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

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

ribociclib (Kisqali)

(Novartis Pharmaceuticals Canada Inc.)

Indication: Ribociclib is indicated: • for the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative stage II and III early breast cancer (eBC), in combination with an aromatase inhibitor (AI). • in pre- or perimenopausal women, or men, the AI should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.

January 6, 2025

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CDA-AMC and do not necessarily represent or reflect the views of CDA-AMC. No endorsement by CDA-AMC is intended or should be inferred.

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Patient Input Template for CDA Reimbursement Reviews

CDA Project Number: PC0395-000
Name of Drug: KISQALI (ribociclib)
Indication: For the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative stage II and III early breast cancer (eBC), in combination with an aromatase inhibitor (AI) in pre- or perimenopausal women, or men, the AI should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.
Name of Patient Group: Breast Cancer Canada and McPeak-Sirois Group for Clinical Research in Breast Cancer
Author of Submission: Kimberly Carson, CEO Breast Cancer Canada

1. About Your Patient Group

Breast Cancer Canada's (BCC) commitment is to save lives through breast cancer research and its outcomes. For the last three decades, you've known us as the Breast Cancer Society of Canada. But with a disease that is ever evolving, we have also evolved. We remain the only national organization in Canada laser focused on precision oncology breast cancer research and education because we believe in building on the outstanding progress in therapeutic outcomes that's been made. Breast Cancer Canada encourages precision oncology research and awareness collaboration among physicians and researchers. Our mission drivers are: Diversity by creating a basis of ethnically diverse breast cancer patients in clinical trials; Acceleration by driving Canadian research from the lab directly to the clinic with precision oncology; Innovation by applying research methodology that utilizes emerging technology; Patient leadership by developing Patient Reported Outcomes (PROs) for breast cancer in Canada, and Connection by rapidly expanding the network of research and sharing of data to support design and running of novel Canadian clinical trials.

About - Breast Cancer Canada (breastcancerprogress.ca)

The McPeak-Sirois Group for Clinical Research in Breast Cancer's vision is to bring together the main players in breast cancer clinical research to make research that cares accessible to as many patients as possible. The organization is a private and unique initiative bringing together public health organizations in Quebec. The McPeak-Sirois Group is a charitable organization supported by Susan McPeak, survivor, and Charles Sirois, a renowned entrepreneur and caregiver to his wife. By joining forces, hospitals that are members of the McPeak-Sirois Group ensure that more people affected by breast cancer can access the best treatments available and that valuable practices based on the latest knowledge are shared within the medical community though Research that cares. All actions taken by the Group are focused on the best interest of the Breast Cancer patient. Whether it be in the selection of Member institutions, research protocol selection or the sharing of best practices, based on the most recent knowledge, within the medical community. In just a few years, the McPeak-Sirois Group has become one of the most important breast cancer clinical research consortia in Canada.

McPeak • Sirois – Recherche clinique en cancer du sein (mcpeaksirois.org)

2. Information Gathering

INFORMATION SOURCE: SURVEY TO HORMONE RECEPTOR POSITIVE, EARLY STAGE 2 & 3 BREAST CANCER PATIENTS

November 14 to 18th , 2024 we surveyed our Breast Cancer Canada (BCC) and McPeak Sirois (MPSG) communities using validated patient reported outcomes measures (PROMs) to capture the lived experience of Canadians diagnosed with early-stage breast cancer[1].

188 survivors responded to the survey and confirmed their diagnosis of hormone receptor positive (HR+), HER2 negative (HER2-) early stage 2 or 3 breast cancer (EBC) currently receiving endocrine therapy (ET). The age at diagnosis of responders was n=54 at age 49 or younger (29%), n=58 at age 50-59 (31%), n=75 over age 60 years (40%) and n=1 who did not answer. Ethnicity was primarily White at 94% with Filipina, Chinese, Black, Metis and South Asian comprising 6% of survey responders. Cross country representation included 44.6% from Western Canada (BC, AB, SK & MB), 37% from Ontario, 9.5% from Quebec and 8% from Atlantic provinces (NS, NB & NL). Eight (8) of 188 HR+/HER2- EB respondents, currently on ET, contributed their experience on Ribociclib for the indication under review, as a doublet adjuvant treatment regimen.

BCC has included patient reported outcomes (PRO) evidence from our national ethics approved PROs Registry, PROgress Tracker[2], on the significant quality of life impact of financial toxicity as a direct result of breast cancer diagnosis, treatment and supportive care costs.

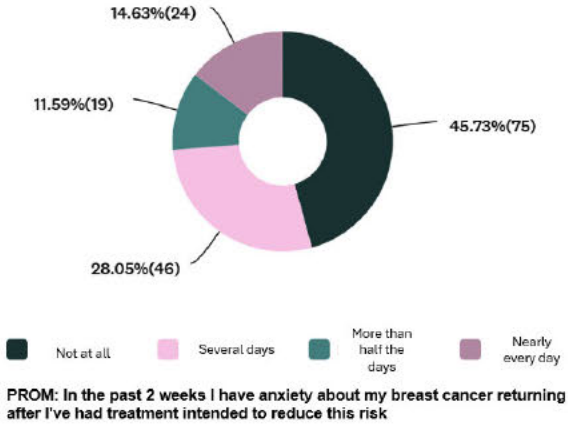
BCC also reviewed the outcomes from the randomized phase III NATALEE trial[3] publications / congress abstracts' and conferred with our breast cancer clinical specialist partners from the Research Excellence, Active Leadership (REAL) Breast Cancer Canadian Alliance on our questions regarding the study evidence.

3. Disease Experience

EARLY-STAGE DISEASE AND PREVENTION OF RECURRENCE

Surgery, chemotherapy and radiation are treatments commonly experienced by HR+ / HER2- EBC patients. This period brings acute management of mental health (i.e. shock, coping) and treatment side effects. When this initial therapy period is over and there are no longer cancer-related symptoms, the long-term lived experience is where the true resilience of a "new normal" from curative intent therapy can have an ongoing impact on daily living. In addition, survivors can be managing side effects of extended endocrine therapy for 5-10 years. Despite this, our BCC survey responders indicate that they are willing to accept current standard long-term ET and related side effects to reduce the risk of their cancer recurrence with 54% of respondents (Figure 1) experiencing some degree of anxiety about recurrence.

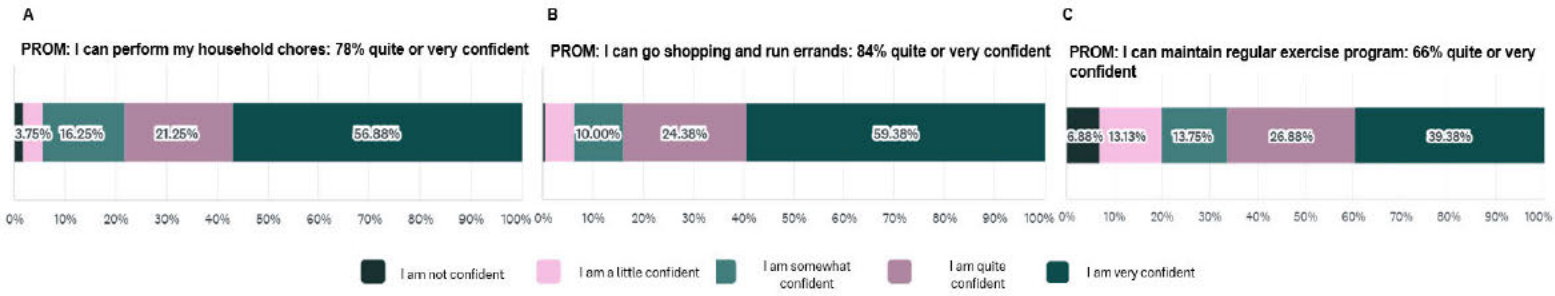
Figure 1. 54% of HR+ / HER2- Stage II/III EBC patients experience a consistent degree of anxiety through each week about cancer recurrence



(n=164 / 188)

In terms of daily living, post acute multimodality therapy, early-stage HR+ / HER2- breast cancer survivors responding to this survey are able to maintain activities with 78% 'quite' or 'very confident' to complete household chores, 84% 'quite' or 'very confident' to complete shopping & errands, however fewer (66%) feel 'quite' or 'very confident' in being able to maintain regular exercise following a breast cancer diagnosis and related curative treatment. (Figure 2 A, B, C)

Figure 2. Lived experience of n=160 / 188, HR+ / HER2- EBC Stage II & III patients' ability to maintain daily activities post acute multimodality therapy.
How would you rate your level of confidence:



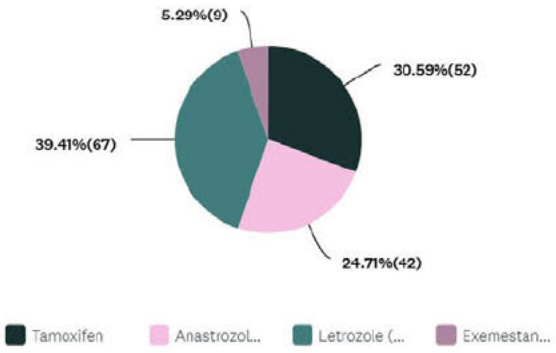
Regardless of age or stage, patients' goal for HR+ / HER2- EBC cancer therapy is to ultimately cure their breast cancer with the highest degree of confidence that will prevent recurrence of advanced disease, while offering the lowest rate of disruption to normal living from treatment short and long-term side effects.

4. Experiences With Currently Available Treatments

LIVED TREATMENT EXPERIENCE WHILE TAKING STANDARD OF CARE ENDOCRINE THERAPY

Our survey included 177 of 188 HR+ / HER2- EBC survivors who provided details on their prescribed oral adjuvant endocrine therapy (ET) following acute curative multimodal treatment, with 30.5% receiving Tamoxifen, 25% Anastrozole, 39.5% Letrozole and 5% Exemestane. (Figure 3)

Figure 3. Endocrine therapy agents prescribed to survey respondents for HR+ / HER2- stage 2 or 3 breast cancer



Duration of ET ranged across surveyed survivors where 14.5% are in the first year of treatment, 20.5% in the second year, 17% in the 3rd year, 8.5% in 4th year and 39.5% are within or have completed a total of 5 years. Of the lived experience 5.5% of survivors required early discontinuation due to toxicity; and 3.5% felt they could have remained on ET if they had access to experienced adverse event management support. None of those surveyed expressed experiencing a breast cancer recurrence. Cost can be a significant burden, particularly among survivors under the age of 55, with more detail on financial toxicity provided in Section 8.

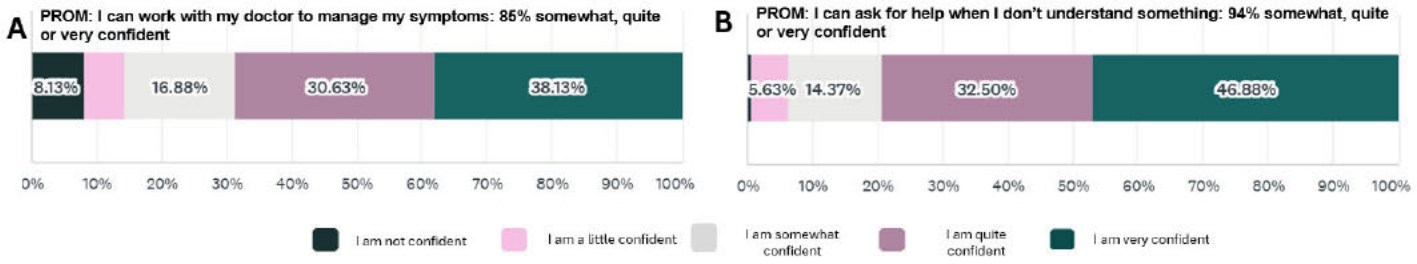
MANAGING DAILY LIFE ACTIVITIES AND RELATIONSHIPS WHILE ON ENDOCRINE THERAPY:

HR+ / HER2- EBC survivors with high-risk of recurrence are more likely to experience long-term impact of acute multimodality treatment such as difficulty with full mobility, lymphedema and work / employment ability equal to pre-breast cancer capabilities. In the context of the focus of this review of Ribociclib added to current standard adjuvant oral ET, post-multimodal curative therapy, our survey explored patient reported outcomes of impact in areas of daily activity and maintaining relationships while on single agent ET and the combination treatment. While on ET alone, 90% of survivors described being confident in managing [cancer-treatment] symptoms during daily activities (15% 'somewhat confident'; 35% 'quite confident'; 40% 'very confident'). In a related PROM, 90% of surveyed survivors feel confident in their ability to keep [cancer-treatment] symptoms from interfering with relationships among family and friends (19% 'somewhat confident'; 35% 'quite confident'; 36% 'very confident').

DRUG / DISEASE STATUS AND SELF EFFICACY:

Survey responders expressed a high ability for self-efficacy in managing treatment and cancer related issues, indicating a high degree of confidence while managing oral at-home ET. Patient reported outcomes (Figure 3) reveal 85% are 'somewhat (16.8%), quite (30.6%) or very confident' (38%) to work with their doctor to manage treatment-related symptoms (taking potential influence of lack of access to primary physician with the shortage in Canada). Additionally, 94% of survivors expressed confidence in asking for help when they don't understand something (14.3% somewhat; 32.5% quite; 46.8 very confident). With this high degree of self-efficacy confidence, survivors are managing oral, long-term therapy quite well.

Figure 4. Self-Efficacy confidence of HR+ / HER2- EBC survivors lived experience with vast majority able to A) manage [cancer-treatment] symptoms with their doctor (85%) and B) request help when in need of more understanding (94%). (n=160/188)



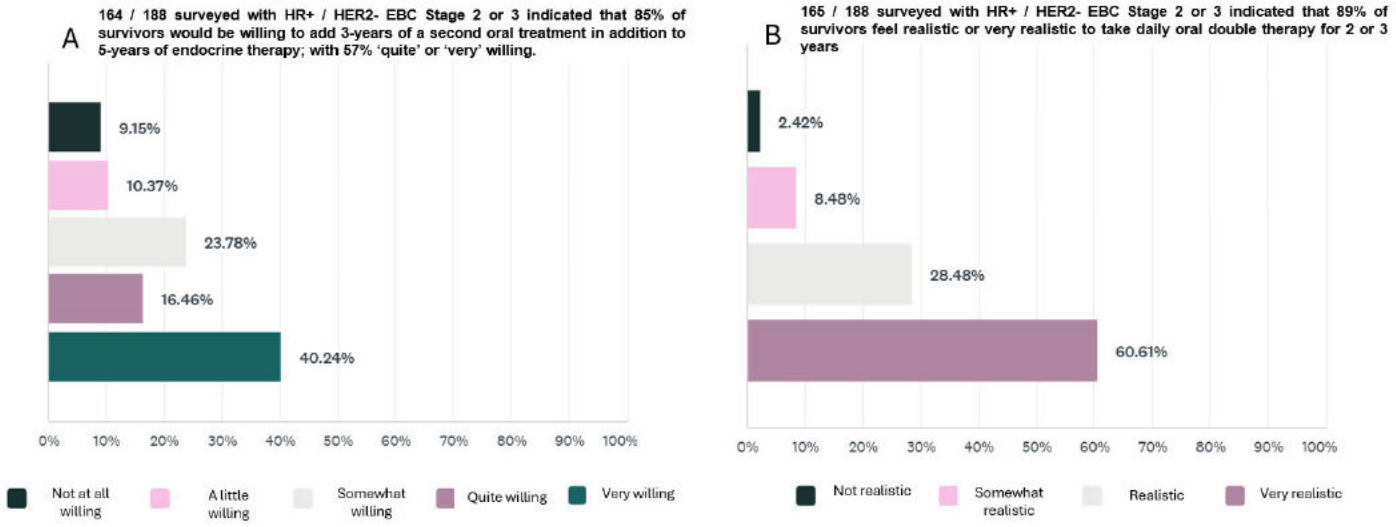
5. Improved Outcomes

PATIENTS SEE VALUE IN ADDING 3-YEARS of ORAL TREATMENT to ENDOCRINE THERAPY

Regardless of age or stage, patients' goal for HR+ / HER2- EBC cancer therapy is to ultimately cure their breast cancer with the highest degree of confidence that will prevent recurrence of advanced disease. Patients are highly aware of recent evidence and peer or survivors' experience, that long-term recurrence rates are happening after the traditional 5-year mark. HR+/ HER2- EBC is associated with an approximate 50% rate of long-term recurrence after the 5-year mark from initial diagnosis[3]. After the 5-year mark, as survivors move forward with a new normal, the devastation to patient and family cannot be measured when there is a delayed recurrence, particularly when the patient is a caregiver to others (i.e. children or aged parents). There is a significant domino effect, for example BCC has fielded many calls from survived spouses that their retirement fund is depleted, and house is being sold in order to financially support their loved one during the course of their recurrent metastatic disease until end of life. These stories, long-term data and death rate in Canada having not lowered in over 2 decades indicates current therapy for HR+ / HER2- EBC at high-risk of recurrent disease is not enough to prevent and lower advanced cancer recurrence rates. With ~70% of BC cases being HR+, primarily detected in an early stage, and despite advances in chemotherapy, clearly the hormone driver is an area of critical therapeutic focus to prevent recurrence of advanced disease leading to death. **Novel HR+ targeted treatments are needed in addition to or replace standard endocrine therapy. There remains a significant unmet need to improve treatment for HR+/HER2- high-risk EBC survivors while the disease is still curable, and impact the death rate of recurrent breast cancer in Canada.**

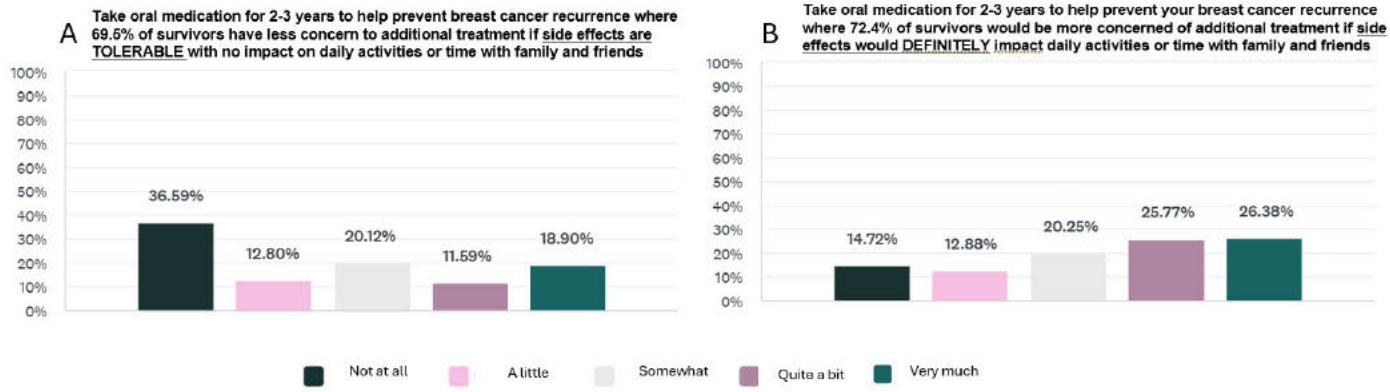
Our survey asked HR+ / HER2- EBC survivors about their willingness to add 3-years of a second oral treatment to their planned use of ET if it offered an additional 5% chance of preventing breast cancer from returning. Figure 5 A shows most of our responders (85%) would be 'somewhat', 'quite' or 'very' willing to add 3-years of a second oral agent to their current regimen of ET, with the majority (57%) indicating 'quite' and 'very' willing. In addition, figure 5 B indicates that 89% of survivors surveyed feel it is 'realistic' or 'very realistic' to take daily oral doublet adjuvant therapy for 2 or 3 years.

Figure 5 A and B. 85% of survivors (figure A) surveyed with HR+ / HER2- EBC Stage 2 or 3 indicated that they would be willing to add 3-years of a second oral treatment in addition to 5-years of endocrine therapy for a 5% risk reduction of recurrence; with 89% stating (figure B) their ability to take daily oral doublet adjuvant therapy for 2 or 3 years, as realistic or very realistic.



Our survey went further to explore survivors' willingness to take doublet oral therapy for 2 to 3 years in combination with 5 years of ET for improved chance of preventing cancer recurrence and balancing the impact of treatment adverse events on quality living. Two questions were asked, based on the degree of concern, for adverse events impacting daily activities and time with family / friends. Figure 6 A shows 69.5% of survey respondents indicated their level of concern as 'not at all', 'a little', or 'somewhat concerned' with almost half (49%) expressing 'not at all' or 'little concern' to be on oral medication for 2-3 years to help prevent breast cancer recurrence where side effects are tolerable and no impact on daily activities (chores, shopping, caregiving to others, sleeping, appetite) and time with family / friends. When the degree of treatment toxicity is raised to the level where there would be a definite impact on daily living and time with family and friends, Figure 6 B shows fewer survivors (27.6%) that would rate a low degree of concern as 'not at all' or 'a little bit' when adding a second oral agent to ET.

Figure 6 A & B. 164 / 188 surveyed with HR+ / HER2- EBC Stage 2 or 3 indicated treatment in the adjuvant setting must improve recurrence rates while offering the lowest degree of disruption to normal living from treatment side effects.



With the majority of 72.4% responding survivors expressing greater concern around more debilitating side effects, ('somewhat' [20%], 'quite a bit' [25.7%] or 'very much' [26%]) clearly treatment in the adjuvant setting must improve recurrence rates while offering the lowest impact of disruption to normal living from treatment-related side effects.

The Phase III NATALEE trial evaluated adjuvant ribociclib + ET (R+ET) in a population of HR+/HER2- patients at high risk for recurrence. The results demonstrated, across all high-risk sub-groups, that treatment with ribociclib + ET doublet in the adjuvant setting had a significantly longer invasive disease-free survival (iDFS) and distant disease-free survival (DDFS) compared to those treated with ET alone at the study 4-year landmark analyses.[4,5] **The addition of ribociclib to ET in high-risk HR+ / HER2- EBC, to increase the rate of iDFS by 5%, is meaningful to 85% of survivors who responded to our survey that are currently receiving ET alone. Our survey also showed the majority of survivors (89%) felt they realistically could take 3 years of doublet oral therapy.**

The NATALEE trial demonstrated that the ribociclib + ET combination has manageable side effects.[6,7] The NATALEE trial Quality of Life (QOL) data from four validated PROMs consistently show functional (physical, social, and emotional) and global health status, breast cancer symptoms, mobility, self-care and mental health (anxiety and depression) were not impacted by adding Ribociclib to ET. **These patient reported outcomes support the potential addition of side effects as being manageable when adding Ribociclib to ET. Our survey of HR+ / HER2- EBC stage 2 and 3 survivors reinforced that ~70% of these patients are willing to add 2-3 years of a new drug to ET where side effects will have minimal negative impact on daily living, and feel confident in self-efficacy to manage side effects and dose adjustment (if needed) in collaboration with clinician support. Our survey compliments the findings of the NATALEE trial QoL results as meeting the goals of therapy that are meaningful to survivors.**

6. Experience With Drug Under Review

The Breast Cancer Canada / McPeak Sirois Group survey of HR+ / HER2- Stage 2 and 3 breast cancer survivors identified 8 people that have received ribociclib + endocrine therapy (R+ET) in this clinical setting. Majority, 7 / 8 survivors were under the age of 60 years at diagnosis, 62% had dense breasts, 7 people were white and 1 Metis ethnicity. In terms of geo-location, 3 reside in Ontario, 3 in Quebec and 2 in British Columbia.

Due to the nature of curative intent adjuvant therapy for breast cancer patients at high-risk of recurrence, it is too early to survey survivors on iDFS and DDFS efficacy outcomes lived experience. Therefore, the interest in meeting therapeutic goals using novel doublet therapy and it's benefit, versus the degree of side effects experienced on the impact of daily living taking adjuvant R+ET during active treatment, is most relevant lived experience to describe at this time. Although we do note that no survey respondents described having experienced a breast cancer recurrence while taking R+ET.

CONFIDENCE IN TAKING 3-YEARS OF DUAL THERAPY IN THOSE EXPERIENCED WITH RIBOCICLIB + ET:

In our survey of HR+ / HER2- EBC, 6 of 8 survivors on R+ET (figure 7) described having a low degree of concern in balancing quality daily living while tolerating side effects of doublet therapy for the therapeutic advantage of further reducing the risk of recurrence ('none' n=4 and 'somewhat' n=2) with 1 of 8 survivors on R+ET having stopped treatment due to side effects.

Figure 7. Of those surveyed while taking Ribociclib + ET, 85% felt therapeutic advantage to reduce the risk of recurrence had minimal to no concern of the tradeoff for manageable treatment side effects. N=8

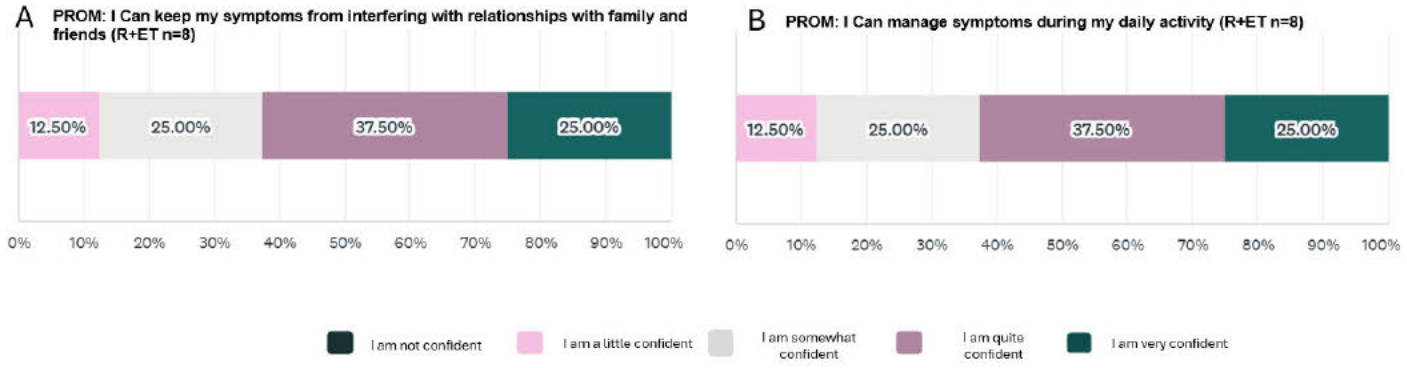
In terms of realistic confidence to take daily oral medication for 3 or more years, 3 of 8 survivors receiving R+ET, felt this was realistic while 4 / 7 felt it was very realistic. The duration of experience on R+ET therapy of the surveyed survivors spanned 2 years for three (3) survivors, 3 years for two (2) survivors, and three (3) survivors had completed doublet therapy while now completing 5 years of ET. Our survey did not ask questions on how ribociclib was accessed; however, it is presumed at least 5 of 8 received treatment as participants on the NATALEE trial given their duration of use or completion of doublet therapy. At the time of this HTA submission, there is not an open drug patient support program for adjuvant ribociclib.

LIVING FUNCTIONALITY MAINTAINED ON RIBOCICLIB + ET:

Our survey also asked of survivors who have taken R+ET their ability to manage symptoms [treatment side effects] during daily activities. 5 of 8 (62.5%) responded 'very' and 'quite' able, indicating a high degree of daily function while 2 of 8 responded 'somewhat' able indicating clinical support may be needed for some.

These survey results remained consistent for routine function across many domains of daily living with 5 of 8 and 2 of 8 (62.5% quite + very; 87.5% when adding 'somewhat') survivors taking R+ET: Ability to keep my symptoms [side effects] from interfering with relationships with friends and family; and ability to perform household chores and go shopping or run errands. (Figure 8 A and B). 5 of 8 (62.5 %) felt a mid to positive level of confidence in maintaining a regular exercise routine (3 / 8 'very' confident; 1 / 6 'quite'; 1 / 8 'somewhat' confident).

Figure 8 A and B. Of those surveyed while taking Ribociclib + ET, 87.5% (n= 6 / 8) respondents expressed high degrees of confidence in maintaining relationships and ability to perform chores or errands.

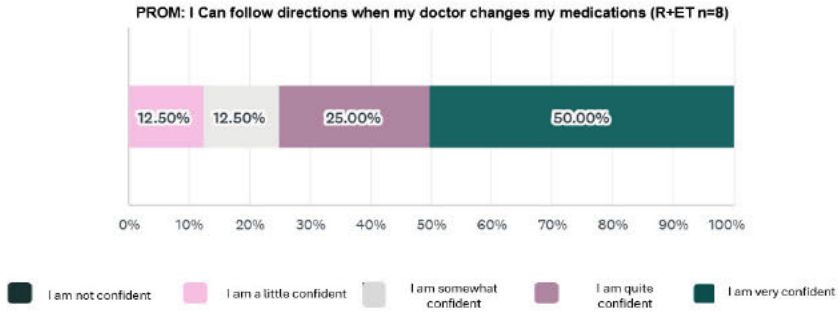


These survey responses indicate the majority of HR+ / HER2- surveyed survivors have experienced had a high degree of functional daily living with R+ ET oral therapy. With no compromise in activities for the majority of the survivors surveyed on R+ET, this reflects the quality-of-life data reported from the NATALEE trial.

SELF-EFFICACY AND CLINICAL SUPPORT IN MANAGEMENT of DUAL THERAPY:

Our survey identified a high degree of self-efficacy where 6 of 8 (87.5%) respondents on R+ET felt 'very', 'quite' or 'somewhat' confident working with their doctor to manage symptoms [side effects]. (Figure 9) However, 3 of 8 (37.5%) expressed a lower degree of confidence when managing their medication if having no help at all (3 / 8 'a little' confident). None of those surveyed with experience taking R+ET expressed a total 'lack of confidence' in any of the self-efficacy questions about managing oral R+ET therapy related to drug dosing, side effect management or seeking clinical support.

Figure 9. Of those surveyed while taking Ribociclib + ET, 87.5% (n= 6 / 8) respondents expressed high degrees of confidence in working with their doctor to manage treatment side effects.



These survey responses on seeking physician help to manage treatment side effects, although representing a small number of experienced people on R+ET, were proportionally consistent at 85% for the larger group of respondents (n=152 / 160) taking single agent ET. Our survey did also suggest the need for initial treatment education and experienced clinical support to manage side effects and dosing changes effectively for those on doublet oral R+ET.

Breast Cancer Canada / McPeak Sirois Group strongly support the Survivor and Clinician (REAL Alliance) viewpoint to have ribociclib + ET accessible through public health cancer care services. We will endeavor to monitor this novel approach to endocrine positive breast cancer at high-risk for recurrence, on the positive impact on survivors' confidence and anxiety around cancer recurrence and, ultimately, a reduction in the Canadian death rate from recurrent advanced breast cancer that has not been observed in over 20 years.

7. Companion Diagnostic Test

To our knowledge, biomarker testing required to identify HR+, HER2- breast cancer subtype and risk of recurrence (i.e. genomic OncoType Dx) is broadly publicly available.

8. Anything Else?

Financial toxicity resulting from a breast cancer diagnosis is a detrimental short- and long-term impact for patients and their families.

Recent evidence from Breast Cancer Canada's PROgress Tracker[1], a national, ethics approved breast cancer registry of patient reported outcomes collecting the lived breast cancer experience as decision-grade data, has demonstrated significant financial toxicity for survivors under the age of 55 years. Data drawn from 228 survivors who had completed COST-FACIT PROM financial toxicity questionnaires every three months since the Registry opened in October 2023, illustrates the financial burden associated with a breast cancer diagnosis. All reported data reached statistical significance[6]. The majority of study participants were diagnosed with early-stage breast cancer (93%). 36% of younger patients under age 55 report financial hardship affecting themselves or their families, while only 13% of older patients over age 55 experience the same. Employed survivors, 36% under age 55, are also more likely to face financial strain compared to 13% of employed survivors over age 55. 28% of survivors under age 55 have more had difficulty covering treatment costs compared to 17% of those older than age 55.

Public funding for curative intent oral or IV treatment is crucial, particularly for HR+/HER2- EBC survivors who uniquely face, compared to other solid cancer tumour types, 5-10 years of long-term endocrine therapy to reduce the risk of recurrence while also report significant financial hardship directly related to BC diagnosis. Private insurance co-pays over the long-term and additional supportive care out-of-pocket costs to manage survivorship treatment side effects, have significant financial ramifications notably for those diagnosed under the age of 55. Quality of living impact include reduced retirement savings requiring retirement at an older age, and/or an inability to afford their lifestyle before breast cancer (i.e. house downsizing, higher caregiving costs, reduced wages for employment accommodations and/or inability to afford vacation or post-secondary education for children).

Based on the robust evidence presented in this document, we urge the CDA to incorporate ribociclib into the treatment paradigm for all high-risk HR+/HER2- EBC patients eligible on the NATALEE trial. The collective lived experience of our patient survivor community underscores the clinical significance of this recommendation.

References

1. Breast Cancer Canada data on file: survey of Stage 2 and 3 breast cancer survivors in Canada with Hormone receptor positive, HER2 negative breast cancer, currently or completed adjuvant endocrine therapy. November 14 – 18, 2024.
2. Leduc, S., Gibson, A.W. et al. PROgress Tracker Breast Cancer Registry: A Breast Cancer Canada initiative. J Clin Oncol 42, 2024 (suppl 16; abstr e23018). https://meetings.asco.org/abstracts-presentations/236660
3. Pedersen RN, Esen BÖ, Mellemkjær L, et al. The Incidence of Breast Cancer Recurrence 10-32 Years After Primary Diagnosis. J Natl Cancer Inst. 2022;114(3):391-399. doi:10.1093/jnci/djab202
4. Fasching PA, Stroyakovskiy D, Yardley DA, et al. Adjuvant Ribociclib Plus Nonsteroidal Aromatase Inhibitor in Patients With HR+/HER2– Early Breast Cancer: 4-Year Outcomes From the NATALEE Trial.
5. Hortobagyi GN, Lacko A, Sohn J, et al. A phase III trial of adjuvant ribociclib plus endocrine therapy versus endocrine therapy alone in patients with HR-positive/HER2-negative early breast cancer: final invasive disease-free survival results from the NATALEE trial. Ann Oncol. 2024;0(0). doi:10.1016/j.annonc.2024.10.015

6. Barrios CH, Harbeck N, Hortobagyi GN, et al. 113MO NATALEE update: Safety and treatment (tx) duration of ribociclib (RIB) + nonsteroidal aromatase inhibitor (NSAI) in patients (pts) with HR+/HER2− early breast cancer (EBC). ESMO Open. 2024;9. doi:10.1016/j.esmoop.2024.103101

7. Fasching PA, Slamon D, Nowecki Z, et al. VP3-2023: Health-related quality of life (HRQoL) in the phase III NATALEE study of adjuvant ribociclib (RIB) plus a nonsteroidal aromatase inhibitor (NSAI) vs NSAI alone in patients (pts) with HR+/HER2- early breast cancer (EBC). Ann Oncol. 2023;34(10):951-953. doi:10.1016/j.annonc.2023.08.007

8. Breast Cancer Canada (BCC) 2024 Progress Report on Breast Cancer in Canada, reporting data from BCC's PROgress Tracker Breast Cancer Registry on the analysis of financial toxicity and a breast cancer diagnosis; Breastcancerprogress.ca, October 2024. https://breastcancerprogress.ca/2024-progress-report/

Appendix: Patient Group Conflict of Interest Declaration

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

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

   No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   Yes, University of Calgary assisted in data analysis of PROgress Tracker Breast Cancer Registry on financial experience of breast cancer survivors.

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
BCC - Gilead Sciences Canada				x
BCC – AstraZeneca Canada				x
BCC – Novartis Canada				x
BCC – Lilly Canada				x

BCC - Merck + AstraZeneca Canada				x
BCC – Daiichi Canada		x		
MPSG – Pfizer Canada				x
MPSG – Lilly Canada				x
MPSG – AstraZeneca Canada				x
MPSG – Gilead Sciences Canada				x
MPSG – Seagen Canada				x
MPSG – Novartis Canada				x
MPSG – Merck 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: Kimberly Carson
Position: CEO
Patient Group: Breast Cancer Canada
Date: **December 28, 2024**

CADTH

CADTH Reimbursement Review
Patient Input

Name of the Drug and Indication	Ribociclib (Kisqali) is indicated for the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative stage II and III early breast cancer (eBC), in combination with an aromatase inhibitor (AI) in pre- or perimenopausal women, or men, and the AI should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.
Name of the Patient Group	Canadian Breast Cancer Network
Author of the Submission	JK Harris
Name of the Primary Contact for This Submission	JK Harris
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

The Canadian Breast Cancer Network (CBCN) is Canada's 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

CBCN is a member of the Canadian Cancer Action Network. We commit to their Code of Conduct Governing Corporate Funding adherence.

2. Information Gathering

Information for this submission was collected via:

CBCN's 2022 Triple Negative Breast Cancer Patient Survey

CBCN conducted and distributed an online survey to patients who had been diagnosed or were currently living with breast cancer. 981 people completed the English-only survey. CBCN contacted patients through the membership databases of CBCN, social media, and other patient organizations. Survey questions comprised of a combination of scoring options and free form commentary. 111 of the 981 had stage II or III HR-positive, HER2-negative breast cancer.

Stage II and III HR-positive, HER2-negative respondents reported that they lived in the following provinces:

- 30% were from Ontario (39 respondents).
- 21.5% were from British Columbia (24 respondents).
- 13.5% were from the Maritimes, where 5 respondents each were from Nova Scotia and Newfoundland and Labrador, 4 respondents were from New Brunswick, and 1 respondent was from Prince Edward Island.
- 12.5% were from Alberta (14 respondents).
- 8% were from Saskatchewan (9 respondents).
- 7% were from Quebec (8 respondents).
- 1.8% were from other regions, where 1 respondent each was from the North West Territories and Manitoba.

These respondents also reported on their age at the time of the survey, and first language:

- 11% spoke a first language other than English, where 6 respondents spoke French as a first language, and 6 spoke European languages other than French or English.
- 4.5% were 40 years of age, or younger (5 respondents).
- 39.5% were between 41-55 years of age (44 respondents).
- 48.5% were between 56-70 years of age (54 respondents).
- 4.5% were older than 71 years of age (5 respondents).

CBCN's 2017 Breast Cancer Patient Survey

CBCN conducted and distributed an online survey to patients who had been diagnosed or were currently living with breast cancer. Survey questions comprised of a combination of scoring options and free form commentary. CBCN contacted patients through the membership databases of CBCN and other patient organizations.

216 patients participated in the survey. 17 of the 216 respondents had stage II or III HR-positive, HER2-negative breast cancer. One of these 17 respondents only completed the survey questions related to their subtype of breast cancer, and not the remaining survey questions. Therefore, only the completed 16 responses are included in the following analysis and throughout this submission.

Patients reported the following about where they live:

- 4 respondents were from British Columbia
- 3 respondents each were from Ontario and Saskatchewan.
- 2 respondents each were from Manitoba, Quebec, and Newfoundland and Labrador.
- 1 respondent each were from Alberta and Nova Scotia.

Respondents also reported on their age at the time of the survey, and first language:

- 2 respondents spoke French as a first language, while the remaining respondents reported they spoke English as a first language.
- 1 respondent was between 30-40 years of age.
- 6 respondents were between 41-50 years of age.
- 8 respondents were between 51-60 years of age.
- 1 respondent was between 61-70 years of age.
- No respondents were younger than 30, or older than 71 years of age.

Key Informant Interview

CBCN was not able to speak with stage II or III patients taking ribociclib for the treatment of HR-positive, HER2-negative breast cancer. In September and October 2017, we interviewed two Canadian metastatic breast cancer patients living with HR-positive, HER2-negative breast cancer that had direct experience with ribociclib for a different indication. Their experiences related to treatment efficacy, risks associated with side effects, and the social impacts of accessing ribociclib are included in this submission.

Printed Sources

CBCN reviewed current studies and grey literature. We identified issues and experiences shared among many women living with breast cancer. We also collected data from the clinical trial related to the treatment in question.

3. Disease Experience

A diagnosis of early stage HR-positive, HER2-negative breast cancer effects people tremendously. A breast cancer diagnosis impacts the emotional and physical well-being of patients, as does breast cancer treatment itself. Most early stage patients will undergo a variety of treatments. This may include surgery, chemotherapy, hormone therapy, targeted therapy and radiation. These treatments cause a significant impact on the lives of patients. Additionally, attending treatment appointments and side effects from treatments are disruptive to patient's lives.

HR-positive, HER2-negative is the most common subtype of breast cancer. Between 70-80% of all breast cancer diagnoses will be HR-positive, HER2-negative.[1] This type of breast cancer has the presence of the progesterone and/or estrogen hormone, but not the HER2 protein. HR-positive breast cancer types have a high risk of recurrence and patients value treatment options which address this increased risk. For HR-positive, HER2-negative patients, there are limited options of targeted therapies. Patients with this subtype of breast cancer can use hormone therapy, but these treatments may lose effectiveness over time. As a result, HR-positive breast

[1] https://cbcn.ca/en/subtypes-of-cancer

cancer patients have a greater reliance on systemic treatments. Systemic therapies such as chemotherapy are less effective and have greater side effects than targeted therapies[2].

4. Experiences With Currently Available Treatments

The Goals of Current Therapy

Current treatments for early stage breast cancer have two aims. The first is to shrink or remove the tumor, and the second is to prevent recurrence or spreading of the cancer. Treatment effectiveness and treatment options available to patients will vary depending on the subtype of breast cancer, location of the cancer, and what symptoms patients experience. A breast cancer diagnosis is not monolithic, and people diagnosed with stage II and III HR-positive, HER2-negative breast cancer have unique needs. As demonstrated by survey responses in the following sections, this patient group desires treatments that eliminate disease, reduce the risk of recurrence, and have minimal side effects.

In our 2022 Survey, stage II and III HR-positive, HER2-negative breast cancer respondents had the following experiences with therapies:

- 98% had received or were currently receiving surgery (109 patients).
- 86.5% had received or were currently receiving hormone therapy (96 patients).
- 75.7% had received or were currently receiving radiation therapy (84 patients).
- 63% had previous or current treatment with chemotherapy (70 patients).
- 8% had previous or current treatment with biologics or targeted therapies (9 patients).

Key Factors for Decision-Making Around Treatment

In both our 2017 and 2022 Surveys, the following were identified as key factors that influence respondent's treatment decision-making.

- Effectiveness of the Treatment. This relates to how well the treatment stabilized disease.
- Prolonged Quality of Life. Patients value productive, active lives with minimal disruption to daily routines.
- Reduced Risk of Recurrence. This means reducing the chances that breast cancer will come back or spread.
- Side Effect Management. Patients want minimal risk while stabilizing their disease.
- Cost and Accessibility of Treatments. This relates to the affordability and ease of accessing treatments.

[2] https://www.cbcn.ca/en/subtypes_of_breast_cancer

Effectiveness of the Treatment:

In both the 2022 Survey and the 2017 survey, efficacy of treatment was a high priority for patients. The 2022 Survey found that 90% of stage II and III HR-positive, HER2-negative breast cancer patients rated how well a therapy works to treat their cancer as either important, or very important. In our 2017 Survey, 14 of 16 (87.5%) stage II and III HR-positive, HER2-negative breast cancer respondents rated treatment efficacy as the most important factor in treatment decision making.

Prolonged Quality of Life:

In addition to efficacy, patients routinely cited quality of life as a key factor in making treatment decisions. In our 2017 Survey, 93.8% of stage II and III HR-positive, HER2-negative breast cancer patients rated quality of life was either important, or very important to them when considering treatment options. In the same survey population, 12 of 16 (75%) respondents indicated that mobility was either an important, or very important consideration when deciding on treatment options.

Reducing Risk of Recurrence:

In the early stage of breast cancer, patients routinely cite reducing the risk of recurrence as a key factor in treatment decision making. In our 2017 Survey, all 16 stage II and III HR-positive, HER2-negative breast cancer respondents rated reducing the risk of recurrence as either important, or very important when deciding on treatment options. Moreover, research demonstrates some patients consider treatments that reduce the risk of recurrence by less than 5% as worthwhile.[3]

In our 2022 Survey, we provided respondents with a list of topics and concerns related to breast cancer and asked them about their current interest in the given topic. Information on new treatments and research (61.7%) and fear of recurrence (61.7%) were the top rated topics of interest among respondents diagnosed or living with non-triple negative subtypes of breast cancer (HR-positive, HER2-negative breast cancer or HR-negative, HER2-positive breast cancer).

Taken together, the tremendous value patients place on reducing the risk of recurrence is evident.

Side Effect Management:

In addition to treatment efficacy, prolonged quality of life, and reducing the risk of recurrence, patients have an expectation that the benefits of treatment will come with manageable side effects. This includes long term side effects. In our 2017 Survey, 12 of 16 (75%) stage II and III HR-positive, HER2-negative breast cancer respondents indicated that minimal side effects was

[3] https://pmc.ncbi.nlm.nih.gov/articles/PMC10625390/#s0004

the most important factor in treatment decision making. In our 2022 survey, 74.8% of stage II and III HR-positive, HER2-negative breast cancer respondents indicated the same.

These concerns were reiterated anecdotally. In our 2017 Survey, early stage HR-positive, HER2-negative patients noted:

> *"Although I was told about the side effects, I was not told about longer term side effects. I felt that I took the responsibility of being informed and did more searching so I asked the right questions- [it] felt like a full time job at first but I was sure of my decisions by doing this"*

> *"The side effects of the treatments caused a lot of other health problems, which I am still dealing with and recovering from."*

Cost and Accessibility of Treatments:

The financial burden associated with early 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: [4]

- 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.

In our 2017 Survey, 87.5% of stage II and III HR-positive, HER2-negative respondents reported that their diagnosis either had some, or a very large impact on their finances.

Our 2022 Survey indicated that among stage II and III HR-positive, HER2-negative patients:

- 33% were prescribed treatments not covered publicly.
- 48.5% were prescribed support medication not covered publicly.
- 2.7% reported that the cost of support medication or treatment medication prevented them from taking the drug.

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

These concern were reiterated anecdotally by early stage HR-positive, HER2-negative patients:

> *"Cost of travel to have tests done, see oncologist etc. is in the thousands when living in remote areas. This is a huge issue in my area." – 2022 Survey respondent*

> *"Although I had access to health insurance through work it was not 100% and included a cap on spending. [One treatment] alone maxed the plan before treatment was complete." – 2017 Survey respondent*

> *"Financial security is a big issue. With no income and so far no government assistance my retirement savings have been impacted. Also, I am uncertain of when I will be able to begin searching for a job again or when I will be successful in my search." – 2017 Survey respondent*

Need for Personal Choice

Discussions with breast cancer patients has demonstrated the imperative for personal choice. One aspect of choice is the availability of treatments. This refers to both Health Canada approval, and national public funding. A second aspect of choice relates to options about which treatment to take. In our 2022 Survey, 78% of stage II and III HR-positive, HER2-negative respondents reported they were provided with the information needed to make treatment decisions. In the same survey population, 85.5% reported that they felt either very comfortable, or somewhat comfortable participating in making treatment decisions. In our 2017 Survey, all 16 stage II and III HR-positive, HER2-negative respondents reported the same.93.75% of these respondents also reported they were given the opportunity to be involved in the decision-making process for their treatment.

Researchers have observed this imperative for patient choice in the context of aromatase inhibitors (AIs). The high burden of side effects associated with AIs can result in non-adherence. However, patients often switch to a different AI to address treatment toxicity. Researchers recognize that while all AIs work in the same way, the option to switch from one AI to another can be effective in reliving treatment related toxicity.[5] Choice in treatment is also important as what works for one patient might not work for another.

5. Improved Outcomes

For early stage breast cancer patients, treatment efficacy and reducing the risk of recurrence is of great concern. Like any other treatment for early stage breast cancer, patients have an expectation that ribociclib (Kisqali) will effectively treat their cancer, reduce the risk it will return, and offer a good quality of life.

[5] https://ascopubs.org/doi/10.14694/EdBook_AM.2014.34.e25

The NATALEE trial, a phase III multi-center, randomized, open-label trial, evaluated the efficacy and safety of ribociclib with endocrine therapy as an adjuvant treatment in patients with HR-positive, HER2-negative, early breast cancer, using 4-year analysis.

This study used invasive disease free survival (iDFS) as the primary endpoint. Secondary endpoints were distant disease–free survival, recurrence–free survival, overall survival, safety, quality of life, and pharmacokinetics. These secondary endpoints reflect the value patients place on treatment choice, reducing the risk of recurrence, safety, effectively treating cancer, and manageability of side effects. At 3 years, distant disease–free survival was 90.8% and 88.6% in the treatment and control arms respectively. At 3 years, recurrence-free survival was 91.7% and 88.6% in the treatment and control arms respectively. The NATALEE trial reported a 25% relative risk of recurrence reduction, and a 5% absolute risk of recurrence reduction. The median duration of follow-up for overall survival was 30 months.[6]

Adverse Effects[7]

The data from NATALEE showed that ribociclib combined with NSAI had greater side effects than NSAI alone (any grade 97.9% vs 87.1% respectively) while the safety profile of ribociclib was consistent with previous studies, and no new safety signals were identified. Commonly reported side effects of any grade were: neutropenia, arthralgia, nausea, headache, and fatigue. Commonly reported side effects of grade 3 or higher were: neutropenia, increased alanine aminotransferase, and increased aspartate aminotransferase.

56.9% of patients treated with ribociclib reported serious side effects, versus 16.1% in the control arm. At the time of the data cutoff, deaths from any cause were reported in 60 patients (2.4%) and in 74 patients (3.0%) in the treatment and control arms respectively. No deaths were considered to be related to the trial treatment.

Impact of Treatment Options to Patients

Additional treatment options that can reduce the risk of recurrence, relieve cancer-related symptoms, and improve a patient's quality of life have a significant impact on patients. When living with no or with minimal cancer-related symptoms, and with minimal side effects from treatment, patients are able to reduce the impact of cancer on their ability to care for children and dependents, continue with their employment, 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] https://www.nejm.org/doi/full/10.1056/NEJMoa2305488

[7] https://www.nejm.org/doi/full/10.1056/NEJMoa2305488

Value to Patients

HR-positive breast cancer patients value reducing their risk of recurrence. Although an individuals risk of recurrence is determined by a myriad of factors, it is known that stage II and III HR-positive breast cancer is associated with a greater risk of recurrence. Endocrine therapy (ET) is one treatment used to address this risk of recurrence, but the effectiveness of ET alone can diminish over time. As ET effectiveness diminishes, the effectiveness of reducing the risk of recurrence also diminishes. In this context, patients value greater choice in treatments that can reduce their risk of breast cancer recurrence.[8]

6. Experience With Drug Under Review

CBCN was not able to speak with stage II or III patients taking ribociclib for the treatment of HR-positive, HER2-negative breast cancer. In September and October 2017, we interviewed two Canadian metastatic breast cancer patients living with HR-positive, HER2-negative breast cancer that had direct experience with ribociclib for a different indication. Their experiences related to treatment efficacy, risks associated with side effects, and the social impacts of accessing ribociclib are discussed below.

Patient Profile

In September and October 2017, CBCN connected with two Canadian patients who had different levels of experience with the treatment under review in the metastatic setting. At the time of the interviews, Patient 1 was between the age of 51-55 years old, and had been on ribociclib for 3 months. She accessed ribociclib through a clinical trial in Ontario. Ribociclib is the first treatment she had been prescribed for her metastatic breast cancer. Patient 2 was between 45-49 years old at the time of the interview, and had been on ribociclib for 5 months. She accessed ribociclib through a clinical trial in Quebec. She had previously been treated with surgery, radiation and goserelin.

Treatment Goals

Each patient's health care provider informed them about the possible risks of this treatment, and that every patient may have a different t side effects. Both patients expressed that they found the side effects to be very minimal. Patient 1 expressed that she had experienced mild nausea and fatigue in the first month and occasional indigestion. She considered all the symptoms to be very minor and easily tolerable. Patient 2 shared that she had experienced thinning hair and a lowered white blood cell count, but that neither of these conditions were intolerable to her.

> *"If this is cancer treatment, bring it on! This is nothing compared to what other chemo agents do to patients!" – Patient 1*

[8] https://pmc.ncbi.nlm.nih.gov/articles/PMC10625390/#s0004

"There are no side effects with this treatment that are not acceptable to me. I had fears about my white blood cells being lowered, but so far I would say the impact has been very minimal. " – Patient 2

The Social Impact of the Treatment

Neither Patient 1 nor Patient 2 discussed the financial impact of the treatment. They did discuss the impact that access to ribociclib had on their quality of life and ability to be productive.

Both patients spoke about the benefit of having access to ribociclib. Patient 1 stated that at the time of diagnosis, she was not able to be active. Before she was diagnosed, she would go for 75 kilometer bike rides. Just prior to her treatment, she was unable to exercise. Following her treatment, she was able to be active and had resumed cycling.

"I am grateful for being able to resume my life without missing a beat… I feel so blessed to be able to access this treatment. The fact that if I lived somewhere else I would not have access to this treatment is heartbreaking". – Patient 1

"I have so much hope accessing a new medicine-I feel like I'm doing something to be able to heal… I wish all women could get access to it. It made me forget about cancer for a while. I don't have to be at the hospital so much and I don't have to give up my life, I can just live with cancer" – Patient 2

Overall, both patients expressed that they valued accessing ribociclib to control their cancer, live well with cancer, and have manageable treatment side effects. These testimonies from patients who used ribociclib in the metastatic setting demonstrate the manageability of side effects, and positive impact treatment had on patient's lives. This is in line with the value stage II and III HR-positive, HER2-negative breast cancer patients place on quality of life, and minimal side effects.

Companion Diagnostic Test

Not applicable

7. Anything Else?

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.

   CBCN connected with the manufacturer, Novartis, to learn about the results of the NATALEE clinical trial.

   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.

   As a member of the Canadian Cancer Action Network, the Canadian Breast Cancer Network is committed to adhering to the Code of Conduct Governing Corporate Funding.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No. The Canadian Breast Cancer Network compiled and wrote this submission independently.

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
Gilead				X
Eli Lilly				X
Novartis				X
Roche				X
Pfizer				X
AstraZeneca				X

Janssen			X	
Merck				X
TerSera	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: JK Harris

Position: Health Policy and Advocacy Lead

Patient Group: Canadian Breast Cancer Network (CBCN)

Date: December 23, 2024

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Kisqali ® (ribociclib)
Indication: Adjuvant treatment of HR-positive, HER2-negative early breast cancer
Name of Patient Group: Quebec Breast Cancer Foundation
Author of Submission: Patricia Quintana

1. About Your Patient Group

For 30 years, the Quebec Breast Cancer Foundation (QCBF) has been committed to defending the interests and well-being of people affected by breast cancer and their loved ones. Our contribution is especially noteworthy in the area of medical and scientific advances. We invest in innovation and cutting-edge research and in patient-support programs, ranging from prevention to cure.

The QCBF works to save lives and improve the quality of life of people living with breast cancer by:

- Funding research and innovation,
- Defending patient rights and offering support,
- Generating cutting-edge knowledge and a sense of community,
- Leading prevention and education, activities and raising awareness.

Website: www.rubanrose.org

2. Information Gathering

<The QCBF has asked among the members of its Facebook private group ‘’Club Stade 4” if anyone has had any experience with Kisqali®. As well, one of our peer support helpline members, [redacted] 49 years (diagnosed at age 44 with metastatic breast cancer) has been taking this drug for almost five years. The QCBF has asked if anyone was willing to share their experience with the medication. All patients live in the Quebec province area. Meanwhile, the QCBF has conducted literature research (PubMed, etc.) and social media to collect the necessary information to complete this form.

3. Disease Experience

[redacted] one of the QCBF peer support helpline members, has agreed to share details about her experience with breast cancer and Kisqali®. She thinks breast cancer stage 1,2 and 3 are quite different from stage 4 (metastatic), as metastasis are patients’ worst fear, and experiences differ depending on metastasis localisation. Also, she perceives earlier stages patients do not receive further support once their treatment is complete. [redacted] suffers nausea, gastric reflux and extreme fatigue, the latter has had a significant impact in her work life. She takes a rest during evenings to cope with the fatigue and articular pain. Likewise, vaginal dryness has a significant impact on her relationship with her partner.

4. Experiences With Currently Available Treatments

Besides Kisqalli®, [redacted] takes also letrozole daily. She does not have any trouble for swallowing pills but she has a blood test once per month or every two months. Every month she has a bone scintigraphy. Every year, she's followed by her surgeon and has to pass a bone densitometry. She suffers from insomnia and articular pain. Her main concern is the immunosuppression which also impacts her quality of life as her concerns limit the number of activities she gets involved in. She is also worried about the long-term side effects of her medication.

As she has access to her medication through private insurance given by her employer, she's concerned about losing or having to change her employment.

5. Improved Outcomes

[redacted] is concerned about the long-term effects of her medication as well as the efficacy. While she is keeping a positive attitude regarding advanced breast cancer, the fatigue and articular pain are limiting factors in her daily life. Since her diagnosis, she has received help from her family and friends. She expects future treatments will help her and other patients to better cope with side effects.

6. Experience With Drug Under Review

[redacted] has had access to Kisqali® through private insurance provided by her employer. One of her main concerns is to be able to access her medication. She took this medication almost immediately after being diagnosed, therefore she is unable to make a comparison of her health before/after Kisqali®. As her, many women with advanced breast cancer who have approached the QCBF, have expressed their concerns about survival. As the new data about the impact of Ribociclib on patients overall survival demonstrates a significant improvement, this represents a possibility to respond to an important need not yet fulfilled.

For [redacted] the main concerns regarding Kisqali® can be summarized to: aide effects, long term side effects and means to access the medication in case her private insurance is no longer available

7. Companion Diagnostic Test

<Not applicable>

8. Anything Else?

<Not applilcable >

Appendix: Patient Group Conflict of Interest Declaration

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

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

   No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

No

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Astra Zeneca				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: Patricia Quintana
Position: Coordinator, Funding and Support Programs
Patient Group: Quebec Breast Cancer Foundation
Date: January 3rd, 2025

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: ribociclib (Kisqali)

Indication: Ribociclib for the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative stage II and III early breast cancer (eBC), in combination with an aromatase inhibitor (AI), in pre- or perimenopausal women, or men, the AI should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.

Name of Patient Group: Rethink Breast Cancer

Author of Submission: Jenn Gordon

1. About Your Patient Group

Rethink Breast Cancer (Rethink) is a Canadian charity known for making positive change. Rethink educates, empowers and advocates for system changes to improve the experience and outcomes of those with breast cancer, focusing on historically underserved groups: people diagnosed at a younger age, those with metastatic breast cancer and people systemically marginalized due to race, income or other factors. We foster spaces to connect, listen, empower and rethink breast cancer, together. Rethink's strategic priorities and organizational direction are guided by the unique, unmet needs identified by breast cancer patients and their families.

Programs and Activities

- Rethink Breast Cancer builds community, bringing patients with various stages of breast cancer together through our private and public social spaces as well as in-person events
- Rethink runs patient retreats and facilitates peer-support
- Rethink creates and runs education forums and conferences
- Rethink creates support and education tools, resources and content
- Rethink funds and supports breast cancer research

You can find out more by visiting:

Rethink Breast Cancer Instagram
Rethink Breast Cancer Website

2. Information Gathering

For over 20 years, Rethink has been working closely with breast cancer patients in Canada. We learn from and listen to the community to understand their values, priorities and pain points to help drive change and system improvements. Each year, we learn from the patients we serve, survey and collaborate with. We learn from the 24 individuals that we work extremely closely with as key patient advisors; the 50 patients that share their stories on our blog; the 500 patients that participate in our virtual support groups; the 2,200 members of our private peer-support network; and the 43,000 people that have joined our Instagram community. We listen, learn, engage and have conversations in all these spaces.

For this submission, we have drawn on our general observations and insights gathered through programming and meetings with breast cancer patients as described above. Rethink also conducted in-depth telephone interviews between August 2024 and December 2024 with 4 patients who have experience with ribociclib for HR+, HER2- high risk early breast cancer.

3. Disease Experience

The majority of the people in the Rethink community are diagnosed at a younger age, between 20 and 50 years old. When younger people get breast cancer it may be more aggressive, which can lead to tougher treatments. In addition, those diagnosed in their 20s, 30s and early 40s face age-specific issues such as fertility or family-planning challenges, diagnosis during pregnancy, childcare, impact on relationships, body image, dating and sexuality, feeling isolated from peers who don't have cancer, career hiatuses, and financial insecurity. The physical and emotional toll that a breast cancer diagnosis and treatment takes on a young person's life is devastating and traumatic.

When it comes to those in the community who have been told their breast cancer is at a higher risk of recurrence, treatment is less about controlling an aspect of the illness and more a deep desire to take on whatever treatment(s) are needed to decrease the chance of recurrence and metastasis. They are facing mortality prematurely and many express a goal to treat aggressively to optimize treatment. Here's what patients from our community with early-stage breast cancer had to say about the importance of reducing their risk of recurrence:

"I think when anyone gets a cancer diagnosis, you're always scared of the illness coming back. Especially when I have young kids that I want to be there for, and I have a lot of things I want to do myself. It's not only my kids, but also my life too. I want to be able to enjoy it. Because I feel that I'm doing anything and everything that's available out there to have a lower chance of recurrence, it gives me peace of mind. It gives me less anxiety in my life." –[redacted]

"I am generally a fan of treatment - the more aggressive the better. In fact, after having chemo done, I advocated to have a total axillary LN dissection, and I also had my ovaries out last year. Again, I don't

mind treatment at all, even the side effects that come with it - I'm more concerned about the prospect of mortality." –[redacted]

"I want to try anything to prevent recurrence, I want to add it to my exercise routine and healthy diet in my bag of tricks." –[redacted]

"I had the perspective of, "I'll do it all"; anything I could do to help prevent recurrence I wanted to do. It was worth having any possible additional side effects to know that I was doing everything I could to reduce my risk of recurrence." –[redacted]

"I have three young kids, so I was really willing to do anything possible to would have done anything to help prevent the cancer from returning" -[redacted]

4. Experiences With Currently Available Treatments

Current treatment for HR positive HER2 negative early breast cancer depends on the specifics of each individuals' diagnosis and the characteristics revealed on their pathology report. It is usually treated with a combination of surgery, chemotherapy, radiation therapy, and targeted hormone therapy, which can reduce the risk of early-stage breast cancer coming back. Some patients with higher risk, and certain genetic mutations, may also opt for an oophorectomy.

There is also currently one CDK4/6 inhibitor, abemaciclib, that is available to this patient population to help reduced the risk of recurrence. The intent to treat population for ribociclib is broader than the abemaciclib intent to treat population, which would allow more patients to access a therapy that has proven to help reduce risk of recurrence. In addition, the side effect profile between abemaciclib and ribociclib is different, the duration of treatment is different, and the dosing schedule is different. Having two options for patients and clinicians to choose from is important as co-morbidities might dictate which therapy is more suitable, patient preference around side effects/dosing/duration is an important consideration, and specifics of their diagnosis may dictate that one treatment is more suitable than the other.

5. Improved Outcomes

Each individual patient brings their own personal values and goals to their discussions with their oncology team. Communication and trust in their team is essential. In our experience working closely with many young high risk breast cancer patients, we find most are willing to trade toxicity for confidence in knowing they've "thrown everything they could" at the cancer. In other words, they will choose to endure additional side-effects and impacts on quality of life from the toxicity of a stronger therapy to ensure they are doing everything they can to treat what they know is an aggressive form of breast cancer. That was a take-away mentioned by patients who were interviewed specifically for this submission and other early-stage

breast cancer submissions.

Reducing the risk of recurrence is of particular importance to younger women, under the age of 50, who don't just want to have their cancer in remission for 5 or 10 years, but rather for several decades as they are still young, may be in the middle of raising kids, still have a lot they want to accomplish in their careers and their lives.

6. Experience With Drug Under Review

Rethink conducted in depth phone interviews with four patients with high-risk early breast cancer who have experience with ribociclib.

Patient #1: [redacted]

I was diagnosed in the summer of 2018 at the age of 38. I felt a lump and went to get it checked out. Within 1 month I received my diagnosis. I had stage 3 HR+ breast cancer and received surgery, chemotherapy, radiation, and targeted therapies.

I wasn't aware of ribociclib at the time and finished active treatment in March of 2019. I had reconstruction and recovered from reconstruction before starting ribociclib. My oncologist shared the option of joining the ribociclib trial. I realized I was committing to a 5-year trial that was randomized and I wouldn't know until later if I was receiving ribociclib or not. I was taking tamoxifen and switched to an aromatase inhibitor in order to participate in the trial.

Being a young woman, and also a mom of two daughters, I wanted to help advance breast cancer science, whether it was for me or for others.

Leaving active cancer treatment felt scary, and being able to stay connected with my oncologist and being followed for 5 years provided some reassurance that I was looking for. The trial will be finished in January 2025, but I was informed that I was on the ribociclib arm.

Being diagnosed with cancer at 38 was terrifying. I had no family history, I had no risk factors for being diagnosed with breast cancer. Not having something to point to say "this is why I got cancer' was really destabilizing. The uncertainty and fear, and anxiety was very real; anxiety over every little headache for example.

I had the perspective of, "I'll do it all"; anything I could do to help prevent recurrence I wanted to do. It was worth having any possible additional side effects to know that I was doing everything I could to reduce my

risk of recurrence. Although, I don't think that most of my side effects were a result of the ribociclib, I think they were mostly from taking the Zoladex and letrozole. The biggest impact and challenge was that instead of easing into natural menopause, it was like being thrown off a cliff into a medical menopause. Body aches, weight gain, fingernails splitting, thinning hair, aching feet the second I got out of bed. But all of these side effects were most likely not from the ribociclib, so adding it, didn't really impact my quality of life negatively.

I feel amazingly fortunate to be in the trail, and I am thrilled to know I received the drug. It helps my mental health a huge amount. But knowing that I have accessed something in addition to the standard of care makes me feel fortunate.

I have friends who have been diagnosed who can't access ribociclib because it hasn't been approved yet. I'm really glad to see that the results of the trial showed a positive impact and that I was able to access this treatment when I did.

I have two daughters. They're 11. When I was diagnosed with breast cancer, I was faced with the idea that there was a possibility that I wouldn't be here for them; which is something that I had always just taken for granted. The idea that I would miss out on the ability to help them through their life, was too much to bear. Having access to all the treatments that are available gives me reassurance that I have done everything I can to reduce my risk of recurrence. I feel fortunate that I had access to ribociclib. Getting breast caner is incredibly unlucky at my age, and especially concerning and anxiety causing when there's not way to pin-point how to stop it; so, this treatment helps with that. It also helped me have a sense of control in a situation where so many things are out of my control.

It's been 6 years, I am still on the hormone reducing medications, I am off ribociclib. I am back to a job that I love and that I find a lot of meaning in. I am active with friends and within my community. My girls are starting middle school this year and I am back to being a person who is living their life, and that's not something I will every take for granted again.

Patient #2: Wishes to remain anonymous

I had just finished my school degree in June of 2023, when I was diagnosed with breast cancer in July of that same year at the age of 35. I was diagnosed with HR+, stage 2 or 3 breast cancer, grade 2, with two tumours, one 2.5cm and one 1.5cm.

In August 2023 I started on ribociclib + Zoladex + letrozole. I am being treated at a teaching/research hospital which I feel has made a big difference in giving me the option to try new therapies. My oncologist mentioned that he had seen good results with this therapy in some of his other patients He also mentioned that the side effect profile was better than some of the other therapies. I had surgery in March

of 2024, with clear margins, although small in certain spots. The tumour was 30% dead at the time of surgery.

Given that I had just finished school, I had no job, no benefits and no EI hours to use. A social worker helped me apply for several foundations for funds, and the manufacturer co-pay is what is currently covering the cost of ribociclib. Without the assistance program from Novartis, there is no way I could afforded $5,000 per month on my own.

I was able to look for work, secure a job, and then work at that job all while going through treatment. The most noticeable side effects were the medically induced menopause which was a result of the other drugs I was taking as a part of my treatment, not the ribociclib. I did experience neutropenia which was believed to be a result of the ribociclib, but my physician was able to help manage this, and I managed the impact on her immune system by wearing a mask when riding transit, working, or in situations where I may have higher exposure to viruses. It is disruptive trying not to get sick, I often need to isolate myself from friends and family if they are sick, which can be hard.

My oncologist did reduce my dose after surgery and this seemed to really help manage the neutropenia.

I did not lose my hair, which was really nice, and also really helpful because I didn't have to tell people I was sick, which is huge when you're looking for work. It's hard to apply for work when you look sick.
The nausea only happened a few times, but that was manageable. I received some heart scans at the beginning, but it was determined that I was fine, so we stopped the heart scans.

Also, taking an oral drug meant that I wasn't at the hospital all the time.

Patient #3: [redacted]

I was diagnosed with breast cancer in May 2019 at the age of 41. I found my own lump and went to my family doctor who referred me for an ultrasound, and then I went to Princess Margaret Hospital for a biopsy. I was diagnosed with Stage 2 HR-positive breast cancer. My tumour was 1.9cm and grade 3 with lymph node involvement. While the tumour was relatively small, the lymph node involvement and grade 3 was what made it harder to deal with and more serious in terms of risk of recurrence.

I went on to have surgery, with immediate reconstruction on the affected breast. I then started chemotherapy at Sunnybrook, 4 weeks after surgery with dose dense ACT. This was followed by radiation for 3 weeks, also at Sunnybrook.

I did a lot of research, a lot of reading, and was looking to do anything I could to reduce my risk of recurrence. I asked my oncologist about studies I could participate in. She had heard about the palbociclib trial, which was closed, but shared that they did have the NATALEE trial for ribociclib open and

that I qualified for that trial. I was randomized to receive the drug, which felt to me like was like God answering my prayers. I don't know how to put into words how lucky I feel to have received that cancer drug because I would have done anything to reduce my risk of recurrence.

I have three young kids, so I was really willing to do anything possible to would have done anything to help prevent the cancer from returning. I was incredibly happy to be put in the arm of the trial that received ribociclib. I took this therapy for three years, along with an aromatase inhibitor and Zoladex. I did go off the drug for a short period of time while I had a prophylactic mastectomy on my other breast, which also helped ease my fears of having the cancer return.

I started ribociclib with original dose of 400mg, but there was an issue with my liver. We cut the dose to 200mg and that solved the liver issues, and I didn't have any additional liver issues for the remainder of the time I was taking the drug.

It's hard to know whether the side effects were from the ribociclib or the AI, being thrown into menopause was what caused most of my side effects. There was a lot of fatigue. After my diagnosis I started working out religiously to help manage the side effects. I also changed my diet to help manage side effects and reduce my risk of recurrence. I also experienced really dry eyes. I am still on AI and a monthly injection of Zoladex. I have just come up on the 5-year mark so am finishing up these treatments.

I am willing to endure the side effects. You cannot put a price on offering that choice to someone and giving them the option to take that therapy. I consider myself extremely lucky to be put into the study and to receive the drug. I really hope that this becomes available to anyone that it could help.
I would do this 1000 times over to reduce my risk of recurrence. I really hope than anyone in my situation is able to access this and is given this choice.

Patient #4 – [redacted]

I was 41 at when I was diagnosed in June 2018 with stage 3B HR-positive Her2-negative invasive ductal carcinoma, which had also spread to the lymph nodes. I found the lump myself and was referred for a diagnostic mammogram and eventually a biopsy.

I received surgery, 5 ½ months of chemotherapy and 5 or 6 weeks of radiation. My oncologist was the one who mentioned the study with ribociclib to me and I indicated right away that I was very interested in participating if I met the criteria. If it wasn't for my oncologist being so involved in research and discussing this option with me, I would not have know about this trial option.

I was on the ribociclib arm of the trial and received ribociclib in combination with an aromatase inhibitor and Zoladex. I took ribociclib for the recommended time frame of three years and was able to take the

recommended dose of 400mg for the full three years. I did have low neutrophil count a couple of times but would just take an extra week off and that would resolve it, this only happened a couple of times.

At the beginning of the study there were lots of initial visits to the hospital for monitoring, so it was a fairly big time commitment for the first couple of months, but then once the initial testing was complete and it was determined that I wasn't experiencing any serious side effects then the frequency of visits for monitoring decreased.

I did have some side effects but couldn't really tell if it was from ribociclib or the other drugs. It's mostly menopausal symptoms that I have felt and everything that goes with that medically induced menopause. It didn't do anything to reduce my quality of life though, the side effects have not impacted my ability to do anything I want to do. In fact, taking these therapies has actually allowed me to start doing the things I did before.

I joined trial for a couple of reasons, part of it was for me, reducing the risk of the cancer coming back; part of it was also being able to contribute to research to help others who are diagnosed in the future. I would not have been able to afford this drug if I had to pay out of pocket; I have a good job, but still, the cost of this would have prevented me from taking it so I appreciate that I was able to access ribociclib and have the cost covered through the trial. It was a gift.

The cost benefit of providing people with this drug to reduce the risk of recurrence is much cheaper than treating someone for stage IV cancer. I am working full time, am a contributing member of society, I pay taxes; this is a much more cost-effective way of dealing with cancer than paying for the cost of treatments for someone with a stage IV diagnosis. Ideally, this should become standard of care so that anyone who could benefit has access.

I am enjoying the post treatment phase of my life. I am a mom, a wife, and I have a busy fulfilling career. I am grateful that I was able to have all of the treatments that I did to help prevent the cancer from returning.

7. Companion Diagnostic Test

N/A

8. Anything Else?

We'd like to emphasize that young, high-risk breast cancer patients want more effective tools in their toolbox that will help improve their chances against this challenging disease that's turned their life-plans upside-down.

As we ponder "anything else," we think about those in our metastatic breast cancer community that we know so well—and their loved ones. We think about those we've lost. Too, too many at such a young age over the years. Their families will never be the same. The CDK 4/6 inhibitors have been more of a game-changer in our community than we could have ever imagined, and by providing another option for early-stage patients to reduce their risk of recurrence, we can help patients and families avoid a metastatic breast cancer diagnosis. This therapy provides another option for those with HR+ HER2- breast cancer that is at a high risk of recurrence, and can give patients a tangible way to help achieve their goa of reducing their risk of recurrence.

And, finally, as more and more oral therapies are developed for the treatment of breast cancer, barriers to care increase in some provinces for patients who are under the age of 65. It is important that provinces recognize that younger people with cancer are having to navigate yet another challenge when trying to access optimal care to reduce their recurrence. Economic reports continue to demonstrate the treating an early-stage breast cancer has significantly lower costs to the health system then treating metastatic breast cancer. Ensuring the recurrence reducing treatments are accessible to all patients helps ensure optimal outcomes for patients and for the health system.

Appendix: Patient Group Conflict of Interest Declaration

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

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

   No.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No.

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis 2024				X
Novartis 2023				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: Jenn Gordon

Position: Lead, Strategic Operations and Engagement

Patient Group: Rethink Breast Cancer

Date: January 2, 2025

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0395-000
Generic Drug Name (Brand Name): ribociclib (Kisqali)
Indication: for the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative stage II and III early breast cancer (eBC), in combination with an aromatase inhibitor (AI). • in pre- or perimenopausal women, or men, the AI should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.
Name of Clinician Group: OH (CCO) Breast Cancer Drug Advisory Committee
Author of Submission: Dr. Andrea Eisen and members of the OH (CCO) Breast Cancer Drug Advisory Committee

1. About Your Clinician Group

OH(CCO)'s Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

Information was gathered by email correspondence.

3. Current Treatments and Treatment Goals

High risk ER+, HER2-ve breast cancer patients treated with adjuvant intent.

Additional therapy added to endocrine backbone.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Patients with high-risk ER positive, HER2 negative breast cancer have a significant rate of recurrence despite existing standard of care. Currently, abemaciclib is a funded treatment option in this patient population. The ribociclib indication under review would extend treatment eligibility to the node negative patient population, and also expand the eligibility to include node positive patients at lower risk for recurrence. In addition, ribociclib would provide an alternative treatment option with a different toxicity profile than abemaciclib.

5. Place in Therapy

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

Ribociclib will be added to standard endocrine therapy. Ribociclib would likely become the preferred standard of care regimen due to difference in toxicity profile from that of abemaciclib.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Patients who meet the NATALEE trial eligibility would be best suited:

- stage IIB and stage III breast cancer patients were eligible.
- Stage IIA breast cancer patients were eligible if
    - At least 1 lymph node involved
    - Or if node negative,
        - have a grade 2 tumour with a Ki-67 >=20%, or
        - have a grade 2 tumour and were considered to be in a high genomic risk group by molecular profiling, or
        - have grade 3 tumour.
- The patient could have received adjuvant/neoadjuvant endocrine treatment for up to 12 months before randomization.*

*Note - The DAC supports the use of ribociclib in legacy patients who may have received curative endocrine treatment beyond the 12 months, but within a reasonable time frame (e.g., the patient with high-risk disease who has been on endocrine therapy for 15 months.)

Patients least suitable would be patients with prior CDK4/6 inhibitor, or have uncontrolled heart disease, or cardiac repolarization abnormalities. However, legacy patients on abemaciclib who may wish to switch over to ribociclib (because of side effects) should be considered.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Patients receiving adjuvant therapy get monitored as per standard of practice.

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

Discontinue if intolerable toxicity or disease progression.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

In an outpatient setting, by clinicians with expertise in the treatment and management of side effects (QT prolongation, cytopenias).

6. Additional Information

Abemaciclib is given for 2 years while ribociclib is given for 3 years, which will increase the need for clinical monitoring for patients (e.g., blood work, clinic visits) for an extra year.

One DAC member has indicated a lack of support for adjuvant ribociclib for the following reasons: the NATALEE trial data did not demonstrate any overall survival benefit. the use of adjuvant ribociclib poses a significant burden to both patients and the health care system; and ribociclib is associated with toxicity that may be challenging to manage.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   OH (CCO) provided a secretariat function to the group.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Andrea Eisen
Position: Lead, OH-CCO Breast Cancer Drug Advisory Committee (OH-CCO Breast DAC)
Date: 27-Nov-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

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

Declaration for Clinician 2

Name: Dr. Ronita Lee
Position: Member, OH-CCO Breast DAC
Date: 29-Nov-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	X			

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

Declaration for Clinician 3

Name: Dr. Haider Samawi
Position: Member, OH-CCO Breast DAC
Date: 29-Nov-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	x			

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

Declaration for Clinician 4

Name: Dr. Orit Freedman
Position: Member, OH-CCO Breast DAC
Date: 29-Nov-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 4: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**

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

Declaration for Clinician 5

Name: Dr. Olexiy Aseyev
Position: Member, OH-CCO Breast DAC
Date: 29-Nov-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 5

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis	x			

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

Clinician Group Input

Generic Drug Name (Brand Name): Ribociclib (KISQALI)
CDA Project Number: PC0395-000
Indication: Ribociclib is indicated:

- For the adjuvant treatment of patients with hormone receptor-positive, human epidermal growth factor receptor 2-negative stage II and III early breast cancer, in combination with an aromatase inhibitor.
- In pre- or perimenopausal women, or men, the AI should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.

Name of Clinician Group: REAL Alliance
Author of Submission: Dr. Karen Gelmon, Medical Oncologist at the BC Cancer Agency, Vancouver Coastal Health Research Institute – VCHRI, Professor of Medicine at the University of British Columbia
REAL Alliance Members in support of this submission: Dr. Jean-Francois Boileau, Dr. Christine Brezden-Masley, Dr. Stephen Chia, Dr. Scott Edwards, Dr. Jan-Willem Henning, Dr. Anil Abraham Joy, Dr. Nathalie Levasseur, Dr. Mita Manna, Dr. Sandeep Sehdev, Dr. Christine Simmons.
Clinicians that agree with the REAL Alliance Clinical Input and in support of the submission: Dr. Nayyer Iqbal, Dr. Maged Salem, Dr. Silvana Spadafora.

1. About Your Clinician Group

The Research Excellence, Active Leadership (REAL) Canadian Breast Cancer Alliance is an equitable standing nucleus committee of multi-disciplinary, clinical-academic oncologists across Canada and Breast Cancer Canada, a patient organization. Formed in December 2023 in recognition that a national ecosystem of leadership should address evidence-based guidance and recommendations for equitable breast cancer clinical management. REAL Alliance publishes national clinical consensus recommendations, routinely updated, for timely health policy, funding, and consistent clinical adoption based on research evidence and medical specialty expertise to ensure optimal outcomes for breast cancer patients across all provinces and territories in Canada.

2. Information Gathering

Our members met virtually and exchanged views via email to discuss our clinical recommendations for ribociclib in patients with hormone receptor positive (HR+), HER-2 negative (HER2-), early-stage breast cancer (EBC) who are at high-risk of recurrence. Our recommendations were compiled to reflect our clinical opinion as medical specialists in breast cancer on what we believe is best for our patients. Our opinion is based on literature review, level 1 data from clinical trials, and recent data releases from international congresses, as well as our collective clinical expertise. We urge CDA to consider our clinical recommendation as per the evidence in this document along with the submissions put forward by patient advocacy groups to make an informed decision regarding the place in therapy for ribociclib in patients with HR+/HER2– EBC at high-risk for recurrence. The collective expertise from this group equates to decades of clinical experience in the management of patients with breast cancer.

3. Current Treatments and Treatment Goals

HR+/HER2- early breast cancer is associated with long-term risk of recurrence

In Canada, breast cancer remains one of the most commonly diagnosed cancers among women, with HR+/HER2– subtype comprising approximately 70% of cases.[1,2] Most women (>90%) with HR+/HER2- tumors will present with EBC and receive multimodal treatment that includes locoregional and systemic therapies. However, despite advances in the treatment of HR+/HER2- EBC, this disease is associated with a long-term risk of recurrence with ~ 50% of recurrences happening more than 5 years after diagnosis.[1,3,4]

Our ultimate goal in treating patients with HR+/HER2- EBC is to cure them of their cancer (i.e., prevent recurrence) and to minimize any treatment-related adverse events. The treatments include surgery, radiotherapy and (neo)adjuvant systemic therapy consisting of chemotherapy and/or endocrine therapy (ET) with oral tamoxifen or aromatase inhibitors.[5,6] The clinical assessments to measure the effectiveness of treatment are recurrence-free survival by measuring invasive disease-free survival (iDFS) and overall survival (OS). Thus, the goals of systemic treatment for EBC are to prolong recurrence-free survival and overall survival (iDFS and OS) while minimizing treatment-related adverse events (AEs) to preserve quality of life.[7]

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

50% of recurrences happen >5 years after diagnosis

Despite the effectiveness of current systemic therapies, relapse remains a significant challenge, highlighting the need for more effective strategies to prevent recurrence in patients with HR+/HER2- EBC. This risk persists not only in the years immediately following diagnosis but can extend for decades, with nearly half of recurrences occurring more than five years after initial treatment.[3] Data from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) and real-world studies emphasize the long-term risk, with 10-year recurrence rates with lymph node positive patients ranging from 15% to 40%.[8] While patients treated after the year 2000 benefited from improved adjuvant treatments, the long-term risks of distant recurrence persists (figure 1).[8] Even among patients with lymph node negative EBC, the 10-year risk of distant recurrence remains substantial at 7.5% and appears to be increasing at a constant rate with each passing year. At 20 years, the distant recurrence risk for patients with node-negative disease was reported to be as high as 22%.[3] This elevated recurrence for node-negative disease has also been confirmed in recent data from the control arm in the NATALEE trial evaluating a CDK4/6 inhibitor with 5-year adjuvant ET showing a 10% 3-year invasive disease recurrence rate for node-negative patients with a higher risk (T4N0, T3N0, or T2N0 with additional criteria (grade [G]2 with Ki-67≥20% or high genomic risk, or G3).[9] In fact, real-world evidence from the US indicates how this cohort of node-negative HR+/HER2− EBC has a similar recurrence risk as patients with 1-3 affected nodes (N1)(figure 2).[10] While extending ET to 10 years modestly reduces recurrence risk, it does not significantly improve survival and is associated with increased adverse effects, such as bone pain, fractures, and osteoporosis.[11] Furthermore, recurrence usually manifests in the form of distant metastatic disease, which is an incurable disease. Current endocrine therapeutic strategies are failing to prevent the recurrence of advanced breast cancer despite targeting the driver of the disease which is the endocrine receptor. There remains a significant unmet need to optimize treatment of patients with HR+/HER2- breast cancer, in the early-stage setting to prevent recurrences, when the disease is still curable.

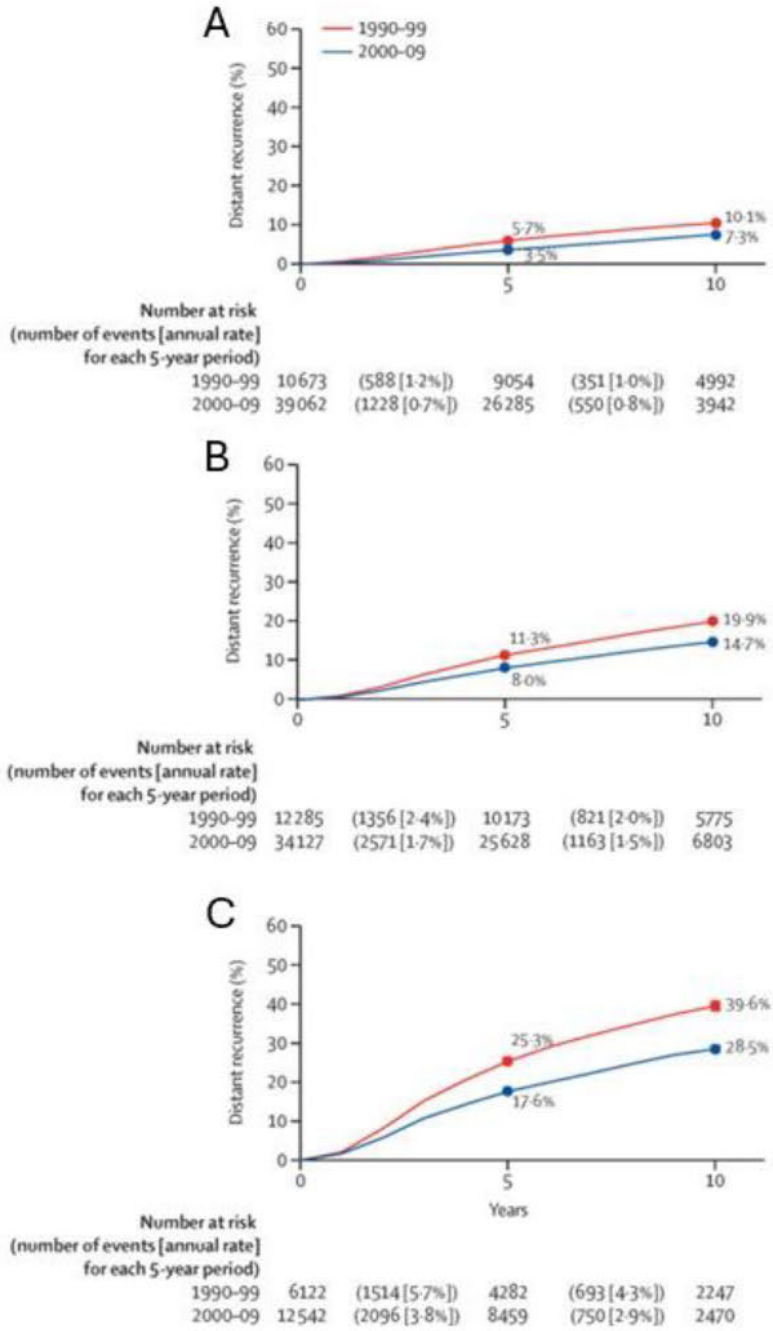


Figure 1. Risk of distant recurrence by period of enrolment among 155 746 women from 151 trials treated with 5 years of endocrine therapy for HR+ disease. Molecular risk of distant recurrence in HR+ EBC consistently increases over time despite nodal status in node-negative (A), node-positive N1 (B) and node-positive N2 (C).
Source: Early Breast Cancer Trialists' Collaborative Group. Lancet. 2024 Oct 12;404(10461):1407-1418

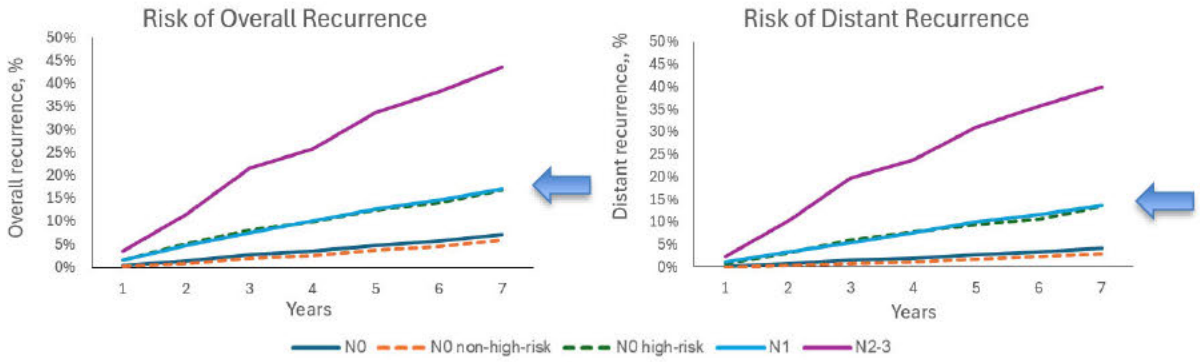


Figure 2. Overall (left) and distant (right) recurrence risk in patients with node negative and node positive HR+/HER2− EBC from 7564 US electronic health records. Real-world data illustrating how N0 high-risk patients have similar risk of both overall and distant recurrence to that of patients with N1 node-positive disease.
Source: Jhaveri K, et al. ESMO 2024. Poster 292P

Emerging evidence supports the role of adding CDK4/6 inhibitors to endocrine therapy in the adjuvant setting to reduce the risk of recurrence for patients with HR+/HER2- EBC.[9,12–15] Both the FDA and the European committee for medicinal products for human use (CHMP) now recognize the benefits of adding CDK4/6 inhibitors to ET in these populations, with abemaciclib and ribociclib approved for such use.[16–18] In addition, the NATALEE clinical trial demonstrated a reduction in risk of recurrence for a population not previously studied (i.e., node-negative disease and a broader population of patients with node-positive disease), while offering a manageable safety profile with less diarrhea compared to other agents in this class.[13,14]

5. Place in Therapy

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

NATALEE trial is the first HR+/HER2- EBC randomized trial to include patients with Stage II and Stage III EBC, regardless of nodal status.[9,13,14]

The Phase III NATALEE trial evaluated adjuvant ribociclib + ET in a population of HR+/HER2- patients at risk for recurrence. Patients with Stage II and Stage III disease comprised 40% and 60% of the study population, respectively. Patients with N0 disease (no nodal involvement) accounted for ~27% of the study population and patients with N1 disease made up ~40% of the study population; the remaining evaluated 20% of patients had a higher burden of nodal involvement (N2+).

The results demonstrated that patients treated with ribociclib + ET in the adjuvant setting had a significantly longer iDFS compared to those treated with ET alone at both the 3-year and 4-year landmark analyses. At 3 years, iDFS rates were 90.4% versus 87.1% in favour of ribociclib (HR=0.748; 95% CI: 0.618-0.906; P<0.001).[13] At 4 years, the iDFS rates were 88.5% versus 83.6%, also favouring ribociclib (HR=0.715; 95 CI: 0.609-0.840; P<0.0001).[9,14] **The difference between the groups increased over time, with a delta of 2.7% at 3 years and 4.9% at 4 years.** These results suggest a potential **carry-over effect**, where the benefits of ribociclib persist and the divergence between the treatment curves continues to expand even after the 3-year ribociclib treatment is completed. In other words, while the risk continues to increase over time for the control arm, in the ribociclib study-arm, there is a statistical protective benefit from developing local and distant recurrences.

Notably, there was a consistent iDFS benefit in favour of ribociclib across all key subgroups, including patients with Stage II disease (HR 0.644; 95% CI 0.468-0.887), **patients with N0** disease (HR 0.666; 95% CI 0.397-1.118) and **men/premenopausal women** (HR 0.677; 95% CI 0.523-0.877).[9,14]

Distant disease-free survival (DDFS), a secondary endpoint and surrogate for overall survival, also demonstrated a consistent benefit with ribociclib with the difference between the arms increasing over time (3-year delta of 2.7% and a 4-year delta of 4.5%).[13] This represents a 29% risk reduction at the 4-year landmark analysis.[9,14] Overall survival remains immature, as would be expected in an adjuvant trial with a short follow-up. Other agents have received HTA approval in Canada (and globally) based on trials with iDFS or event-free survival (EFS) as the primary objective.[17,19] The NATALEE trial demonstrated significant disease-free benefits at the 4 year landmark analysis, which is one year after completion of 3 years of treatment.[9,14]

Thus, based on these results, we recommend that ribociclib, in combination with ET, be made available as a treatment option for patients with HR+/HER2- EBC adjuvant setting with node-positive or high-risk node-negative disease as per the NATALEE trial eligibility criteria.

The NATALEE trial demonstrated manageable AEs when adding ribociclib to ET with a 20% discontinuation rate, while on 3-years of therapy.[9] Dose modification due to AEs were mainly observed in the first four months of treatment, consistent with other CDK4/6 inhibitor clinical trials.[20] Neutropenia was the most frequent AE requiring dose reduction or discontinuation in the NATALEE trial. Of note, there are some AEs that are equal in the two arms in the NATALEE trial, as ET alone is known to be associated with some AEs, such as arthralgias, headache, fatigue and hot flushes.

Given our experience with CDK4/6 inhibitors in the metastatic setting, we know the importance of having more than one treatment option. Diarrhea can be a debilitating AE. A patient with EBC is generally fit and well after the peri-operative treatment (surgery/radiation/chemotherapy) is completed. They will often go back to work and resume their regular life. Grade 1 level of diarrhea can significantly disrupt a person's routine with 4 bowel movements a day. Abemaciclib is associated with higher AE grade and incidence of diarrhea.[15] The NATALEE trial demonstrated that the ribociclib + ET combination has a manageable safety profile, where AEs are notably predictable (e.g., liver transaminitis, neutropenia) in the first four months of initiating therapy and are detected with routine bloodwork, as patients are usually asymptomatic.[20] Oncologists have become very competent in monitoring and managing ribociclib associated side effects because this agent is the preferred CDK4/6i in the metastatic setting.[21] Furthermore, the quality-of-life data confirms a minimal effect of AEs on patient's lives, during 3-years of combination therapy.[22] Thus, it is important that clinicians and patients have treatment options within this drug class.[23]

The current treatment paradigm provides adjuvant ET for HR+/HER2- EBC patients over a 5-year period, with some patients who have node positive EBC continuing ET for a longer duration. Following surgery and chemotherapy (where applicable), the addition of combination oral agent adjuvant therapy with ribociclib and ET can be incorporated into current standard practice for 3 of the 5 years with ET.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

We recommend ribociclib for all HR+/HER2- EBC patients at high-risk of recurrence using the NATALEE study criteria, including men and pre and postmenopausal women, regardless of nodal status. This population has been shown to clearly derive iDFS benefit. Of note, the T2N0 sub-population must have grade 2 disease plus an additional risk factor of either high genomic risk (i.e.OncoType Dx / MammaPrint etc.) or Ki67 score of ≥20%, or, have grade 3 disease[9,13,14], **thereby reducing the number of eligible N0 patients** that would routinely be prescribed ET and are currently included in current practice volumes. Ribociclib should ideally start within 12 months of beginning standard (neo)adjuvant ET and continue for 3 years in combination with ET. In patients with a BRCA mutation who undergo a year of adjuvant olaparib therapy, ribociclib initiation may occur slightly beyond the 12-month window. This adjustment accommodates the completion of olaparib without overlapping toxicities. After finishing ribociclib, patients should stay on their regular ET for a total of 5 to 10 years, as recommended by a medical oncologist.

Least suitable patient populations would include patients ineligible for the NATALEE study or contraindicated to CDK4/6 inhibitors.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Monitoring for recurrence would occur only if clinically indicated, as per the current standard of care for ET.

Monitoring is required most notably in the first four months after ribociclib initiation, which includes monitoring of blood work for toxicities and ensuring adherence to ET + ribociclib. AEs are manageable with early intervention including dose reduction and standard supportive care. For baseline cardiac assessment with ECG, the US label indicates that an ECG is required in all patients prior to starting ribociclib and repeated at approximately Day 14 of the first cycle, and as clinically indicated.[24] A similar indication by Health Canada is anticipated.

Current health systems in place can incorporate this follow up monitoring, with consideration of health system monitoring models that utilize pharmacists and nurses, where necessary, at no additional clinical workflow burden.

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

Ribociclib + ET combination therapy should be discontinued at the first evidence of recurrent disease or in the case of persistent toxicity, as per the product monograph.

5.5 What settings are appropriate for treatment with ribociclib? Is a specialist required to diagnose, treat, and monitor patients who might receive ribociclib?

Oncologists with experience in treating breast cancer patients are required for the initial treatment recommendation and early monitoring of ribociclib + ET combination therapy. Pharmacy/nursing expertise can support the management of oral agents and routine AE screening, including assessing for treatment adherence

6. Additional Information

Of note, and per current standard practice, men and premenopausal women also receive goserelin (ovarian function suppression).

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ADDENDUM:

Declaration for Jean-Francois Boileau

Name: Dr. Jean-Francois Boileau

Position: MD

Date: 12/5/2024 | 3:58:11 PM PST

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Jean-Francois Boileau

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	X			
Genomic Health	X			
NanoString Technologies	X			
Pfizer	X			
Lilly		X		
Novartis		X		
Merck		X		
AstraZeneca	X			
Allergan	X			
Abbvie	X			
RNA Diagnostics Inc	X			
Bristol Myers Squibb	X			
Exact Sciences	X			

New or Updated Declaration for Christine Brezden-Masley	
Name	*Dr. Christine Brezden-Masley*
Position	*Medical Oncologist and Associate Professor of Medicine, University of Toronto*
Date	*February 21, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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**
Astellas	☐	☐	☒	☐
Eli Lilly	☐	☐	☒	☐
Astra Zeneca	☐	☐	☒	☐
Pfizer	☐	☐	☒	☐
Merck	☒	☐	☐	☐
BMS	☐	☒	☐	☐
Amgen	☐	☐	☐	☐
Beigene	☒	☐	☐	☐
Gilead Sciences	☐	☒	☐	☐
Novartis	☐	☐	☒	☐
Seagen	☐	☒	☐	☐
Hoffman La Roche	☒	☐	☐	☐

Declaration for Stephen Chia

Name: Dr. Stephen Chia

Position: Medical Oncologist, BC Cancer Breast Tumour Group Chair Date: Feb 20, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Stephen Chia

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		
Eli Lilly	X			
AstraZeneca		X		
Daiichi Sankyo	X			
Merck	X			
Gilead	X			
Hoffmann LaRoche	X			

Declaration for Scott Edwards

Name: Scott Edwards

Position: Clinical Oncology Pharmacy Specialist at the Cancer Care Program in St. John's Newfoundland

Date: 9/10/2024 | 4:15:51 PM PDT

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Scott Edwards

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Astellas	X			
AstraZeneca	X			
Apobiologix	X			
Gilead	X			
Novartis	X			
Pfizer		X		
Ipsen	X			

Declaration for Clinician Karen Gelmon

Name: Dr. Karen Gelmon

Position: Medical Oncologist, Department of Medical Oncology, British Columbia Cancer Agency, Professor of Medicine, University of British Columbia

Date: December 16, 2024

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Karen Gelmon

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca		x		
Eli Lilly	x			
Gilead Sciences	x			
Novartis	x			
Pfizer	x			
Seagan	x			
McGill University	x			
CIHR	x			
Merck	x			
City of Hope Hospital	x			
Celuity	x			

Declaration for Clinician Dr. Jan-Willem Henning

Name: Dr. Jan-Willem Henning

Position: Medical Oncologist, Clinical Associate Professor, Tom Baker Cancer Centre, University of Calgary, Canada. Correct

Date: 2/13/2024 | 2:03:36 PM EST

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Jan-Willem Henning

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca		X		
Eli Lilly	X			
Gilead Sciences	X			
Novartis		X		
Pfizer		X		
Seagan		X		
University of Toronto	X			
Rethink Breast Cancer	X			

Declaration for Anil Abraham Joy

Name: Dr. Anil Abraham Joy

Position: Medical Oncologist

Date: 12/6/2024 | 10:28:40 AM EST

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Anil Abraham Joy

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca		X		
BMS	X			
DS	X			
Gliead		X		
Eli Lilly	X			
Merck	X			
Novartis	X			
Pfizer	X			
Roche	X			

Declaration for Nathalie Levasseur

Name: Dr. Nathalie Levasseur

Position: Médical Oncologist

Date: 12/5/2024 | 6:34:23 PM PST

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Nathalie Levasseur

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie	X			
AstraZeneca		X		
Eli Lilly		X		
Exact Sciences		X		
Gilead		X		
Knight Therapeutics		X		
Merck	X			
Novartis		X		
Pfizer		X		
Roche	X			
Seagan	X			
TerSera	X			

Declaration for Clinician Dr. Mita Manna

Name: Dr. Mita Manna

Position: Medical Oncologist, Saskatoon Cancer Center and Provincial Disease Site Lead for Breast Oncology in Saskatchewan Assistant Professor at the University of Saskatchewan, MD FRCPC

Date: 2/13/2024 | 9:54:14 AM PST

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Mita Manna

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca		X		
Ipsen	X			
Advanced Accelerator Applications	X			
Knights Therapeutics	X			
Eli Lilly		X		
Gilead Sciences		X		
Novartis		X		
Pfizer	X			
Bristol Myers Squibb	X			
Merck		X		
McGill University	X			

Declaration for Clinician Dr. Sandeep Sehdev

Name: Dr. Sandeep Sehdev

Position: Medical Oncologist, lead of breast cancer disease site group at The Ottawa Hospital Cancer Centre. Assistant Professor, U of Ottawa.

Date: 10-FEB-2024

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Sandeep Sehdev

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca			X	
Novartis			X	

Declaration for Christine Simmons

Name: Dr. Christine Simmons

Position: PI - medical oncologist

Date: 12/13/2024 | 11:27:58 AM EST

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Christine Simmons

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca	x			
Knight	x			
Gilead	x			
Pfizer	x			
Novartis	x			
Bayer	x			
Lilly	x			
Merck	x			
Eisai	x			

Declaration for Dr. Nayyer Iqbal

Name: Nayyer Iqbal

Position: Professor, Department of Oncology and Medical Oncologist

Date: 12/6/2024 | 10:41:07 PM EST

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Nayyer Iqbal

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Bayer	X			
Ipsen	X			
Eisai	X			
Janseen	X			
Pfizer	X			
Novartis	X			
Astella	X			
Tolmar	X			
Astra Zeneca	X			
BMS	X			

Declaration for Dr. Maged Salem

Name: Maged Salem

Position: Medical oncologist. The Moncton Hospital

Date: 12/10/2024 | 3:28:02 AM PST

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Maged Salem

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			
Lilly	X			
pfizer	X			
Roche	X			
AZ	X			
Gilead	X			

Declaration for Dr. Silvana Spadafora

Name: Silvana Spadafora

Position: Principal Investigator, Consultant

Date: 12/9/2024 | 9:04:13 AM EST

☒**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Silvana Spadafora

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Pfizer	X			
Astra Zeneca	X			
EliLilly	X			
Novartis	X			