CADTH

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	**Adam Waiser**
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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 (Cytoxan)	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 it's benefits. We asked our Scientific Advisory Committee (medical oncologists) about this drug and it's 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