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

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

pembrolizumab (Keytruda)

(Merck Canada Inc.)

Indication: Pembrolizumab for the treatment of adult patients with FIGO 2014 Stage III-IVA cervical cancer, in combination with chemoradiotherapy (CRT).

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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Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Pembrolizumab (Keytruda ®)
Indication: Pembrolizumab for the treatment of adult patients with FIGO 2014 Stage III-IVA cervical cancer, in combination with chemoradiotherapy (CRT)
Name of Patient Group: Colorectal Cancer Resource & Action Network (CCRAN) in collaboration with the Canadian Cancer Survivor Network (CCSN) and HPV Global Action
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 patient-focused mandate to serve cancer patients outside of the colorectal cancer space through its health technology assessment (HTA) patient evidence submissions, educational events and advocacy initiatives. 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

To help capture the advanced and metastatic cervical cancer patient perspective for this submission, CCRAN reached out to 10 Canadian gynecological oncology clinicians / KN-A18 trial investigators between **February 7th – 18th, 2025** via email to request their assistance in identifying cervical cancer patients who had experience with the therapy under review, with follow up emails through to **March 7th, 2025**. The email contained a patient recruitment poster (**APPENDIX A**) 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 cervical cancer journey in general. Some Canadian clinicians commented that they did not have any patients who had accessed the therapy as it has yet to be funded in Canada. HPV Global Action engaged several Medical Advisors and additional partners in an effort to identify patients who had/have experience with the therapy under review. Clinician investigators commented that it was difficult to identify patients due to the blinded nature of the trial and gynecologic oncologists noted a lack of available patients on the protocol due to an easier access pathway for another immunotherapy through a compassionate access program.

Given the lack of access to this therapeutic protocol in Canada, CCRAN determined that in order to truly be able to provide this expert review committee with the patient's lived experience, international patient perspectives would be required. Thus, on **February 7th, 2025** CCRAN reached out to a U.S.-based women's cancer patient advocacy group (SHARE Cancer Support), and additionally to U.S.-based groups Cervivor and the Foundation for Women's Cancer on **February 24th, 2025.** These groups were provided with the patient recruitment poster (**APPENDIX A**) to share within their networks to help secure the patient perspective.

A social media outreach campaign (**APPENDIX B**) was shared and promoted within CCRAN, CCSN, and HPV Global Action networks, from **January 19th – March 14th, 2025.** Calls for patient recruitment were contained in CCSN's newsletters on **January 29th & February 25th, 2025.**

Previously curated data from a cervical cancer survey which was released on **April 4th, 2022,** and closed on **May 10th, 2022** (**APPENDIX C**) was utilized to inform this submission in respect of the disease experience and the experience with previously available treatments.

These extensive efforts resulted in five patient interviews, the transcripts of which can be found in **APPENDIX D.**

3. Disease Experience

As the only cancer type exclusively diagnosed in individuals assigned female at birth, gynecological cancers are plagued with inequities, including chronic underfunding in research and treatments (NYSTF, 2022; Nature, 2023), as described in a recent submission **(PC0366-001)** for endometrial cancer. This underinvestment is part of a broader issue affecting women's health in general (Nature, 2024).

In recent years, cervical cancer incidence has been increasing in Canada, and it is considered to be the fastest rising cancer in Canadian females (Canadian Partnership Against Cancer, n.d.). The median age of diagnosis is 47, and cervical cancer is the third most commonly diagnosed cancer in younger women aged 25 – 44 (Caird et al., 2022); further emphasizing the urgent need for our society, and this committee, to direct efforts and funding to prevention, research and treatment options for this pathology. Cervical cancer disproportionately impacts individuals from equity-denied communities in Canada, who experience higher incidence rates (Canadian Partnership Against Cancer, n.d.) and are more likely to face challenges with health literacy, health system navigation, and receiving culturally appropriate support and care.

Cervical cancer develops as a result of a persistent infection with an oncogenic genotype of the human papillomavirus (HPV) (Caird et al., 2022), which provides significant opportunity for elimination of the disease through vaccine-prevention (World Health Organization, 2025). However, since HPV is acquired through a sexually-transmitted infection, cervical cancer patients often face stigma, guilt, and shame related to their cancer diagnosis, despite the fact that the vast majority of the population develops an HPV infection at some point throughout their lives (National Cancer Institute, 2022).

In its earlier stages, cervical cancer frequently does not have any signs or symptoms. As the disease progresses and invades nearby tissues, symptoms may include abnormal vaginal bleeding including between periods, unusually long or heavy periods, after menopause and after sexual intercourse; abnormal vaginal discharge; bleeding after a pelvic exam; pain during sexual intercourse; difficulty urinating or having a bowel movement; leaking of urine or feces from the vagina; or pain in the pelvis or lower back (Canadian Cancer Society, 2025).

Interviewed patients shared their experiences with diagnosis:

Patient A was diagnosed with stage IIIb cervical cancer at the age of **63** after having her post-menopausal bleeding dismissed by multiple healthcare providers.

Patient B received the news that she had stage IVa cervical cancer at the age of **41**, after imaging that was ordered following her 4th diagnosis of a urinary tract infection in a brief period of time.

Patient C started having cellular dysplasia at the age of **27** after testing positive for HPV. She was later diagnosed with invasive cervical cancer at the age of **34** and has since experienced 2 recurrences.

Patient D was diagnosed at the age of **54** with stage IIIc cervical cancer after experiencing some intermittent vaginal bleeding and mild lower back pain.

Patient E received her diagnosis at the age of **48** after experiencing significant clotted discharge. Her oncologist prescribed pembrolizumab following her recurrence, but her access was denied, and she felt compelled to share her perspectives to inform this submission.

Three of the interviewed patients spoke to an element of dismissal of their symptoms and the impacts that the COVID-19 pandemic had on their delayed diagnoses:

"I was getting blood every now and then. Nobody really caught it. I had gone to a couple of clinics and there was bullshit about it being post-menopausal and all that. Even my family doctor didn't push it…" **– Patient A**

"My only symptom that was outwards that I noticed was frequent urination, everyone said I was getting older, I was diagnosed with a UTI 4 times. I was having to run to the bathroom every 5 minutes. Because of COVID I was having trouble getting into my primary care provider and when I did, they wanted me to wait [for testing]" **– Patient B**

"…We just got through COVID, everything had been shut, you couldn't get in to see anybody." **– Patient D**

Patient A experienced pain prior to her diagnosis, ***"I kept feeling like I had to urinate and there was no urine and then there was pain where the tumour was growing. It was the pain, I couldn't take the pain anymore, so I went to the ER."***, though for many, the disease itself is not painful.

The intimate nature of the disease necessitates that patients undergo regular intrusive physical pelvic examinations, often with the use of a colposcope. **Patient A** vulnerably shared the invasive experience of her diagnosis: ***"I waited about 11 – 12 hours at the emergency. Then a doctor that came, a gynecologist, he put his hand in me."***

Patients B & D both shared that they felt they had been delivered a death sentence upon learning the news of their diagnosis:

"I honestly… I was devastated. I honestly thought I was going to die. I thought it was a death sentence. That's the first thing you think of when you hear of an advanced cancer." **– Patient B**

"Petrified. Overwhelmed. I felt like it was a death sentence. Alone. You feel really alone. Our healthcare system is so broken." **– Patient D**

In some patients, the treatment for HPV can be complex and arduous, causing significant distress and disruption to quality of life before even progressing to the point of malignancy. **Patient C** went through such traumatic treatments for HPV that when she eventually progressed to invasive cancer, she felt a sense of relief: *"when I first received the diagnosis, I was actually relieved because I had gone through so much for "pre-cancer" and I was never actually able to share that I have cancer. I take issue with the way that cervical cancers are staged. So, it was actually validating."* Her treatments for HPV-induced dysplasia included multiple loop electrosurgical excisions procedures (LEEPs), a hysterectomy, post-hysterectomy brachytherapy on her vaginal cuff, and laser therapy on her vagina, vulva, and anus for persisting dysplasia.

The most important aspect of the disease to manage was reported by the majority of interviewed patients as controlling the spread of the disease. As **Patient C** states, *"Trying to catch it before it spreads further. That's the one thing I can control in all of this."* The ability to be actively involved in their care and treatment decisions was prioritized by patients, who are empowered and permitted to feel just a little bit more control when doing so. Surveyed patients identified living with uncertainty, fatigue, and anxiety, panic attacks or depression as the most commonly reported problems living with cervical cancer.

Cancer takes away the ability to plan for the future. **Patient E** shared, *"Ever since I was hit by cancer, I feel like my life is limited. I can't plan ahead. I can only plan in a very short range. Your life is on hold. You just never know when it will come back."* **Patient C** has been forced to plan out her life in short intervals for the past 14 years while living through this journey: *"It was very difficult to be having surgery or biopsies every 3 months. I felt like I was living my life in 3-month intervals. I couldn't plan any vacations. It was like, 'the cancer hasn't returned, let's get away for the weekend.' It's the only thing you can think about. It's the one problem in your life. Everything else doesn't quite matter. To deal with that - 14 years of every 3 months - was very, very hard."*

The impact of cancer is not limited to the patient. Cancer's toll has a ripple effect which is cast throughout the patient's loved ones, workplace, and community. When asked about the impact that cancer has had on interviewed patients' loved ones, some heart-wrenched replies were provided:

"It's been really hard…. My daughter started college in another state the day before I started treatment. I couldn't go with her to move into school, and it was hard on my daughter knowing I might not be there when she got back." **- Patient B**

"It's been very difficult. Both my husband and I are in therapy because of it. He worries a lot about me dying…. It's been really challenging on our mental health, for both of us." **– Patient C**

"Well, it's been emotionally debilitating for [my husband]. He wants to fix it, but can't. Watching someone you love go through this has got to be some form of hell." **– Patient D**

4. Experiences With Currently Available Treatments

Treatment for stage III – IV cervical cancer typically includes surgery, chemoradiation, and sometimes brachytherapy, chemotherapy, and/or targeted therapies. Cervical cancer survey respondents report treatment with cisplatin, caroboplatin/pacilitaxel/bevacizumab, palliative care, alternative methods, and pembrolizumab.

Patient B was initially treated with 27 external radiation and 5 brachytherapy sessions over 3 days, and 4 cycles of cisplatin, a therapeutic which she was unable to complete due to low platelet levels. **Patient C** went through extensive treatment regimens over 13 years for the treatment of her dysplasia and cancer: multiple LEEP procedures, a hysterectomy, brachytherapy, laser therapies, and a partial vaginectomy. Despite these intensive treatments, she recurred with advanced stage disease and required a total pelvic exenteration: *"They took what was left of my vagina, my bladder, my rectum… They created a neovagina and I have a permanent colostomy and urostomy."* **Patient D** was initially treated with cisplatin and external beam radiation. **Patient E** received a radical hysterectomy followed by chemo, radiation and brachytherapy.

Patients B & D were both initially treated with chemotherapy and radiation, and shared that the radiation therapy, in particular, was a grueling experience:

"It was really rough. I am 5'9" and I got down to 113 lbs. I lost a lot of weight. I couldn't eat. I thought it was the chemo, but they said it was the radiation …. I would literally have an orange or popsicle and consider it a good day."

"Oh, brutal. Brutal! Basically, I was beyond fatigued, no appetite, I lost a lot of weight. I attribute it more to the radiation."

The extent of the adverse effects of currently available treatments can have a remarkable, detrimental effect on health-related quality of life. **Patient B** shared, ***"I couldn't work. I slept a lot. I just went to treatment and came home and laid on the couch. I was very weak."*** **Patient D** describes the impact of her quality of life as ***"huge",*** sharing ***"I did nothing. I had no quality of life. Went no where, did nothing, very depressed. Alone, just pretty useless, I guess."*** With the rising rates of cervical cancer impacting younger women, the potential impact on fertility is quite significant, as was experienced by **Patient C:** ***"The hysterectomy obviously took away any option for me to get pregnant, so that was a big thing."***

All too often, the significant impact of treatment on sexual health and functioning is dismissed or inadequately addressed in both clinical care and research (Agrawal, 2022; Barcellini et al., 2022). Interestingly, but perhaps unsurprisingly, female patients are less likely to be asked about sexual health than male patients (Agrawal, 2022). Females who undergo pelvic radiation therapy have poor sexual outcomes, with many having lasting impacts of sexual and vaginal functioning (Angel et al., 2023). As **Patient C** shared, ***"With brachytherapy – the biggest impact was the need for vaginal dilators. Having to use those daily was quite frustrating. My vaginal canal was shrinking. It made having penetrative sexual intercourse painful. That impacted my life and my marriage."*** A recent study evaluating patient-reported outcomes found that cervical cancer patients self-report high rates of sexual distress, dysfunction, and menopause symptoms, yet these symptoms are often under-reported to their healthcare teams (Chuk et al., 2024). **Patient C**, who later faced a pelvic exenteration in her early 30s, shares that her and her husband's ***"sexual health is non-existent."*** Once again, this highlights one of the many inequities faced by women experiencing cervical cancer.

5. Improved Outcomes

When asked what improvements they would like to see in drug therapies accessible in Canada, interviewed patients expressed access to treatments as a key priority:

"I would like to see [pembrolizumab + chemoradiation] available. Period. Because I think it's going to save lives." **– Patient A**

"I would like everyone to be offered Keytruda and other drugs because I feel like it gives us all more of a chance…. No one should not have access to a drug that may save their lives. To know there is a drug out there and you can't get access to it, and it's saving other people is incredibly frustrating and sad." **– Patient B**

"Access to things that are available to save your life." **- Patient D**

Interviewed patients residing in the United States of America, where access to the therapeutic protocol under review is more widely available, shared the pain of seeing their Canadian counterparts not being able to access immunotherapeutics: ***"I'm here [interviewing with you] today for my Canadian friend who couldn't access immunotherapy - she tried so hard and then she couldn't get it and she died. Her oncologist in Canada fought hard but she just couldn't get access. For her, I want other people to have that opportunity."*** **– Patient B**

Patient D, a Canadian patient who accessed the therapeutic expressed a similar sentiment with respect to access to therapeutics in Canada, sharing that ***"…as a Canadian, it's overwhelming to see all the extras that go on in the States and that they have so much, it's so unfair. To sit there with your doctor and hear that's not coming to Canada for years… it's not right. That in itself is some form of a death sentence. It's very unfortunate, unfair."***

Additionally, interviewed patients shared that they valued oral administration, or, for intravenous therapy, a shorter administration time than traditional chemotherapeutics, as well as access to support and educational materials, ***"medication that doesn't leave you feeling so crummy"***, and earlier access to more targeted treatments that can slow or prevent progression of disease. The therapeutic under review offers the benefits, improved outcomes, and provides an experience that is in alignment with these reported patient values. For example, when asked about the ease of use of pembrolizumab (**Q29**), the responses clearly indicate that patients find pembrolizumab easy to use:

"You don't feel anything. The only thing I didn't like was being poked with the needle. It changes nothing, you don't even feel it." **– Patient A**

"100%. It's quicker. The infusion itself is 30 minutes. The longest part is waiting for the pharmacy to bring it. When I had chemo, it was like a 6-hour infusion…. I'm laughing when I'm in there, they don't need to give me the pre-meds - the Benadryl and the steroids, and all that." **– Patient B**

"It's probably the easiest treatment option that's been provided to me. Because there's not the severity of side effects. It's really just the inconvenience of getting the infusion, rather than feeling badly after treatment." **– Patient C**

"Yes. Way shorter time, as far as when you're at the hospital. And you don't have to take any pre-meds." **– Patient D**

All interviewed patients shared that they believed that pembrolizumab had the desired improvements that they would wish to see in new therapeutics (**Q34**) – short infusion time, minimal side effects, and robust response. **Patient A** emphatically stated, *"I would like to see this available. Period. Because I think it's going to save lives."*

6. Experience With Drug Under Review

Patient A accessed pembrolizumab in combination with 5 cycles of chemotherapy and radiation, followed by pembrolizumab monotherapy in first line therapy through a clinical trial, beginning in March 2021 and she continued the pembrolizumab monotherapy for 2 years.

Patient B accessed pembrolizumab in combination with carboplatin + paclitaxel for 4 cycles, followed by pembrolizumab monotherapy, beginning in January 2023. She had received 34 of 35 cycles of pembrolizumab at the time of the interview. She had undergone chemoradiation previously and had briefly achieved a no evidence of disease (NED) status prior to starting the therapeutic under review.

Patient C started paclitaxel and cisplatin in combination with pembrolizumab and radiation therapy in July 2024. She had completed 6 cycles of combination therapy and 2 cycles of monotherapy with pembrolizumab at the time of the interview.

Patient D was treated with pembrolizumab in combination with carboplatin + paclitaxel for 6 cycles, beginning in September 2023, followed by pembrolizumab monotherapy from February 2024 – December 2024. In December, Avastin was added to her pembrolizumab therapy. She did not receive radiation therapy as she shared that the lymph node disease that remained following her prior treatment was not well-located for radiotherapy.

Patient E shared that despite her medical oncologist's requests for access to pembrolizumab, she has not been able to access the therapeutic under review, thus she felt compelled to participate in the patient interviews. She had just experienced another recurrence. As such, **Patient E** will not be further referenced within Section 6 of the submission.

During the brief period of combination therapy with pembrolizumab and chemotherapy +/- radiation therapy, patients share they experienced the anticipated adverse effects that are commonly observed with the current standard of care therapy, including: fatigue, vaginal pain and discomfort, pain with urination, nausea, intestinal cramping, diarrhea, systemic infections, hair loss, weight loss, dehydration, weakness, and dizziness. Given that these adverse effects are commonly reported with the standard of care treatment (Cancer Research UK, 2023; Palagudi et al., 2024), and these described symptoms resolved when patients transitioned to pembrolizumab monotherapy, it is reasoned that **the addition of pembrolizumab to standard of care chemoradiation did not worsen the patient experience** during this phase of treatment. The short duration of initial treatment of pembrolizumab in combination with chemoradiotherapy lends itself to increased tolerability and limits the impact of cumulative effects, particularly when framed against long-standing chemotherapeutic treatment as is the current standard of care. For the balance of the treatment regimen, patients are treated with a precision immunotherapeutic which is highly efficacious while maintaining a lower side effect profile when compared to its cytotoxic chemotherapeutic counterparts.

During pembrolizumab monotherapy, patients shared few adverse effects during treatment, with a general sense that any side effects were *"very minor"* and well worth the inconvenience. These adverse events included one episode of shortness of

breath which resolved with treatment (the patient could not confirm whether or not she was diagnosed with pneumonitis), minor joint pain which was managed with Claritin, some fatigue (though it was unclear if this was related to resumption of a busy life), and exacerbation of pre-existing conditions including psoriasis and hypothyroidism.

Patients A & D were both experiencing pain from their cancer prior to commencing treatment with the therapeutic under review. Both patients experienced full alleviation of their pain following treatment. **Patient A,** in particular, had been experiencing significant symptoms that disrupted her quality of life, ***"I was having pain in my lower pelvis, near the cervix, the tumour was pushing on my bladder every time I moved. I kept feeling like I had to pee, but I couldn't pee. The tumour was pushing on the bladder and it hurt."*** She shared that ***"The pain went away after day 1. It was the first time I slept."***

Remarkably, interviewed patients shared that, by-and-large, they have been able to resume 'normal' life while undergoing pembrolizumab monotherapy, as **Patient B** revealed: ***"Other than going every 3 weeks for my treatment, I don't feel like I'm in cancer treatment."*** Patients reported that they were able to resume work, travel, going out socially, and generally just living their lives as they would without the burden of cancer because the treatment was so easy to tolerate and patients achieve such a remarkable response. Avoiding long-term cytotoxic treatment and immune-compromising chemotherapeutics was viewed by patients as an important value and a significant benefit of pembrolizumab. In the words of **Patient C,** ***"During chemo the constant hospitalizations were a huge impact. I was immunocompromised, I had to be very careful about who I was in contact with, I wasn't eating in restaurants. Whereas with pembro, I live my life and just plan around my infusions."***

When asked to rate quality of life while on pembrolizumab monotherapy (**Q24**), participants reported a remarkable average rating of **8.9 out of 10!** Here's what the patients had to say:

"10, 10, 10! It was amazing, fantastic! Because it was curing me, I was getting better, there was no pain, I was having fun, I was able to do what I wanted to do, it didn't block me from doing what I wanted to do." **– Patient A**

"I would say honestly a 9 – 10. I'm back at work, number one. I've gone to Scotland, Ireland, New York, I just got back from Aruba. I've been to Seattle. I'm living my life. I'm travelling to see my daughter. I work fulltime as a teacher and I couldn't work when on the other treatment. I'm NED and living my life." **– Patient B**

"With pembro, I would say like an 8. You know it doesn't impact very much, the only thing that it impacts is having to go for lab work, follow up, infusion. A minor disruption. I still have my port, which isn't glamourous, but it's minor. It's the easiest of all the treatments." **– Patient C**

"When I was on the Keytruda standalone I would rate my quality of life as high as an 8. I was able to do more, it's more of a mindset as opposed to the physical. I was capable of a lot more than I allowed myself to do. But, I started hot yoga, and I could do things. The support isn't there. It's mental. That's the biggest thing for me." **– Patient D**

Accessing the therapeutic under review appears to relieve some of the significant psychological burden of cancer as well. Patients expressed a great deal of relief and an ease of the mental burden of cancer when accessing pembrolizumab, as if the ability to access immunotherapy lifts some of the considerable weight of a cancer diagnosis: ***"I think there's a comfort in knowing that I'm on something so that my immune system can be trained to fight this. It gives you more hope. Especially because its so easily tolerated. It really is good for the spirits."*** **[Patient C].** Notably, this is consistent with the perspectives expressed by patients accessing pembrolizumab for other indications in recent submissions **[PC0377-000 & PC0383-000].** In respect of pembrolizumab, **Patient B** shared ***"I thought of it like my superpower".*** In fact, both patients who had completed or nearly completed their treatment regimen actually expressed a reticence to discontinue their therapy after two years of treatment:

"I'm really convinced that the pembro was a key element in the cocktail that I got. The fact that I stayed on it for 2 years, I was thrilled about it… it gave me confidence. It made me calmer, it gave me a little more calmness and confidence that I was going to get through this. I even felt bad the last day of treatment, I was like, 'no more?' It was like it was my friend." **– Patient A**

"I kind of don't want to go off it after my next treatment. I feel good, I don't mind being on it at all." **– Patient B**

In addition to the profoundly positive impact on quality of life, interviewed participants have achieved a remarkable and durable response while on the therapy. **Patients A & B**, who began treatment in March 2021 and January 2023, respectively, both shared that they had achieved a no evidence of disease status. **Patient A** shared the excitement when her and her treating oncologist both reviewed her initial imaging results, ***"I'm not a doctor, but the two images were just remarkable."*** **Patient C,** who began treatment for her aggressive recurrence in July 2024 shared, ***"they haven't really seen any issues with anything coming back."*** **Patient D**, who achieved a good response for almost one year, recently experienced some potential lymph node involvement and has stayed on the pembrolizumab with the addition of Avastin in response to these latest findings. During the shared decision-making with her treating oncologist, she shared, ***"I thought, 'how do we know the pembro is not keeping it at bay?' So, I really fought to stay on it."***

A key theme that emerged overall was **gratitude** for being able to access pembrolizumab. When asked if they believed it was worth it to access the therapeutic protocol under review (**Q31**), participants shared an overwhelming appreciation:

"Oh my God, 100 out of 10!! ...I'm lucky. I cannot believe how lucky I am to have gotten it. I'm in shock - I feel like I owe the world big time. Right time, right place, right timing, right doctors, everything just aligned." **– Patient A**

"100% ... I feel very grateful. I know that this has not been an opportunity given to everyone I know." **– Patient B**

"I'm just grateful that it became available to my type of cancer." **– Patient C**

"For sure. For sure, yes. I feel I'd be dead with out it, because it would just keep growing. I'm thankful." **– Patient D**

7. Anything Else?

There is a significant and urgent unmet need for additional precision therapeutics for the treatment of cervical cancer in Canada. The interviewed patients emphatically called for urgent access to this therapeutic for the benefit of women, and all individuals with a cervix, in Canada. When asked if they would recommend that pembrolizumab + chemoradiation be made available to all patients who qualify for it (**Q35**), here is what patients had to say:

"100% absolutely. Absolutely!" **– Patient A**

"Yes, 100%. It's giving people that had no hope, so much hope. I know people that tried it when they had 2 months to live, and then later went NED. It's a miracle to see, I want everyone to have that opportunity to see if it works for their cancer." **– Patient B**

"Absolutely!!" **– Patient C**

"Yes. I personally truly believe that the pembro boosting your own immunity, it makes so much sense. Chemo kills everything, so we need what can be in your body to help the good stuff, to fight, to build." **– Patient D**

"Oh yeah! Not only for me, but to all the patients." **– Patient E**

A positive funding recommendation for pembrolizumab in combination with chemoradiation would represent progress, and hope, in a cancer type that is under-supported and has derived little benefit from the advancements stemming from the new era of precision medicine within the Canadian treatment landscape. Furthermore, as referenced in **PC0366-001 & PC0383-000,** gynecological cancers, impacting only those assigned female at birth, receive disparate funding and research, while women uniquely face the challenge and societal burden of being primary caregivers. Gynecologic cancers are plagued by inequities in respect of support, funding, and research advancement. Providing access to this drug will help to reduce this disparity, marking a step towards closing the gap in funding and equity for women's health in Canada. Women facing cancer often times carry the psychological and mental burden of continuing their responsibilities as mothers, grandmothers, and wives, in addition to any paid professional obligations, while also battling a devastating disease. When cervical cancer patients are able to access therapeutics which are effective and convenient, with minimal side effects, such as pembrolizumab in combination with chemoradiotherapy, it is not only the patient who benefits, but the many individuals for whom she cares, ultimately reducing the burden of cancer at a societal level. The gynecological medical oncologist referenced in the patient input submission **PC0381-000** articulates this so well based on their extensive clinical experience:

"There are two groups: the older group who are not well so they are trying to balance their own needs and trying to take care of their own spouses who are themselves not well because they have underlying conditions. And a younger patient group who are taking care of their parents and taking care of their own kids, so the stress of both ends is really difficult, the disruption is unbelievable. Women being the primary caretaker is unbelievable when they themselves are diagnosed with a critical illness. It is quite drastic. This is every conversation I have. It is unique taking care of women. I hear: 'How am I supposed to do this?'!!"

On behalf of cervical cancer patients in Canada, **we strongly recommend that the expert committee issue a positive funding recommendation for the therapeutic protocol under review.** Pembrolizumab in combination with chemoradiotherapy offers cervical cancer patients with a treatment option providing a robust response, with minimal adverse effects, high ease of use, and a good quality of life reported during the pembrolizumab monotherapy treatment regimen – aspects that are highly valued by patients and their families. The therapeutic has permitted interviewed patients to re-engage in their everyday lives, workplaces, and with family, and community, which creates a ripple effect that extends far beyond each individual patient. The author leaves this committee with the final comments from cervical cancer patients, who passionately called for funded access to this therapy in Canada:

"It keeps you alive. Bottom line. You're alive! There's no pain, you're alive, it's great. What more do you want?! It gives you your life." **– Patient A**

"I think it's important because it's one of the few cancer drugs that still gives you quality of life. I'm running around teaching 8- or 9-year-olds, and I couldn't have done that on the other drugs. I've lost a lot of sisters that didn't have access and maybe they would have been here today." **– Patient B**

"I think that it's so important that when it comes to cancer that any of the latest advancements, any drug therapies that have been shown to improve outcomes, should be utilized. To lag behind the standard of care is detrimental to patients." **– Patient C**

"I think it needs to be there for all. There's something out there showing really great, promising results, let's do it. These are people. It seems like sometimes it's a lucky wheel spin for some and it's not fair." **– Patient D**

"Anything that can prevent spread, or slow down the spread, that's what we should do." **– Patient E**

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
Merck				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: **March 23, 2025**

DO YOU HAVE CERVICAL CANCER?

Have you taken Pembrolizumab (Keytruda®) in combination with chemoradiotherapy?

Pembrolizumab in combination with chemoradiotherapy is currently under a funding review in Canada for the treatment of high-risk locally advanced cervical cancer.

We really need your help!

By participating in a 45-minute phone interview, you can share valuable insights from your cancer journey and experience with the therapeutic protocol under review. Your perspective will help to inform the patient input submission which will have a meaningful impact on the funding recommendation in Canada.

Make your voice heard! Your input could help get this therapy funded in Canada.

[redacted] [redacted]

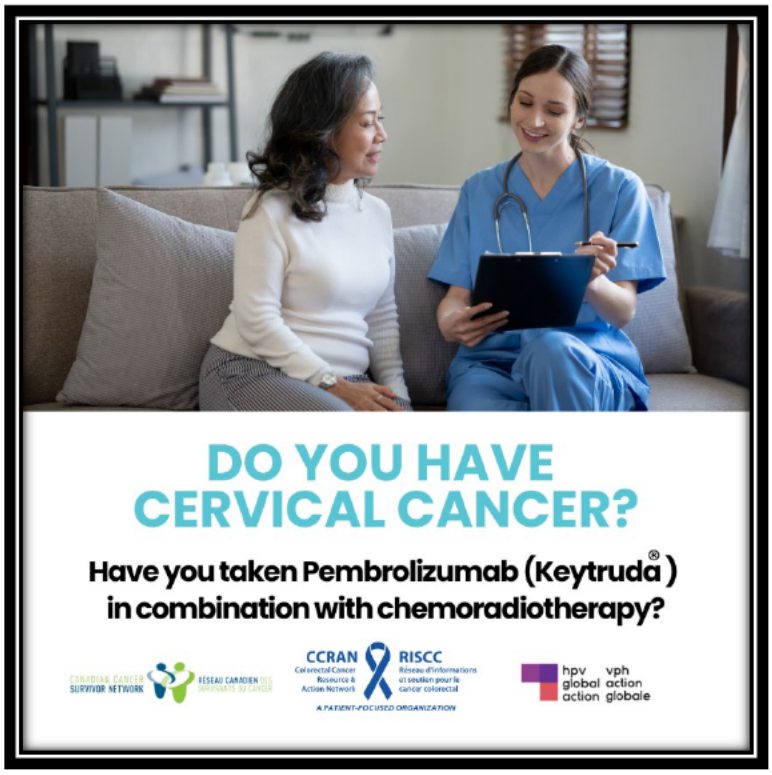
CANADIAN CANCER SURVIVOR NETWORK | RÉSEAU CANADIEN DES SURVIVANTS DU CANCER

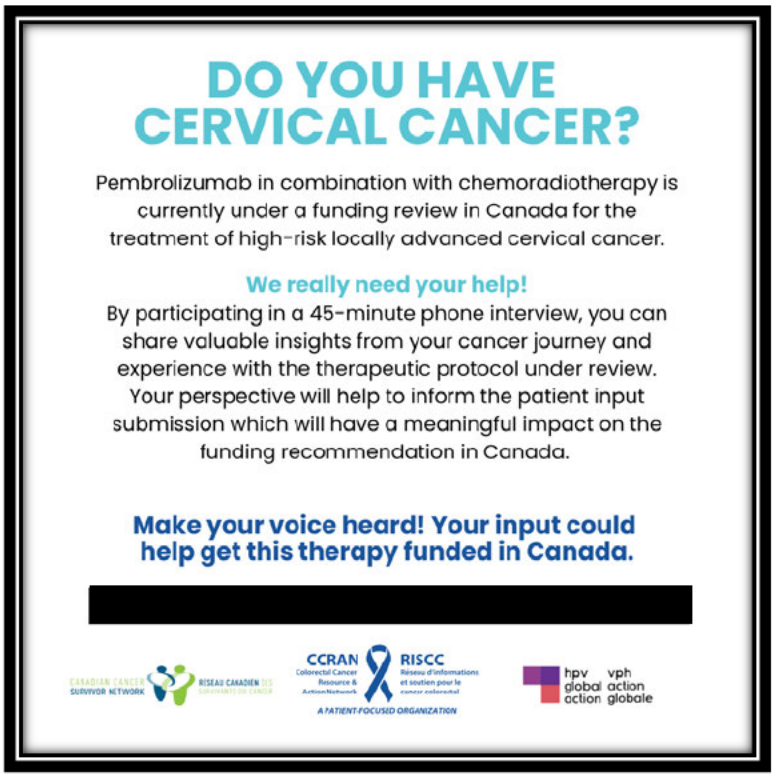
CCRAN Colorectal Cancer Resource & Action Network | RISCC Réseau d'informations et soutien pour le cancer colorectal

A PATIENT-FOCUSED ORGANIZATION

hpv global action | vph action globale

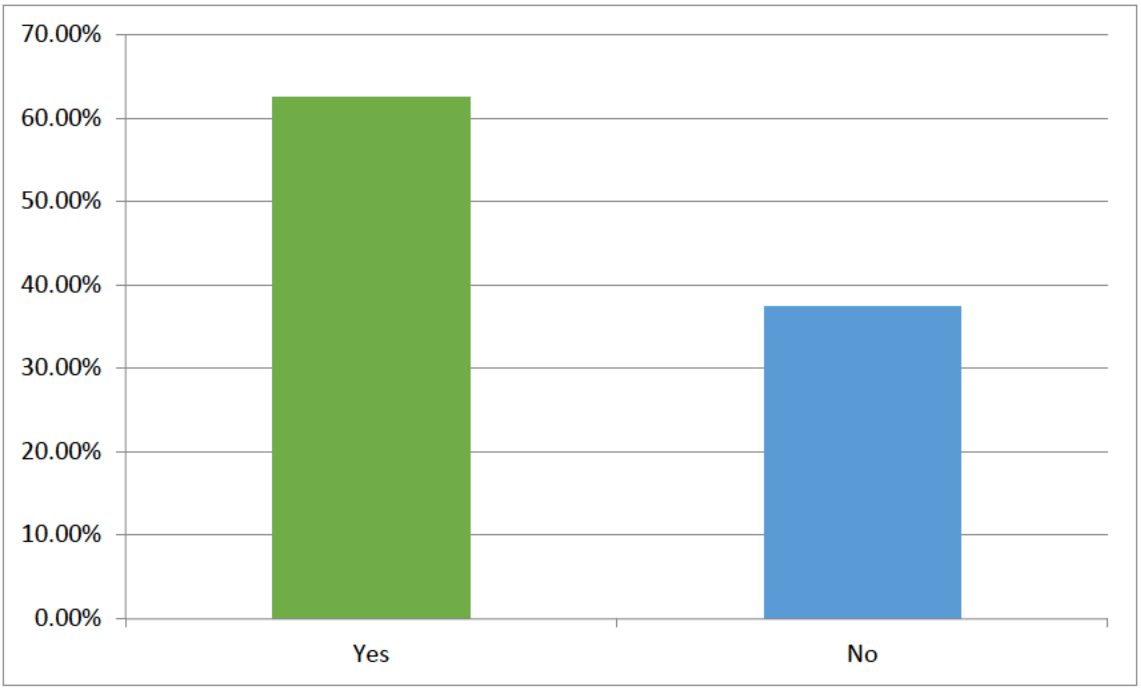
APPENDIX B: SOCIAL MEDIA PATIENT OUTREACH CAMPAIGN





Cervical Cancer Patient Survey Results

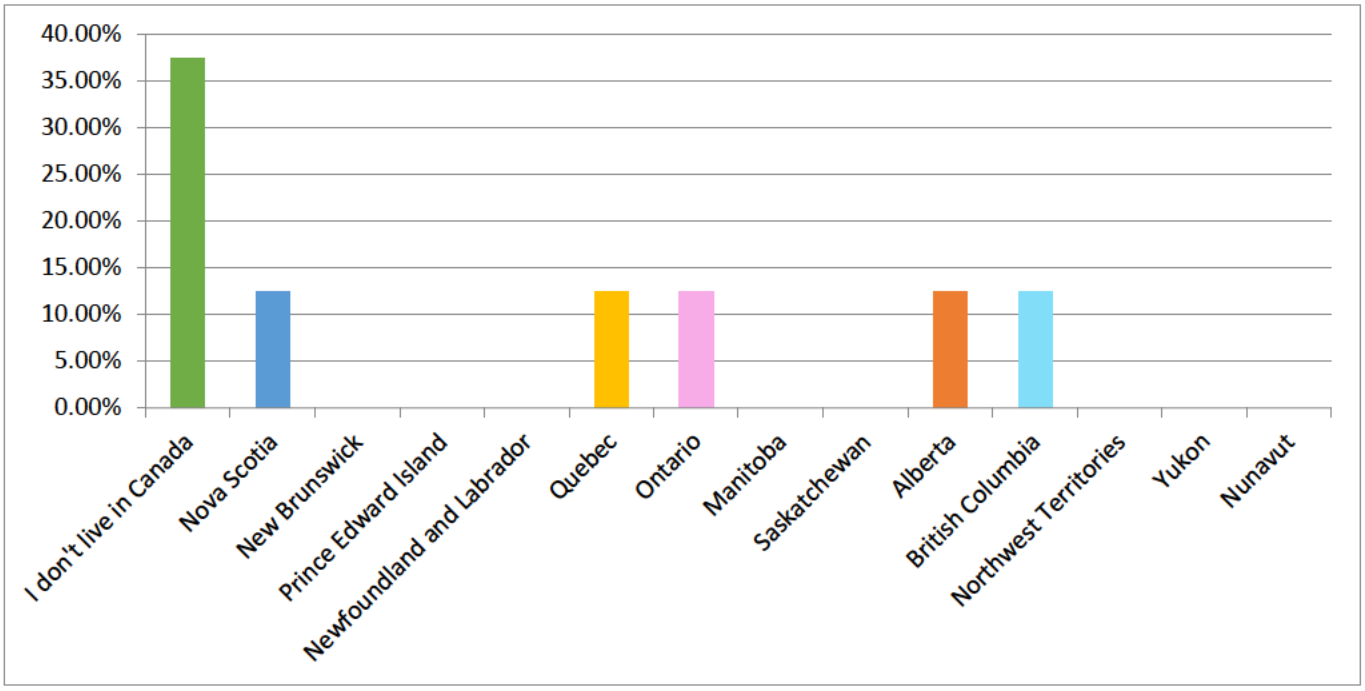
Q1 Are you a Canadian resident?



Answer Choices	Responses	
Yes	62.50%	5
No	37.50%	3
	Answered	**8**
	Skipped	**0**

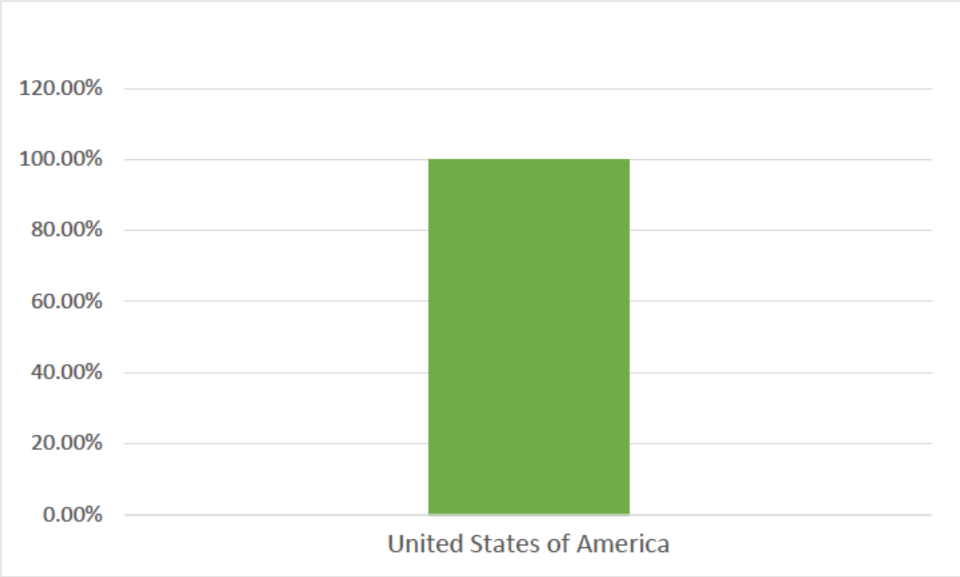
Cervical Cancer Patient Survey Results

Q2 If you are a resident of Canada, what province or territory do you reside in?



Answer Choices	Responses	
I don't live in Canada	37.50%	3
Nova Scotia	12.50%	1
New Brunswick	0.00%	0
Prince Edward Island	0.00%	0
Newfoundland and Labrador	0.00%	0
Quebec	12.50%	1
Ontario	12.50%	1
Manitoba	0.00%	0
Saskatchewan	0.00%	0
Alberta	12.50%	1
British Columbia	12.50%	1
Northwest Territories	0.00%	0
Yukon	0.00%	0
Nunavut	0.00%	0
	Answered	**8**
	Skipped	**0**

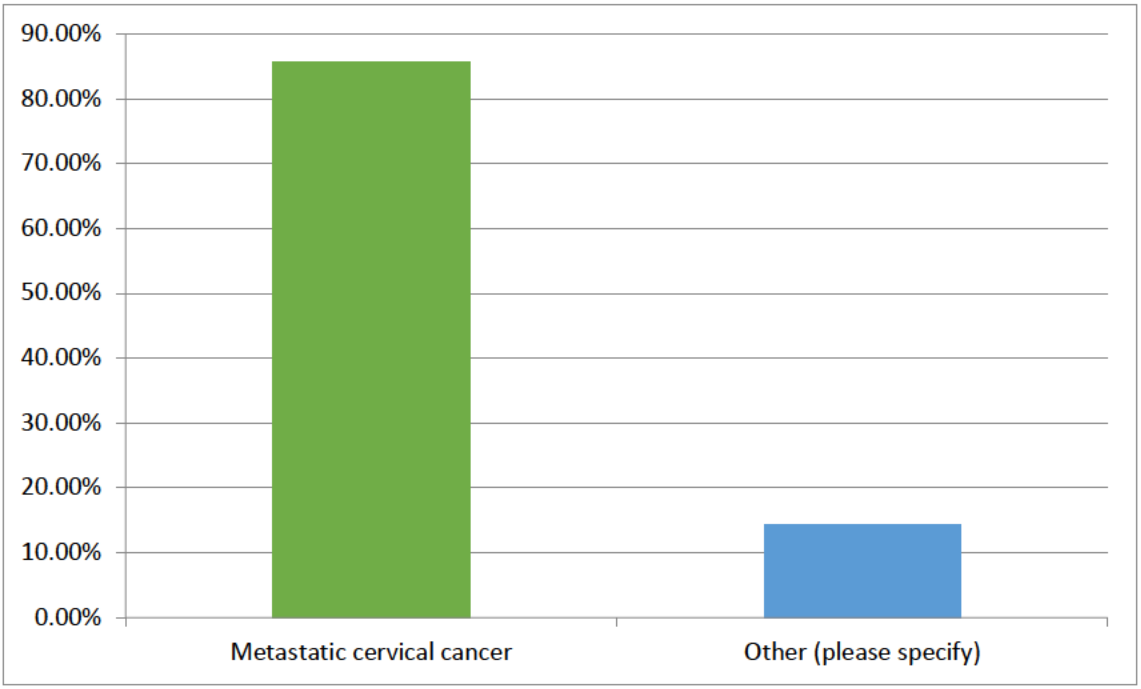
Q3 If you are not a resident of Canada, what country do you reside in?



Answer Choices	Responses	
United States of America	100.00%	3
	Answered	**3**
	Skipped	**5**

Cervical Cancer Patient Survey Results

Q4 What stage/type of cervical cancer do you have?

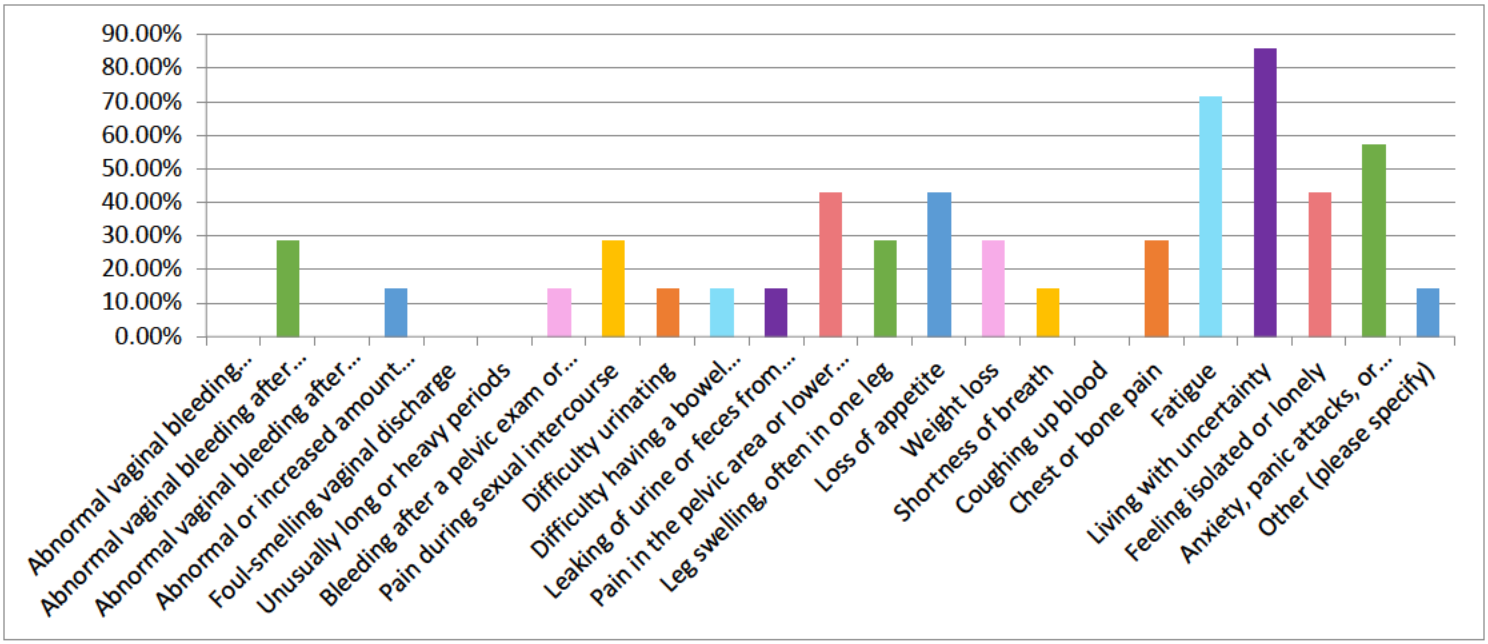


Answer Choices	Responses	
Metastatic cervical cancer	85.71%	6
Other (please specify)	14.29%	1
	Answered	**7**
	Skipped	**1**

Respondents	Response Date	Other (please specify)
1	Apr 07 2022	3C1 Squamous Cell Cervical Cancer

Cervical Cancer Patient Survey Results

Q5 What are the symptoms or problems you experience with cervical cancer that affect your day-to-day living and quality of life?



Answer Choices	Responses	
Abnormal vaginal bleeding between periods	0.00%	0
Abnormal vaginal bleeding after menopause	28.57%	2
Abnormal vaginal bleeding after sexual intercourse	0.00%	0
Abnormal or increased amount of vaginal discharge	14.29%	1
Foul-smelling vaginal discharge	0.00%	0
Unusually long or heavy periods	0.00%	0
Bleeding after a pelvic exam or vaginal douching	14.29%	1
Pain during sexual intercourse	28.57%	2
Difficulty urinating	14.29%	1
Difficulty having a bowel movement	14.29%	1
Leaking of urine or feces from the vagina	14.29%	1
Pain in the pelvic area or lower back that may go down one or both legs	42.86%	3
Leg swelling, often in one leg	28.57%	2
Loss of appetite	42.86%	3
Weight loss	28.57%	2
Shortness of breath	14.29%	1
Coughing up blood	0.00%	0
Chest or bone pain	28.57%	2
Fatigue	71.43%	5
Living with uncertainty	85.71%	6

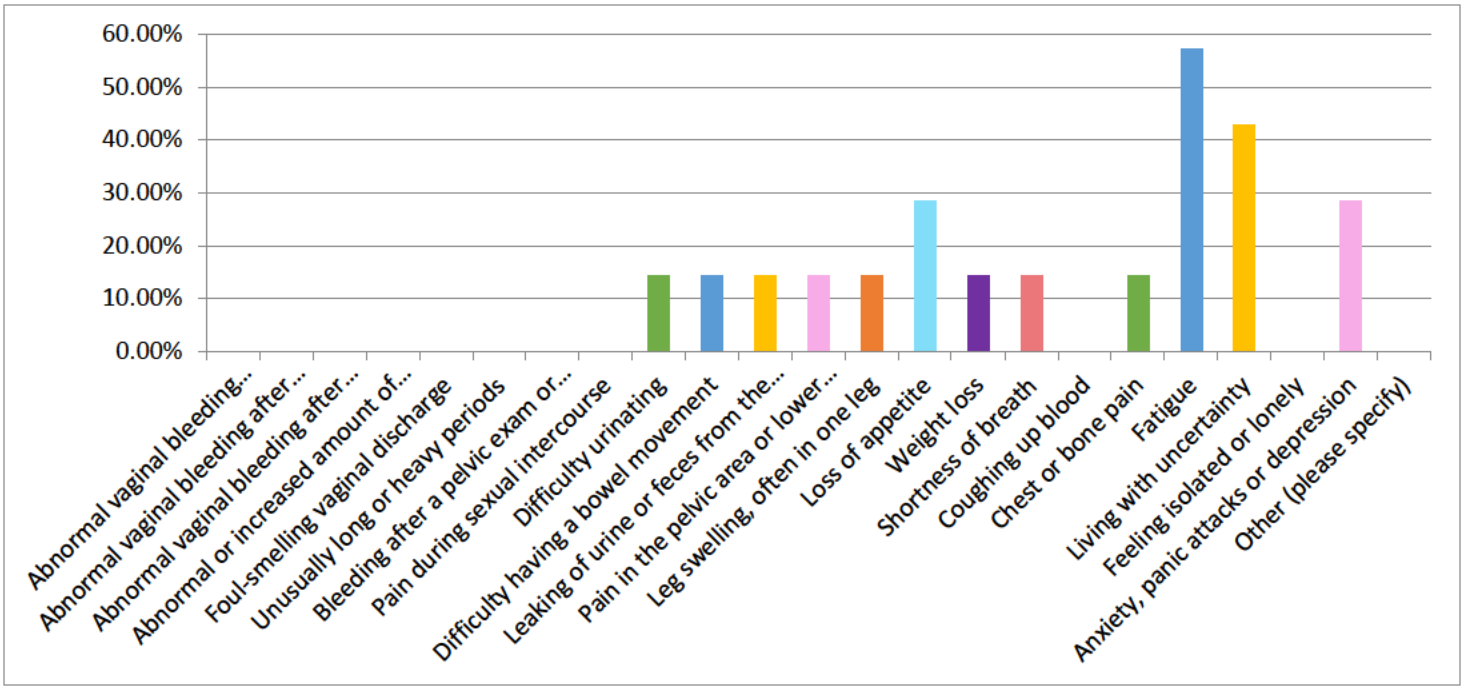
Cervical Cancer Patient Survey Results

Feeling isolated or lonely	42.86%	3
Anxiety, panic attacks, or depression	57.14%	4
Other (please specify)	14.29%	1
	Answered	**7**
	Skipped	**1**

Respondents	Response Date	Other (please specify)
1	Apr 11 2022	Chronic fatigue syndrom, neurologic pain, emotional disregulation caused probably by Cisplatine.

Cervical Cancer Patient Survey Results

Q6 Of the symptoms you checked above, which are the most important to you to control? Please pick your top 3:

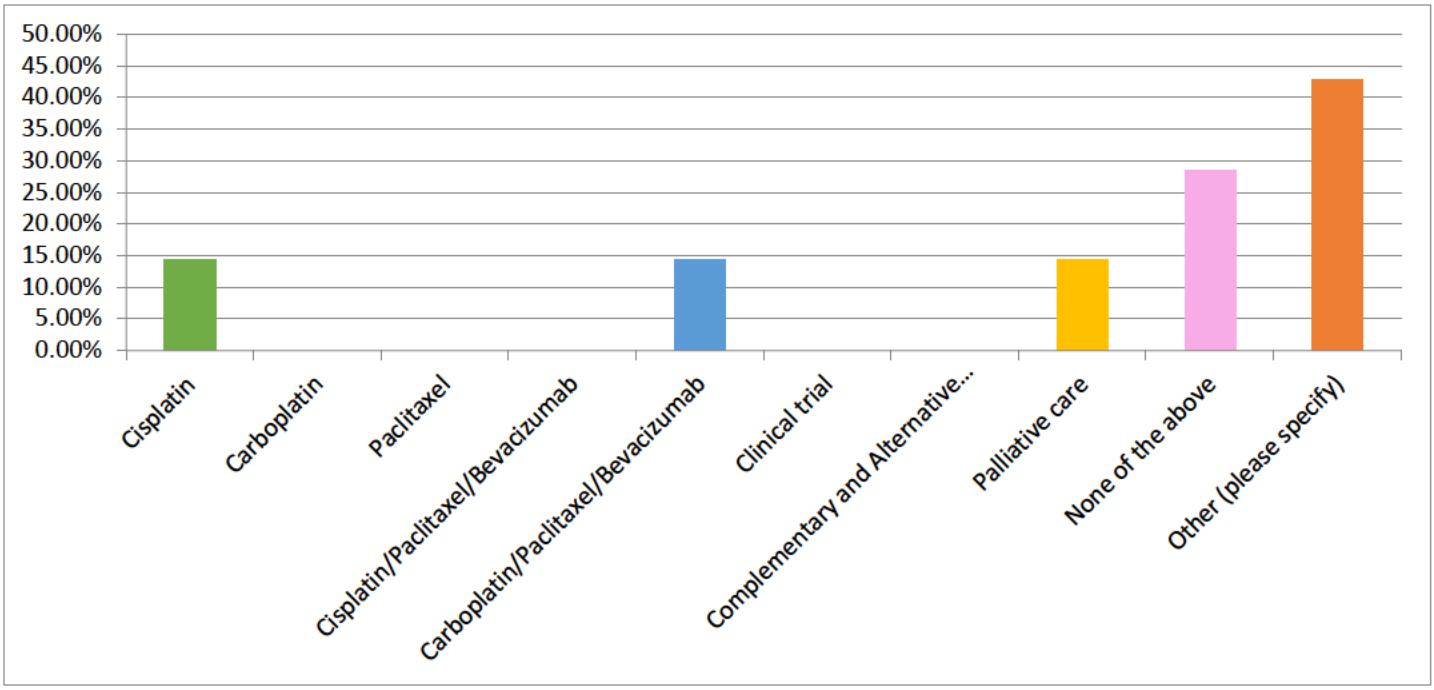


Answer Choices	Responses	
Abnormal vaginal bleeding between periods	0.00%	0
Abnormal vaginal bleeding after menopause	0.00%	0
Abnormal vaginal bleeding after sexual intercourse	0.00%	0
Abnormal or increased amount of vaginal discharge	0.00%	0
Foul-smelling vaginal discharge	0.00%	0
Unusually long or heavy periods	0.00%	0
Bleeding after a pelvic exam or vaginal douching	0.00%	0
Pain during sexual intercourse	0.00%	0
Difficulty urinating	14.29%	1
Difficulty having a bowel movement	14.29%	1
Leaking of urine or feces from the vagina	14.29%	1
Pain in the pelvic area or lower back that may go down one or both legs	14.29%	1
Leg swelling, often in one leg	14.29%	1
Loss of appetite	28.57%	2
Weight loss	14.29%	1
Shortness of breath	14.29%	1
Coughing up blood	0.00%	0
Chest or bone pain	14.29%	1
Fatigue	57.14%	4
Living with uncertainty	42.86%	3

Feeling isolated or lonely	0.00%	0
Anxiety, panic attacks or depression	28.57%	2
Other (please specify)	0.00%	0
	Answered	**7**
	Skipped	**1**

Cervical Cancer Patient Survey Results

Q7 What therapies/treatments are you currently using to treat cervical cancer? Please check all that apply.

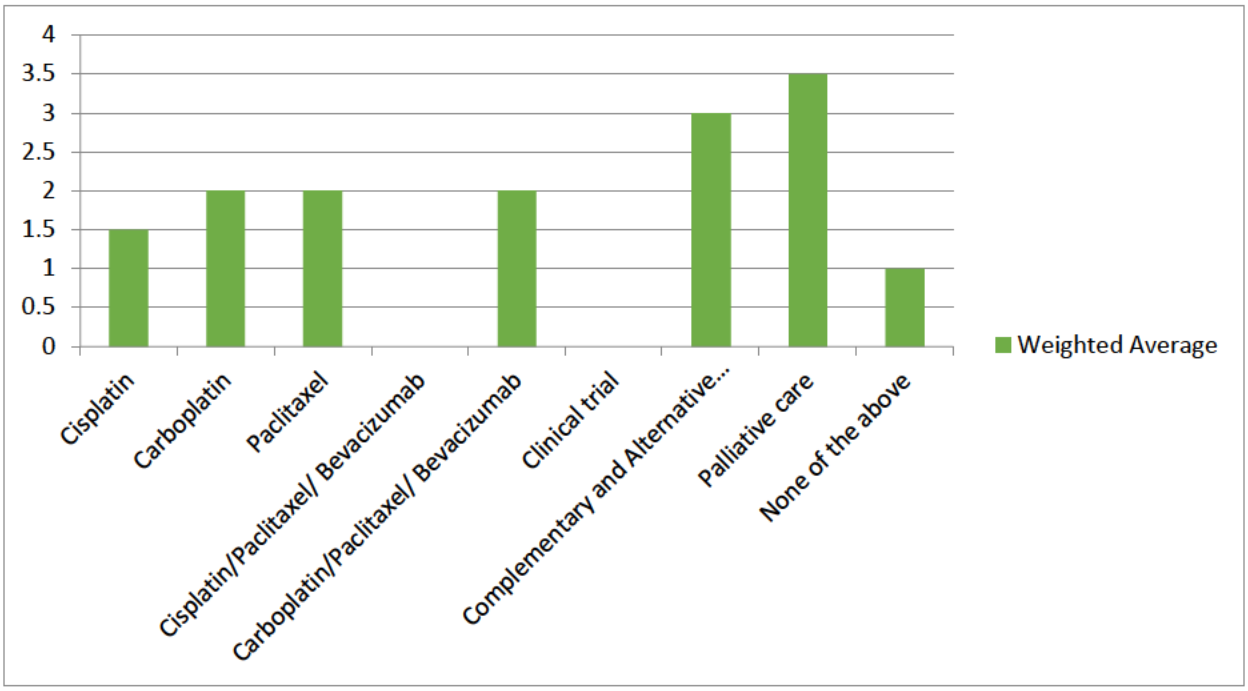


Answer Choices	Responses	
Cisplatin	14.29%	1
Carboplatin	0.00%	0
Paclitaxel	0.00%	0
Cisplatin/Paclitaxel/Bevacizumab	0.00%	0
Carboplatin/Paclitaxel/Bevacizumab	14.29%	1
Clinical trial	0.00%	0
Complementary and Alternative Medicines	0.00%	0
Palliative care	14.29%	1
None of the above	28.57%	2
Other (please specify)	42.86%	3
	Answered	**7**
	Skipped	**1**

Respondents	Response Date	Other (please specify)
1	Apr 11 2022	This is my second recurrence. Have had cisplatin, carboplatin, paclitaxel in the past. Am currently using alternative methods and staying current with my oncologist. Have permanent chest tubes for ease of breathing.
2	Apr 11 2022	In remission.
3	Apr 07 2022	Keytruda

Cervical Cancer Patient Survey Results

Q8 Out of your selections above, how effective have the therapies/treatments been at controlling your cancer? Please check all that apply.



Answer Choices	Responses	
	Very effective	
Cisplatin	50.00%	2
Carboplatin	0.00%	0
Paclitaxel	0.00%	0
Cisplatin/Paclitaxel/ Bevacizumab	0.00%	0
Carboplatin/Paclitaxel/ Bevacizumab	0.00%	0
Clinical trial	0.00%	0
Complementary and Alternative Medicines	0.00%	0
Palliative care	0.00%	0
None of the above	100.00%	1
Other (please specify)		

Cervical Cancer Patient Survey Results

Answer Choices	Responses	
	Somewhat effective	
Cisplatin	50.00%	2
Carboplatin	100.00%	2
Paclitaxel	100.00%	2
Cisplatin/Paclitaxel/ Bevacizumab	0.00%	0
Carboplatin/Paclitaxel/ Bevacizumab	100.00%	1
Clinical trial	0.00%	0
Complementary and Alternative Medicines	0.00%	0
Palliative care	0.00%	0
None of the above	0.00%	0
Other (please specify)		

Answer Choices	Responses	
	Not very effective	
Cisplatin	0.00%	0
Carboplatin	0.00%	0
Paclitaxel	0.00%	0
Cisplatin/Paclitaxel/ Bevacizumab	0.00%	0
Carboplatin/Paclitaxel/ Bevacizumab	0.00%	0
Clinical trial	0.00%	0
Complementary and Alternative Medicines	100.00%	1
Palliative care	50.00%	1
None of the above	0.00%	0
Other (please specify)		

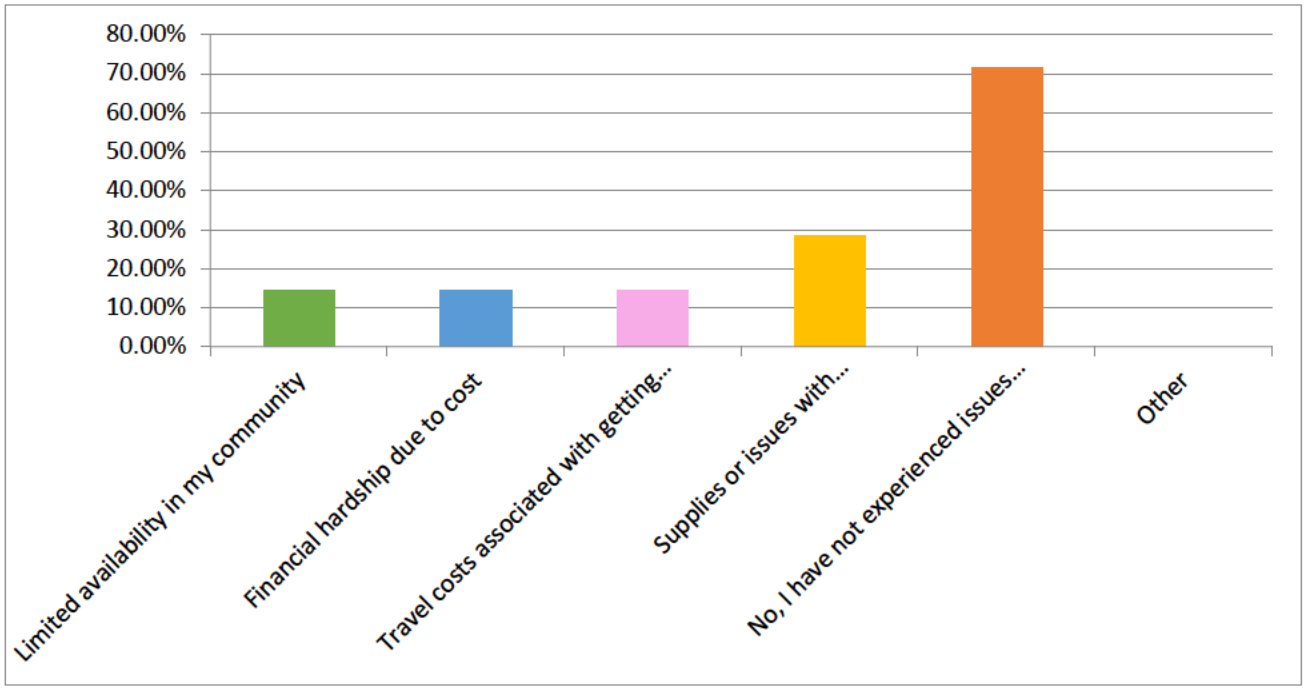
Answer Choices	Responses	
	Not effective at all	
Cisplatin	0.00%	0
Carboplatin	0.00%	0
Paclitaxel	0.00%	0
Cisplatin/Paclitaxel/ Bevacizumab	0.00%	0
Carboplatin/Paclitaxel/ Bevacizumab	0.00%	0
Clinical trial	0.00%	0
Complementary and Alternative Medicines	0.00%	0
Palliative care	50.00%	1
None of the above	0.00%	0
Other (please specify)		

Cervical Cancer Patient Survey Results

Answer Choices	Total	Weighted Average
Cisplatin	4	1.5
Carboplatin	2	2
Paclitaxel	2	2
Cisplatin/Paclitaxel/ Bevacizumab	0	0
Carboplatin/Paclitaxel/ Bevacizumab	1	2
Clinical trial	0	0
Complementary and Alternative Medicines	1	3
Palliative care	2	3.5
None of the above	1	1
Other (please specify)	2	
	Answered	**7**
	Skipped	**1**

Respondents	Response Date	Other (please specify)
1	Apr 11 2022	Radiotherapy and SBRT (very effective)
2	Apr 07 2022	Keytruda- very effective

Q9 Have you had issues accessing current therapy? If yes, please check all reasons that apply.

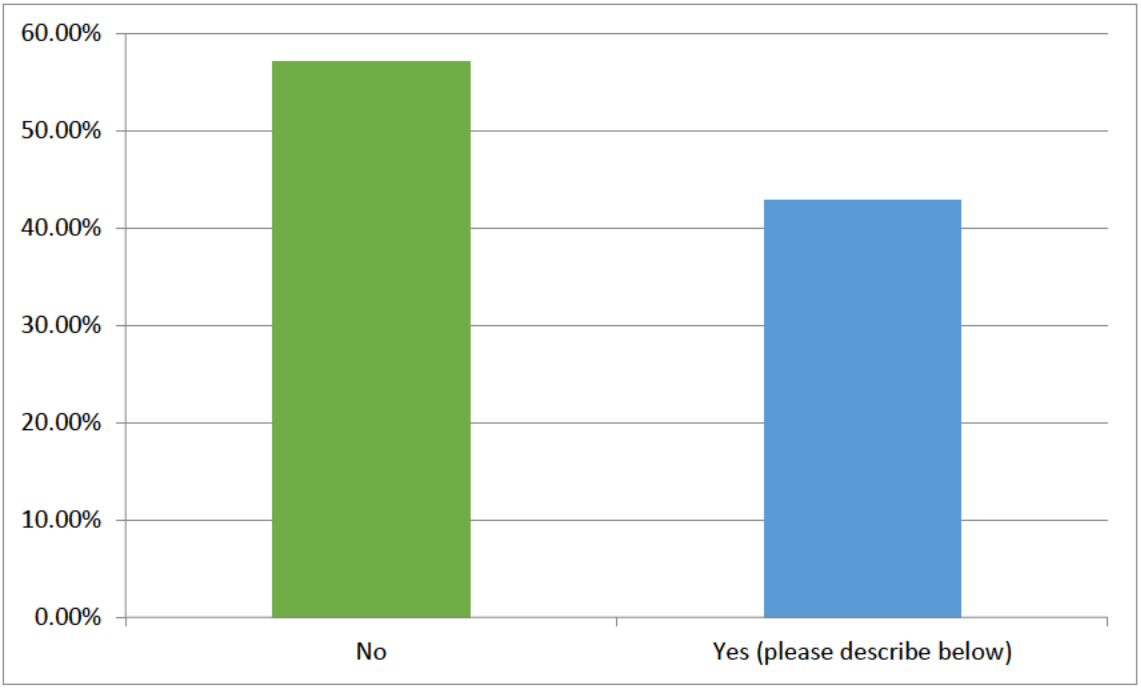


Answer Choices	Responses	
Limited availability in my community	14.29%	1
Financial hardship due to cost	14.29%	1
Travel costs associated with getting therapy/treatment	14.29%	1
Supplies or issues with administration	28.57%	2
No, I have not experienced issues accessing my therapy	71.43%	5
Other	0.00%	0
Other (please specify)		1
	Answered	**7**
	Skipped	**1**

Respondents	Response Date	Other (please specify)
1	Apr 11 2022	Impossible to receive Bevacizumab in 2015 (not approved by INESSS) Impossible to access genomic testing in 2015. No clinical trial available at my hospital (CHUM).

Cervical Cancer Patient Survey Results

Q10 Are there any needs in your current therapy that are not being met?



Answer Choices	Responses	
No	57.14%	4
Yes (please describe below)	42.86%	3
	Answered	**7**
	Skipped	**1**

Respondents	Response Date	Description
1	Apr 11 2022	Controlling lymphedema.
2	Apr 11 2022	Would like to access genomic testing like what is offered by Foundation Medecine (https://www.foundationmedicine.com/press-releases/810ab983-14c8-425e-bb16-1eeae7aba5d6) Would like to access scientific in order to decide which clinical trial is the best for my individual needs (I contact Cancer Commons - a US non-profit organisation for that)
3	Apr 11 2022	xyz

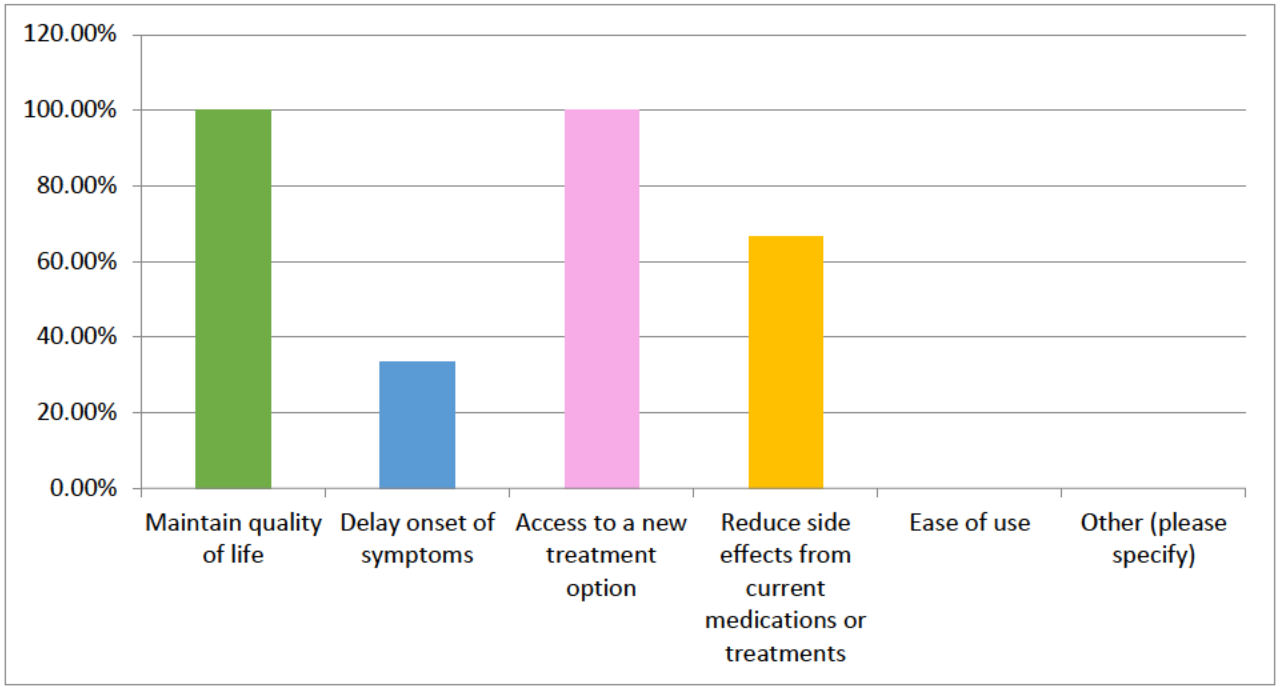
Q11 EXPECTATIONS OF A NEW DRUG: Please complete this question only if you have NOT been treated with Keytruda (pembrolizumab).

Based on the needs in the previous question, how much of an improvement would be needed from the new drug to make it better than current treatment? Please describe:

Respondents	Response Date	Responses
1	Apr 11 2022	Any improvement would help
2	Apr 11 2022	- Genomic testing would give an idea of which drug to use - Having access to the best clinical trial for my personnal situation, anywhere in Canada. - Two drugs are better than a single one. - Scientific data on survival and quality of life.
3	Apr 07 2022	As of right now, my cancer is controlled. If the cancer spreads, Keytruda would be an option to control or prevent further spread
	Answered	**3**
	Skipped	**5**

Q12 EXPECTIONS OF A NEW DRUG: Please complete this question only if you have NOT been treated with Keytruda (pembrolizumab).

Which of the following issues would you hope that a new drug would address to manage your disease? Please check all that apply.



Answer Choices	Responses	
Maintain quality of life	100.00%	3
Delay onset of symptoms	33.33%	1
Access to a new treatment option	100.00%	3
Reduce side effects from current medications or treatments	66.67%	2
Ease of use	0.00%	0
Other (please specify)	0.00%	0
Answered		**3**
Skipped		**5**

Q13 EXPECTIONS OF A NEW DRUG: Please complete this question only if you have NOT been treated with Keytruda (pembrolizumab).

What side effects or symptoms would you be willing to tolerate in a new drug? Please describe.

Respondents	Response Date	Responses
1	Apr 11 2022	Hair loss, weakness, fatigue,
2	Apr 11 2022	What could be worst than chemo? ;)
3	Apr 07 2022	Honestly anything if it were able to extend my life and help me fight
	Answered	**3**
	Skipped	**5**

Q14 EXPERIENCE WITH Keytruda (pembrolizumab): Please complete this question only if you HAVE been treated with Keytruda (pembrolizumab).

Please describe the positive and negative effects of Keytruda (pembrolizumab), in your experience.

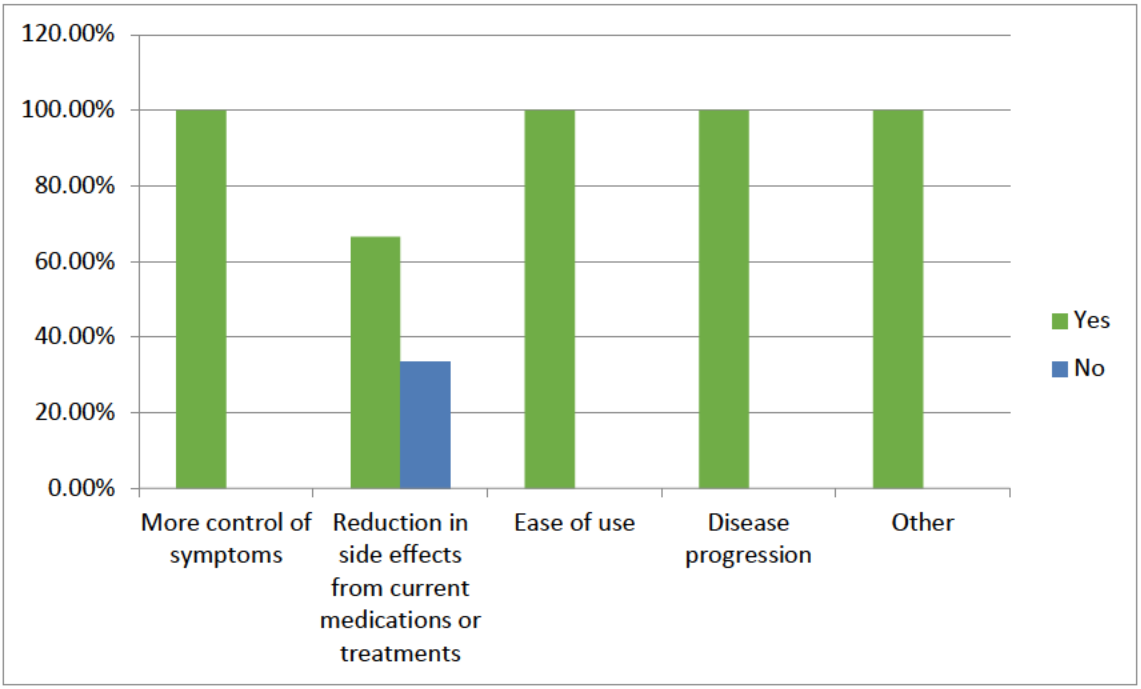
Answer Choices	Responses	
Positive Effects	100.00%	3
Negative Effects	66.67%	2
	Answered	**3**
	Skipped	**5**

Respondents	Response Date	Positive Effects
1	May 09 2022	Minimal side effects. it was great. i barely felt anything at all.
2	Apr 07 2022	My tumor has reduced to being NED in 9 months..
3	Apr 07 2022	No evidence of disease

Respondents	Response Date	Negative Effects
1	May 09 2022	i could only get it in a clinical trial. i can only have a set number of treatments.
2	Apr 07 2022	
3	Apr 07 2022	Grade 2 interstitial nephritis, resolved

Q15 EXPERIENCE WITH Keytruda (pembrolizumab): Please complete this question only if you HAVE been treated with Keytruda (pembrolizumab).

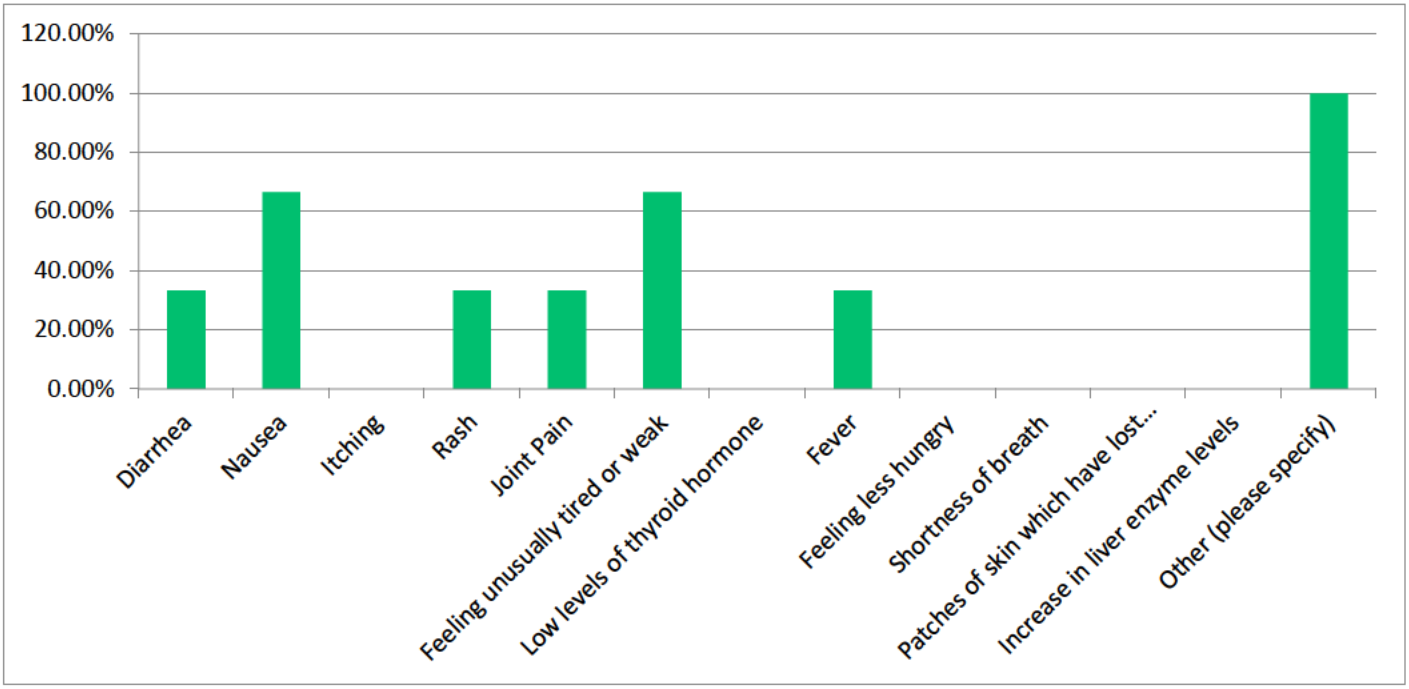
Are you better able to manage the following issues on Keytruda (pembrolizumab) than on your previous therapy?



	Yes		No		Total
More control of symptoms	100.00%	3	0.00%	0	3
Reduction in side effects from current medications or treatments	66.67%	2	33.33%	1	3
Ease of use	100.00%	3	0.00%	0	3
Disease progression	100.00%	3	0.00%	0	3
Other	100.00%	1	0.00%	0	1
Other (please specify)					1
				Answered	**3**
				Skipped	**5**

Q16 EXPERIENCE WITH Keytruda (pembrolizumab): Please complete this question only if you HAVE been treated with Keytruda (pembrolizumab).

What adverse effects were caused by Keytruda (pembrolizumab)?



Answer Choices	Responses	
Diarrhea	33.33%	1
Nausea	66.67%	2
Itching	0.00%	0
Rash	33.33%	1
Joint Pain	33.33%	1
Feeling unusually tired or weak	66.67%	2
Low levels of thyroid hormone	0.00%	0
Fever	33.33%	1
Feeling less hungry	0.00%	0
Shortness of breath	0.00%	0
Patches of skin which have lost colour (vitiligo)	0.00%	0
Increase in liver enzyme levels	0.00%	0
Other (please specify)	100.00%	3
Answered		**3**
Skipped		**5**

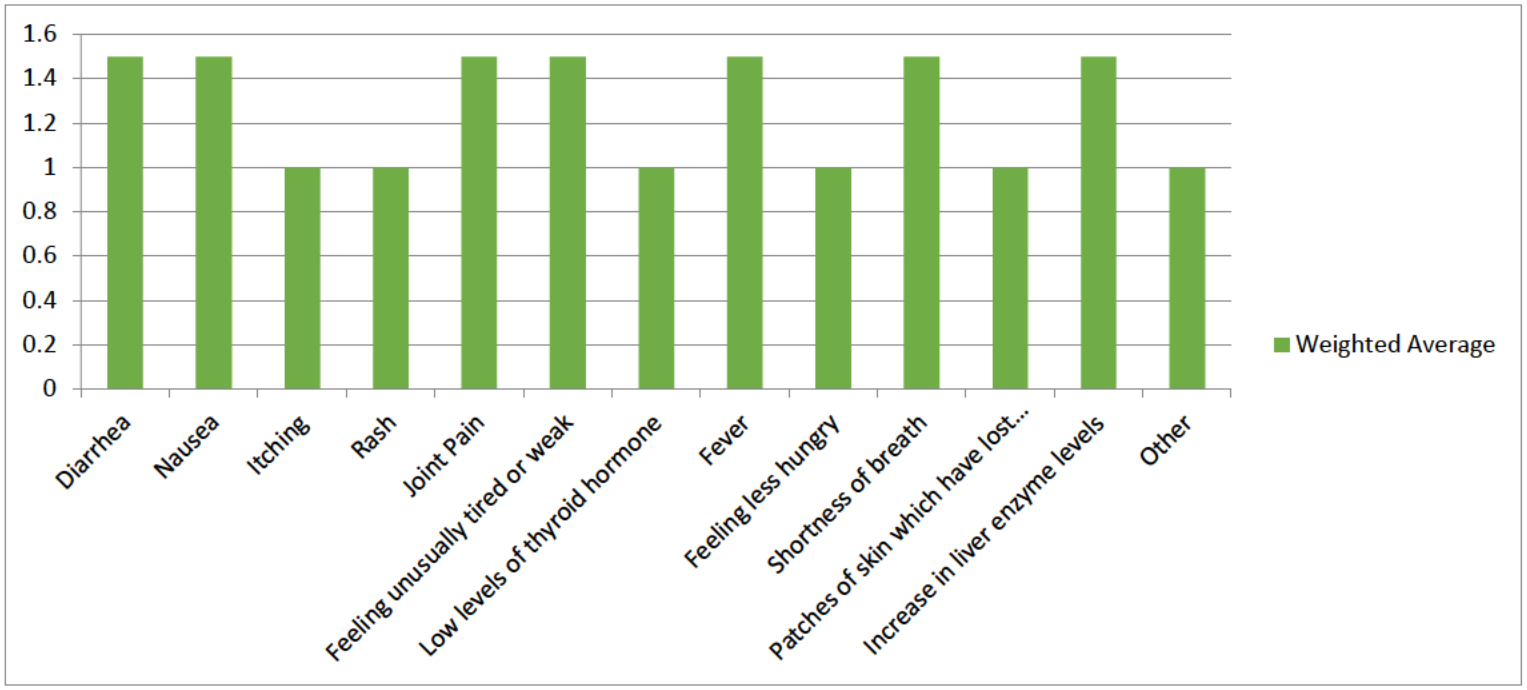
Cervical Cancer Patient Survey Results

Respondents	Response Date	Other (please specify)
1	May 09 2022	i didn't really have any side effects
2	Apr 07 2022	Dry skin and nail breakage.
3	Apr 07 2022	Interstitial nephritis

Cervical Cancer Patient Survey Results

Q17 EXPERIENCE WITH Keytruda (pembrolizumab): Please complete this question only if you HAVE been treated with Keytruda (pembrolizumab).

Which adverse effects are acceptable and which ones are not?



	Acceptable		Not acceptable		Total	Weighted Average
Diarrhea	50.00%	1	50.00%	1	2	1.5
Nausea	50.00%	1	50.00%	1	2	1.5
Itching	100.00%	2	0.00%	0	2	1
Rash	100.00%	2	0.00%	0	2	1
Joint Pain	50.00%	1	50.00%	1	2	1.5
Feeling unusually tired or weak	50.00%	1	50.00%	1	2	1.5
Low levels of thyroid hormone	100.00%	2	0.00%	0	2	1
Fever	50.00%	1	50.00%	1	2	1.5
Feeling less hungry	100.00%	2	0.00%	0	2	1
Shortness of breath	50.00%	1	50.00%	1	2	1.5
Patches of skin which have lost colour (vitiligo)	100.00%	2	0.00%	0	2	1
Increase in liver enzyme levels	50.00%	1	50.00%	1	2	1.5
Other	100.00%	2	0.00%	0	2	1
Other (please specify)					1	
					Answered	**3**
					Skipped	**5**

Cervical Cancer Patient Survey Results

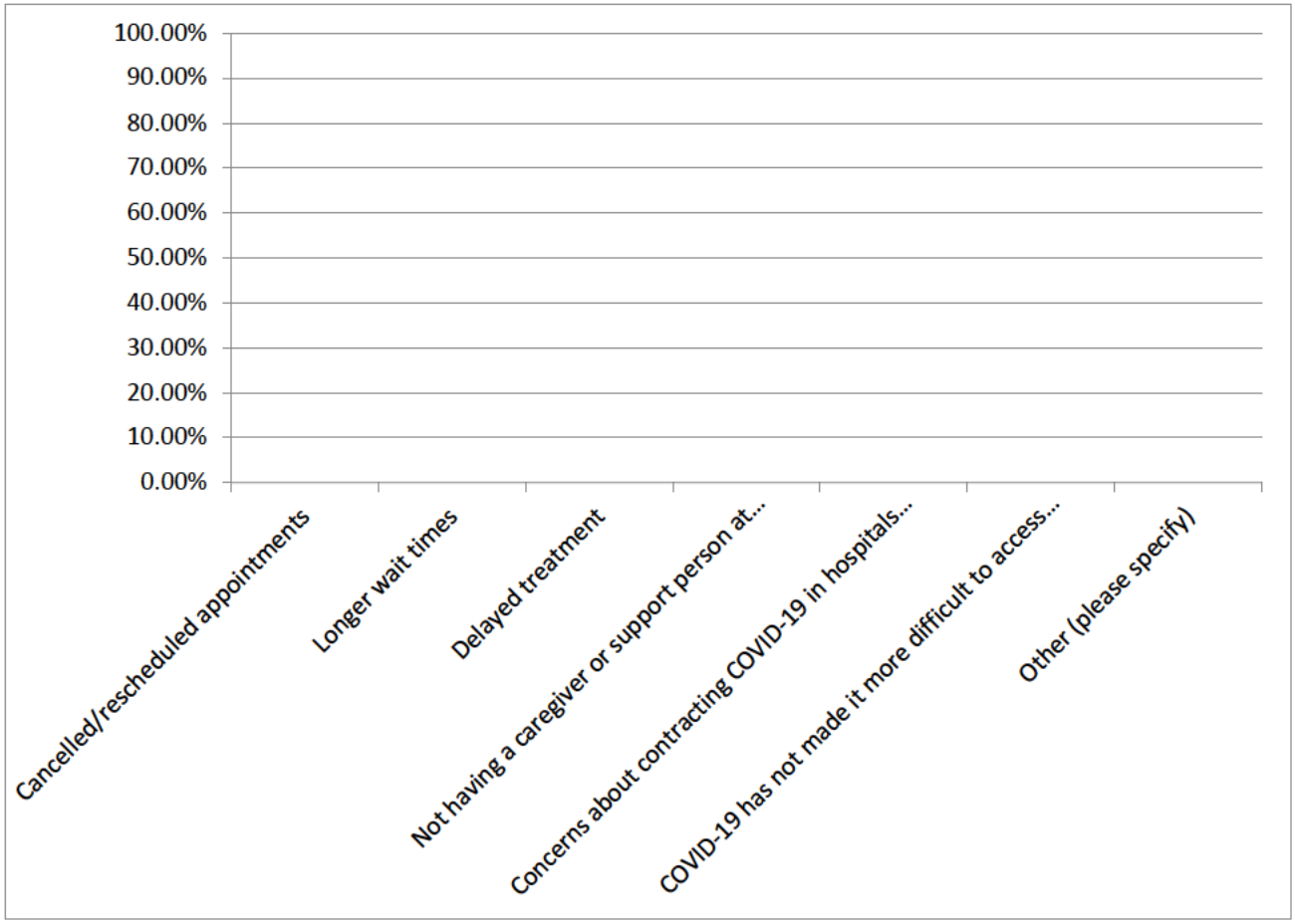
Respondents	Response Date	Other (please specify)
1	May 09 2022	didn't really experience anything

Q18 EXPERIENCE WITH Keytruda (pembrolizumab): Please complete this question only if you HAVE been treated with Keytruda (pembrolizumab).

What expectations do you have for your long-term health and well-being as a result of taking Keytruda (pembrolizumab)?

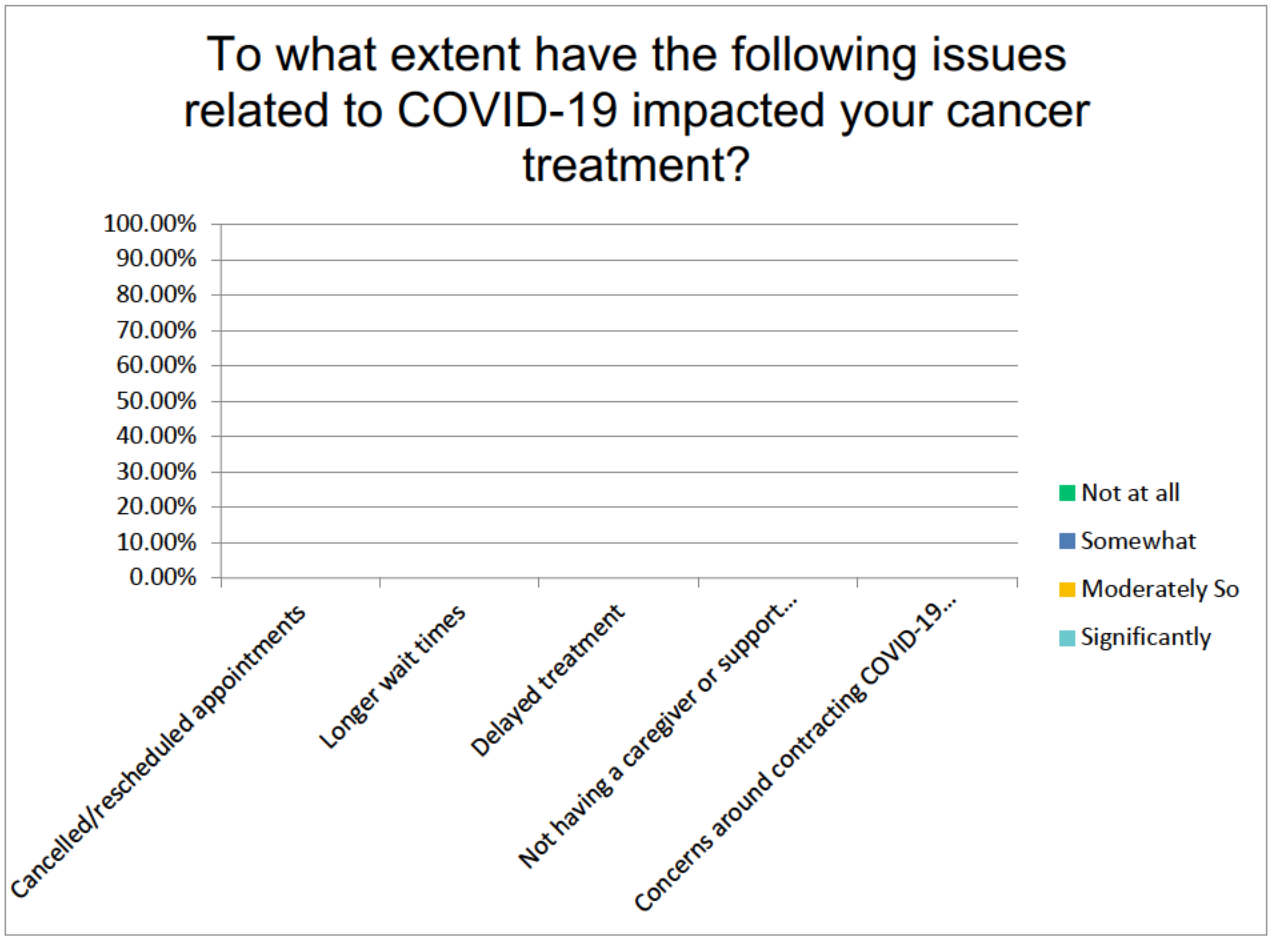
Respondents	Response Date	Responses
1	May 09 2022	to continue to live as long as i can with good quality of life. this drug has been wonderful and easy for me. it really hasnt been toxic or made me sick like the chemos. i hope i get to stay on it for a long time.
2	Apr 07 2022	Better quality of life and not having my cancer spread.
3	Apr 07 2022	No evidence of disease!
	Answered	**3**
	Skipped	**5**

Q19 How has COVID-19 made it more difficult for you to access treatment?



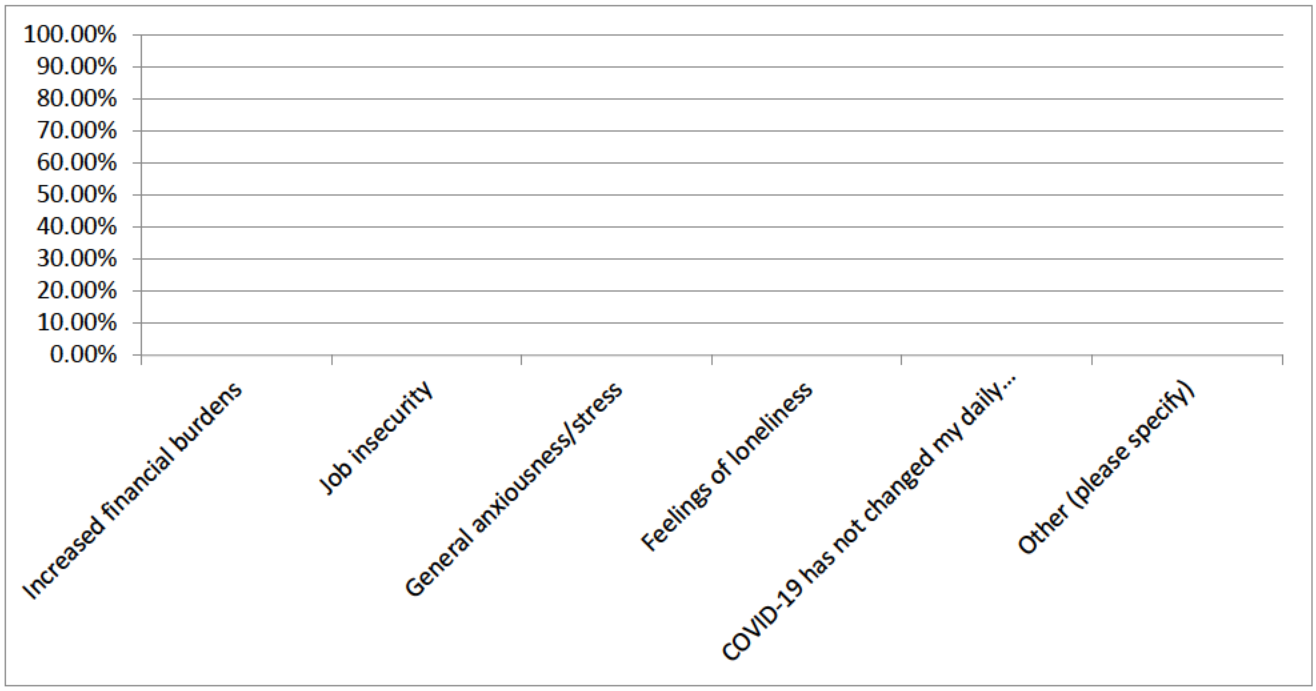
Answer Choices	Responses	
Cancelled/rescheduled appointments	0.00%	0
Longer wait times	0.00%	0
Delayed treatment	0.00%	0
Not having a caregiver or support person at appointments	0.00%	0
Concerns about contracting COVID-19 in hospitals or clinics	0.00%	0
COVID-19 has not made it more difficult to access treatment	0.00%	0
Other (please specify)	0.00%	0
Answered		**0**
Skipped		**8**

Q20 To what extent have the following issues related to COVID-19 impacted your cancer treatment?



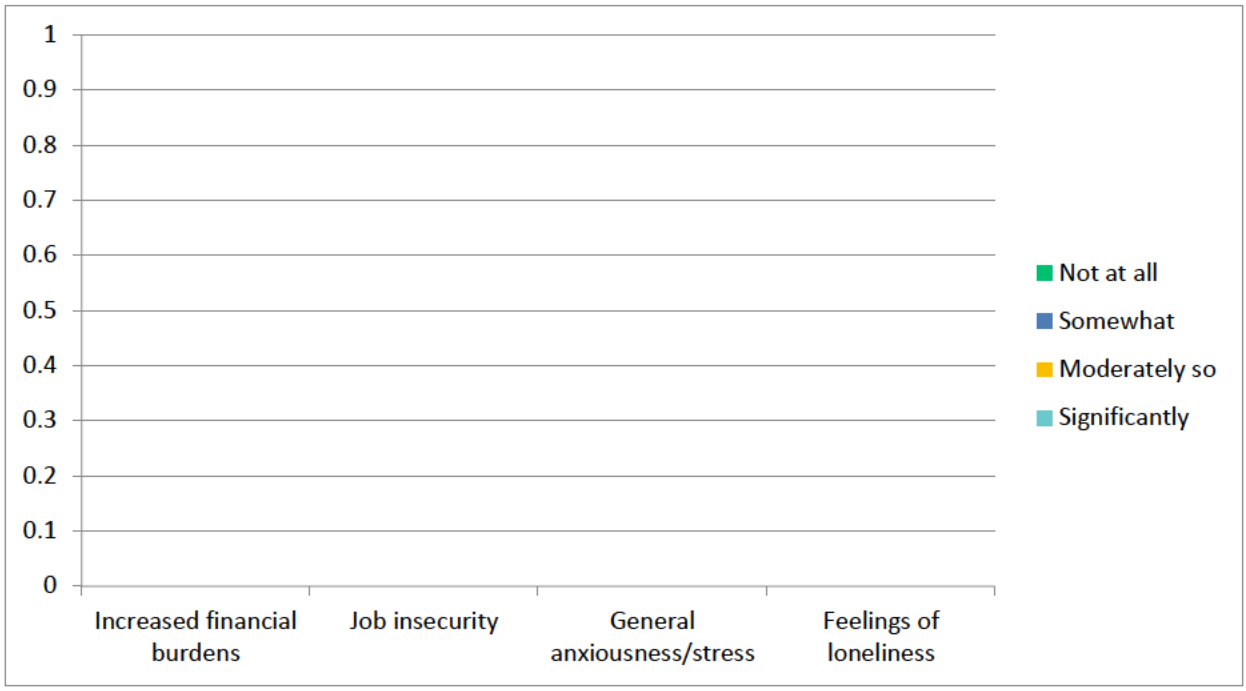
	Not at all	Somewhat	Moderately So	Significantly	Total
Cancelled/rescheduled appointments	0	0	0	0	0
Longer wait times	0	0	0	0	0
Delayed treatment	0	0	0	0	0
Not having a caregiver or support person at appointments	0	0	0	0	0
Concerns around contracting COVID-19 in hospitals or clinics	0	0	0	0	0
Other (please specify)					0
			Answered		**0**
			Skipped		**8**

Q21 In what ways has COVID-19 changed your daily life as a cervical cancer patient?



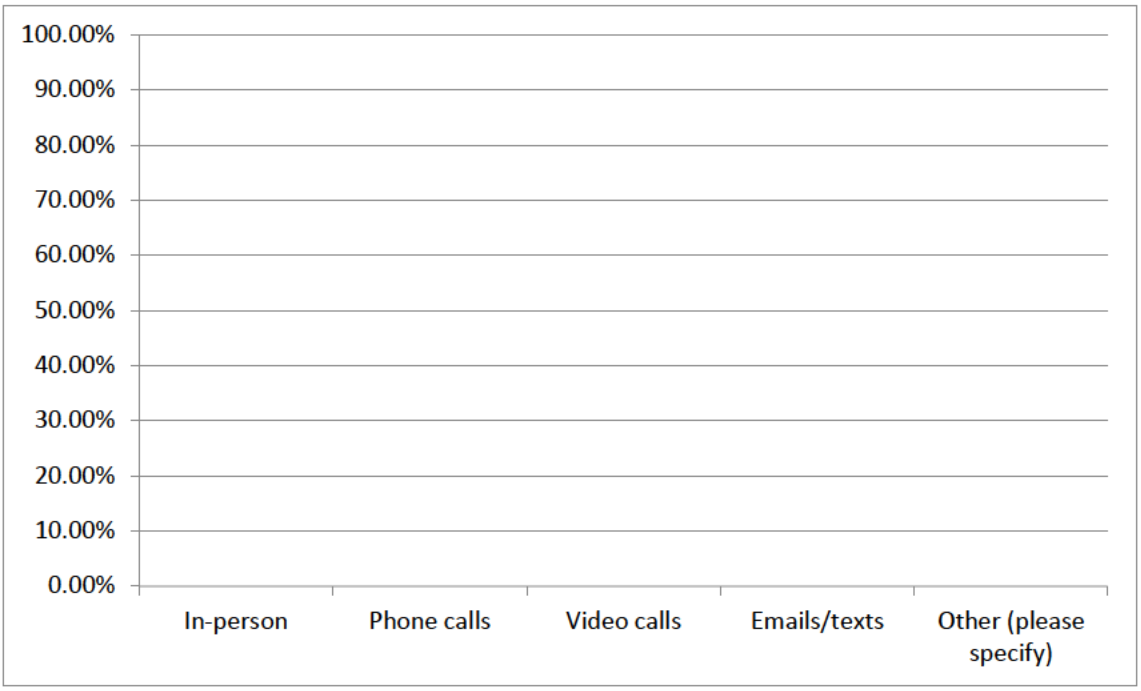
Answer Choices	Responses	
Increased financial burdens	0.00%	0
Job insecurity	0.00%	0
General anxiousness/stress	0.00%	0
Feelings of loneliness	0.00%	0
COVID-19 has not changed my daily life	0.00%	0
Other (please specify)	0.00%	0
	Answered	**0**
	Skipped	**8**

Q22 To what extent have the following issues related to COVID-19 impacted your daily life?



	Not at all	Somewhat	Moderately so	Significantly	Total
Increased financial burdens	0	0	0	0	0
Job insecurity	0	0	0	0	0
General anxiousness/stress	0	0	0	0	0
Feelings of loneliness	0	0	0	0	0
Other (please specify)					0
				Answered	**0**
				Skipped	**8**

Q23 How have you communicated with your doctor during the pandemic? Check all that apply.



Answer Choices	Responses	
In-person	0.00%	0
Phone calls	0.00%	0
Video calls	0.00%	0
Emails/texts	0.00%	0
Other (please specify)	0.00%	0
Answered		**0**
Skipped		**8**

Q24 If you have had virtual doctor appointments during the pandemic, have they been satisfactory? If not, please explain why.

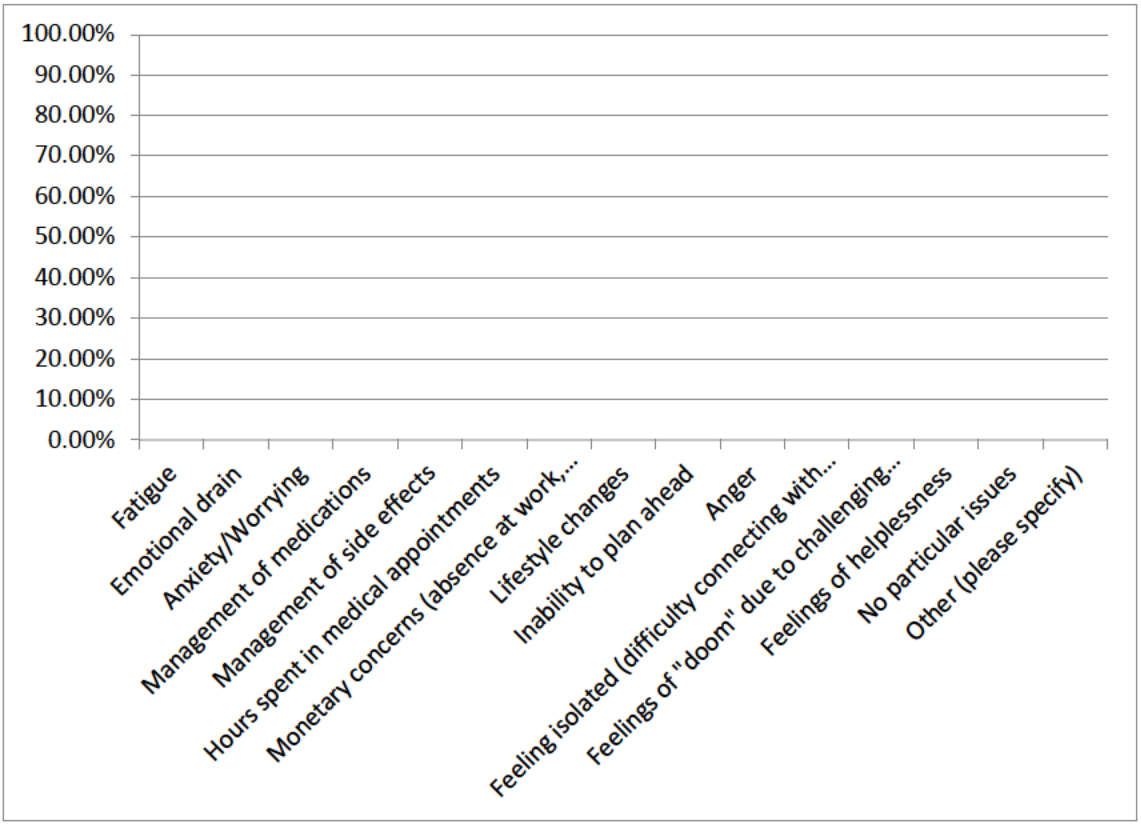
Answered	**0**
Skipped	**8**

Q25 Is there anything else that you would like to add or share with us before completing this survey?

Answered	**0**
Skipped	**8**

Q26 QUESTIONS FOR CAREGIVERS This section of the survey is for individuals who are caring for a loved one with Metastatic Cervical Cancer.

What are the issues you encounter or have encountered as a caregiver for someone with cervical cancer? Check all the apply.



Answer Choices	Responses	
Fatigue	0.00%	0
Emotional drain	0.00%	0
Anxiety/Worrying	0.00%	0
Management of medications	0.00%	0
Management of side effects	0.00%	0
Hours spent in medical appointments	0.00%	0
Monetary concerns (absence at work, driving expenses, etc.)	0.00%	0
Lifestyle changes	0.00%	0
Inability to plan ahead	0.00%	0
Anger	0.00%	0
Feeling isolated (difficulty connecting with friends, geographical remoteness)	0.00%	0
Feelings of "doom" due to challenging prognosis	0.00%	0
Feelings of helplessness	0.00%	0

No particular issues	0.00%	0
Other (please specify)	0.00%	0
	Answered	**0**
	Skipped	**8**

Q27 How has caring for someone with cervical cancer affected your daily routine or lifestyle?

Answered	**0**
Skipped	**8**

Q28 What are the most challenging adverse effects related to your loved one and their current therapy or treatment?

Answered	**0**
Skipped	**8**

Q29 Is there anything else that you would like to share with us about your experiences as a caregiver?

Answered	**0**
Skipped	**8**

CCRAN Colorectal Cancer Resource & Action Network
RISCC Réseau d'informations et soutien pour le cancer colorectal
A PATIENT-FOCUSED ORGANIZATION

APPENDIX D: PEMBROLIZUMAB + CHEMORADIATION CERVICAL CANCER PATIENT INTERVIEW DATA					
INTERVIEW QUESTION	**RESPONDENT A [PATIENT]**	**RESPONDENT B [PATIENT]**	**RESPONDENT C [PATIENT]**	**RESPONDENT D [PATIENT]**	**RESPONDENT E [CANADIAN PATIENT WHO HAD ACCESS TO PEMBROLIZUMAB DENIED]**
PART A: DEMOGRAPHICS/INFORMATION GATHERING					
1. Interview date, time & method	March 4, 2025; 12:00 pm ET; telephone interview	March 4, 2025; 3:00 pm ET; telephone interview	March 10, 2025; 10:00 am ET; telephone interview	March 12, 2025; 12:00 pm ET; telephone interview	March 13, 2025; 10:00 am ET; telephone interview
2. Patient's current age, age at diagnosis, gender identity	67; 63; female	44; 41; female	39; 27; female	56; 54; female	50, 48, female
3. City, province / state	Montreal, Quebec	Quincy, Massachusetts, USA	South Orange, New Jersey, USA	Airdrie, Alberta	Sault Ste Marie, Ontario
4. **A. MARITAL STATUS S/M/D/CL** **B. CHILDREN**	Common law No children	Married 1 daughter – age 21	Married No children	Married 2 children – 28 & 30	Married 2 daughters – 19 & 23
5. Outreach method: (Canadian clinician, US clinician, etc.)	Canadian Clinician	U.S. Patient Group	U.S. Patient Group	Facebook Support Group	U.S. Patient Group
6. Treatment centre	Montreal, Victoria Hospital, Glen Campus	Dana Farber	University Hospital, Newark NJ	Tom Baker Hospital	Sudbury North Health Sciences Cancer Center
PART B: DISEASE EXPERIENCE & EXPERIENCES WITH CURRENTLY AVAILABLE TREATMENTS					
7. When were you first diagnosed with cancer? And with what type of cancer? At which stage was your disease diagnosed?	"December 29, 2020; cervical cancer stage IIIb"	"July 19 2022; stage IVa cervical cancer, squamous cell"	"At age 27 I tested positive for HPV and started having dysplasia, so at some point that's considered stage 0 and then I was 34 when I had invasive cancer (stage IaI), and I've had 2 recurrences since then. I was still IaI with my 2nd recurrence, but my most recent recurrence this past year might be stage 4 since it recurred on my rectum. Cervical cancer."	"That would have been 2022, in April. Cervical. 3c2."	"April 2022. Cervical cancer, stage Ib2"

8. Were you symptomatic which led to investigations? Tell me a bit about your journey?	"I was getting blood every now and then. Nobody really caught it. I had gone to a couple of clinics and there was bullshit about it being post-menopausal and all that. Even my family doctor didn't push it, she was more interested in selling me Prolia for my bones. Then I just got so much pain, so there was no choice. I kept feeling like I had to urinate and there was no urine and then there was pain where the tumour was growing. It was the pain, I couldn't take the pain anymore so I went to the ER."	"My only symptom that was outwards that I noticed was frequent urination, everyone said I was getting older, I was diagnosed with a UTI 4 times. I was having to run to the bathroom every 5 minutes. Because of COVID I was having trouble getting into my primary care provider and when I did, they wanted me to wait from June to December for testing, so I switched primary care providers and got an ultrasound of my kidneys. It found a urinoma – they then sent me for CT and the found a 8 x 9 cm mass and lymph node involvement. I started out stage IIIb and they upped it to stage IVa as they weren't sure if it was going into my bladder."	"I tested positive for HPV at 27 and then was under very strict surveillance. I had had multiple LEEP procedures, like a little melon scoop of my cervix. Eventually there wasn't enough cervical tissue left and I had to have a hysterectomy. The hysterectomy was where they found the stage 1a1 cancer. I then had brachytherapy 9 months post-hysterectomy because I had persistent dysplasia on my vaginal cuff. That was 2020. Between the brachy and 2023 I was having laser therapies for the dysplasia on my vagina, vulva, and anus. I had a partial vaginectomy at 37 years old. They didn't get surgical margins, they got cut margins, so they unfortunately did cut the tumour in surgery. It was pretty close to my rectum and they were trying to avoid the rectum and need for ostomy. 9 months following surgery I was getting pain. I was denied PET scans by my insurance company. I waited for my appointment, and then they did a CT and it showed the recurrence. The tumour was on my rectum. I had a total pelvic exenteration. They took what was left of my vagina, my	"Just intermittent bleeding was the only symptom that I had. How do I even start? Of course, we just got through COVID, everything had been shut, you couldn't get in to see anybody. I finally saw a gynecologist and I was bleeding again, and she said go to the ER, and I went to the ER. I was having a little bit of lower back pain at the time I was diagnosed as well."	"I didn't have any symptoms at all. I was 48 at the time. I was in the initial stage OF menopause, and I wasn't having my cycle since 2019. Then in 2022 I had big blood clots discharged. That was crazy with not having a cycle for a long time. I went to my family doctor right away and they sent me for x-ray and ultrasound and nothing was wrong. And then they did a test and found out I had cervical cancer. I had a radical hysterectomy in April 2022. 2 lymph nodes were removed and they said it was all clear and no treatment was needed. But in April 2024 it came back, in the same spot. We were getting ready to celebrate the 2-year anniversary, and instead we were going through it again. My med onc really wanted me to go on immunotherapy and applied for special access. She asked if it was accepted would I take it, and I said yes, but then it was rejected and I couldn't have it. So, I continued on chemo. I just had my MRI 2 days ago and based on the report they found something on my rectum and it has spread again. April is coming, April is my curse, I guess."

			bladder, my rectum… They created a neovagina and I have a permanent colostomy and urostomy. After that, the pathology showed some very local lymph node involvement, they look at about 25 and 3 showed cancer, but the pelvic lymph nodes were non cancerous, and it was decided despite surgery, let's do the Keytruda, chemo and radiation to squash anything microscopic that might still be in my system."		
9. How was your cancer detected/ diagnosed?	"I waited about 11 – 12 hours at the emergency. Then a doctor that came, a gynecologist, he put his hand in me. And then he sent me to another gynecologist at the clinic by the hospital and he did a physical exam. He was the one that told me I had cancer."	"It was through a CT scan that they first found it and then I went to Dana Farber and my grandmother used to work there, she told me 3 doctors to go see. First, I saw the surgeon and he did a CT and colposcopy, and he told me it was cancer. He said it was too big to operate so he sent me to an oncologist, who was one of the other doctors my grandmother wanted me to see."	"All through surveillance. The first 2 was through GYN exams with speculum and biopsies from that. The rectal tumour was CT and PET and ultimately a biopsy through my anus and rectum that confirmed that it was cancerous."	"They took a small biopsy from my cervix at my gynecologist's office."	"The first time it started with a pap and then I had a physical biopsy with my gyne in Sault Ste. Marie. She said it was cancer and referred me to a gyn onc in Sudbury, which is a 3-hr drive one way. My oncologist and the radiologist together examined me and did another biopsy and confirmed the cancer. This was all during COVID. I had to do everything on my own, nobody else could go into to the hospital. And then 2 years later it was discovered by a physical exam, I had MRI again, CT and PET. We should be able to have access to PET scans more often, not until it's too late. The recurrence in 2024, I had 2 tumours, and it was the PET scan that caught the 2nd tumour near the rectum."

10. How did you feel when you were delivered the diagnosis of cancer?	"I'll give you the strangest answer in the world. I'm an oral historian and I had been working on an apology project for 15 – 20 years, we were supposed to do the public apology before and then covid came. I got a call from Ottawa to say we were going to do the apology online with the Prime Minister in the spring, so I was on cloud nine - I had been working on this for almost 20 years. I was on the ceiling at the time, I was so excited. And then the doctor came in and told me I had stage iii cancer. It was so extreme, 2 extremes at the same time, you can't even imagine. I was crying walking home, dealing with 2 very extreme emotions at the same time, dealing with heaven and hell within 5 minutes. It was amazing, but at the same time I was scared, I didn't want to die."	"I honestly, I was devastated. It's funny because I always thought I would cry and I did, but not when he was in the room. I walked out and that's when I broke down. I honestly thought I was going to die. I thought it was a death sentence. That's the first thing you think of when you hear of an advanced cancer. I was disappointed I couldn't get a hysterectomy, why couldn't they just cut it all out? I know better now."	"This one it depends on the phasing, when I first received the diagnosis after my cystectomy I was actually relieved because I had gone through so much for "pre-cancer" and I was never actually able to share that I have cancer. I take issue with the way that cervical cancers are staged. So, it was actually validating. But then it was obviously quite disappointing to hear about the recurrences. It was quite devastating. Though I have to say that I had kind of expected that a pelvic exenteration was in my future. I knew my cancer was aggressive and I had never articulated it to anyone, but I just knew it was coming."	"Petrified. Overwhelmed. I felt like it was a death sentence. Alone. You feel really alone. Our healthcare system is so broken."	"I was thinking, 'why me? Is this real?' That's really how I felt. 'Oh my God, is this a joke?' I didn't have symptoms, I didn't have anything wrong with me. Ever since I was hit by cancer, I feel like my life is limited. I can't plan ahead. I can only plan in a very short range. Your life is on hold. You just never know when it will come back. Nobody will understand until they have cancer."
11. Please share with me the date of your advanced or metastatic diagnosis.	"January 15, 2021 I got the diagnosis, and then they started running all the tests, the month of February was all the tests, then March they started the treatment."	"July 19, 2022"	"May 22, 2024"	"Well, I guess it was right then, it was April 2022."	"April 1, 2024 was the exam, and then the PET scan found the second tumour, so maybe May 1, 2024."
12. Location of your metastatic disease, if applicable.	N/A	"Potentially in the bladder and the lymph nodes. And it was blocking my left ureter. That was what was causing the only outward symptom."	"Rectum and lymph nodes."	"They could see some in my lymph nodes, but no other organs or anything."	"Rectum and lymph nodes."
13. Did you undergo biomarker testing for your cancer?	"I have no idea."	"They did check when the biopsied and they did a PD-L1. I was positive."	"No, I don't know."	"No, the only thing they did test after my first round of chemo was PDL1. I don't know what my result was, it	"I don't know. I was never informed of any of that."

				was positive, but I didn't get a number."	
14. Is there an aspect of your disease that, to you, is more important to control than others?	"My whole thing was it was during COVID times and I had this work event I was thinking about. I was dealing with all the media nationally, I didn't know what would happen, if I would lose my hair, if I would have moments that I couldn't think. When I started, I thought I have to do this my way, not the cancer victim bullshit, I created a concept that it was going to be 'Team [Patient Name]'. I knew people that worked there and they were all pissed off at the antivaxxers, so I made it my mission to make it a good experience for the staff. I trusted them. I trusted the medicines. I wasn't thinking about me or the cancer. I was thinking about them. It was a lot of fun – I re-branded how to have cancer. The team was great, everyone got in on the concept and it changed the whole experience. I was doing this while doing my work with the apology… I'd have treatment and then go to do an interview on CBC."	"I'll be honest I really didn't know anything about cervical cancer at the time. I educated myself quickly. Rather than go on google I joined a lot of support groups and got a lot of my knowledge from other women who had been through it. I had such confidence in my medical team immediately."	"I mean the most important thing to me is maintaining my follow up and scans. It's the control I have over this disease is trying to catch it before it comes to nasty. That's been my life for the last 14 years. Trying to catch it before it spreads further. That's the one thing I can control in all of this."	"Spread. Stop the spread. What can you do to get these lymph nodes under control."	"I would keep control of the spreading. Be in control to access different scans and prevent it getting worse."
PART C: EXPERIENCES WITH CURRENTLY AVAILABLE TREATMENTS					
15. What therapies did you receive before pembrolizumab + chemoradiation, if any?	N/A	"I had 27 external radiation and 5 brachytherapy sessions over 3 days, and 4 cisplatin therapies, I was supposed to have more but my platelets dropped."	"Surgery plus the brachytherapy."	"I had cisplatin and radiation (external beam radiation). My first round was chemo and radiation and then when I had the follow up PET that's when they saw it spreading in the lymph nodes and that's when I started on the carbo and	"I started with a radical hysterectomy. I had chemo, cisplatin. I had 25 rounds of radiation, and 3 rounds of brachytherapy. For brachytherapy I have to go to

				pembro. That started in September of 2023."	London, Ontario. It's like a road trip."
16. Did those treatments control your cancer? Y or N Please explain.	N/A	"Yes, it did. 3 months after the brachytherapy I was NED on PET."	"I think so because the issue was really the HPV not being fought off. It did and it didn't. I recurred because there's no way the virus can be removed by my body. So, I guess, yes, the first time, no the second time. I believe the tumour being cut is why I recurred in my rectum."	"I'm going to say controlled it, mostly yes, other than a couple lymph nodes, the tumour's gone but the lymph nodes were there."	"Yes, based on the imaging it shows that it is disappearing and it's under control, until my most recent scan, which I'll know today. "
17. Please describe your quality of life on those treatments.	N/A	"It was really rough. I am 5'9" and I got down to 113 lbS. I lost a lot of weight. I couldn't eat. I thought it was the chemo, but they said it was the radiation. I couldn't eat. I would literally have an orange or popsicle and consider it a good day. I couldn't work. I slept a lot. I just went to treatment and came home and laid on the couch. I was very weak."	"It was very difficult to be having surgery or biopsies every 3 months. I felt like I was living my life in 3 month intervals. I couldn't plan any vacations. It was like, 'the cancer hasn't return, let's get away for the weekend.' It's the only thing you can think about. It's the one problem in your life. Everything else doesn't quite matter. To deal with that - 14 years of every 3 months - was very, very hard. I still tried to take those moments when I wasn't in treatment and enjoy my life, but it's always in the back of your mind. The hysterotomy obviously took away any option for me to get pregnant, so that was a big thing. My husband and I are fine not having children, but it was a big impact. I gained a lot of weight. Once I recovered from the hysterectomy I exercised a lot, so that's a positive that it	"Oh, brutal. Brutal! Basically, I was beyond fatigued, no appetite, I lost a lot of weight. I attribute it more to the radiation. It was huge. I did nothing. I had no quality of life. Went no where, did nothing, very depressed. Alone, just pretty useless, I guess. Your outing was going to the hospital every 3 weeks and being there for the day."	"I consider myself very lucky. I have family support, my husband and kids have been there for me. I didn't have a lot of crazy side effects from the chemo, I didn't lose my hair. I consider myself very lucky. I only lost a little bit of weight, not too much."

			motivated me to exercise after. With brachytherapy – the biggest impact was the need for vaginal dilators. Having to use those daily was quite frustrating. My vaginal canal was shrinking. It made having penetrative sexual intercourse painful. That impacted my life and my marriage. It's really impacted my vaginal wall. The other issue was radiation damage to my surrounding tissue – my bladder and rectum - and then this impacted things when I had my vaginectomy, so it impacted some treatment options and sequencing later because of the radiation damage."		
18. How long did it take before you progressed on each of those previous therapies?	N/A	"I don't know. But before the brachy my tumour had only shrunk down to 5 cm, so I was feeling very discouraged, but they told me to have faith in brachytherapy."	"After brachy, it was about 2 years after when the invasive cancer returned."	"So, gosh I guess 3 months after I finished, I'd say 4 months all together."	"From the first to the second, 2 years exactly. One thing that really made me confused was when we found out the second time, in April 2024, but before that 6 months prior I had the follow up with my onc. They didn't see anything, everything was good. So, it seems like only 6 months from 0 to 2 cm tumour."
19. Was there any particular aspect of the disease that was difficult to control while on those previous therapies? If so, please explain.	N/A	"Honestly, it was more the loss of my appetite was probably the hardest. I felt very weak, no energy. I remember at one point looking in the mirror and seeing how thin I was. I remember it was scary, I wasn't sure if I would survive it. I was wasting away, it was tough. Definitely harsh treatment."	"So, I had to do kegel exercises to strengthen my bladder after the vaginectomy. And then I had anal fissures and it was very painful for me to pass stool. I had to take MiraLAX every day to have a soft stool consistency."	"No."	"No."

PART D: EXPERIENCE WITH THERAPY UNDER REVIEW					
20. How did you become aware of pembrolizumab + chemoradiation?	"My surgical oncologist told me, she just offered it to me. I called a girlfriend of mine and she worked in a pharma company and she told me it was really good, she really encouraged me to do it. It was great, it was amazing, I'm so happy that I did it. I was SO happy!!"	*Author's Note: pembrolizumab + chemo (4 cycles of carboplatin + paclitaxel and pembro, then switched to Keytruda only)* "I had heard about pembro through my support groups, but my doctor had actually mentioned it to me. She said if you agree, no matter what your results are, I would like you to do it. She assured me that I wouldn't feel as bad as with chemo, she thought I would do better on it. I said, 'I'll give it a try, I trust you.'"	"It was after my pathology came back and the tumour board had reviewed my case and my gyn onc said based on the lymph node involvement I should have chemo, and paclitaxel, cisplatin, and then Ketyruda which would continue 2 years after I completed chemo. I had radiation too."	*Author's Note: pembrolizumab + chemo (carboplatin + paclitaxel) for 6 cycles, then pembro monotherapy starting Feb 7, 2024); no radiation – "the lymph nodes remaining were not in a prime location to do radiation"]* "Honestly through my support group that I'm a part of. Also, my NP. She had brought it up probably even when I first started treatment, but they didn't want to throw everything at it all at once either."	"I read a lot after I had this cancer thing. I read a lot online. Its not all true, but I find a lot of ppl on support groups from different parts of the world on different drugs, and they have different options."
21. How did you access the therapy under review? E.g., clinical trial, private insurance, self pay, special access?	"Clinical trial."	"Covered through insurance. We have state insurance that we pay for through his job. They never questioned my doctor's decision."	"Insurance."	"Provincial insurance."	N/A
22. Access: **A. When did you receive pembrolizumab + chemoradiation (date)?**	"The first day – March 2021."	"It was January, the last week, in 2023."	"July 2024"	"September 2023"	N/A
B. In what line of therapy?	"First line."	"Right from the start she knew she would put me on in after, so she called it adjuvant therapy."	"It was my first time accessing drug therapy."	"I'm not sure."	N/A
C. How many cycles of pembrolizumab did you receive?	"I was on it for 2 years, it started every 3 weeks and then at some point it switched to every 6 weeks and I got double the dose. I had chemo in the beginning for 5 cycles."	"I have received 34 of 35. One more to go in 3 weeks. Just had number 34 on Friday."	"I had 6 cycles with the cisplatin and paclitaxel, and then I have had 2 cycles on its own. I will continue until January 2027."	"6 cycles of combo therapy; pembrolizumab monotherapy from Feb 7 – Dec 20 every 3 weeks; and then they added Avastin to pembrolizumab starting Dec 20, 2024."	N/A
D. If you received radiation therapy as a part of your treatment, what type of	"Yes, radiation followed by brachytherapy."	N/A	"I had external beam radiation as a part of the treatment plan, I received this starting in Jan 2025."	N/A	N/A

radiotherapy did you receive?					
23. Side effects: **A. Have you experienced any side effects while on this therapy? Yes/no**	"Yes. Only one."	"Very minimal."	"Yes."	"Yes."	N/A
B. What were those side effects? Please describe them.	"The only one was about a year later. I was going away and I was having shortness of breath and they gave me cortisone or something like that to take and then it went away. Nothing else, I actually I gained weight – there were no other side effects. The only days that were really hard were the days after brachytherapy. They knocked me out during treatment, but after the 4 weeks of brachy your vagina is burnt and when you try to urinate it's like fire coming out of your vagina. Of all the therapy, that was the worst."	"First when I had it with the chemo and I was worried if I was going to be able to do it. Sometimes I have a little minor bit of joint pain that goes away with Claritin. I have some fatigue, but im also 44 and a teacher, so I don't know if you can say it's the Keytruda *laughs* I had some psoriasis when I was sick with strep throat, but I had a little bit as a kid and they thought the Keytruda brought the psoriasis back out. I had phototherapy and they were able to fix it quickly."	"What was difficult during the chemo is I was very fatigued, nauseous, and because of the big surgery and the urostomy I had numerous systemic infections, some kidney infections, so I was hospitalized a number of times. They ended reducing my dose of paclitaxel, which helped with stopping infections and reducing the depth of fatigue. With radiation – intestinal cramps, diarrhea, nausea. With pembro, I haven't really experienced anything."	*Combination therapy*: "Lost my hair, lost a bunch of weight, never nauseous as far as throwing up, dehydration, weakness, dizziness, things like that." *Pembrolizumab monotherapy*: "I've been pretty good. I do take the Claritin because I was getting a sore knee and that was recommended for joint pain. Other than that, I've been pretty good. Severe constipation though. It affected my thyroid. I've been on Synthroid for many years previous and it started to really decline with the pembro, I think that's a very minor side effect. For me personally, I've had no other side effects. I think it was an existing issue for me, and maybe got a little bit worse. It's more fear-based than physical side effects."	N/A
24. On a scale of 1-10, how would you rate your QoL while on pembrolizumab + chemoradiation / pembrolizumab monotherapy? **1 being very poor and 10 being very good. Please explain.**	"10, 10, 10! It was amazing, fantastic! Because it was curing me, I was getting better, there was no pain, I was having fun, I was able to do what I wanted to do, it didn't block me from doing what I wanted to do. The only thing that pissed me off was that I couldn't have my home-made tomato sauce. I was getting life, they	"I would say honestly a 9 – 10. I'm back at work, number one. I've gone to Scotland, Ireland, New York, I just got back from Aruba. I've been to Seatle. I'm living my life. I'm travelling to see my daughter. I work fulltime as a teacher and I couldn't work when on the other treatment. I'm NED and living my life. Other than	"With pembro, I would say like an 8. You know it doesn't impact very much, the only thing that it impacts is having to go for lab work, follow up, infusion. A minor disruption. I still have my port, which isn't glamourous, but it's minor. It's the easiest of all the treatments."	*Combination therapy*: "I'm gonna say to average it out, I would say a 3. Just the fatigue, the weight loss, the dizziness, with your immune system completely tanked, you can't really go anywhere, do much, pretty low functioning. Freezing cold, too."	N/A

	were curing me, why would it not be amazing?"	going every 3 weeks for my treatment, I don't feel like I'm in cancer treatment. If I'm going away I can call them and push my treatment out a week, no big deal, it's much more relaxed. When I tried the double dose at 6 weeks that's when I got the strep and psoriasis, we didn't know if that was why, but just stayed at 3 week interval. I like going every 3 weeks, it's a comfort, I get my bloodwork done. I kind of don't want to go off it after my next treatment. I feel good, I don't mind being on it at all."	"The combo treatment – oh my gosh. It was like a 2. The way I felt was just awful. During chemo the constant hospitalizations were a huge impact. I was immunocompromised, I had to be very careful about who I was in contact with, I wasn't eating in restaurants. Whereas with pembro, I live my life and just plan around my infusions."	*Pembrolizumab monotherapy*: "I gotta say improving, it took a long time, but my side effects were minimal. When I was on the Keytruda standalone I would rate my quality of life as high as a 8. I was able to do more, it's more of a mindset as opposed to the physical. I was capable of a lot more than I allowed myself to do. But, I started hot yoga, and I could do things. The support isn't there. It's mental. That's the biggest thing for me." *Pembrolizumab + Avastin:* "Now I would say I'm at about a 5 or better. Having the Avastin added, the fatigue is more again and the immunity is compromised, you're back on that cautious train."	
25. Did you have any cancer symptoms before starting the therapy? If so, what were they?	"I was having pain in my lower pelvis, near the cervix, the tumour was pushing on my bladder every time I moved. I kept feeling like I had to pee but I couldn't pee. The tumour was pushing on the bladder and it hurt."	"No, but I was still having minor issues with my stent in, and it was annoying me, but once I got that out, no."	"Less of the cancer and more just the healing from the surgery."	"Just the little bit of lower back."	N/A
26. If you did have cancer symptoms before starting the therapy, did the therapy help resolve those cancer symptoms? If so, which ones?	"The pain went away after day 1. It was the first time I slept. Everything. Right away. Within less than 24 hours."	N/A	N/A	"Yes."	N/A
27. How was response confirmed to pembrolizumab + chemoradiation? Was it	"I don't know how they knew. For one thing is that before I started brachy, after the 5 weeks of chemorads	"It was perfect. The only thing I had at one point was I had a lymph node light up in my neck but they were	"I think they can only really see through imaging, and they haven't really seen any issues with anything coming	"So, they did a scan and they were saying I was doing good when I finished my combo therapy, and then when they	N/A

clinically (symptoms resolved and you felt better), biochemically (tumour marker went down), or radio-graphically (imaging scan results)?	and the immune when my oncologist looked at the pre- and post- scan, she showed it to me and she put it up on the screen and was like 'oh my God, oh my God' and I was like 'what's wrong?' and she gets on the phone and started sending my picture out – she wanted to share the results right away, I could tell the results were very good. She showed it to me and asked if she could share it with others, I said of course. They still had to go in and get the dust of the cancer out of there, but it was amazing. I'm not a doctor, but the two images were just remarkable. That was the first time I saw the difference. And I was feeling better right away. The imaging made me feel even more thrilled and happy, I knew we were moving along. I didn't have time to think about the cancer, we were moving along and I was focused on work. I completely trusted the therapy. I was thrilled to death I was on the immunotherapy."	confident it was because I had had strep and COVID-19 and then I went back for imaging again and it was gone. They said it wasn't cancer. I get a PET scan and pelvic exam every 3 months."	back. I've had CT and will have a PET in 2 – 3 months."	did a scan in July they had noticed some spread. I thought to stay on it, that can happen. Then they scanned again in November and still saw some lymph node involvement, some potential spread, it's difficult to see with the inflammation. I thought, 'how do we know the pembro is not keeping it at bay?' So, I really fought to stay on it."	
28. Have you ever had to stop pembrolizumab + chemoradiation? Why or why not?	"I stopped when I had the lung issues. It went away but I was going away to Europe too for 6 weeks, so I stayed off it and then when I came back I started again."	"They paused it just that one time when I had the rash. Paused one treatment and once I saw the derm she said its psoriasis there's no danger and I could go right back to it. The derm said in retrospect she didn't need to stop it."	"Yes. We had to delay by a week or two because of the infections with chemo. I have not had to stop pembro on its own."	"Just the pembro part, no we've never had to pause it. My bloodwork has always been good. When I was on the chemo combo, we did have to push it back a week because my neutrophils were low."	N/A

29. Has pembrolizumab + chemoradiation been easier to use than any previous therapies? / Has pembrolizumab + chemoradiation been easy to use? Why or why not?	"It was absolutely nothing. You don't feel anything. The only thing I didn't like was being poked with the needle. It changes nothing, you don't even feel it."	"100%. It's quicker. The infusion itself is 30 minutes. The longest part is waiting for the pharmacy to bring it. When I had chemo, it was like a 6-hour infusion. I'm laughing when I'm in there, they don't need to give me the pre-meds - the Benadryl and the steroids, and all that. Just the infusion and the flushing. I go and get my bloodwork and my IV in, I see the doctor or the NP to check my bloodwork and they say I'm good and I go. I needed a blood transfusion, platelet transfusion, and magnesium, on chemo, and nothing on Keytruda, its so much easier."	"The pembro alone, absolutely. Like I said, it's probably the easiest treatment option that's been provided to me. Because there's not the severity of side effects. It's really just the inconvenience of getting the infusion, rather than feeling badly after treatment."	"Yes. Way shorter time, as far as when you're at the hospital. And you don't have to take any pre-meds, nothing like that."	N/A
30. How has your journey impacted your caregiver /family?	"I don't have kids, my parents have passed away. It's been amazing, totally positive. I came from parents who enjoyed life and my parents impacted me to do the same. The only difference is after cancer, I don't feel guilty about anything anymore. I've always loved life and my experience makes me love it even more. My husband couldn't come in [due to pandemic protocols] and one day I had a window spot in the chemo suite and he showed up with a sign and was dancing outside like a fool. It was so cute. I was having fun but I was very aware that not everyone was having fun, so I	"It's been really hard. My mom and my husband are my biggest care takers. My daughter started college in another state the day before I started treatment. I couldn't go with her to move into school and it was hard on my daughter knowing I might not be there when she got back. My mom had a hard time with me losing hair, she started sobbing when she saw me. My mom came to a lot of treatments with me, my husband did too, but he had to work, since I was not. They were very supportive.	"It's been very difficult. Both my husband and I are in therapy because of it. He worries a lot about me dying. We talk about it a lot. I think because of the surgery and the chemo and the radiation, because he has seen me so sick this past year, it's hard for him to think of me as healthy again, or that I'm doing well. I had to increase my anxiety meds. It's been really challenging on our mental health, for both of us. Our sexual health in non-existent. I'm still healing from my total pelvic exenteration and I'm having a lot of discharge and a lot of dryness. It's definitely impacted that aspect."	"Ohhh, huge. My husband I gotta say has been amazing. My support on that front has been phenomenal. I'm very lucky. Well, it's been emotionally debilitating for him. He wants to fix it but can't. Watching someone you love go through this has got to be some form of hell. There's no way you can do this on your own, I just cant imagine. For me I feel that the emotional support is greatly lacking. I would love to get to the point that I can be a patient advocate and help others. The hospitals are just so medical."	"I guess he just wants to give me all his support, treats me like a princess when in in chemo. My daughters they didn't know what to say, they did their best to support me. They're all with me, they're trying to support me. My most recent MRI, my husband said, oh know, not again! My husband has a positive mindset."

	was very aware of that. I didn't want to offend anyone. I didn't let them call me a patient, I was a guest. Everyone had rules and regulations to follow and they got into it, but we were having fun."	My husband took leave as was needed, but he took PFMLA and it was intermittent. He is the primary breadwinner, so he had to keep working. My insurance is through his job, so he had to keep working."			
31. Was it worth accessing pembrolizumab + chemoradiation? Why or why not? Please describe the impact it has had on your life.	"Oh my God, 100 out of 10!! I believe it helped me, honest to God, I tell my friends thank God I ended up at this hospital and ended up on this drug. If I was on another drug I might have had a different outcome. I believe this and there is no way I can prove it, but I'm convinced it's the immuno that helped me. Convinced. I'm convinced that was a major factor in getting the cancer out of my system. I believe my parents were watching over me and that's why I ended up and this hospital and getting access. I'm lucky. I cannot believe how lucky I am to have gotten it. I'm in shock - I feel like I owe the world big time. Right time, right place, right timing, right doctors, everything just aligned. I don't know what I did right. I'd like to give back, I think it's fate coming back to you."	"100%. I've seen people the same stage as me, and I had the pemrbo and tolerated it well and am still NED, and a lot of my friends weren't offered the pembro and recurred. I was facing a 16% 5-year survival rate and I'm so glad that she offered it to me and I hope it taught my body how to fight cancer if it comes back. I know the further out you get the better it looks, and I'm now 25 months so the hope is that any cancer cells are dead. I feel very grateful. I know that this has not been an opportunity given to everyone I know. I am REALLY grateful that I was in a place that I am. My husband wanted to move back to the UK, and I said I will not leave Boston and my oncologist. I am grateful for where I live when I got sick."	"I think so, I'm just grateful that it became available to my type of cancer. I think there's a comfort in knowing that I'm on something so that my immune system can be trained to fight this. It gives you more hope. Especially because its so easily tolerated. It really is good for the spirits."	"For sure. For sure, yes. I feel I'd be dead with out it, because it would just keep growing. I'm thankful. That being said, as a Canadian it's overwhelming to see all the extras that go on in the States and that they have so much, it's so unfair. To sit there with your doctor and hear that's not coming to Canada for years… it's not right. That in itself is some form of a death sentence. It's very unfortunate, unfair. I've been very involved in my care. There's so many people, some who have passed, that aren't their own advocate and just go along with what the doctor says. It's not enough."	N/A
32. Did accessing pembrolizumab + chemoradiation allow you to fulfill or accomplish anything that you would not have otherwise been able to	"100%. Absolutely. I think the pembro was the most essential part of the mix of everything. I remember my doctor saying we have to treat aggressively, because the cancer was I aggressive. I	"I do. I feel like it helps give me confidence that I was able to fight this thing. I think I travelled and had the confidence and ease because I was being checked every 3 weeks.	"You know I'm hoping that this allows me to live a longer life you know. So yeah, it's the fact that I'm still here, which that small fact is so meaningful to people with cancer. We know	"Yeah, I think the pembro is the perfect drug. The perfect drug for keeping things at bay, preventing new growth. It's allowed me to be where I am today.	N/A

do had you not accessed the therapy? Please explain.	don't think I would have been the same without the pembro… I don't know where I would have been. But when I got the lung issues I was thrilled… (*laughs*) I was thrilled – it confirmed that I was on the drug and not the placebo and I was just thrilled. I'm really convinced that the pembro was a key element in the cocktail that I got. The fact that I stayed on it for 2 years, I was thrilled about it. Staying on it for 2 years, it gave me confidence. It made me calmer, it gave me a little more calmness and confidence that I was going to get through this. I even felt bad the last day of treatment, I was like, 'no more?' It was like it was my friend."	I feel like I'm doing better physically after radiation and I got physically better once I was on the pembro. I thought of it like my superpower."	how precious life is. We know how it can be stripped from you, so yeah."	I'm just thankful to have access to it."	
33. What improvements would you like to see in drug therapies?	"I don't know other drugs, I only know what I got, so I can't compare it."	"I would like everyone to be offered Keytruda and other drugs because I feel like it gives us all more of a chance. I have a friend in Canada, and she tried to get access to another immunotherapy, and sadly she passed away. Maybe it wouldn't have saved her, but you never know. No one should not have access to a drug that may save their lives. To know there is a drug out there and you can't get access to it, and it's saving other people	"Getting away from infusions and having something you can swallow would be an amazing advancement. There's no blood test for cervical cancer, so I would like to see that. Not having to spend an entire day while having infusions. I was arriving at 9am and leaving at 7pm, so a shorter infusion time or pills would be a huge advancement. Medication that doesn't leave you feeling so crummy."	"Access to things that are available to save your life. Putting this information out there. There are so many things that people have no idea about. What it does to you. There's just so little information, nothing is offered, they just tell you a drug name and that's the extent of it."	"Make it stop going everywhere. If there is a way we can prevent it before the cancer stops to travel, we should do that. Once it starts to travel, it might be too late."

		is incredibly frustrating and sad."			
34. Do you believe pembrolizumab, has those desired improvements? Why or why not?	"I would like to see this available. Period. Because I think it's going to save lives."	"I do, because I have seen people even now on my Keytruda page that were told it wouldn't work because of their PDL1 and I've seen them become NED. I've seen not just people like me, but others who were told they were not curative and now they are NED years later. And it gives a quality of life option where people can try something else if you can't handle chemo. Sometimes your body needs a break from the harsh drugs. We're walking, taking our dogs out hiking, working, and I couldn't do anything like that on chemo. I was lucky if I could walk up the stairs to say hi to my nephew, I couldn't hardly hold the baby. I'm not immunocompromised anymore like when I was on chemo - then if I got the flu it could kill me. It's now better that I can be around anything. As a teacher, I'm exposed to everything, so it's nice that I don't have to worry about it more than anyone else. It doesn't knock out your immune system, more than anything it makes it go into overdrive."	"Yeah, the fact that it's the quickest infusion I had – it's 30 min so that is great. And the fact that the side effects are really minimal. It's huge."	"Yes, just personal experience on my last scan, I had a CT not too long ago, and there was nothing there. That's a big improvement."	"No one can really see this, but if we can focus on how to prevent it from spreading that would be something we should put more effort in. Maybe we can be put on immunotherapies earlier than the terminal stage, once it's too late. Access to immunotherapy earlier. This is what I need right now, if we can do this earlier, maybe there will be less patients in the terminal stage."
35. Would you recommend that pembrolizumab + chemoradiation be made	"100% absolutely. Absolutely!"	"Yes, 100%. For instance, my oncologist, who I regard as one of the best in the world, she has told me that that	"Absolutely!!"	"Yes. I personally truly believe that the pembro boosting your own immunity, it makes so much sense.	"Oh yeah! Not only for me, but to all the patients. That would be a way to prevent the cancer from spreading, in

available to all patients who qualify for it?		16% survival rate is outdated and a lot of it is from pembro, she said she cannot believe how many of her patients are going NED after advanced or metastatic disease. It's giving people that had no hope, so much hope. I know people that tried it when they had 2 months to live, and then later went NED. It's a miracle to see, I want everyone to have that opportunity to see if it works for their cancer."		Chemo kills everything, so we need what can be in your body to help the good stuff, to fight, to build."	an earlier stage. Slow down the spread, or even stop the spread. Less patients in the last stage. If there is something we can do to prevent, we should do it. Just like vaccinations. If we can do something in an earlier stage to prevent a recurrence, we should do that."
36. Do you wish to add anything about why accessing pembrolizumab + chemoradiation is so important to cancer patients and caregivers?	"It keeps you alive. Bottom line. You're alive! Theres no pain, you're alive, it's great. What more do you want?! It gives you your life. The radiation did more damage to my bones, but the pembro did nothing other than a little blip along the way. And you're being followed, so anything would be caught right away. That drug was incredible. I have nothing bad to say. I was on TV, I was writing for the Toronto Star, I was doing my work and you couldn't tell."	"I think it's important because it's one of the few cancer drugs that still gives you quality of life. I'm running around teaching 8- or 9-year-olds and I couldn't have done that on the other drugs. I've lost a lot of sisters that didn't have access and maybe they would have been here today. I'm here today for my Canadian friend who couldn't access immunotherapy - she tried so hard and then she couldn't get it and she died. Her oncologist in Canada fought hard but she just couldn't get access. For her, I want other people to have that opportunity. She smiled up until the end. It was her greatest wish to have other people get access."	"I think that it's so important that when it comes to cancer that any of the latest advancements, any drug therapies that have been shown to improve outcomes, should be utilized. To lag behind the standard of care is detrimental to patients. It might be Keytruda now, and maybe something else in the future. It's really about utilizing all therapies to save your patients."	"I believe if it's going to work your quality of life will come around a lot quicker. I think it needs to be there for all. There's something out there showing really great, promising results, let's do it. These are people. It seems like sometimes it's a lucky wheel spin for some and it's not fair. Sometimes it really depends on the doctor you have, how involved they are, how active they are with getting you to a cure, that's the end goal, and then quality of life matters."	"Oh, I think not only that kind of drug, but all kinds of drugs. It's to prevent the disease from getting worse. Anything that can prevent spread, or slow down the spread, that's what we should do. Treatment should be about prevention."

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: **PC0411-000**
Generic Drug Name (Brand Name): **pembrolizumab (Keytruda)**
Indication: Pembrolizumab for the treatment of adult patients with FIGO 2014 Stage III-IVA cervical cancer, in combination with chemoradiotherapy (CRT).
Manufacturer Requested Reimbursement Criteria[1]:
Pembrolizumab for the treatment of adult patients with FIGO 2014 Stage III-IVA cervical cancer, in combination with chemoradiotherapy (CRT).
Name of Clinician Group: Ontario Health (Cancer Care Ontario) Gynecologic Cancer Drug Advisory Committee ("OH (CCO) Gyne DAC")
Author of Submission: Dr. Rachel Kupets

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 email/Teams meeting.

3. Current Treatments and Treatment Goals

Current treatment is concurrent chemoradiation. Other treatment option includes induction chemotherapy followed by standard chemorad (INTERLACE protocol).

Treatment goals include: Overall survival, progression-free survival, improved 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.

Need new treatments that would improve OS and PFS for this patient population

5. Place in Therapy

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

Pembrolizumab with chemoradiation followed by pembrolizumab will fit into the current treatment paradigm as first-line treatment with curative intent.

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?

Patients who are best suited for treatment are FIGO Stage III and IV patients who have not received prior treatment.

Least suitable for treatment – patients who are unable to tolerate radiation, chemotherapy, or immunotherapy

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?

Tumour imaging per RECIST v1.1 criteria – in the pivotal study, tumour imaging was scheduled at week 12 after the completion of chemoradiotherapy, every 12 weeks in years 1 and 2, every 24 weeks in year 3, and once yearly thereafter.

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

Disease progression, treatment-related toxicities, or patient's choice.

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 can be given in the outpatient setting. Systemic treatment will be managed by medical oncologists or gynecologic oncologists.

6. Additional Information

NA

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.

   OH (CCO) 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. Rachel Kupets
Position: Lead, Ontario Health (Cancer Care Ontario) Gynecologic Cancer Drug Advisory Committee
Date: 28-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 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**
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: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

☐ 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 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 3

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

☐ 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 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: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

☐ 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 4

	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 5

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

☐ 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 5: Conflict of Interest Declaration for Clinician 5

	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.

Canada's Drug Agency
L'Agence des médicaments du Canada
Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

Reimbursement Review

Clinician Group Input

Project Number: PC0411-000
Generic Drug Name (Brand Name): Pembrolizumab
Indication: Pembrolizumab for the treatment of adult patients with FIGO2014 Stage III-IVA cancer, in combination with chemotherapy (CRT)
Name of Clinician Group: Society of Gynecologic Oncology of Canada (GOC)
Author of Submission: Lesley Roberts

1. About Your Clinician Group

The Society of Gynecologic Oncology of Canada (GOC) is a non-profit multidisciplinary organization. It is the national society representing health care professionals including physicians, nurses, pharmacists, and scientists involved in the treatment and prevention of gynecologic cancer. GOC strives to improve the care of women with, or who are at risk of, gynecologic cancer by raising standards of practice, encouraging ongoing research, promoting innovation in prevention, care and discovery, and advancing awareness.

Website: https://gyneoncology.ca/

2. Information Gathering

The information in this submission represents data from completed and published clinical trials, as outlined in the references below. These were identified through a literature specifically focusing on trials investigating treatments for locally advanced cervical cancer. Physician members of the Board of Directors of GOC, representing Gynecologic Oncology physicians across the country, were also surveyed regarding their expert opinion on the treatment of locally advanced cervical cancer.

References:

Colombo et al. 2021. Pembrolizumab for persistent, recurrent, or metastatic cervical cancer. *New England Journal of Medicine*. 385:1856-1867.

Keys et al. 1999. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. *New England Journal of Medicine*. 340:1154-1161.

Lorusso et al. 2024. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG3047/KEYNOTE-A18): a randomized, double-blind, phase 3 clinical trial. *Lancet*. 403:1341-1350.

Morris et al. 1999. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. *New England Journal of Medicine*. 340:1137-1143.

Rose et al. 1999. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *New England Journal of Medicine*. 340:1144-1153.

Thomas, GM. 1999.

Improved treatment for cervical cancer — concurrent chemotherapy and radiotherapy. *New England Journal of Medicine*. 340:1198-1200.

Whitney et al. 1999. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group Study. *Journal of Clinical Oncology*. 17:1339-1348.

3. Current Treatments and Treatment Goals

Cervical cancer ranks as the fourth most prevalent cancer among women globally, with 660,000 new cases diagnosed each year (World Health Organization, 2024) and one woman dying of cervical cancer every two minutes (World Health Organization 2018). In Canada, an estimated 1,600 new diagnoses of cervical cancer and 400 deaths from the disease occur annually (Brenner et al., 2024; Canadian Cancer Statistics Advisory Committee, 2023). Despite both the World Health Organization and the Canadian Partnership Against Cancer (CPAC) setting targets for the eradication of cervical cancer, the incidence of cervical cancer is rising nationally. Canada has seen the incidence of cervical cancer increase by an average of 3% per since 2015, surpassing the rate of growth of all other cancers in women (Canadian Cancer Statistics Advisory Committee, 2023).

The five-year net survival for cervical cancer in Canada is 74% (Canadian Cancer Society). Prognosis, however, varies significantly by stage. Multiple updates and alterations to the staging system used for cervical cancer (FIGO) have made accurate identification of prognosis challenging. Most importantly, until 2018, nodal metastases were recognized as a poor prognostic factor but were not included in the staging system due to global access to imaging. While early stage (stage I) and locally advanced disease (Stage II, III, and IVA) are often treated with curative intent, survival rates differ significantly. Stage IA cervical cancer is associated with a 93% 5-year survival, whereas Stage III disease is associated with a 5-year overall survival of 32-35% (Canadian Cancer Society). Provincial level data suggests that the stage distribution for cervical cancer is shifting, with the proportion of cervical cancer initially diagnosed as locally advanced increasing (Cancer Care Ontario, 2022).

Locally advanced cervical cancer includes Stage II, III, and IVA disease. The standard of care in Canada for these patients is concurrent cisplatin and external beam pelvic radiation followed by brachytherapy, which was established through a series of clinical trials published in 1999 (Keys et al, 1999; Morris et al, 1999; Rose et al, 1999; Whitney et al, 1999). There have been no updates to the treatment algorithm of locally advanced cervical cancer since that time. The addition of radiation-sensitizing chemotherapy (specifically, cisplatin 40 mg/m2 weekly) concurrent with administration of external beam pelvic radiation demonstrated improved progression free and overall survival in these trials. This treatment regimen remains the standard of care for non-operable, locally advanced cervical cancer and is provided with curative intent. However, as demonstrated by the survival statistics, the rate of cure remains low.

Recent studies have demonstrated the effectiveness of pembrolizumab in the treatment of metastatic or recurrent cervical cancer. Pembrolizumab is an immune checkpoint inhibitor, which blocks PD-1. In the KEYNOTE-826 trial (Colombo et al, 2021), the addition of pembrolizumab to standard of care chemotherapy improved progression-free survival (HR 0.62, 95% CI 0.50-0.88, P<0.001) and overall survival (HR 0.64, 95% CI 0.50-0.91, P< 0.001). This regimen has subsequently become the standard of care in Canada for metastatic (Stage IVB or not a candidate for curative-intent concurrent chemoradiation) or recurrent cervical cancer.

The recently published KEYNOTE-A18 trial investigated the effectiveness of pembrolizumab in addition to standard radiation-sensitizing chemotherapy for patients with locally advanced cervical cancer receiving curative intent concurrent chemoradiation. Patients with FIGO 2014 Stage IB2-IIB with node-positive disease or Stage III-IVA regardless of nodal status were enrolled in the trial. Concurrent chemoradiation was administered as per standard of care. Pembrolizumab was administered at a dose of 200 mg every 3 weeks with chemoradiotherapy, followed by 15 cycles of pembrolizumab 400 mg every 6 weeks. The addition of pembrolizumab to concurrent chemoradiotherapy significantly improved progression-free survival (68% vs 57%, HR 0.70, 95% CI 0.55-0.89, p = 0.0020). Overall survival data are not yet mature, but early overall survival data demonstrate a non-significant improvement with pembrolizumab (87% vs 81%, HR 0.73, 95% CI 0.49 – 1.07). The addition of pembrolizumab to concurrent chemoradiation is the first advancement in the treatment of locally advanced cervical cancer since the addition of radio-sensitizing chemotherapy to radiation in 1999.

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.

As described above, the overall survival rate of Stage III-IVA cervical cancer remains poor, in the range of 32-35% in Canada. The currently available treatment (concurrent chemoradiation) is administered with curative intent, though 5-year rates of progression-free survival and overall survival remains low. Improved and updated treatments in locally advanced cervical cancer are an area of significant unmet need, as treatment algorithms have not significantly changed in the past two decades. More effective treatment options to improve curative potential and to reverse the course of the disease are required.

5. Place in Therapy

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

Pembrolizumab, as an immune checkpoint inhibitor, would function as a complement to the currently available treatment of chemoradiation. This regimen would be used as a first-line treatment for patients with FIGO 2014 Stage III (regardless of nodal status) or Stage IVA undergoing curative intent therapy. Given the observed benefit in KEYNOTE-A18, if approved it would be anticipated that this would cause a shift in the current treatment paradigm, such that any candidate patient initiation chemoradiation would also receive pembrolizumab. As this is a first line, curative-intent therapy, trying other treatments prior to initiating treatment with chemoradiation plus pembrolizumab would not be appropriate.

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?

Newly diagnosed patients with FIGO 2014 Stage III (irrespective of nodal status) or Stage IVA histologically confirmed squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the cervix with no previous cancer-directed treatment are most likely to respond to chemoradiation plus pembrolizumab. Companion diagnostic testing is not required, as KEYNOTE-A18 (Lorusso et al, 2024) enrolled all comers of the appropriate stage and histology. Treatment responses were stratified by PD-L1 status, a diagnostic test that is current used for recurrent/metastatic cervical cancer patients initiating treatment. This diagnostic tool is widely available across centers in Canada. The hazard ratios for progression or death were similar in the PD-L1 positive subgroup (HR 0.72, 95% CI 0.56 – 0.92) and PD-L1 negative subgroup (HR 0.61, 95% CI 0.18 – 2.07). Numbers in the PD-L1 subgroup were very small (60 participants), which likely accounts for the wide confidence interval observed. Given this subgroup analysis, it is not possible to identify of subgroup of patients who are most likely to exhibit a treatment response to chemoradiotherapy plus pembrolizumab.

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?

Initial imaging prior to initiating chemoradiation plus pembrolizumab would include an MRI pelvis and CT scan or CT-PET scan for staging. No planned diagnostic imaging is required on chemoradiation, though can be considered on an as needed basis directed by symptoms or clinical findings. Response to chemoradiation plus pembrolizumab would be assessed clinically and radiologically with physical examination and tumor imaging via CT or MRI three months after completion of chemoradiation. Ongoing response to therapy be based on clinical assessment (symptom burden and physical examination) and radiologic tumor burden assessment via CT or MRI every three to six months. Tolerability of treatment and clinical assessment is performed prior to every cycle of therapy (every 6 weeks).

A clinically meaningful response to treatment would be defined as clinical and radiographic resolution of disease control with tolerable toxicity.

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

- Disease progression:
    - Disease progression can be identified clinically or radiologically.

- Adverse events:
    - Grade 4 immune-related adverse events warrant permanent discontinuation of treatment
    - Grade 2-3 immune-related adverse events necessitate holding treatment, and can be managed as per standard guidelines (O'Cearbhaill et al, 2022; Schneider et al, 2021)
    - Grade 2-4 adverse events associated with cisplatin, or pembrolizumab may warrant dose reduction or treatment discontinuation
    - Most commonly reported grade 3 or higher adverse events with this treatment regimen included: anemia, neutropenia, diarrhea, neutropenia, and hypothyroidism
- Patient preference:
    - Patients can and may choose to discontinue treatment at any time, irrespective of adverse events or disease response

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]?

Treatment regimen would be administered as outpatient therapy in a comprehensive cancer center setting and is best prescribed by specialist physicians (medical oncologists, radiation oncologists, gynecologic oncologists) with experience and knowledge in treating gynecologic cancer.

6. Additional Information

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CDA-AMC 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. CDA-AMC may contact your group with further questions, as needed. Please see the *Procedures for 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 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: Lesley Roberts
Position: Gynecologic Oncologist, Assistant Professor at University of Manitoba; Advocacy Director, Society of Gynecologic Oncology of Canada
Date: 30-03-2024

☒ **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**
AstraZeneca	X			
AbbVie	X			

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

Declaration for Clinician 2

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

☐ 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 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 3

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

☐ 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 3

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 4

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

☐ 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 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: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

☐ 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 5: 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
Add company name				
Add company name				

Add or remove rows as required				

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