CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Tucatinib is indicated in combination with trastuzumab and capecitabine for treatment of patients with locally advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received prior treatment with trastuzumab, pertuzumab, and trastuzumab emtansine, separately or in combination.**
Name of the Patient Group	**Rethink Breast Cancer**
Author of the Submission	**Adam Waiser**
Name of the Primary Contact for This Submission	**MJ DeCoteau**
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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 who are concerned about and affected by breast cancer through education, support and advocacy. Since 2001, we have been building community for those diagnosed with breast cancer at a younger age, providing support and resources to help them live the best quality of life. We represent their voices 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. Because up to 30% of all breast cancers become metastatic, Rethink Breast Cancer has always worked closely with young MBC patients. Our community experiences tremendous loss from this life-limiting disease and our organization places a major focus on the unmet needs of those living with MBC. 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 2 and April 7, 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 Tukysa treatment experience. Potential respondents were identified through messages to Rethink Breast Cancer's mailing list as well as the Rethink's closed Facebook group and partner organizations. Messages were also posted on Rethink's public Facebook, Instagram and Twitter channels as well as the Breastcancer.org, Cancer Connection and Cancer Survivors Network online discussion forums.

A total of 51 women completed the patient survey. Of these respondents, 37 are from Canada (representing Alberta, British Columbia, Manitoba, Nova Scotia, Ontario, Quebec & Saskatchewan), 12 are from the United States, 1 is from Mexico and 1 chose not to answer. All 51 respondents have been diagnosed with HER2-positive locally advanced unresectable or metastatic breast cancer, and 6 respondents have treatment experience with Tukysa. The latter group of patients will be profiled in section 6. Five of the respondents in this group agreed to participate in telephone interviews with Rethink 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?

7 respondents were diagnosed in 2020, 8 were diagnosed in 2019, 6 were diagnosed in 2018, 3 were diagnosed in 2017, 8 were diagnosed in 2016, 6 were diagnosed in 2015, 8 were diagnosed in 2014 and 5 were diagnosed earlier.

21 respondents are currently receiving first-line treatment, 5 are receiving second-line treatment, 9 are receiving third-line treatment or higher, 8 are receiving treatment after recurrence, 2 are under surveillance following treatment, 3 have no evidence of disease and 3 indicated that they are in a different phase of treatment.

14 respondents reported brain metastases from their breast cancer.

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 51 respondents provided information about the medications they had undergone since their diagnosis. Trastuzumab and pertuzumab were by far the most common forms of treatment. Trastuzumab emtansine, capecitabine and paclitaxel were the only other medications reported by more than 4 respondents.

Medications Received	n	Medications Received	n
Trastuzumab (Herceptin)	49	Trastuzumab deruxtecan (Enhertu)	1
Pertuzumab (Perjeta)	45	Carboplatin (Paraplatin)	1
Trastuzumab emtansine (Kadcyla)	12	Vinorelbine (Navelbine)	1
Capecitabine (Xeloda)	10	Palbociclib (Ibrance)	1
Paclitaxel (Taxol)	9	Ribociclib (Kisqali)	1
Docetaxel (Taxotere)	4	Fulvestrant (Faslodex)	1
Trastuzumab, pertuzumab and trastuzumab emtansine	4	Pertuzumab, trastuzumab and hyaluronidase-zzxf (Phesgo)	1
Lapatinib (Tykerb)	3	Zoledronic acid (Zometa)	1
Nab-paclitaxel (Abraxane)	3	Abemaciclib (Verzenio)	1
Neratinib (Nerlynx)	2	Anastrozole (Arimidex)	1
Tamoxifen (Nolvadex)	2	Denosumab (Xgeva)	1
Eribulin (Halaven)	2	SYD985	1

Fatigue was the most commonly reported side effect of these treatments (86%, n=49), followed by diarrhea (71%), nausea (49%) and insomnia (45%).

Diarrhea and fatigue were most commonly cited by respondents as the most-difficult-to-tolerate side effects of these treatments. Nausea, loss of appetite, neuropathy, skin problems and breathing difficulties were also cited by multiple respondents.

A majority (69%, n=51) of respondents did not have difficulty accessing treatment. However, 22% reported that they were unable to access treatment because it was unavailable in Canada. 28% of respondents (n=50) also reported that they needed financial assistance due to the costs associated with breast cancer.

Some of the general comments about previous treatments include:

- Taxol reduced mets early in treatment. Herceptin, Perjeta continue to keep me stable. So far side effects are tolerable, but my quality of life has diminished.
- Xeloda is rough, feet are on fire constantly and hands hurt. Shortness of breath at times and weak. Will be 2 years in June. Herceptin seems to be fine - just get tired and I did well with the Perjeta.
- They all worked well for a while until I had to change. Abraxane caused neuropathy and heavy leg syndrome, Verzenio caused occasional diarrhea and even though I have had just one treatment of Eribulin, I feel more neuropathy and heavy leg syndrome.
- Grateful to have these targeted therapies.
- Targeted treatment has been a dream compared to all body chemo.

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). Respondents ranked all of the outcomes as important, but prioritized long-term health outcomes with 48 of 51 patients giving the highest score to controlling disease progression and 46 of 49 patients doing the same with preventing recurrence.

It may be worth noting that the respondents to this survey gave lower scores to reducing symptoms and managing side effects than metastatic breast cancer respondents from other surveys. This may reflect distinctive patient values for women with HER2-positive metastatic breast cancer. However, we should also allow that it may be a function of the limited sample size.

Importance of outcome	1 - not important	2	3	4	5 – very important	Average
Controlling disease	0.00% 0	1.96% 1	0.00% 0	3.92% 2	94.12% 48	4.90 51
Reducing symptoms	0.00% 0	5.88% 3	31.37% 16	19.61% 10	43.14% 22	4.00 51
Maintaining quality of life	0.00% 0	0.00% 0	0.00% 0	23.53% 12	76.47% 39	4.76 51
Managing side effects	0.00% 0	6.00% 3	22.00% 11	24.00% 12	48.00% 24	4.14 50
Preventing recurrence	0.00% 0	2.04% 1	0.00% 0	4.08% 2	93.88% 46	4.90 49

Comments from respondents include:

- The ultimate goal is to maximise longevity and personally, I can tolerate many side effects if it means I can live longer.
- I just want to live.

Respondents were also asked to rate how much they would be willing to tolerate new side effects from therapies that can control disease profession. On a scale of 1 (will not tolerate side effects) to 10 (will tolerate side effects), the average score was 7.2 (n=49), suggesting a strong tolerance for side effects for therapies that can improve long-term health outcomes.

Rating	Responses	Rating	Responses
1	0.00% 0	6	10.20% 5
2	0.00% 0	7	14.29% 7
3	6.12%	8	22.45%

	3		11
4	0.00% 0	9	6.12% 3
5	6.12% 3	10	34.69% 17

Comments included:

- Being alive and staying alive is my goal.
- It's very hard on my quality of life but I want to live.
- I suffer daily to live for today and any other day that I'm blessed to have.
- I just want more time with my daughter and husband. I would tolerate anything for more time.
- I can adapt.

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?

Six respondents received Tukysa for treatment of HER2-positive locally advanced unresectable or metastatic breast cancer. Four of these respondents received Tukysa in combination with trastuzumab and capecitabine following prior treatment with trastuzumab, pertuzumab, and trastuzumab emtansine, separately or in combination.

- Patient A is from the United States. She was diagnosed in 2016 and is currently undergoing second-line treatment. She was shifted to the Tukysa-Herceptin-Xeloda combination to better treat her brain metastases. She has been receiving Tukysa for 3-6 months.
- Patient B is from Ontario. She was diagnosed in 2013 and is currently receiving third-line treatment or higher. She has been receiving Tukysa for less than three months.
- Patient C is from Ontario. She was diagnosed in 2017 and is currently receiving treatment after a recurrence. She has brain metastases. She received Tukysa for less than three months and was forced to discontinue treatment due to the side effects.
- Patient D is from Alberta. She was diagnosed in 2014 and is currently receiving third-line treatment or higher. She has brain metastases. She has been receiving treatment with Tukysa for less than three months.

One respondent did not receive Tukysa in combination with trastuzumab and capecitabine:

- Patient E is from the United States. She was diagnosed in 2018 and currently has had no evidence of disease for more than two years. She had brain metastases. She has been receiving Tukysa for 3-6 months. Her Tukysa dosage was lowered due to the side effects. She also has treatment experience with zoledronic acid and paclitaxel.

One respondent did not receive Tukysa in combination with trastuzumab and capecitabine or following prior treatment with trastuzumab, pertuzumab, and trastuzumab emtansine, separately or in combination.

- Patient F is from the United States. She was diagnosed in 2019 and is currently receiving third-line treatment or higher. She has brain metastases. She has been receiving Tukysa for 6-12 months. She was previously treated with paclitaxel, anastrozole, denosumab, zoledronic acid, a craniotomy as well as one session of high-dose radiation.

Treatment Experience

Patients were asked to rate the change to their quality of life on Tukysa compared to other therapies they had received on a scale of 1 (much worse) to 5 (much better). Respondents felt strongly that Tukysa helped control disease progression and prevented recurrence. The responses in other areas were generally close to neutral.

Change to quality of life on Kadcyla	1 – much worse	2	3	4	5 – much better	Average
Metastatic cancer symptoms	0.00% 0	0.00% 0	40.00% 2	40.00% 2	20.00% 1	3.80 5
Drug side effects	0.00% 0	16.67% 1	50.00% 3	16.67% 1	16.67% 1	3.33 6
Maintaining quality of life	16.67% 1	0.00% 0	16.67% 1	33.33% 2	33.33% 2	3.67 6
Controlling disease progression	0.00% 0	0.00% 0	0.00% 0	40.00% 2	60.00% 3	4.60 5
Preventing recurrence	0.00% 0	0.00% 0	0.00% 0	20.00% 1	80.00% 4	4.80 5
Ability to work	20.00% 1	0.00% 0	40.00% 2	20.00% 1	20.00% 1	3.20 5
Ability to sleep	0.00% 0	16.67% 1	33.33% 2	33.33% 2	16.67% 1	3.50 6
Ability to drive	20.00% 1	0.00% 0	20.00% 1	40.00% 2	20.00% 1	3.40 5
Ability to perform household chores	33.33% 2	00.00% 0	16.67% 1	0.00% 0	50.00% 3	3.33 6
Ability to care for children	33.33% 2	16.67% 1	16.67% 1	0.00% 0	33.33% 2	2.83 6

Comments include:

- I am feeling better than I previously was. It has helped to reduce symptoms. (Patient B)
- It's not bad at all. I've been on a lot of treatments and this one isn't so bad. (Patient D)

Side Effects

Diarrhea was the most commonly reported side effect of Tukysa (5 of 6 respondents). Decreased appetite, fatigue, nausea, hand-foot syndrome were also reported by multiple respondents.

When asked how much they could tolerate the side effects associated with Kadcyla on a scale of 1 (completely intolerable) to 10 (completely tolerable), the average rating was 7. However, this represented a divided response. Patients C and F gave scores of 1 and 3 respectively, while all other respondents gave scores of 8 or higher.

Patient comments included:

- Initially, side effects of nausea, vomiting and diarrhea were bad but with the right meds to control that, I'm doing really well and feel great. (Patient A)
- Side effects are manageable. Some mild diarrhea at the beginning, but managed with some Imodium. (Patient B)
- This drug was horrible for me. Side effects not tolerable at all. Mind you, no dose reduction was suggested either. Not sure I would have done them.(Patient C)

Treatment Options

Chemotherapy was the only alternative treatment suggested if Tukysa was unavailable.

Patients also reflected on the importance of having a treatment option for brain metastases:

- It's a huge relief that we're making progress in treating brain mets because right now, that's the thing that's liable to take me down. (Patient A)
- I was happy. We were all happy to find out that I had an option. (Patient D)
- At least giving people the opportunity to make the decision is critical. Everyone should have the choice to try it or not. (Patient E)

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?

Recommend Tukysa: When asked if they would recommend Tukysa to other patients with breast cancer, five patients said that they would. Patient C was the sole dissenter.

Asked to elaborate, respondents commented:

- Is very tolerable so far and seems to be working. The effectiveness with brain mets is especially important and I am hopeful. (Patient A)
- So far so good. Cancer is stable based on last scan. Hopeful that this can continue. (Patient B)
- Side effects are horrible (Patient C)
- I don't mind as long as it keeps me alive. I don't like how much pills I have to take. (Patient D)
- Absolutely fantastic drug. As an attorney/freelance medical editor, nothing was more devastating than learning that my brain has been affected. I don't care how I look; I don't care if I am fatigued or bloated or have painful hands...I am my brain, and my ability to conduct complex analysis. I wish I could personally thank every researcher involved in the design of this drug, and any drug with the capacity to cross the blood/brain barrier. (Patient E)
- I'm glad that I have the opportunity to take Tukysa. I feel that it's extending my life. (Patient F)
- 100% - it is a Life-saver for me. Feeling healthier and able to go back to my routine. (Patient B)
- While I see from the comments posted by others taking Tukysa that some people experience side effects that they feel are intolerable, the fact that this formulation permits access to the brain is a game-changer and should encourage anyone with the ability to access it to try it. In the event that side effects are, in fact, intolerable, thereby dictating a medication switch, Tukysa should be initially approached as an opportunity. As Canadians will well understand, "You miss 100% of the shots you don't take." (Patient E)
- Hopefully, it gets approval worldwide. (Patient A)

Key Points:

1. All respondents agreed that Tukysa helped to control disease progression and prevent recurrence compared to other therapies that they had received.
2. Breast cancer patients prioritize long-term health outcomes and are usually willing to tolerate side effects from therapies that can control disease progression.
3. There are no drugs currently indicated for treatment of brain metastases.

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 Seattle Genetics 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 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
Seagen 2020			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: April 19, 2021