

CADTH Reimbursement Review

Patient Input

Pertuzumab (Perjeta)
(Hoffman-La Roche Limited)

Indication: Early stage breast cancer

CADTH received patient input from:
Canadian Breast Cancer Network
Rethink Breast Cancer

May 7, 2021

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CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

CADTH Reimbursement Review Patient Input Template

Name of the Drug and Indication	Perjeta in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either 2 cm in diameter or node positive).
Name of the Patient Group	Canadian Breast Cancer Network
Author of the Submission	██████████
Name of the Primary Contact for This Submission	██████████
Email	██████████
Telephone Number	██████████

1. About Your Patient Group

Describe the purpose of your organization. Include a link to your website.

The Canadian Breast Cancer Network (CBCN) is a leading, patient-directed, national health charity committed to ensuring the best quality of care for all Canadians affected by breast cancer through the promotion of information, education and advocacy activities.
www.cbcn.ca

The Canadian Breast Cancer Network is committed to strict adherence to the Code of Conduct Governing Corporate Funding.

2. Information Gathering

Information for this submission was collected via:

CBCN's 2017 [Lived Experience Breast Cancer Patient Survey](#): An online survey was distributed in English and French to patients living with breast cancer. No patients surveyed had direct experience with the treatment under review. Survey questions comprised of a combination of scoring options and free form commentary. Patients were contacted through the membership databases of CBCN and other patient organizations.

Patient Respondents Profile:

278 early-stage, breast cancer patients responded to the survey in English and French. In this submission, CBCN specifically utilizes the data provided by 52 Canadian, early-stage, HER 2-positive breast cancer patients who responded to our survey.

The respondents all identified as female and primarily (29) spoke English as a first-language, with 7 speaking French as a first language, and 4 respondents selecting other as their first language (split between Cantonese, Polish and Serbo-Croatian), with 12 respondents undeclared. The majority of respondents were from Ontario (12) and Saskatchewan (6), 4 from Quebec, 4 from Nova Scotia, 4 from British Columbia, 2 from Manitoba, 2 from New Brunswick, 2 from Newfoundland and Labrador, 2 from Alberta and 1 from Prince Edward Island. The remainder did not specify their province of residence.

Most of the respondents (21) were between the ages of 40-49 when diagnosed, 15 respondents were in the 50-59 age range, 10 were between 30-39 years, and 3 were between 60-69 years of age, the remainder were undisclosed.

Most respondents were in a relationship (34), while five declared themselves as single, and the rest did not specify their relationship status. Most of the patients (33) had children, with the majority (17) with children 20 years or older, 10 had children between the ages of 13-19, 5 had children 2-5 years of age, 4 had children between 6-12 years of age and 4 had children below 1 year.

Key informant interviews: Phone interviews were conducted in April and May 2021 with 4 Canadian early-stage, breast cancer patients living with high-risk, HER2 positive breast cancer and had direct experience with the treatment under review.

Printed sources: A review was conducted of current studies and grey literature to identify issues and experiences that are commonly shared among many women living with breast cancer.

3. Disease Experience

A diagnosis of early-stage, human epidermal growth factor receptor (HER2) positive breast cancer has a significant impact on the day-to-day life of the patient. The diagnosis of HER2-positive breast cancer, as well as the treatments that are used, impact both the emotional and physical well-being of a patient. In Canada, approximately 20-25% of all diagnosed breast cancer patients have the HER2-positive subtype.

The HER2-positive breast cancer subtype is traditionally associated with more aggressive cancers and a poor prognosis in the absence of HER2-directed therapy with a greater likelihood for central nervous system metastases. It is therefore of critical importance for patients to have targeted anti-HER2 therapies available to them to reduce the risk of disease recurrence. Even so, approximately 15 percent of patients treated with HER2-

directed therapy continue to experience disease relapse, suggesting that novel treatment approaches are urgently needed for this patient population.¹

The primary aspect to control for patients with early-stage, high-risk HER2-positive breast cancer is reducing the risk of recurrence and disease progression to improve patients' overall survival. Clinical research shows that HER2-positive patients have around five times the recurrence risk of HER2-negative patients and decreased five-year, recurrence-free survival rates than those with other breast cancers. Some of the side effects of HER2 positive breast cancer and the therapies used to manage this disease include: cardiac toxicity, fever, cough, muscle pain, fatigue, diarrhea and nausea. Many of these symptoms have the ability to impact daily life, primarily: fatigue, pain and nausea. Therefore it is important for patients to have access to therapies that will extend their life expectancy without significantly increasing side effects that will negatively impact their daily lives.

Inflammatory breast cancer (IBC) is a rare and aggressive form of the disease characterized by red, itchy, swollen, warm and tender breasts. When diagnosed, it is always considered locally advanced. This is because it has already spread to surrounding tissue in the skin and/or lymph nodes. It tends to be more common in younger women and women of African ancestry.² Up to 60% of IBC cases are HER2-positive and the disease tends to have a lower survival rate than other forms of breast cancer. It can be a very aggressive, fast-growing cancer so treatment can also be aggressive. Treatment for IBC involves chemotherapy and targeted therapy-particularly if the cancer is also HER2-positive, surgery (usually mastectomy and axillary lymph node dissection), radiation and further systemic therapy.³

Neoadjuvant treatment of HER2-positive breast cancer in Canada varies across the country. This may be due to restricted access to neoadjuvant treatment in certain parts of the country. However, despite this variation, there is a trend towards increasing use of neoadjuvant treatment for HER2-positive breast cancer, particularly following the demonstrated survival benefits of HER2-directed therapies given later in the disease pathway. A reduction in the size of the tumour may make the disease operable, and in other cases allow for breast-conserving surgery, thereby reducing the need for more complicated procedures like mastectomy and breast reconstruction and their associated risks. Preoperative therapy can also provide a real-time evaluation of tumor response to allow discontinuation of ineffective therapies, and can provide vital prognostic information as a supplement to conventional prognostic data (ie tumour staging, grade, receptor status etc).

¹ Wangchinda, P., Ithimakin, S. Factors that predict recurrence later than 5 years after initial treatment in operable breast cancer. *World J Surg Onc* 14, 223 (2016). <https://doi.org/10.1186/s12957-016-0988-0>

² Inflammatory Breast Cancer Fact Sheet. *National Cancer Institute*. Accessed April 26th, 2021. <https://www.cancer.gov/types/breast/ibc-fact-sheet>

³ Inflammatory Breast Cancer. *Canadian Cancer Society*. Accessed April 27th, 2021. <https://www.cancer.ca/en/cancer-information/cancer-type/breast/breast-cancer/cancerous-tumours/inflammatory-breast-cancer/?region=on>

4. Experiences With Currently Available Treatments

Goals of Current Therapy:

Managing early-stage, HER2-positive breast cancer is always a challenge as patients have more limited treatment options available to them. As HER2-positive breast cancers have been clinically demonstrated to have a higher risk of recurrence than HER2 normal tumors, the goal of therapy is to target cancer cells in the body and reduce the risk of disease recurrence. Currently, most patients receive a combination of the anti-HER2 therapy, trastuzumab (Herceptin), in addition to standard chemotherapy.

This was reinforced in our 2017 survey, most of the HER2+ early-stage breast cancer patients had been or were currently being treated with a combination of surgery, radiation, chemotherapy and the HER2-directed therapy, Herceptin.

Respondents in our 2017 Survey indicated that the following key factors influenced their decision-making around treatments:

1. Effectiveness of the treatment – how well the treatment stabilized their disease and delayed progression of their cancer.
2. Reducing the risk of recurrence without sacrificing quality of life – being able to maintain productive, active lives with minimal disruption to daily routines and avoiding relapse of their cancer.
3. Side effect management – minimizing risk while stabilizing their disease.
4. Cost and accessibility of treatments – affordability and ease of accessing treatments.

Patient Values In Determining Treatment Options:

In our survey of HER2-positive, early-stage breast cancer patients, the majority of respondents (24) were diagnosed with Stage 2 cancer, 11 were diagnosed Stage 1, 13 were diagnosed with Stage 3, 4 did not specify their stage. 5 patients had experienced a recurrence. Most patients had undergone surgery (44 out of the 52 respondents), radiation therapy (33 out of 52 respondents) and chemotherapy (35 out of 52 respondents) as part of their overall breast cancer treatment.

Treatment efficacy:

When asked about deciding on treatment options, patients cited the following as most important to them:

- The effectiveness of the treatment was ranked the most important for patients in deciding on treatment options, with 40 patients declaring it very important to them.
- 38 patients responded that effectiveness of their treatment was the single most important factor in making decisions about their treatment.

- 2 patients stated that avoiding chemotherapy and radiation was the single most important factor for them in making decisions about their treatment, and 1 patient stated that having a choice in therapeutic options was the most important factor for making decisions about their treatment.

"I just wanted to make sure they did everything to get rid of the cancer"-Patient respondent

"If I had to do it over again I would opt out of chemo"-Patient respondent

- Reducing the risk of recurrence was also ranked highly as a priority for patients with 28 patients stating it was very important to them, 2 stated it was important, and 1 patient stated it was somewhat important in their treatment deliberation.

"I only wanted to reduce my risk of recurrence as much as possible. Everything else was secondary. "-Patient respondent

"I worry about reoccurrence"-Patient respondent

Quality of life:

- Maintaining quality of life was also crucial for patients, with 24 patients declaring it very important, 8 stating it was important and 8 stating it was somewhat important.

"My quality of life during and after treatment was the biggest issue for me"-Patient respondent

"Quality of life, & taking treatments extending my life"-Patient respondent

- Maintaining mobility was also essential for patients, with 19 patients stating it was very important to them and 12 stating it was important.
- Maintaining productivity was also a key concern, with 9 patients stating it was very important, 9 patients stating it was important and 13 stating it was a somewhat important factor in their treatment decision-making.

Patient willingness to tolerate treatment side effects

- Minimal side effects was cited by 11 patients as very important, 14 patients as important and 15 patients as somewhat important. Four patients also stated that side effect management was the single most important factor in making decisions about their treatment.

"I was willing to do whatever was best to rid myself of the cancer. I could deal with the side effects and disruption in my life for the long term good." -Patient respondent

"Le dommage à mon système." -Patient respondent

"Les effets de la chimio qui nous sont inconnus et qui fait peur car on en attends parler tellement négativement"-Patient respondent

Factors influencing accessibility:

- Finally, ability to continue childcare duties was ranked by 2 patients as very important, 4 patients as important and 28 patients as not important. CBCN would like to note that the majority of patients who responded to our survey had children over the age of 20 years, and as such it is understandable that for these respondents, childcare was not a concern during their treatment, however for patients with younger children, childcare would be a much more critical factor in determining treatment options.

"I am a mother to 3 children. I wanted to be aggressive in order to increase my chances of survival." -Patient respondent

"le support pour m'aider avec les soins de mon enfant et domestique...mais le plus important le support émotionnel et physique."-Patient Respondent

The Financial Burden Of Treating And Managing Breast Cancer:

The financial burden associated with living with breast cancer extends far beyond any loss of income during a temporary or permanent absence from employment. In addition to the loss of income during illness, breast cancer patients can incur substantial costs associated with treatment and disease management.

Research on the financial impact of breast cancer on patients identified the following:

- 80% of breast cancer patients report a financial impact due to their illness.
- 44% of patients have used their savings, and 27% have taken on debt to cover costs.⁴

These findings were consistent with the responses in our current survey of 52 HER2-positive, early stage breast cancer patients:

- Nine respondents stated that they had experienced a very large financial impact as result of their diagnosis, and 20 stated that they had experienced some financial impact from their diagnosis.
- While at the time of their diagnosis, most respondents (26) were employed full-time, 3 were employed part-time, 4 were self-employed, and 6 were retired, their employment status changed significantly following breast cancer. At the time of our survey, only 10 patient respondents remained employed full-time, 12 were retired,

⁴ Janet Dunbrack, Breast Cancer: Economic Impact and Labour Force Re-entry. Canadian Breast Cancer Network, 2010

5 were part-time, and 5 were on disability and 2 were unemployed. This small snapshot, highlights the significant financial burden placed on early-stage breast cancer patients and their families while undergoing a breast cancer diagnosis.

“Very hard on my family...had to return to work still not feeling strong enough...very hard ...when you’re sick you don’t need this stress on top of everything else..” -Patient respondent

Other barriers included access to private insurance coverage and support medications: While 40 of the 52 patients surveyed reported having private insurance coverage, several (6) also reported challenges accessing medications not publicly reimbursed. Many patients (32) stated that they had been prescribed support medications as part of their treatment and 14 patients stated that their support medications were not provincially reimbursed. Instead, respondents stated that they had to use private insurance (17 respondents) or pay out of pocket (11 respondents) to access medications they had been prescribed.

“Incroyable et très difficile..quand tu es malade...”-Patient Respondent

When I found out how expensive my treatment is, I was absolutely flabbergasted. I had to leave the pharmacy empty handed because a one month supply was over \$1400 and I didn't have the money or amount available on credit. I was told about a form to fill out if my income was below a certain amount but I didn't qualify. So, we paid for it out of pocket and did get some reimbursed from work insurance plan. -Patient Respondent

5. Improved Outcomes

For HER2-positive, early-stage breast cancer patients, reducing the risk of recurrence is of critical concern. Patients have an expectation that Perjeta will provide a possibility for improving their rate of invasive disease-free survival and reduce their risk of recurrence allowing them to live a better quality of life. This is based on the data from the neoadjuvant Phase II NeoSphere study, which showed that nearly 40 per cent of people receiving the combination of Perjeta, Herceptin, and chemotherapy achieved pathological Complete Response (pCR) in the affected breast and local lymph nodes compared to 21.5 per cent of people who received Herceptin and chemotherapy alone. This is further reinforced by data from the Phase II neoadjuvant TRYPHAENA and BERENICE studies, in which pCR rates ranging from 54.7 per cent to 63.6 per cent were achieved across the Perjeta-containing study arms.

Patients are also aware that follow-up data from the NeoSphere trial has suggested that people who received the Perjeta regimen prior to surgery were 31 per cent less likely to experience disease worsening, recurrence or death compared to those who received Herceptin and chemotherapy. People treated with the Perjeta regimen were also 40 per cent less likely to experience disease recurrence or death, suggesting that the pCR

benefit seen with the Perjeta regimen may translate into longer-term improvements in patient outcomes.

Patients understand that Perjeta was approved as neoadjuvant treatment for people with HER2-positive early-stage breast cancer in the U.S. in 2013, and in Europe since 2015. They are aware that there has been a reluctance to accept pCR as a relevant clinical endpoint for approving neoadjuvant therapies in Canada. The breast cancer patient community has expressed general concern that neoadjuvant treatments that have been accepted internationally as standard of care for early-stage breast cancer and having demonstrated value and clinical benefit for patients are not publicly accessible in Canada in the neoadjuvant setting.

It is also of utmost importance to breast cancer patients that neoadjuvant/adjuvant access to HER2-directed agents, like pertuzumab and ado-trastuzumab emtansine, should not end up limiting access to these agents in the metastatic setting. Should patients be treated with HER2-directed therapies in the earlier stage setting, and subsequently progress to a metastatic setting, it is vital that they remain eligible to benefit from these targeted HER2-directed therapies for their metastatic disease.

Adverse Effects

The Phase II NeoSphere trial showed that the Perjeta regimen was not associated with a significant increase in adverse events compared to Herceptin and chemotherapy alone. The most common severe adverse events for the Perjeta regimen were neutropenia (44.9 per cent), febrile neutropenia (8.4 per cent), leukopenia (4.7 per cent) and diarrhoea (5.6 per cent)

Impact Of Treatment Options To Patients

In treating the cancer and reducing the risk of recurrence, this treatment can relieve cancer-related symptoms, and improve a patient's quality of life. When living with no or with minimal cancer-related symptoms, and with minimal side effects from the treatment, patients are able to reduce the impact of cancer on their ability to care for children and dependents, continue with their employment and earn income, spend time with loved ones and participate in their life in a meaningful way by engaging in social activities, travelling, maintaining friendships, and pursuing personal interests.

6. Experience With Drug Under Review

CBCN connected with four Canadian patients with different levels of experience with the treatment:

Patient 1- is a 40 year old woman, diagnosed at age 39 with Stage III, triple positive (estrogen-receptor positive, progesterone-receptor positive, and HER2 positive) invasive ductal carcinoma in October 2020. She is accessing this treatment through her private insurance extended benefits. In addition to Perjeta, she has received Herceptin and chemotherapy.

Patient 2- Is a 52 year old woman with Stage III, triple positive breast cancer patient diagnosed in August 2020. She is accessing this treatment through her private insurance benefits. She has had a lumpectomy, followed by 16 weeks of chemotherapy, 15 cycles of radiation, as well as Perjeta and Herceptin and will soon be initiating hormone therapy as well.

Patient 3- Is a 69 year old woman with triple positive, Stage IIA breast cancer diagnosed in July 2020. She is accessing this treatment through extended private insurance benefits. She has had a partial mastectomy, chemotherapy of doxorubicin, cyclophosphamide, paclitaxel, radiation, Herceptin and Perjeta.

Patient 4- Is a 62 year old woman with triple positive, Stage II breast cancer diagnosed in March 2020. She is accessing this treatment partially (80 percent) through her extended private insurance benefits through her employer, and partially out of pocket (20 percent). Her treatment regimen so far has included surgery, chemotherapy, radiation, Letrozole, Herceptin, Perjeta and a bone therapy.

The Impact of the Treatment on the Disease

All of the patients expressed their gratitude at having access to this treatment. Patient 1 noted her personal satisfaction with the treatment and all of the patients noted their oncologists confidence in using the therapy. Many of the patients cited the possibility of increasing their chance of survival and reducing their risk of recurrence as major factors in deciding to pursue this therapeutic option.

“The clinical trials say it offers a benefit. I think it was a six percent benefit in taking it to prevent recurrence. And also just to shrink the tumour. Because I haven’t had surgery yet. So my tumour was just under five centimeters, so we’re trying to shrink it down. And it’s worked”- Patient 1

“My oncologist suggested it. He said this is the one we need. And so that’s why. And I know it increases the chance of survival by three percent. And then maybe over the years that increase will be even higher. But that’s why I decided to go with it.”-Patient 2

“I thought, if I have access to it, I’m going to use every means I can. Because in my case, my particular cancer, I’ve been told, is what they call curative. So once the treatment is done, I go down to 13 percent probability of ever seeing it again, which is normal for most people, I’m told”- Patient 3

"I see it is good treatment....The result of this treatment, I cannot say. It is still a possibility just to prolong my life."-Patient 4

Assessing Risks Associated with the Treatment

The patients had very different responses to the treatment. Most patients noted that it was very difficult for them to determine if the side effects they experienced were from chemotherapy or from the addition of Perjeta to their treatment regimen. The patients had differing experiences with the tolerability of their side effects but all of the patients ranked their quality of life on Perjeta highly.

Patient 1 experienced mild nausea, gastrointestinal issues and fatigue, but ranked her quality of life as medium and tolerable.

"It's hard to tell because they're all given together....So it's really hard to distinguish which one is causing which side effect. Overall, looking at them all together, it hasn't been that bad".- Patient 1

Patient 2 noted the relative ease of taking Perjeta compared to chemotherapy. She experienced gastrointestinal issues, and vision acuity. She rates her quality of life as high-up to eight or nine out of 10.

"The two infusions seem to be less problematic than the chemo, for example. I have to say I was quite fortunate, but I didn't have anything that was unmanageable. With the chemo, I managed to pass through it okay. It wasn't a picnic, but I got through it. But with the Perjeta, apart from some gastrointestinal issues, I really don't have much of a problem with it at all."- Patient 2

"Not more difficult to tolerate. "It's markedly easier. The chemos were a bit tough. It just took all of my energies out of me. I was really tired with that. I'm still on the tail end of my radiation therapy—of recovering from it—but it's markedly better than it was."-Patient 2

"It's a little hard with this COVID situation. It's a little hard to figure because nobody's normal right now. But on a scale of one to ten, I would probably say eight, nine. I'm still regaining my energies, so I'm not all the way back yet from all the chemo and the radiation. But I'm getting there. I'm feeling better every day."-Patient 2

Patient 3 experienced fatigue and increased muscle and joint pain. She ranks her quality of life as good, at a 5 out of 10, although she is concerned about the tolerability of her joint pain. She does not want to suspend her treatment, despite her pain, as she wants the possibility of increased survival.

"That's a big question for me. I started Perjeta when I started my second round of chemotherapy, the second drug. At the beginning it didn't seem to affect me. I was still on the chemo drug. So it was very easy for me. I could feel some side effects, I thought, from the chemo, a few days after, but then I was fine. It was every two weeks. Aside from the side effects that I got from the beginning, the loss of hair and all that, the second round of chemotherapy, I didn't have any bad side effects in terms of my bones or joints or muscle aches. And I had already started the Perjeta." -Patient 3

"I worry because I don't know where it's coming from. If it is side effects from the Perjeta. Maybe I'm among the percentage that causes this side effect. How do I determine if it's from the Perjeta or if it's still all the effects that I'm getting from the chemo. My quality of life is good. I just feel very frustrated because I can't do the things I used to do"-Patient 3

Patient 4 experienced weakness, diarrhea, gastrointestinal issues, neuropathy in her hands, sleep issues and muscle aches. She noted that she is not clear if these symptoms are caused by her Perjeta regimen. She ranks her quality of life highly as a 7 or 8 out of 10.

"I tolerate very well this treatment...My side effects are mild, very, very mild. They're not so strong. " -Patient 4

"I rate my quality of life at about seven or eight out of ten. At the beginning...I was very, very weak and sick, but after that, I slowly, slowly was okay. And still I am okay. Now I would say I am going to normal life."-Patient 4

Alternatives To The Treatment

Most of the patients noted that without access to Perjeta, they would have either had to forego the treatment, or fight to advocate for access to the treatment. While Patient 3 was uncertain of what her other treatment options may be, Patient 2 mentioned that without this treatment, she would have likely been left with only Herceptin or chemotherapy as an alternative treatment and Patient 4 noted that without Perjeta-Herceptin, she did not have any other choices.

"That's a hard question to answer. I'm very grateful it is available. I would probably look at the funding program. I wasn't sure if my extended benefits were going to cover it, so then the next step was to go and look at Roche . They have a program where they fund the drug. So looking at that in order to get it or starting a GoFundMe. I have a friend who offered to start a GoFundMe page to pay for it. And if it wasn't approved in Canada, I'd start looking at what additional more aggressive drug treatments are available or if there was a clinical trial."-Patient 1

"Without Perjeta, I'd have to use Herceptin alone maybe. I'm glad we were able to do this. When you have cancer, you want to use every means to stop it. So I'm very happy that my insurance covered it and that I could make use of it. " -Patient 2

"The doctor appears to have the notion that it does have some curative effect, or she wouldn't have recommended it to me. I'm just glad that I was able to take advantage of every possibility. Something to deal with the cancer that I got."-Patient 3

"If I didn't have the Perjeta, I think I would be getting Herceptin alone, maybe?" -Patient 3

"My oncologist suggested it. There were no other choices."-Patient 4

The Social and Financial Impact of the Treatment

The patients discussed the financial impact of the treatment and specifically addressed what having access to Perjeta meant to them and their families. Since all of the patients accessed the treatment through their private insurance benefits, with Patient 4 also paying out of pocket, they all noted the lack of public reimbursement for the treatment and the value of having additional therapeutic options available to them.

Patient 1 noted the value of the treatment itself, coupled with the need for Canadian patients to have access to the same standards of care used in other jurisdictions.

“Having just that additional little bit of peace of mind that I’m doing everything that I can. I’m pretty young. I’ve got a young family. I’ve got a three-year-old. So I need to be able to say that I’ve done everything that I possibly can to beat it. So having that peace of mind that I’m getting the same care that others are getting elsewhere in the world, so I don’t have to look at going somewhere else and all the costs and finances involved. If there was a breakthrough treatment that was working in the U.S. but not available in Canada, having to somehow try to finance going there to go get that treatment.” -Patient 1

“The drug works and women should be able to get access to it. You know, there’s been clinical trials that show its effectiveness, and it’s so important that Canadians are getting the same treatment that others are getting elsewhere in the world. Having a cancer diagnosis is such a stressful thing to go through. Just knowing that the care that we’re receiving is top-notch is so important. That everything is being done to try and save our lives. I think it’s so important there’s new drugs coming out other than Perjeta as well. Just to get them available for Canadian women is so important.”-Patient 1

Patients 2 and 3 both discussed their gratitude at being able to access the treatment and the value of the therapy for patients in general.

“I’ll know better in time how good the effect of it was on me and whether it did the job or not. I’m talking to you early on that. Like I say, I’m just glad to have access to it. Because any little help is something, especially when you’ve got cancer patients who are basically just trying to add days and weeks and months to their lives. So I’m glad I have this.” -Patient 2

“I was so happy that I was able to get it. Because like I said, my doctor said this is the one we really need. Finally, when my insurance approved it, I was over the moon happy. It’s a blessing that I can actually get it.”-Patient 3

Patient 4 delved into the financial burden of paying out of pocket for their treatment and the challenges of accessing the medication financially. She highlighted the need for public reimbursement of the therapy to ease the financial strain on patients and their families.

“Regarding funding. Because even when they asked me for my group insurance, and they said my insurance would cover Perjeta 80 percent, and the other 20, I should cover myself. But the first dosage was double. It means one infusion is \$3800-something. It means around \$8000 I’m supposed to pay for the first infusion. And now I’m going to this treatment, there will be a total of 16 infusions. Every time I will pay \$3800. It is a lot for one person to cover this every three weeks.”-Patient 4

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

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.

CBCN did connect with the manufacturer, Roche Canada, to connect us with patients with experience on the treatment.

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.

All other research, interviews and outreach to patients was conducted independently by the Canadian Breast Cancer Network, as was the compilation of information and data for the writing of this submission.

The Canadian Breast Cancer Network is committed to adhering to the Code of Conduct Governing Corporate Funding

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.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Roche Canada				x

I hereby certify that I have the authority to disclose all relevant information with respect to any

matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Niya Chari

Position: Director of Health Policy and Public Affairs

Patient Group: CBCN

Date: May 4, 2021

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	Perjeta in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either 2 cm in diameter or node positive).
Name of the Patient Group	Rethink Breast Cancer
Author of the Submission	
Name of the Primary Contact for This Submission	
Email	
Telephone Number	

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

Rethink Breast Canada's mission is to empower young people worldwide who are concerned about and affected by breast cancer through education, support and advocacy. Since 2001, we have been building community for young women dealing with breast cancer and providing support and resources to help them live the best quality of life. We represent the voice of young women dealing with breast cancer and strive to ensure their needs and values are heard and considered in all aspects of breast cancer treatment and care at all stages of their breast cancer experience. www.rethinkbreastcancer.com

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered in **Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

Online patient surveys were conducted between March 23 and April 19, 2021. The survey asked questions about the impact of breast cancer on the lives of patients, the effect of current treatments and their willingness to accept side effects for improved health outcomes. The

survey also included questions directed to patients with Perjeta treatment experience. Potential respondents were identified through messages to Rethink Breast Cancer's mailing list as well as the Young Women's Network and partner organizations. Messages were also posted on Facebook and Twitter as well as the Cancer Connection online discussion forum.

A total of 62 women completed the patient survey. Of these respondents, 37 are from Canada (representing Alberta, British Columbia, New Brunswick, Ontario, Quebec and Saskatchewan), 22 are from the United States, and 1 is from Mexico, Macedonia and Portugal. 7 respondents agreed to participate in telephone interviews with staff members to discuss their treatment experience and elaborate on their feedback.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

All 62 respondents were diagnosed with HER2-positive breast cancer in stage 1, 2, or 3. Of these respondents, 41 have treatment experience with Perjeta, 39 had been diagnosed with locally-advanced, inflammatory or early-stage breast cancer when they began receiving Perjeta, 40 received Perjeta in combination with trastuzumab and chemotherapy, and 38 received Perjeta as neoadjuvant therapy. In total, 35 respondents match the full indication for this review.

Most respondents were diagnosed in the last two years - 4 were diagnosed in 2021, 31 were diagnosed in 2020, 12 were diagnosed in 2019, 5 were diagnosed in 2018, 6 were diagnosed in 2017 and 4 were diagnosed earlier.

16 respondents are currently receiving neoadjuvant therapy, 18 are currently receiving adjuvant therapy, 23 have had a pathological complete response, 1 is receiving treatment after recurrence, 2 have completed treatment and 2 have had disease progression.

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

All 62 respondents provided information about the treatments they had undergone since their diagnosis. Herceptin was by far the most commonly received form of treatment. No other drug was reported by more than 12 respondents.

Treatments Received	n	Treatments Received	N
Trastuzumab (Herceptin)	56	Capecitabine (Xeloda)	2

Trastuzumab emtansine (Kadcyla)	12	Cyclophosphamide (Cytosan)	2
Carboplatin (Paraplatin)	11	Letrozole (Femara)	2
Pertuzumab, trastuzumab, and hyaluronidase (Phesgo)	10	Taxotere, Carboplatin, Herceptin and Perjeta (TCHP)	2
Docetaxel (Taxotere)	10	Neratinib (Nerlynx)	1
Paclitaxel (Taxol)	7	Zoledronic acid (Zometa)	1
Unspecified chemotherapy	6	Doxorubicin (Adriamycin)	1
Adriamycin and Cyclophosphamide (AC)	5	Fluorouracil, epirubicin, cyclophosphamide and docetaxel (FEC-D)	1
Radiation	4	Anastrozole (Arimidex)	1
Adriamycin, Cyclophosphamide and Taxol (AC-T)	3	Leuprorelin (Lupron)	1
Goserelin (Zoladex)	3	Exemstane (Aromasin)	1
Tamoxifen (Nolvadex)	2		

Fatigue was the most commonly reported side effect of these treatments (80%, n=61), followed by diarrhea (64%), nausea (44%) and insomnia (39%).

Fatigue was most frequently cited as the hardest-to-tolerate side effect of these treatments. Diarrhea, nausea, neuropathy and taste changes were also cited by at least 10% of respondents.

Most respondents (73%, n=62) did not report any difficulty accessing treatment.

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Rethink Breast Cancer asked patients to evaluate the importance of different outcomes for their breast cancer treatment on a scale of 1 (not important) to 5 (very important). Eliminating cancer cells, preventing recurrence and preventing metastases were overwhelmingly rated as the most important results suggesting that patient values prioritize long-term health outcomes over more immediate concerns like reducing symptoms or managing side effects.

Importance of outcome	1 - not important	2	3	4	5 – very important	Average
Controlling disease progression	0.00% 0	0.00% 0	1.67% 1	0.00% 0	98.33% 59	4.97 60
Reducing symptoms	0.00% 0	0.00% 0	1.67% 1	0.00% 0	98.33% 59	4.97 60

Maintaining quality of life	0.00% 0	6.67% 4	11.67% 7	18.33% 11	63.33% 38	4.38 60
Managing side effects	1.64% 1	13.11% 8	16.39% 10	22.95% 14	45.90% 28	3.98 61
Preventing recurrence	0.00% 0	0.00% 0	0.00% 0	3.28% 2	96.72% 59	4.98 61

Respondents were also asked if they would be willing to tolerate new side effects from new drugs to extend life expectancy. On a scale of 1 (will not tolerate side effects) to 10 (will tolerate significant side effects), respondents gave an average score of 8.57, supporting the conclusion that patient values prioritize health outcomes. It should be noted that patients who received Perjeta gave an even higher score of 8.8 (n=40).

Comments included:

- I am willing to suffer side effects if there is solid evidence that it will eliminate cancer cells and prevent recurrence. The fear of recurrence is a burden that cancer survivors need to live with everyday.
- I will tolerate whatever symptoms I have to so that I can survive and take care of my children.
- This is rough to answer! I just finished chemo and feel like there's no way I'd ever do it again. Period. But at the same time how do you not do *whatever* it takes to stay alive? I'd undergo near death side effects in order to avoid death....

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

35 respondents match the full indication for this submission – they had been diagnosed with locally-advanced, inflammatory or early-stage breast cancer (either >2cm in diameter or node positive) when they began receiving Perjeta, they received Perjeta in combination with trastuzumab and chemotherapy, and they received Perjeta as neoadjuvant therapy.

Of these 35 respondents, 20 received Perjeta as neoadjuvant therapy for a total mastectomy, 7 received Perjeta in preparation for a lumpectomy, 2 for a modified radical mastectomy, 1 for a skin-sparing mastectomy, 3 for an unspecified mastectomy and 2 respondents declined to answer the question. Three of these procedures were reported to include reconstruction. 15 respondents continued to receive Perjeta after surgery; all other respondents completed their course of treatment.

At the time of the survey, 11 respondents had received for Perjeta for 0-3 months, 11 had received it for 3-6 months, 12 had received it for 6-12 months and 1 respondent had received it for more than one year.

21 respondents achieved pathological complete response within one year of their breast cancer surgery, 1 did not and 13 were unsure or did not answer. Of the 21 respondents who achieved pCR, only 1 has since had a recurrence; the other 20 remain free of cancer cells.

Quality of Life

Patients were asked to rate the change to their quality of life on Perjeta compared to other treatments they had received on a scale of 1 (much worse) to 5 (much better). Respondents felt that Perjeta had improved their quality of life in every listed area. In fact, no category received a score lower than 3.8. However, preventing recurrence and eliminating cancer cells received the highest scores overall.

Change to quality of life on Perjeta	1 – much worse	2	3	4	5 – much better	Average
Eliminating cancer cells	0.00% 0	0.00% 0	15.79% 3	15.79% 3	68.42% 13	4.53 19
Preventing recurrence	0.00% 0	0.00% 0	13.33% 2	13.33% 2	73.33% 11	4.60 15
Cancer symptoms	0.00% 0	5.56% 1	5.56% 1	22.22% 4	66.67% 12	4.50 18
Drug side effects	0.00% 0	13.64% 3	22.73% 5	27.27% 6	36.36% 8	3.86 22
Maintaining quality of life	0.00% 0	4.35% 1	17.39% 4	30.43% 7	47.83% 11	4.22 23
Ability to work	0.00% 0	0.00% 0	40.00% 6	20.00% 3	40.00% 6	4.00 15
Ability to sleep	6.67% 1	6.67% 1	26.67% 4	20.00% 3	40.00% 6	3.80 15
Ability to drive	0.00% 0	0.00% 0	13.33% 2	20.00% 3	66.67% 10	4.53 15
Ability to perform household chores	0.00% 0	0.00% 0	40.91% 9	31.82% 7	27.27% 6	3.86 22
Ability to care for children	0.00% 0	0.00% 0	13.33% 2	46.67% 7	40.00% 6	4.27 15

Comments included:

- Taking Perjeta has offered me peace of mind in addition to its treatment benefits.
- I did not experience any side effects that were very concerning. I feel better that it was an added drug that helped with eliminating cancer and prevent reoccurrence
- Overall, I am very happy I had access to Perjeta. My tumor did not respond to AC but had an excellent response to Taxol + H+P
- Positive: side effects are tolerable, my tumor shrunk from 7.5 cm to 1.1 cm. Negatives: diarrhea and nausea, lack of taste/bad taste in my mouth causing foods to taste horrible.
- Good so far. This treatment needs to be added to Ontario Cancer Care so all have in Ontario have access to this drug.
- Thankful for knowing there is a drug out there that can help eliminate a chance of reoccurrence.

It should be noted that several patients said that they had difficulty distinguishing which effects were due to Perjeta and which were due to the other drugs they were concurrently receiving.

Side Effects

Diarrhea and fatigue were the most commonly reported side effects of Perjeta (84% and 81% respectively, n=32) followed by alopecia (38%), neutropenia (25%) and nausea (22%). However, respondents overwhelmingly described these side effects as tolerable.

When asked how much they could tolerate the side effects associated with Perjeta on a scale of 1 (completely tolerable) to 10 (completely intolerable), the average score was 8.82 with no respondent giving a score lower than 5. We would like to note that this is the highest score ever recorded in a survey conducted by Rethink Breast Cancer.

Rating	Responses	Rating	Responses
1	0.00% 0	6	9.09% 3
2	0.00% 0	7	3.03% 1
3	0.00% 0	8	18.18% 6
4	0.00% 0	9	6.06% 2
5	6.06% 2	10	57.58% 19

Comments included:

- Compared to the first chemo I was on, the side effects were minor
- Totally worth it

Several respondents also emphasized that they willing to tolerate the side effects associated with Perjeta because of its medical value:

- Even if there were stronger side effects, I think they would have to be pretty severe to have wanted to stop taking [Perjeta]
- Anything that's led to my post-op NED result was well worth it
- If you have a scan or you have another ultrasound and you see the reduction in the tumor so quickly, it had an impact on anxiety, on positivity, on quality of life
- Symptoms are temporary, I would rather not feel well for a short term and be here cancer free for the long term.

During telephone interviews, a few respondents noted that they had some difficulties with the loading dose even as they found the rest of their Perjeta treatment to be manageable.

Other Feedback

Some respondents commented on the benefit of having a targeted treatment for HER2-positive breast cancer:

- Knowing that it's out there, it was great to have access to something that partnered so well in targeting the HER2 factor
- As soon as I saw the studies that said the dual-targeted therapy HER2 gives you an added benefit in neoadjuvant and in adjuvant, I wanted to have it for myself

Due to the lack of coverage approximately 30% of respondents (n=34) had to find an alternative source to access Perjeta for neoadjuvant treatment.

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

8. Biosimilar

If the drug in review is a biosimilar (also known as a subsequent entry biologic), please outline any expectations or concerns held by patients, caregivers, and families about the biosimilar. If the biosimilar was less expensive than the brand name drug, what would the impact be for patients, caregivers, and families?

9. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

Patient Recommendation

When asked if they would recommend Perjeta to other patients with breast cancer, 100% of respondents who matched the full indication said that they would.

Asked to elaborate, respondents commented:

- If Perjeta assists in eliminating HER2+ cancers and keeping them away, as I believe it has, I see it as a must for anyone facing these odds.
- The ultimate goal is CURE. With a pCR from the quadruplet, it makes it all worth it. A further decrease in risk of recurrence with very little added toxicity is also very important to reduce anxiety levels.
- This is standard of care in so many places. It is a mystery to me that Canada has not recognized its contribution to improving Breast Cancer patients' survival rate.

- Just for the fact that it is a drug that would add to preventing reoccurrence with minimal side effects I found it very beneficial.
- It's working! Side effects are a small price to pay in order to get this cancer out of my body!!!
- It is helping to shrink tumor. Causes diarrhea but it is manageable for the benefit it provides. After 1 treatment, there was noticeable difference.
- I would definitely recommend it to anyone who was in the same position as me

Key Points:

1. Every respondent who received Perjeta said that they would recommend it to other patients with breast cancer.
2. Patient values prioritize long-term health outcomes.
3. The outcomes reported by respondents who received Perjeta were overwhelmingly positive.
4. Perjeta improved the average quality of life for respondents in every listed category.
5. Respondents rated the side effects of Perjeta as the most tolerable of any therapy reviewed by Rethink Breast Cancer.

Appendix: Patient Group Conflict of Interest Declaration

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

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

We asked Roche to provide us with information about the general characteristics of the drug and its benefits. We asked our Scientific Advisory Committee (medical oncologists) about this drug and its benefits and whether it addressed an unmet need. Adam Waiser is a freelance health technology assessment writer who we contracted to help us with writing this submission.

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.

We contracted Adam Waiser to help us develop the survey we used to collect the data used in this submission. All telephone interviews were conducted by Rethink Breast Cancer staff. Adam Waiser helped us analyze the findings of our survey and interviews.

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.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Hoffmann-La Roche Limited				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: MJ DeCoteau
Position: Executive Director
Patient Group: Rethink Breast Cancer
Date: May 3, 2021