to complete continuous treatment with nivolumab and ipilimumab, while 25% of respondents had to stop treatment earlier than planned or skip doses due to side effects or complications.

One patient commented in the survey: *"Please let patients know the top side effects - the adrenal & thyroid issues! My cortisol was down so low, I was near death".*

This underscores the critical need to encourage patients and caregivers to promptly report any side effects related to nivolumab and ipilimumab. Timely reporting allows the medical team to intervene early, prevent complications from worsening, and help minimize unnecessary treatment discontinuation.

Conclusion and Summary Statement

When asked to describe why access to nivolumab and ipilimumab is important to them, survey respondents and interviewees replied with the following open-ended responses:

- *"I have stage 4 colon cancer and [the combination treatment] has resulted in having no evidence of disease for 5 years. It's so effective and life changing for people who have these types of colon cancer. It needs to be accessible to all."*
- *"It gives me hope and is a lot easier to tolerate."*
- *"It cured me within 3 months of having a recurrence for which I was told I had no surgical options. It saved my life. I have been NED for 5 years thanks for Opdivo."*
- *"Diagnosed in 2022 after severe abdominal pain. Surgery in April 2023 to remove 6kg of omentum, spleen, some small intestine and colon. All visible cancer was removed plus hot chemotherapy after removal before closure. Cancer was detected 3 months later with PET scan. Started nivolumab and ipilimumab in August 2023. June 2024 PET scan showed mass had shrinkage. November 2024 CT showed more shrinkage. Oncologist says mine isn't curable but treatable."*
- *"This treatment is giving me hope to live a normal life span with continued maintenance course of treatment."*
- "*I wouldn't be here now if I hadn't gotten into the nivo-ipi clinical trial. Radiation was out of the question, surgery wasn't possible based on where my tumours were located, and chemo certainly wasn't working. There were definitely huge challenges associated with participating in the clinical trial. Although I had some side effects, I was always so grateful to have options available that worked".*
- "*After a little over one year of treatment, I went from extensive metastasis to no evidence of disease, which has persisted to this day [just under 5 years]"*

When reflecting on his experience with the combination therapy, Patient 12 indicated that he was ready to take a lot of discomfort if it meant there was a tangible reward involved – with nivolumab plus ipilimumab, the "*reward was huge*". In comparison, with chemotherapy, he was not willing to make that trade-off. He described chemotherapy as offering very minimal benefit for the severity of side effects he experienced while receiving it. Despite the side effects he did experience on nivolumab plus ipilimumab, Patient 12 indicated that it was well worth it, as he was able to regain his life back. When his children saw him in 2019 as he was beginning treatment nivolumab plus ipilimumab, they were not sure if they would see him alive again. After three months on the combination therapy, he went from being immobile and in severe pain, to flying home to watch his daughter graduate from university.

In summary, public access to nivolumab plus ipilimumab for patients with MSI-H/dMMR metastatic colorectal cancer would grant patients in this setting an additional, highly effective therapeutic option that can prolong life and maintain/improve their quality of life.

7. Companion Diagnostic Test

For patients with metastatic colorectal cancer, treatment with nivolumab plus ipilimumab is primarily determined by MSI-H/dMMR biomarker testing. MSI-H/dMMR testing is typically covered in Canada for these patients, with some provinces automatically testing for MSI/dMMR in all newly diagnosed cases. This may vary according to the province/territory and healthcare institution, but MSI/dMMR testing is considered part of the standard of care.

No patients or caregivers who participated in the survey or interview indicated any specific challenges with companion diagnostic testing.

Among interviewees, Patients 12 and 13 underwent private comprehensive biomarker testing. Having already received multiple lines of therapy, they chose to pursue more extensive biomarker testing to explore additional treatment options, which ultimately led them to consider nivolumab and ipilimumab.

Patient 14 who was treated in the US indicated that MSI testing was done automatically following his emergency surgery to remove the colorectal tumour that was obstructing his small intestine. He noted that he was not sure how the cost of testing got distributed, but it was likely a combination of insurance and deductibles which in the greater scheme of things were negligible to him.

Patient 15 did not undergo biomarker testing, but rather, the recommendation to pursue immunotherapy came from the results from genetic testing, which she received under public healthcare coverage in Canada due to her multiple cancer diagnoses.

8. Anything Else?

If publicly funded, nivolumab in combination with ipilimumab would represent a significant therapeutic advancement for the MSI-H/dMMR metastatic colorectal cancer patient population across all lines of therapy.

We strongly support a positive funding recommendation for this combination therapy. It responds to a clear need expressed by patients and caregivers for more effective treatment options in the advanced colorectal cancer setting. This therapy offers the potential to meaningfully extend survival while maintaining quality of life. Many patients with metastatic disease are faced with the prospect of lifelong chemotherapy, which is often not sustainable due to severe side effects and its significant negative impact on quality of life. Public funding for nivolumab and ipilimumab would give eligible patients access to a promising immunotherapy that may not only improve outcomes but also offer the possibility of long-term remission—without requiring continuous treatment.

Appendix 1: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, 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.

   No.

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.

   No.

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbvie			x	
Amgen Canada Inc				x
AstraZeneca Canada Inc				x
Bayer Inc				x
Boehringer Ingelheim Ltd				x
Hoffmann-La Roche				x
Innovative Medicines Canada				x
INCYTE			x	
Janssen Inc				x
Pfizer Canada Inc				x
Taiho Pharma Canada			x	
GlaxoSmithKline				x
Novartis			x	
Merck Canada Inc				x
Bristol Myers Squibb Canada				x

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.

Name: Iris Karry
Position: Program Manager
Patient Group: Colorectal Cancer Canada
Date: April 7, 2025

[redacted]

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Nivolumab and Ipilimumab (Opdivo® and Yervoy®)
Indication: Nivolumab is indicated for the first-line treatment of adult patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer, when used in combination with ipilimumab.
Name of Patient Group: Colorectal Cancer Resource & Action Network (**CCRAN**) in collaboration with the Canadian Cancer Survivor Network (**CCSN**).
Author of Submission: Cassandra Macaulay, Chief Research Officer, CCRAN

1. About Your Patient Group

CCRAN is a national, not-for-profit patient advocacy group championing the health and wellbeing of Canadians touched by colorectal cancer and others at risk of developing the disease, by providing support, education and advocacy to help improve patient outcomes by way of longevity and quality of life. CCRAN has expanded its mandate to serve cancer patients outside of the colorectal cancer space through its health technology assessment (HTA) patient evidence submissions, educational events, advocacy initiatives and patient programming. It collaborates with other tumour type patient advocacy groups to help achieve its expanded mandate because, collectively, it can achieve far more than it could working in silos. (www.ccran.org)

2. Information Gathering

Author's Note: It was initially anticipated that this submission may open in the latter half of 2024, thus information gathering efforts began quite early. This proved to be helpful given the difficulty in connecting with patients who had accessed this therapy.

To help capture the unresectable and metastatic MSI-H colorectal cancer patient perspective for this submission, CCRAN reached out to Canadian medical oncologists / Checkmate 8HW trial investigators beginning on **July 24th, 2024,** through to **February 14th, 2025,** via email to request their assistance in identifying colorectal cancer patients who had experience with the therapy under review, with follow up emails throughout this period. The email contained a patient recruitment poster [redacted] which clinicians could share with patients or their caregivers who may be willing to participate in a telephone interview to provide their lived experience with the therapy under review, in addition to their cancer diagnosis, treatment journey and colorectal cancer journey in general. The Canadian clinicians who responded to outreach commented that they had not treated any MSI-H colorectal cancer patients who had been able to access the therapeutic protocol, with one clinician commenting that access to the combination therapy of nivolumab + ipilimumab was desperately required.

Given the lack of access in Canada, CCRAN determined that in order to truly be able to inform this committee with the patient's lived experience, a pivot to an international outreach campaign would be required. Thus, also beginning on **July 24th, 2024,** CCRAN reached out to U.S.-based medical oncologists treating colorectal cancer via email to request assistance. Follow up to these American clinicians continued through **March 7th, 2025**.

After experiencing significant difficulty in connecting with patients who had accessed the therapeutic under review, on **February 10th, 2025,** CCRAN requested email introductions to European-based Checkmate 8HW trial investigators via industry professionals at *Bristol Myers Squibb Canada Co.* in an effort to further provide this committee with the patient's lived experience. Following e-introductions, and independently, CCRAN later reached out to 3 European-based clinicians on **February 18th – 19th, 2025.** The patient recruitment poster was subsequently translated into French and provided to a clinician in France who treated patients who may be interested in sharing their lived experiences. French patients were requested to reach out to CCRAN and were provided with a French copy of the patient questionnaire, to be completed in French, and later translated to English for the purposes of including their feedback in this submission. Translations were completed by a bilingual CCRAN staff member. The English patient recruitment poster and questionnaire were provided to clinicians in Italy, who graciously administered the questionnaires during oncologic visits.

A social media outreach campaign ([redacted] was shared within CCRAN and CCSN networks, from **July 16th, 2024 – March 15th, 2025.**

Two U.S.-based patient organizations, GI Cancers Alliance and Colon Cancer Alliance, were contacted via email on **July 25th, 2024,** with requests to share the social media outreach campaign within their networks.

To help further inform the committee with respect to the experience with the disease and with other administered treatments, previously curated data from CCRAN's national colorectal cancer survey to inform a recent submission [**PC0330-000**] which was released **March 21st – April 17th, 2024,** and completed by **77** metastatic colorectal cancer patients or their respective caregivers, was utilized ([redacted]

These extensive efforts resulted in two **(2)** telephone interviews with U.S.-based patients who had accessed the therapeutic combination; translated, written questionnaires completed by two **(2)** patients treated in France; written questionnaires completed by two **(2)** patients treated in Italy, and one **(1)** telephone interview with an MSI-H metastatic colorectal cancer patient in Canada who has been unable to access the therapeutic under review, which represents the Canadian patient perspective. The transcripts and written responses from these patient interviews can be found in [redacted]

3. Disease Experience

Colorectal cancer is the fourth most commonly diagnosed cancer in Canada, representing 11% of all cancer cases, and it is the second leading cause of cancer death (Brenner et al., 2024) nationally. Colorectal cancer impacts men and women equally, and while incidence is declining amongst the population over 50 years of age, largely due to the implementation of population-based screening programs, incidence is rising rapidly in the population under the age of 50 (Heer et al., 2024), who are currently ineligible for screening programs. This further highlights the need for additional therapeutics to improve longevity and quality of life for these patients living with metastatic cancer.

Patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) disease represent approximately 15% of the colorectal cancer patient population, and this subset of the population has a distinct tumour biology and responds differently to therapeutics. Prior to the advent of immunotherapeutics, the metastatic MSI-H patient population had a dismal prognosis related to poor response to traditional chemotherapeutics. However, MSI-H tumours display high immunogenicity, and as such, have a high sensitivity to immune-checkpoint inhibitors (Ambrosini et al, 2025). Some individuals with an MSI-H colorectal cancer have Lynch syndrome, a hereditary condition increasing the likelihood of developing certain cancers, including colorectal cancer, and particularly before the age of 50 (CDC, 2024).

The average age of onset of interviewed patients was **44 years old**, though participating patients ranged in age from their 20s to their 80s, and thus good representation of the diverse patient population was achieved:

Patient A was diagnosed with stage IV MSI-H colon cancer on Christmas Day in 2016, at the age of **39**. He is now 47 and has spent the ***"past 5 years in remission".*** He has Lynch syndrome and has received treatment in the **U.S**. He was joined in the interview by his wife, **Caregiver A**, who also shared her perspectives.

Patient B was diagnosed with stage IIIc MSI-H rectal cancer in November 2024 at the age of **31**. She was aware of her Lynch syndrome prior to diagnosis and shared she had expected to develop cancer in her lifetime, but didn't expect it to be when she was still so young. She resides in the **U.S.**

Patient C learned she had metastatic colon cancer all the way back in October 2013 at the age of **28,** when she learned she had Lynch syndrome as well. She was pleased to participate from **France**. After a difficult treatment journey that eventually led to accessing nivolumab + ipilimumab, she now has a no evidence of disease status and is 39 years old.

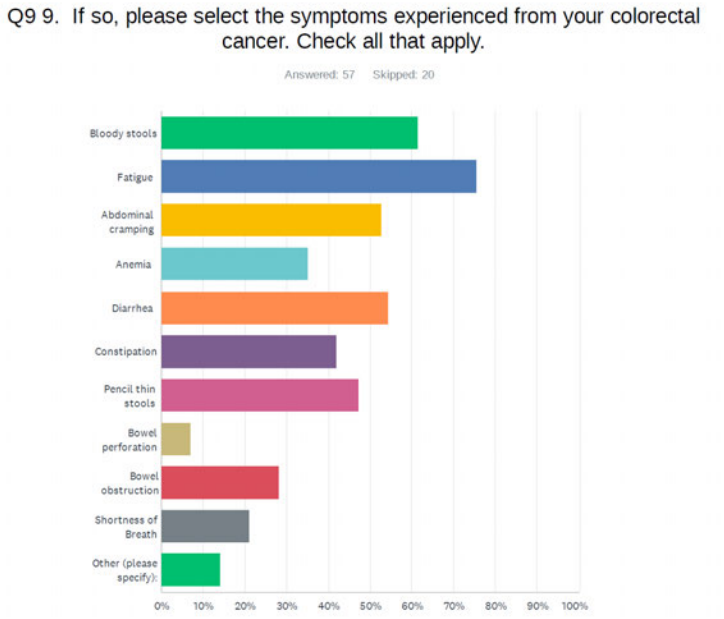
Patient D, from **France,** was diagnosed with unresectable colon cancer in 2013, at the age of **72**. Today, she is 84 and has had no evidence of disease since 2019.

Patient E learned she had MSI-H metastatic colon cancer in 2017, at the young age of **21.** Today, she is 29 years old and has no evidence of disease. She was identified to have Lynch syndrome, despite being the only one in her immediate family to have tested positive. Her oncologist shared that she was very happy to contribute from **Italy**.

Patient F received a diagnosis of stage IV colon cancer in September 2023, at the age of **54**. He is being treated in **Italy.**

Patient G was diagnosed in 2023 with MSI-H & BRAFV600e mutant stage III colon cancer at the age of **63** and recurred with metastatic disease in May 2024. As a **Canadian** patient, she has been unable to access nivolumab + ipilimumab, and, in the setting of a less than robust response to pembrolizumab, she felt compelled to participate and represent the unmet need in Canada.

Given its anatomical location, the pathology often has significant impact on health-related quality of life. By the time the colorectal cancer has advanced or metastasized, patients are frequently symptomatic and experiencing **pain** at the time of diagnosis, as was reported by **87%** of survey respondents and **86%** of interviewed patients. Interviewed and surveyed patients reported symptoms from their cancer, including abdominal or lower back pain or cramping, constipation, diarrhea, nausea, bloating, changes in bowel habits, bloody stools, fatigue, weakness, rectal pain, anemia, bowel obstruction or perforation, urinary retention, lack of appetite, vaginal fistula, rectal fistula, and shortness of breath. Often times, and particularly in younger patients, these symptoms can be dismissed prior to diagnosis, as was the case for **Patient A:** ***"I had abdominal pain beginning March 2016. Pain, constipation, nausea, bloating. It got bad so I saw my regular family doctor in June. My doctor sent me for an ultrasound and then said the report showed gallbladder stones, which were too small for surgery. He told me I had indigestion and prescribed omeprazole. We found out later that the ultrasound report had identified a 10 cm mass that my doctor missed in the report."*** This patient became so symptomatic after developing a complete bowel obstruction that he needed to visit the Emergency Department on Christmas Day, where he was then diagnosed with metastatic colorectal cancer at the young age of 39. **Patient E** shared a similar experience: ***"I felt increasingly tired and weak, attributing it to being in a new environment. I also had intense pain in my right side, but I got used to it over time… When I returned home [from university] for Christmas holidays, I became seriously ill with fever, worsening pain, and almost no appetite. These symptoms led to my first hospitalization, where I was initially diagnosed with Crohn's disease."***



Two of the interviewed patients described a 'preparedness' to receive the news of their cancer diagnosis. As **Patient B** shared, ***"I have Lynch Syndrome so I suppose I wasn't as surprised as someone else my age would be, getting diagnosed with cancer. I was like, 'okay, this is it, it's happening now.'… It was still obviously upsetting because I'm 31, I wasn't really thinking I'd be dealing with this sort of thing yet. I was upset but not surprised."*** Whereas **Patient E** was in such debilitating pain that the news of her cancer came as a ***"strange mix of relief and shock"*** as her diagnosis allowed her to identify and validate the cause of her pain and suffering. But the news of a cancer diagnosis is most often traumatic, not only for the patient, but their family members or care partners as well:

"It was shocking. It was very upsetting and unexpected. When you get a stage 4 diagnosis, you know there is no stage 5. It's the end of the line… It was very difficult to not know what was ahead of you. It was scary, very scary." **– Caregiver A**

"I was especially worried about my mother's reaction, as she has been depressed for a long time, so I suppressed all emotions at the time of the diagnosis and in the weeks that followed." **– Patient C**

"I think it was more traumatic for [my family] then it was for me, everybody wants to fix stuff, but there's nothing they can do." **– Patient G**

Survey respondents identified that the most significant impacts or limitations that having colorectal cancer has on quality of life were related to (i) ability to work, (ii) ability to exercise, and (iii) ability to fulfil family obligations. Psychologically, the most significant impacts were identified as (i) inability to plan for, or think about the future, (ii) chemo brain making them feel forgetful, or 'less than', and (iii) constant fatigue making it difficult to function normally.

The unique experience of living with early age onset cancer (EAOC) has been established and represents a subset of the population with significant unmet needs. Disparities exist due to their earlier stage of life, wherein disruptions exist to work and

education, impacts on fertility, sexual health, and body image, financial consequences, and increased loneliness and isolation, as well as the oftentimes increased severity of their disease biology and late stage of diagnosis (Wildgoose et al., 2024). The impacts were articulated in the interviews with the EAOC patients:

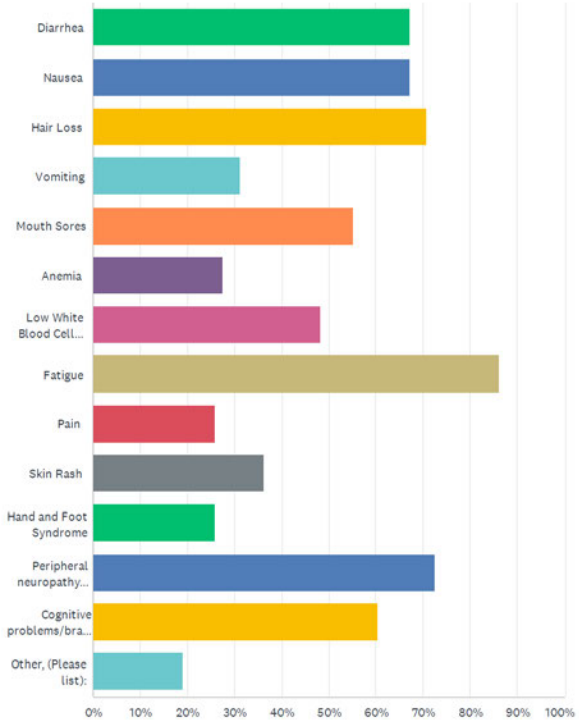
"I think about this timing… it's affected my career, my partner and I's ability to maybe get engaged this year, it's been financially taxing, we wanted to buy a home, and everything has been pushed back - put on pause." **- Patient B**

"Unfortunately, we had to give up on having children because of my illness" **– Patient C**

Patients of all ages often filled the role of care providers before they were diagnosed with cancer. The psychological burden of needing to care for others – children, parents, or other loved ones – while caring for oneself can be particularly challenging. **Patient G**, whose adult son lives with her after becoming disabled as a result of Long COVID, shared, ***"My biggest fear is what happens to him if something happens to me."***

4. Experiences With Currently Available Treatments

The current first line standard of care treatment for MSI-H colorectal cancer is pembrolizumab monotherapy, followed by a variety of chemotherapeutics and/or biologic therapies in second-line and beyond based on the patient's tumour biomarker profile.



Side effects reported from treatment

Patients C, D & F received chemotherapy +/- biological therapy (bevacizumab, panitumumab, and/or Magrolimab) prior to receiving nivolumab + ipilimumab. **Patient G** received adjuvant chemotherapy with FOLFOX for the treatment of her early-stage disease, and has since received pembrolizumab for the treatment of her metastatic disease. Survey respondents accessed FOLFOX, FOLFIRI, FOLFOXIRI, capecitabine, bevacizumab, cetuximab, encorafenib + cetuximab or panitumumab, panitumumab, regorafenib, raltitrexed, cyclophosphamide + DPX (through a clinical trial), and pembrolizumab. Additionally, one anonymous survey respondent accessed nivolumab + ipilimumab, though their responses could not be isolated.

Survey respondents noted a variety of side effects from systemic treatment, as displayed in the graph on the left. The most common side effects reported were fatigue (reported by **86%** of respondents), peripheral neuropathy (**72%**), hair loss (**71%**), diarrhea (**67%**), nausea (**67%**), cognitive problems (**60%**), mouth sores (**55%**), and low white blood cell count (**48%**). Significantly, **69%** of respondents required additional prescription medicines to help manage treatment-induced side effects, and of this, **40%** reported incurring out-of-pocket expenses for those additional medications, which, as had been recently highlighted in the Canadian Cancer Society's *special report on the economic impact of cancer*, results in unjust additional burden on cancer patients.

Additionally, survey respondents reported accessing surgical resection (**67%**), stereotactic radiation therapy (**19%**), external beam radiation therapy (**10%**), as well as radiofrequency ablation, hepatic arterial infusion pump chemotherapy, hyperthermic intraperitoneal chemotherapy, in vivo lung perfusion, living donor liver transplant, cryoablation, trans-arterial radioembolization, trans-arterial chemoembolization, and complimentary therapies for the management of their disease. **Patient B** required a colostomy as her cancer had caused rectal and vaginal fistulas, thus she required diversion surgery. **Patients C, D, and F** underwent toxic systemic treatment which they felt had little to no effect on controlling their cancer ([redacted]:

"No. The Folfox had no effect (at least none that I could notice). As for the Folfiri/Avastin, even though it was harder to endure due to more side effects, I had the impression that it slowed the progression of the disease a little more, but it never cured me." **– Patient C**

"No. Didn't help in my case." **– Patient D**

"No; chemo failed and I do not know why." **– Patient F**

Not only were the chemotherapeutics ineffective in controlling their cancer, resulting in either progression or recurrence, but the interviewed patients reported a poor quality of life while undergoing the *"destructive"* treatment and a negative impact on their mental wellness:

"I tolerated the chemotherapies very poorly. Since I was young, I recovered fairly quickly from the side effects, undesirable as they were, but the sessions drained me, and working in such a state of constant exhaustion was extremely difficult. It was also very hard emotionally because I felt like I was doing all of this in vain, never feeling or seeing any improvement in my condition. Those three years were the hardest of my life, and I wouldn't wish them upon anyone." **– Patient C**

"On chemo my quality of life was horrific, and I would not do it again. I was sick the whole time." **– Patient G**

Unique to the experience of undergoing treatment for cancer at a young age, **Patient C** recalled how difficult it was living with cancer amongst her age-matched peers, and within the typical societal expectations of a young adult. In her own words: *"Overall, having to 'perform' while undergoing treatment was a constant challenge. I had to wear a lot of makeup to hide the paleness and dark circles, use headbands so people wouldn't notice the missing hair, and still manage to excel at work and in my studies."*

Treatment with pembrolizumab is well-established to have a fairly good side effect profile, as is expected with immunotherapies, and **Patient G** expressed that her only side effect was being *"bone-tired"* which she likened to the fatigue experienced during pregnancy. She shared that *"the jury is still out"* on whether she is responding well to the pembrolizumab treatment. She has experienced a decrease in her CEA but has had indeterminate imaging results suspicious for progression, with a differential diagnosis of pseudo-progression. She sought out a second opinion at a prominent U.S. hospital, and one of the recommendations was to move to nivolumab + ipilimumab, but as a Canadian, she has been unable to access it without having to incur prohibitive out-of-pocket expenses.

5. Improved Outcomes

Controlling pain and preventing spread or recurrence emerged as top priorities when interviewed respondents were asked what aspect of the disease is most important to control ([redacted]. **Caregiver A** provided a straight-forward response: *"Preventing death. Stopping the spread of illness and trying to eliminate it. We can deal with all the other stuff. Survival."* **Patients B & E**, both young patients with Lynch syndrome, prioritized preventing recurrence, or the development of a second primary cancer. **Patient C** felt it was very important to control pain and nausea, and **Patient G** highlighted the need to approach management like that of a chronic disease.

In terms of new drug therapies, **92%** of surveyed patients and caregivers reported that it was "very important" (e.g.,10 / 10) that new drug therapies improve their physical condition, and **80%** felt it was "very important" that new therapies bring about an improvement in quality of life. In terms of improvement to therapies, interviewed respondents emphasized the need for ***access*** to emerging precision medicines, with minimal side effects [redacted]):

"I would say an effective treatment that is available for patients, regardless of the type of cancer - colon, breast, whatever. A treatment with minimal side effects. A cure for all." **– Caregiver A**

"The quality of life during treatment, with as few side effects as possible, seems to me to be the most important improvement. From my experience, it is much easier to endure the illness and the follow-up care when you're not feeling unwell for days after each treatment..." **– Patient C**

"Each case should be able to profit from new treatments." **– Patient D**

"I would like to see more personalized treatments that are tailored to the individual patient's genetic makeup and disease characteristics. There is still room for improvement in reducing side effects while maintaining treatment efficacy. Additionally, it would be great to have therapies that are less invasive and can be administered with fewer hospital visits, allowing patients to maintain a higher quality of life during their treatment." **– Patient E**

"*For me, it's more access…. why do you have to jump through all these hoops? We know one-size-fits all doesn't work for all. If there are multiple drugs available at first or second line, why can't we access it right away? Why do I have to do chemo as a stage III MSI-H cancer patient, when we know it doesn't work? We know this, why torture me?"* **– Patient G**

The therapeutic under review appears to provide these desired improvements. In the words of **Patient C**:*"Yes, absolutely. I had no debilitating side effects with this treatment. It made both the cancer and, more generally, Lynch syndrome much more bearable."* In fact, **all** interview participants expressed their belief that nivolumab + ipilimumab should be made available to all patients who qualify for it. As **Patient C** went on to say, *"this treatment saved me, and I believe it could help many other patients."* **Caregiver A** & **Patient G** spoke to the unmet need for access to this therapeutic protocol in Canada, with **Caregiver A** sharing that they wouldn't want their children, who may carry a hereditary syndrome, to move to a country where access to this treatment is not available. **Patient G** was passionate about the current unmet need in Canada and felt that Canadians should have access to the best treatment based on their tumour characteristics, right from the start: *"If it works better, and you had MSI and wanted to live, which would you rather have? The stuff that works better, or the stuff that works almost as good? Of course, you want the stuff that works better. It's like - I don't mind helping you, but I don't want to help you all the way, it's like I don't mind taking the tumour out, but I don't want to sew you up. "*

6. Experience With Drug Under Review

All four interviewed patients [**Patients A, C, D & E**] who had completed their treatment protocol with nivolumab + ipilimumab achieved a **durable and complete response, and, remarkably have maintained a no evidence of disease status for over 5 years.** Even **Patient B**, who had recently started treatment noted biochemical response, with her CEA value returning to normal, as well as a reduction of size of her large, 11 cm rectal tumour, and subsequent alleviation of some of her pain. **Patient F** has achieved disease control while still undergoing treatment.

Patient A accessed nivolumab + ipilimumab in first-line therapy from **January – August 2017** through a clinical trial in the United States.

Patient B began first-line treatment with nivolumab + ipilimumab at the end of **November 2024** and had received 8 cycles at the time of the interview. Her treatment was covered by insurance in the United States.

Patient C started treatment with nivolumab + ipilimumab through participation in a clinical trial in France in **2016**. She shared it was her "last" line of therapy: *"It was the trial of last resort, the final hope."* She completed four cycles of the combination therapy, followed by three years of nivolumab monotherapy as per the trial protocol.

Patient D accessed nivolumab + ipilimumab in **2016**, also through a clinical trial in France. She did not share (or was not aware of) in which line of therapy her treatment was accessed.

Patient E received nivolumab + ipilimumab through a clinical trial in Italy in **2017** as first-line therapy.

Patient F began treatment with nivolumab + ipilimumab in **April 2024** in second-line, funded through the Italian Public Health System.

Patient G has not been able to access nivolumab + ipilimumab in Canada. As such, **Patient G** will not be further referenced within Section 6 of this submission.

For those patients who reported pain as a symptom of their cancer prior to starting therapy with nivolumab + ipilimumab [**Patients B, C, D & E**], all shared that the therapeutic under review has helped to relieve some, or all of their pain, with **Patient D** sharing, *"I thought I had a new life"* after her pain and fatigue were relieved by treatment: *"The symptoms disappeared,*

I felt better and my tumour markers decreased." In the words of **Patient E,** who had been experiencing significant physical discomfort for approximately 9 months prior to her diagnosis**:** *"The therapy with nivolumab and ipilimumab significantly helped resolve my cancer symptoms. Over time, my fatigue and weakness improved, and I regained my strength. The persistent abdominal pain gradually diminished, and my overall physical condition stabilized. The recurring fever and general malaise also disappeared as the treatment took effect. Follow-up scans confirmed a positive response, aligning with my physical improvement. The therapy allowed me to regain a sense of normalcy and significantly improved my quality of life."*

Nivolumab + ipilimumab was well-tolerated by patients, and **Patient D** even reported no side effects of undergoing systemic cancer therapy in her 70s, as did **Patient F**, who is undergoing treatment in his 50s. Adverse effects reported by the balance of the interviewed patients included rash, Reynaud's syndrome, fatigue, weakness, memory loss, leg pain, joint pain, nausea and diarrhea (with the first treatment cycle only), and mild flu-like symptoms / grogginess in the first one or two days following treatment. Additionally, patients did not need to delay treatments due to side effects, with the exception of **Patient C**, who had to postpone only one treatment session by a week due to a transient, asymptomatic increase in lipase levels. Overall, patients felt these side effects were quite tolerable and noted they were able to maintain a high quality of life throughout treatment. In fact, when asked to rate their quality of life while on nivolumab + ipilimumab, patients provided a mean and median rating of **8 out of 10**. Here's what the interviewed patients and caregiver had to say about their quality of life while undergoing treatment for metastatic colorectal cancer with nivolumab + ipilimumab:

"I feel we had the best cancer experience of everyone we know or have come across. That's why we feel so optimistic about the therapy. He got to be here with his kids and enjoy activities with our kids, even during a treatment. He continues to do so, which is a huge blessing. If he had done chemo, we don't think he would be here today… it's the immunotherapy that saved him." **- Caregiver A**

"I've pretty much been able to do everything I normally do… I also teach fitness classes and I had to stop for a bit, but I'm back to teaching as much as I did before." **– Patient B**

"The treatment itself didn't cause me major problems, but I had to travel to Paris for the sessions, which was three hours from my home." **– Patient C**

"The treatment was very well tolerated." **– Patient D**

"The positive response to the treatment and the improvement in my overall health made a significant difference. I was able to return to my normal activities, although some challenges persisted, especially psychologically." **– Patient E**

"I had no side effect, therefore to me, the treatment was great." **– Patient F**

Patients found the treatment protocol easy to use – *"you just had to show up and the nurses did the work"* **[Caregiver A]**, though given half of the interviewed patients accessed the therapy in first line, they noted they did not have anything to compare it to. Though she was not able to provide a direct comparison, **Patient E** felt *"the treatment was manageable with infusions every two weeks, and I experienced fewer and less severe side effects compared to what I might have expected with other therapies."* **Patient G** shared that compared to chemotherapy + biologic therapy, his treatment with nivolumab + ipilimumab was *"much easier because of a very good tolerance and because of a lower time of infusion."*

Experiencing such robust response, with minimal side effects, an administration protocol that can be easily managed, and overall providing the ability to maintain a very good quality of life, as the experiences of the interviewed patients have reflected, is highly valued by patients. **Patient A** shared that he felt if he did not receive nivolumab + ipilimumab he *"would not be here"* and that accessing this therapeutic permitted him to *"be here with my kids and my family"* – truly the most important thing. The therapeutic under review has provided interviewed patients the opportunity to re-engage in their lives, enjoy life's most precious moments with loved ones, participate in their communities, and continue to progress in their careers. Additionally, patients shared that the ability to access doublet immunotherapy has proven to demonstrate a good response to treatment, which has lessened the burden on their loved ones as well. When asked if patients felt accessing nivolumab + ipilimumab was 'worth it', all respondents agreed that it most certainly was, and the responses were quite heart-warming and emphatic:

"1000% I'm glad that we did this. He's here, he can share in important life events. He's here for me, but more importantly for our kids. They didn't have to lose a parent." **– Caregiver A**

"Yes. Definitely… I was able to work back up to everything I was doing beforehand. I'm not really feeling that I'm missing out on anything. I've kept my social life, I am able to keep my fitness, I am able to work." **– Patient B**

"This treatment literally saved my life. I was considered terminal when it was proposed to me, and I responded well to it immediately. It also lacked the severe side effects of chemotherapy, which allowed me to regain an "almost" normal life, even while undergoing treatment." **– Patient C**

"Yes. Because it was beneficial." **– Patient D**

"Yes, it was absolutely worth accessing Nivolumab and Ipilimumab. These therapies gave me the opportunity to feel better and regain control over my health. The impact on my life was profound, as it was a critical turning point in my cancer journey." **– Patient E**

"Yes because of a very good tolerance and because of a lower time of infusion." **– Patient F**

7. Anything Else?

The author concludes that given the feedback provided by patients, the combination therapy of nivolumab + ipilimumab is well tolerated and permits a high quality of life while undergoing treatment, with patients reporting similar experiences as treatment with standard of care pembrolizumab monotherapy. The addition of ipilimumab to nivolumab does not appear to unreasonably impact health-related quality of life and provides **meaningful** clinical benefit. Thus, given the high efficacy of nivolumab + ipilimumab, the data supporting the therapeutic combination as a "potential new standard of care" (Andre et al., 2025), and the extremely positive patient feedback, we **strongly urge the committee to issue a positive funding recommendation for the therapeutic protocol under review**. Additionally, we urge the committee to consider access in first line **and beyond**, so that individuals such as **Patient G**, who have already been treated with immunotherapy, may benefit from access to this highly efficacious combination therapy.

There is an unmet need in Canada for additional therapeutics for the unresectable and metastatic MSI-H colorectal cancer patient population who do not respond well to traditional therapeutics. Patients value precision therapeutics which are targeted to their tumour biology, permit high quality of life as a result of low toxicity, minimal side effect profiles, ease of administration, and provide robust and durable response. According to patient input, nivolumab + ipilimumab exemplifies these values and a positive funding recommendation for this therapy would be in alignment with the patient input gathered within this submission. Additionally, access to a doublet immunotherapeutic protocol for MSI-H colorectal cancer is likely to provide all patients, and in particular, the rapidly increasing number of early age onset patients, with a sense of comfort and security with the knowledge that multiple lines of immunotherapeutic and targeted treatments are available for the management of their disease, easing some of the psychological burden associated with cancer treatment and survivorship.

The author leaves the committee with some final thoughts from those with the lived experience:

"If this treatment option is not available it would be the difference of life and death for a lot of people. I didn't know before that his type of cancer doesn't respond well to chemo, 19 months was what they had said for life expectancy on chemo. 19 months vs 7 years. All the things we have done as a family, he would have missed out on it, he wouldn't be here. It's huge." **– Caregiver A**

"If this is something that could work, it should be discussed with a physician and they should be given the option, rather than a one-size-fits-all approach." **– Patient B**

"Immunotherapy in general is a tremendous breakthrough in cancer care, especially for cancers like mine that have a genetic factor. For me, it was a treatment with almost no side effects and real effectiveness—completely the opposite of chemotherapy." **– Patient C**

"Access to Nivolumab and Ipilimumab is crucial for cancer patients and their caregivers because it offers an effective alternative to traditional treatments with potentially fewer and more manageable side effects. In my case, this therapy not only controlled the disease but completely cured me, allowing me to regain my health and return to a normal life - something that would not have been possible with chemotherapy, or at least not in such a short time.

For patients, it provides hope and the possibility of a full recovery with a less physically and emotionally exhausting treatment journey. For caregivers, it can mean less distress, as they see their loved ones respond well to therapy and ultimately heal. Expanding access to these treatments can make a real difference in the lives of many people facing cancer." **– Patient E**

"Again, I want to say to them, if it was you and you have what I have, would you be giving yourself Keytruda, or would you be giving yourself the drug that has better efficacy?" **– Patient G**

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, 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.

   No

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.

   No

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Bristol Myers Squibb			X	

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.

Name: **Filomena Servidio-Italiano**
Position: **President & CEO**
Patient Group: **Colorectal Cancer Resource & Action Network (CCRAN)**
Date: **April 7, 2025**

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0396-000
Generic Drug Name (Brand Name): Nivolumab Opdivo + Ipilumumab (Yervoy)
Indication: locally advanced (not amenable or suitable for curative intent surgery) or metastatic dMMR/MSI-H colorectal cancer
Name of Clinician Group: The Canadian Gastrointestinal Oncology Evidence Network (CGOEN) with the Medical Advisory Board of Colorectal Cancer Canada (and other CCC-treating physicians).
Author of Submission: Dr. Howard Lim, Medical Oncologist, BC Cancer
with
Dr. Sharlene Gill (BC)
Dr. Jennifer Lynn Spratlin (Alberta)
Dr. Brandon Meyers (Ontario)
Dr. Petr Kavan (Quebec)
Dr. Ravi Ramjeesingh (Nova Scotia)
Dr. Vincent Tam (Alberta)
Dr. Rachel Goodwin (Ontario)
Dr. Hatim Karachiwala (Alberta)
Dr. Benoit Samson (Quebec)
Dr. Jay Easaw (Alberta)

1. About Your Clinician Group

Please describe the purpose of your organization. Include a link to your website (if applicable).

The Medical Advisory Board of Colorectal Cancer Canada works alongside the patient group to ensure its activities and health information are relevant and useful for patients and caregivers. The Canadian GI Oncology Evidence Network (CGOEN) is a virtual and inclusive network of Canadian GI Oncology clinicians who contribute to the knowledge of GI cancer and its treatments, including participating in clinical trials, conducting observational research, and involvement in local/provincial and national clinical guideline developments and health technology assessment.

https://www.colorectalcancercanada.com/about/staff-board-medical-advisory/

2. Information Gathering

Information gathered for this submission was based on relevant data from the Checkmate 8DW Nivolumab/Ipilumumab vs Nivolumab vs chemotherapy in dMMR/MSI-H unresectable colorectal cancer trial and expert evidence-based review by Canadian gastrointestinal cancer specialists.

André T, Elez E, Lenz HJ, Jensen LH, Touchefeu Y, Van Cutsem E, Garcia-Carbonero R, Tougeron D, Mendez GA, Schenker M, de la Fouchardiere C, Limon ML, Yoshino T, Li J, Manzano Mozo JL, Dahan L, Tortora G, Chalabi M, Goekkurt E, Braghiroli MI, Joshi R, Cil T, Aubin F, Cela E, Chen T, Lei M, Jin L, Blum SI, Lonardi S.

Nivolumab plus ipilimumab versus nivolumab in microsatellite instability-high metastatic colorectal cancer (CheckMate 8HW): a randomised, open-label, phase 3 trial. Lancet. 2025 Feb 1;405(10476):383-395. doi: 10.1016/S0140-6736(24)02848-4. Epub 2025 Jan 25. PMID: 39874977 Clinical Trial.

Andre T, Elez E, Van Cutsem E, Jensen LH, Bennouna J, Mendez G, Schenker M, de la Fouchardiere C, Limon ML, Yoshino T, Li J, Lenz HJ, Manzano Mozo JL, Tortora G, Garcia-Carbonero R, Dahan L, Chalabi M, Joshi R, Goekkurt E, Braghiroli MI, Cil T, Cela E, Chen T, Lei M, Dixon M, Abdullaev S, Lonardi S; CheckMate 8HW Investigators. Nivolumab plus Ipilimumab in Microsatellite-Instability-High Metastatic Colorectal Cancer. N Engl J Med. 2024 Nov 28;391(21):2014-2026. doi: 10.1056/NEJMoa2402141.

PMID: 39602630 Clinical Trial.

3. Current Treatments and Treatment Goals

Currently mismatch repair (MMR) deficient or microsatellite high (MSI-H) tumors are present in about 5% of colorectal cancers. Due to this variant, these tumors are more responsive to immunotherapy than standard chemotherapy. Currently, Pembrolizumab is funded for the first line treatment of MMR deficient or MSI-H tumors that are not amenable for surgery or metastatic. This has provided a significant survival advantage over standard chemotherapy as well as positive effects on quality of life. These are the ideal feature of therapy – improving survival while positively impacting quality of life.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

There is about 30-40% of patients who do not respond to pembrolizumab and demonstrate progression of disease within the first 2-3 months of treatment. While the trial compares Nivolumab/Ipilumumab to Nivolumab – Nivolumab and Pembrolizumab are within the same class so it would be reasonable to use Nivolumab as a surrogate comparison to Pembrolizumab.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

The treatment would be the new standard first line treatment for MMR deficient/MSI-H tumors.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

This should be reserved for patients whose tumors are MMR deficient or MSI-H as determined by validated testing. It should be limited to patients who are not amenable for surgical resection or with metastatic disease.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Patients would be undergoing clinical evaluations on a regular basis for clinical response and toxicity. In addition, routine imaging during timed intervals are performed for objective assessments. Similar outcomes to clinical trials are used to determine benefit to treatment. A meaningful response would be patient preference, tolerability of treatment, quality of life, and response on imaging.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Treatment would be discontinued due to disease progression (radiologic or clinical), toxicity, clinician discretion or patient's request.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

This treatment could be reasonably to be given in any centre and by any specialist who is currently treating mCRC patients with systemic therapy.

6. Additional Information

Is there any additional information you feel is pertinent to this review?

<Enter Response Here>

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   No

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

   No

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. **Please note that this is required for <u>each clinician</u> who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Name: Brandon Meyers
Position: Medical oncologist
Date: 07-04-2025

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

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca	x			
Ipsen		x		
Roche		x		
Incyte	x			
Bayer	x			

Name: Ravi Ramjeesingh
Position: Medical Oncologist
Date: April 7, 2025

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

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca		X		
Amgen	X			

Roche	X			
Incyte		X		
Eisai		X		
Ipsen	X			
Merck	X			
Jannsen	X			
Pfizer	X			
Novartis	X			
Knight	X			

Declaration for Benoit Samson

Name: Dr. Benoit Samson
Position: Medical Oncologist
Date: April 7, 2025

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

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

Declaration for Rachel Goodwin

Name: Rachel Goodwin
Position: Medical Oncologist
Date: April 7, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 1 (from last 5 years)

Company	Check appropriate dollar range*

	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis	x			
Ipsen		x		+Independent Education Grant "X"

Declaration for Vincent Tam

Name: Dr. Vincent Tam
Position: Medical Oncologist, Arthur Child Comprehensive Cancer Centre
Date: 04-07-2025

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

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Incyte		x		
AstraZeneca			x	
Merck	x			

Name: Petr Kavan MD
Position: Medical Oncologist, Dpt of Oncology McGill University, Co-chair GI oncology Rossy Cancer Network McGill, CRP program director, LDI Jewish General Hospital McGill University
Date: April 3, 2025

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

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Merck		X		
Takeda	X			

Declaration for Jay Easaw

Name: Jacob Easaw
Position: Professor, Medical Oncology, Cross Cancer Institute, University of Alberta.
Date: 07 May 2025

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

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Takeda	X			
Amgen	X			
Astellas	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician

Name: Hatim Karachiwala
Position: Medical Oncology
Date: April 3, 2025

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

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Astellas		X		
Takeda		X		
Pfizer		X		
Eisai		X		
Amgen		X		
Roche	X			
Tahio		X		
Merck		X		

BMS		X		
AstraZeneca		X		

Declaration for Clinician 1

Name: Sharlene Gill
Position: Medical Oncologist, BC Cancer - Vancouver
Date: 03-04-2025

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

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
BMS	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Jennifer Spratlin

Name: Jennifer Spratlin
Position: Associate Professor, University of Alberta; Medical Oncologist, Cross Cancer Institute
Date: April 7, 2025

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

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Incyte advisor	x			
Astrazeneca advisor	x			
Taiho advisor	x			
Ipsen advisor	x			

BMS advisor	x			
Astellas advisor	x			
BOLD advisor	na			

Name: Howard Lim
Position: Medical Oncologist
Date: April 7, 2025

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

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Roche	X			
Bayer	X			
Amgen	x			
Takeda	x			
AstraZeneca		x		
Astellasx				
BMS		x		
Lilly	x			
Taiho	x			
Eisai		x		
Ipsen	x			
Incyte		x		

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0396-000
Generic Drug Name (Brand Name): nivolumab and ipilimumab (Opdivo and Yervoy)
Indication: Opdivo (nivolumab), in combination with ipilimumab, is indicated for the first-line treatment of adult patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer.

Manufacturer Requested Reimbursement Criteria[1]:
Nivolumab is indicated for the first-line treatment of adult patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer, when used in combination with ipilimumab.

Name of Clinician Group: Ontario Health (Cancer Care Ontario) Gastrointestinal Cancer Drug Advisory Committee ("OH(CCO) GI DAC")
Author of Submission: Dr. Erin Kennedy and the OH(CCO) GI DAC

1. About Your Clinician Group

OH(CCO)'s Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

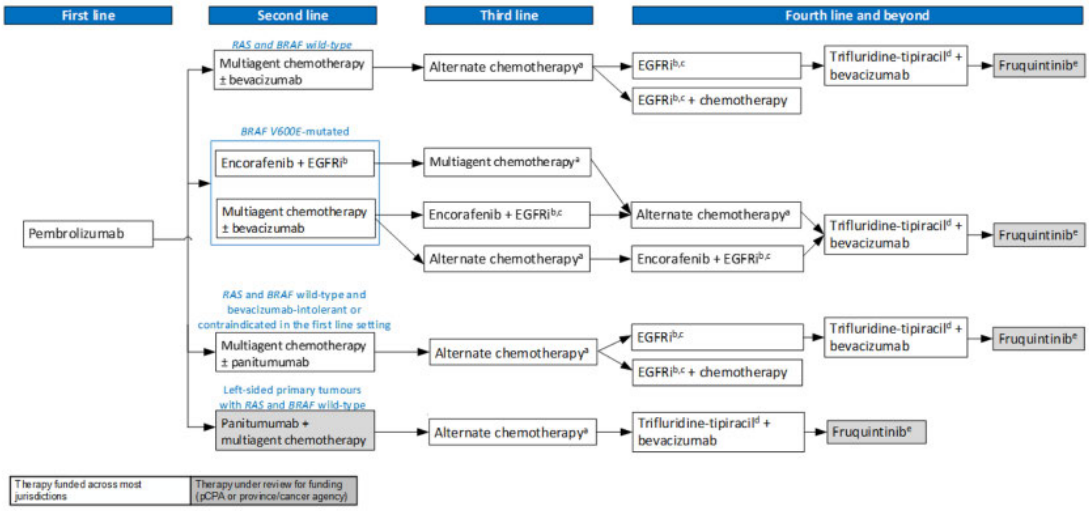
Information was gathered via emails.

3. Current Treatments and Treatment Goals

Our current standard of care for dMMR, MSI-H is pembrolizumab. This is now the second confirmatory trial showing IO (now doublet IO) is better than chemotherapy for 1st line setting. The Ipilimumab/Nivolumab data seems to have a better PFS rate at various time points and less up front resistance to immune therapy compared to the pembrolizumab single arm data (of course this is cross trial comparison).

(Reference for the GI DAC: CDA Provisional Funding Algorithm mCRC)

Figure 2: Provisional Funding Algorithm Diagram for mCRC (MSI-H/dMMR)



dMMR = deficient mismatch repair; EGFRi = EGFR inhibitor; mCRC = metastatic colorectal cancer; MSI-H = high microsatellite instability; MSS = microsatellite stable; pMMR = proficient mismatch repair.

Notes: Pembrolizumab is classified as an immunotherapy. Encorafenib and EGFRis are classified as targeted therapies and not counted as a chemotherapy regimen. Patients with activating *RAS* mutations would follow the same pathway as *RAS* and *BRAF* wild-type; however, they would not be eligible for an EGFRi.

[a] Bevacizumab may be available in combination with 1 line of chemotherapy for the treatment of advanced colorectal cancer (indicated for any line of therapy, provided that the patient is bevacizumab naive).

[b] EGFRis include cetuximab and panitumumab, where available.

[c] This would be the option if an EGFRi was not received in previous lines.

[d] Trifluridine-tipiracil in combination with bevacizumab is for patients who are refractory to chemotherapy and have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapies; anti-VEGF biologics; and, if they have disease that is *RAS* wild-type, anti-EGFR drugs; and have disease progression or demonstrated intolerance to a maximum of 2 prior chemotherapy regimens for the treatment of advanced colorectal cancer. Patients who had received adjuvant or neoadjuvant chemotherapy and had recurrence during or within 6 months of completion could count the adjuvant or neoadjuvant therapy as 1 of the maximum of 2 required prior chemotherapy regimens to qualify. Patients with small bowel or appendiceal adenocarcinoma are eligible for treatment with trifluridine-tipiracil in combination with bevacizumab.

[e] Fruquintinib should be reimbursed for patients who have been previously treated with or are not considered candidates for available standard therapies, including fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy; an anti-VEGF agent; an anti-EGFR agent (if *RAS* wild-type); and either trifluridine-tipiracil or regorafenib.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Aims include: prolong PFS, delay disease progression, prolong life, potentially convert some patients to surgery, reduce the severity of symptoms, minimize adverse events, improve health-related QOL

Using PFS is still a very acceptable end-point for IO based trials. These trials need to use cross-over or they would not accrue patients. Also, now that we have used IO for dMMR, MSI-High patients for years now as standard of care, we have seen patient with pCR sustained with cure.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Many of us were waiting for the Ipilimumab/Nivolumab vs Nivolumab results. Does doublet IO have more efficacy than single IO (Nivolumab). See abstract link. It was positive and did not have significantly higher toxicity.

The GI DAC would now consider Ipilimumab/Nivolumab as the standard of care, especially in patients with liver metastases.

However, having access to single agent IO as 1L treatment will still be important. There will be some patients that we will want to use single agent immune therapy. Example. met colon cancer but there is cirrhosis at baseline: may use IO monotheraoy over doublet. This is just one example.

https://ascopubs.org/doi/10.1200/JCO.2025.43.4_suppl.LBA143#:~:text=Objective%20response%20rate%20(ORR)%20by,concerns%20were%20identified%20(Table).

Prior to the Ipilimumab/Nivolumab data, our current 1L standard of care for patients without IO contraindication is pembrolizumab.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

dMMR, MSI-High is the most robust biomarker predicting response to IO therapy.

Please also refer to 5.1.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

6. Additional Information

<Enter Response Here>

7. Conflict of Interest Declarations

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Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   OH (CCO) PDRP provided secretariat support to the group.

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

   No

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. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Erin Kennedy
Position: Lead, OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Date: 4-April-2025

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

Table 1: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Rachel Goodwin
Position: Member, OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Date: 15-March-2025

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

Table 1: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
BMS				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Michael Raphael
Position: Member, OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Date: 16-March-2025

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

Table 2: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Consolacion Molto Valiente
Position: Member, OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Date: 17-March-2025

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

Table 3: Conflict of Interest Declaration for Clinician 4

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Dr. Suneil Khanna
Position: Member, OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Date: 17-March-2025

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

Table 4: Conflict of Interest Declaration for Clinician 5

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
BMS				
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.