CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Piqray (alpelisib), in combination with fulvestrant, is indicated for the treatment of postmenopausal women and men, with hormone receptor-positive, HER2-negative, PIK3CA mutated advanced or metastatic breast cancer after disease progression following an endocrine-based regimen.**
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 Cancer'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. Because up to 30% of all breast cancers become metastatic, Rethink Breast Cancer has always worked closely with young MBC patients—women who, sadly, leave our community far soon. 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 31 and April 8, 2021. The surveys 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 Piqray 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 and Cancer Survivors Network online discussion forum.

A total of 24 women completed the patient survey. Of these respondents, 4 are from Canada (representing British Columbia and Ontario) and 20 are from the United States. Six of the respondents in this group 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 24 respondents are post-menopausal women who have been diagnosed with HR-positive, HER2-negative, advanced or metastatic breast cancer with a PIK3CA mutation. All of the respondents also have treatment experience with Piqray and received Piqray in combination with fulvestrant. 22 respondents reported that they had been treated with an aromatase inhibitor prior to receiving Piqray, while 2 were unsure. 20 respondents were treated with a CDK 4/6 inhibitor prior to receiving Piqray; 4 were not. In total, 18 respondents completely match the indication for this review.

2 respondents were diagnosed in 2018, 4 were diagnosed in 2017, 3 were diagnosed in 2016, 7 were diagnosed between 2011-2015, and 8 were diagnosed in 2010 or earlier.

11 respondents are currently receiving third-line treatment or higher, 6 are receiving treatment after recurrence, 5 are receiving second-line treatment, 1 is receiving first-line treatment and 1 has had no evidence of disease for six months or less.

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 24 respondents provided information about the treatments they had received since their diagnosis. Every respondent received fulvestrant in combination with Piqray. Over half of respondents were also treated with letrozole or palbociclib.

Treatments Received	n	Treatments Received	n
Fulvestrant (Faslodex)	24	Paclitaxel (Taxol)	2
Letrozole (Femara)	19	Ribociclib (Kisqali)	1
Palbociclib (Ibrance)	17	Goserelin (Zoladex)	1
Exemestane (Aromasin)	10	Denosumab (Xgeva)	1
Anastrozole (Arimidex)	9	Pertuzumab (Perjeta)	1
Tamoxifen (Nolvadex)	6	Trastuzumab (Herceptin)	1
Capecitabine (Xeloda)	6	Trastuzumab emtansine (Kadcyla)	1
Abemaciclib (Verzenio)	3	Doxorubicin, cyclophosphamide and paclitaxel (AC-T)	1
Everolimus (Afinitor)	3	Talazoparib (Talzenna)	1

Most respondents have undergone multiple lines of treatment and reported a wide range of outcomes and side effects.

Fatigue was the most commonly reported side effect of these treatments (100%, n=24), followed by diarrhea (83%), loss of appetite (75%), nausea (54%) and headache (46%).

Fatigue, diarrhea and hyperglycemia were identified as the most difficult to tolerate side effects of previous treatments.

Most respondents (86%, n=21) 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). Controlling disease progression is considered the most important patient value with every respondent giving it the highest possible score.

Importance of outcome	1 - not important	2	3	4	5 – very important	Average
Controlling disease progression	0.00% 0	0.00% 0	0.00% 1	0.00% 0	100.00% 24	5.00 24
Reducing symptoms	0.00%	8.33%	29.17%	25.00%	37.50%	3.92

	0	2	7	6	9	24
Maintaining quality of life	0.00% 0	0.00% 0	4.17% 1	37.50% 9	58.33% 14	4.54 24
Managing side effects	0.00% 0	0.00% 0	25.00% 6	0.00% 6	50.00% 12	4.25 24
Preventing recurrence	12.50% 3	4.17% 1	0.00% 0	8.33% 2	75.00% 18	4.29 61

Comments include:

- Anything that gives people months or years is beneficial.
- As long as it's working, it's tolerable.

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 7.6 and no respondent gave an answer lower than 5, indicating that patient values are willing to tolerate side effects for drugs that can improve long-term health outcomes.

Comments include:

- I have a seven-year-old and nine-year-old. I'm not ready to leave them.
- I will tolerate pretty much anything within reason in order to find and stay on a drug that keeps the tumour burden low.

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?

18 respondents completely match the indication for this review:

1. They have HR-positive, HER2-negative, advanced or metastatic breast cancer.
2. Their breast cancer includes a PIK3CA mutation.
3. They are post-menopausal.
4. They have been treated with Piqray in combination with fulvestrant.
5. They were treated with an aromatase inhibitor and a CDK 4/6 inhibitor prior to receiving Piqray.

The feedback from these 18 respondents will be described in this section.

Patient Experience

All of the respondents had at least 4 months of experience with Piqray: 7 respondents had received Piqray for 4-6 months, 3 respondents had received it for 7-12 months, 2 respondents had received it for 13-18 months, and 5 respondents had received it for 19-24 months.

12 respondents were still receiving Piqray at the time of the survey, 5 stopped receiving it because it did not control their cancer and 1 person stopped receiving it because she could not tolerate the side effects.

10 respondents required a dose reduction due to side effects, 1 respondent had to discontinue treatment before restarting, and 1 person discontinued treatment after the dose reduction failed to alleviate the side effects.

Quality of Life

Patients were asked to rate the change to their quality of life on Piqray compared to other treatments they had received on a scale of 1 (much worse) to 5 (much better). While respondents felt that Piqray had improved their quality of life, the impact seems to have been weak in most areas with no average score higher than 3.61. Drug side effects were the notable exception – most respondents felt these were the same or worse than other treatments they had received.

Change to quality of life on Perjeta	1 – much worse	2	3	4	5 – much better	Average
Controlling disease	5.56% 1	11.11% 2	38.89% 7	22.22% 4	22.22% 4	3.44 18
Metastatic cancer symptoms	0.00% 0	5.56% 1	50.00% 9	16.67% 3	27.78% 5	3.61 18
Drug side effects	16.67% 3	22.22% 4	33.33% 6	22.22% 4	5.56% 1	2.67 18
Maintaining quality of life	0.00% 0	33.33% 6	27.78% 5	27.78% 5	11.11% 2	3.16 18
Preventing recurrence	5.88% 1	0.00% 0	52.94% 9	23.53% 4	17.65% 3	3.47 17
Ability to work	5.88% 1	17.65% 3	52.94% 9	17.65% 3	5.88% 1	3.00 17
Ability to sleep	5.56% 1	5.56% 1	50.00% 9	33.33% 6	5.56% 1	3.27 18
Ability to drive	0.00% 0	5.56% 1	61.11% 11	22.22% 4	11.11% 2	3.38 18
Ability to perform household chores	5.88% 1	17.65% 3	35.29% 6	29.41% 5	11.76% 2	3.24 17
Ability to care for children	0.00% 0	13.33% 2	46.67% 7	33.33% 5	6.67% 1	3.33 15

Side Effects

Large majorities of patients experienced diarrhea (88.9%, n=18), reduced appetite (77.8%), weight loss (72.2%) and alopecia (66.7%). While not cited as frequently, hyperglycemia was often highlighted during patient interviews as being especially hard to manage.

When asked how much they could tolerate the side effects associated with Piqray on a scale of 1 (completely intolerable) to 10 (completely tolerable), the average score was 6.47. However, it should be noted that only two respondents gave a score lower than 5. Thus, it might be more accurate to say that most respondents did not find the side effects associated with Piqray to be intolerable.

Rating	Responses	Rating	Responses
1	5.88% 1	6	5.88% 1
2	0.00% 0	7	5.88% 1
3	5.88% 0	8	17.65% 3
4	5.88% 1	9	11.76% 2
5	23.53% 4	10	17.65% 3

Comments include:

- I wish I had my hair, I wish I didn't have to follow such a strict diet, and every so often and I feel nauseous, but I have stage four cancer. I know that any drug is going to have side effects and this is so much better than Taxol.
- [Nausea] got so bad at one point that I couldn't even stand looking at a picture of food … but that passed.
- I am tolerating, but it is difficult.
- Important to find effective ways to manage SE right away, especially in the first 4 months when there are so SE that are pretty overwhelming.
- I find Piqray extremely manageable … if you do what you're supposed to do.
- This is not an easy drug [repeated multiple times during interview]
- Piqray worked for almost 18 months and was tough but manageable. I did not have any of the major side effects like blood sugar issues or the rash. I got itchy but that was controlled with antihistamines. I do lose my sense of taste and appetite but that was minor and manageable, although I did lose weight.

Several respondents also said that dose reductions made an important difference in helping them manage the side effects associated with Piqray.

When discussing the side effects they had experienced from Piqray, interviewees would often contrast them with the side effects they had experienced with previous treatments. The side effects were described as unpleasant, but generally manageable.

Comments include:

- The reality is - if you have cancer, none of the drugs are without side effects.
- It gave me another year and a half or so without having to go to chemo.

PIK3CA Treatment Option

Respondent feedback about the mental or emotional value of having a dedicated treatment option for PIK3CA-mutated breast cancer was inconclusive. Respondents were broadly split about whether Piqray helped their mental or emotional well-being.

Comments include:

- Absolutely, without this drug I would be going through lines of treatment more quickly. About 40% of MBC have this mutation that up to now had no good treatment option.
- After reading A LOT about Piqray, I was very nervous to start taking it.
- This specific mutation is being attacked and that really made me feel good. And that was one reason why I was willing to put up with a lot in order to stay on that drug.

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.

Piqray has a companion diagnostic, which is used to identify PIK3CA mutations. Of our respondents:

79% of respondents (n=24) have received genomic testing of their tumor – 21% received a blood test, 21% had their tumor biopsied, and 37.5% received both a blood test and a biopsy. Most respondents were tested for a PIK3CA mutation after their cancer became metastatic (30%) or when previous lines of treatment failed (52%).

One of the Canadian patients we interviewed by telephone shared her experience with a companion diagnostic for the P1K3CA mutation to determine eligibility in a clinical trial. Her longest wait times were for a biopsy time and then waiting for results, recalling her wait time for a biopsy was about 3 weeks and her wait time for the results was about 4 weeks. The clinical trial nurse phoned her with the results and her treatment started quickly after that. Reflecting back on the experience with companion diagnostic testing, she shared:

"The biopsy itself took several hours and was challenged by getting enough of a sample for analysis. In one case the sample sent to Switzerland; the more recent sample was sent to California. In both cases I asked that, depending on sample availability, enough material be collected for a Foundation One analysis. My thinking was that if I didn't qualify for the clinical trial, ie. have the mutation, then I would submit a sample for analysis to Foundation One. Cost was an issue.

I think access to liquid biopsy would improve the information flow assuming the blood biopsy provides adequate information. I also think it's important to have access to Foundation One testing when tumours become resistant to treatment. Knowledge and information are power and can help with decision making recognizing that there may not be effective treatments available. It would help with finding clinical trials.

I had a reasonable understanding of why the test was happening. At that time it was the only way to get the mutation confirmed. What was more difficult was understanding how the biopsy would be done and what it would feel like. The radiologist was excellent and clear in his explanation however given the location of my tumours, it is quite a rigorous and somewhat painful process.

I was excited, nervous, and anxious while waiting for the results. Excited because we were moving forward with getting what felt like better information. Nervous because of the unknown, uncertain path forward. And anxious because time was passing without a treatment plan. I have a low tumour burden and keeping it low is key to my ongoing survival and health."

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?

When asked if they would recommend Piqray to other patients with breast cancer, 17 of 18 respondents who matched the full indication for this review said that they would. The lone dissenter indicated that she would rather use Piqray as a last resort. Respondents emphasized that they were willing to tolerate side effects for a drug like Piqray that could potentially control disease progression. However, they also acknowledged that managing these side effects could be a significant challenge.

Asked to elaborate, respondents commented:

- Piqray is kicking my cancer's butt and I have a relatively decent quality of life. I do encourage women to keep their oncologist informed of side effects, to get a dose reduction when possible and to drink a lot of water.
- If it's your only option before IV chemo, then it certainly doesn't hurt to give it a try.
- I finally bought a calendar … after I started in Piqray. I had been scared to plan anything.
- I would suggest they try it but they need to be closely monitored for side effects.
- Piqray controlled my cancer for almost a year and a half, which was a pretty long time, and my side effects were manageable. This treatment was easier to handle than most I'd been on.
- It's very manageable; you can manage the side effects and it really works. It really slows down the cancer.
- This is not an "easy" drug to take given the many and sometimes difficult SE that occur. That said it is the only drug out there targeting this mutation which makes it extremely useful and worth pursuing.
- Is it worth it? Well yeah. Here I am. I thought I would be dying now. I'm not.

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 Novartis 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 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
Novartis				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 14, 2021