CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

inavolisib (Itovebi)

(Hoffmann-La Roche Limited)

Indication: Inavolisib in combination with palbociclib and fulvestrant is indicated for the treatment of adult patients with endocrine resistant, PIK3CA-mutated, hormone receptor-positive (HR+) (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, following recurrence on or after completing adjuvant endocrine treatment.

March 3, 2025

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH 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.

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Patient Input Template for CDA-AMC & INESSS Reimbursement Reviews

CDA Project Number: PC0382-000
Name of Drug: Inavolisib (ITOVEBI®)
Indication: Itovebi® (inavolisib film-coated tablets) in combination with palbociclib and fulvestrant, for the treatment of adult patients with endocrine-resistant, PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, following recurrence on or after completing adjuvant endocrine treatment.
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 METASTATIC HR+ / HER2- BREAST CANCER PATIENTS WITH FIRST RECURRENCE FOLLOWING ADJUVANT THERAPY

An electronic survey was distributed from February 15th – 23rd, 2025 to patients living with a first recurrence (i.e. frontline / 1L) of HR+/HER2- metastatic breast cancer (MBC) through our Breast Cancer Canada (BCC) and McPeak-Sirois (MPSG) communities. The survey responses included 169 survivors responding, with 54 people identified as the target group for this input submission sharing their personal experiences with breast cancer (BC) subtype HR+ / HER2- receiving treatment in the frontline metastatic setting. Of these, 44 people shared that 64% reside in Ontario, 18% from Alberta, 11% from British Columbia, 3% from Quebec and 2% from both Nova Scotia and New Brunswick. The majority of the target survey participants identify as white (86%) with inclusion noted from Black (2%), Chinese (5%), Latin American (2%) and Other (5%) ethnicities.

In addition, an electronic survey was distributed from July 6th – 21st, 2023 to patients living with recurrent HR+/HER2- metastatic breast cancer (MBC) and their caregivers through BCC-MPSG communities. The survey responses included 171 personal experiences with treatment in the recurrent metastatic setting, and their financial impact of living with metastatic breast cancer.

3. Disease Experience

Initial recurrence of people with HR+/HER2- MBC following treatment in the adjuvant setting:

43 responders of our 2025 survey showed the average age of breast cancer diagnosis was 53 years old, of the target survey participants with recurrent HR+ / HER2- MBC (1L). Of this group, 32 responders shared their experience for duration of breast cancer (BC) remission following adjuvant therapy, including endocrine therapy (ET), demonstrating in this sample that 15% had BC recurrence within 18 months, 13% recurred between 19-24 months, 9% within 2 to 3 years, 19% between 3 and 5 years and 44% between 5 to 6 years or longer. 41 responders shared the ET prescribed in the adjuvant setting, with 29% having received tamoxifen, 51% an aromatase inhibitor (27% anastrozole, 22% letrozole, 2% exemestane) and 20% stating they were not prescribed adjuvant ET.

Initial recurrence of people with HR+/HER2- MBC and PIK3CA-mutation following treatment in the adjuvant setting:

This 2025 survey identified 5 people with PIK3CA-mutated HR+/HER2- MBC, notably relevant to this input for frontline inavolisib + palbociclib + ET, sharing the average age at diagnosis to be 56 years old. Four of five shared the time to their recurrence following adjuvant therapy: 1 person who recurred within 7-12 months, 2 people recurred within 2-3 years, and 1 person recurred between 4-5 years, while on endocrine therapy (50% on Tamoxifen and 50% on Anastrozole).

4. Experiences With Currently Available Treatments

Unmet needs for people with frontline HR+ / HER2- PIK3CA-mutated MBC having recurrence following adjuvant ET therapy:

There are no targeted therapies available in first line for PIK3CA-mutated HR+ / HER2- MBC following recurrence on adjuvant ET therapy. This results in a significant unmet need for oral targeted therapy, whereby the patient with this BC subtype must wait for PIK3CA-directed treatment until 2nd and subsequent lines of treatment (2L+). This is notable with data showing a higher degree of ET resistance in PIK3CA-mutated HR+ BC[1] and poor outcomes as demonstrated in MONARCH-2 trial, where this sub-population of patients treated with abemaciclib + fulvestrant had a 5-month shorter progression free survival (PFS) in 1L setting.

In addition, financial insecurity is growing over 40% in the HR+ / HER2- MBC population who receive longer-term therapy as a chronic disease. Based on BCC financial toxicity survey in 2023 in people with this cancer type, their lived experience with financial hardship as a direct result of a breast cancer diagnosis is of high concern that goes beyond treatment side effects and cancer symptom burden.

Frontline treatment experience for people with HR+/HER2- MBC after recurrence despite adjuvant therapy – all survey responders:

Our recent 2025 survey described people's current MBC treatment experience started with rebiopsy at recurrence among 25 / 41 (61%) responders, to confirm recurrence of BC. In addition, 14 / 39 responders shared they had genomic testing completed. 31 responders shared their current frontline MBC treatment, with 64% receiving CDK4/6 inhibitor + ET (35% ribociclib, 26% palbociclib, 3% abemaciclib), 16% receiving ET alone, 10% receiving IV-based chemotherapy and 10% who confirmed receiving treatment but did not disclose the drug prescribed.

Frontline treatment experience for HR+/HER2- MBC with PIK3CA-mutated cancer after recurrence despite adjuvant therapy – survey responders with PIK3CA-mutated BC:

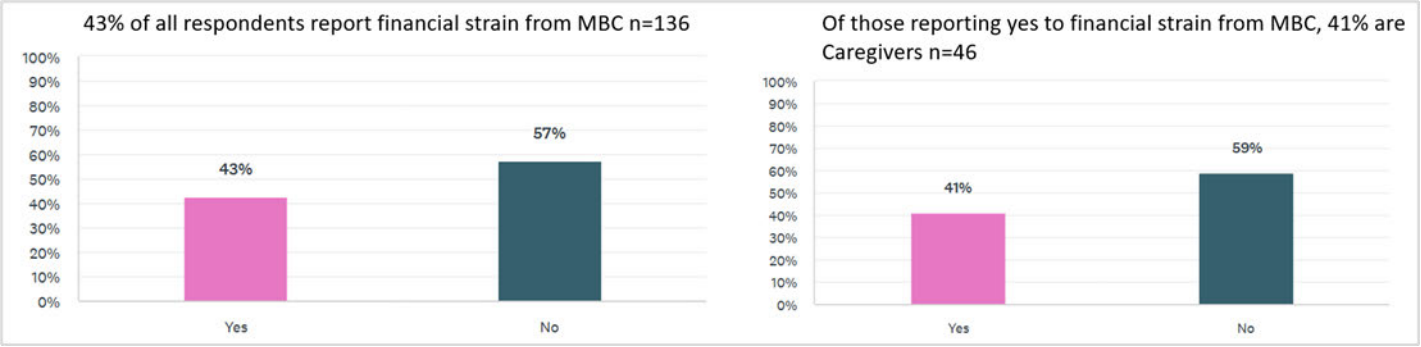
Of the 5 people whose cancer has PIK3CA mutation, at initial recurrence of breast cancer 4 / 5 survivors had a rebiopsy. All five are currently receiving frontline therapy with ribociclib + ET (2 people), palbociclib + ET (1 person), ET alone (1 person) and 1 who confirmed receiving treatment but did not disclose the drug being prescribed. None of the 5 responders are currently on targeted treatment for a tumour mutation nor has received inavolisib added to standard palbociclib + ET.

Oral CDK4/6i + ET has had a positive impact for patients in earlier lines of treatment for HR+/HER2- MBC, with a need to extend this benefit to frontline targeted therapy in patients with poor prognosis, such as PIK3CA-mutated MBC. Patients facing MBC strongly value oral, targeted therapies that provide extended cancer control and meaningful QOL, while delaying chemotherapy.

Financial impact of metastatic breast cancer:

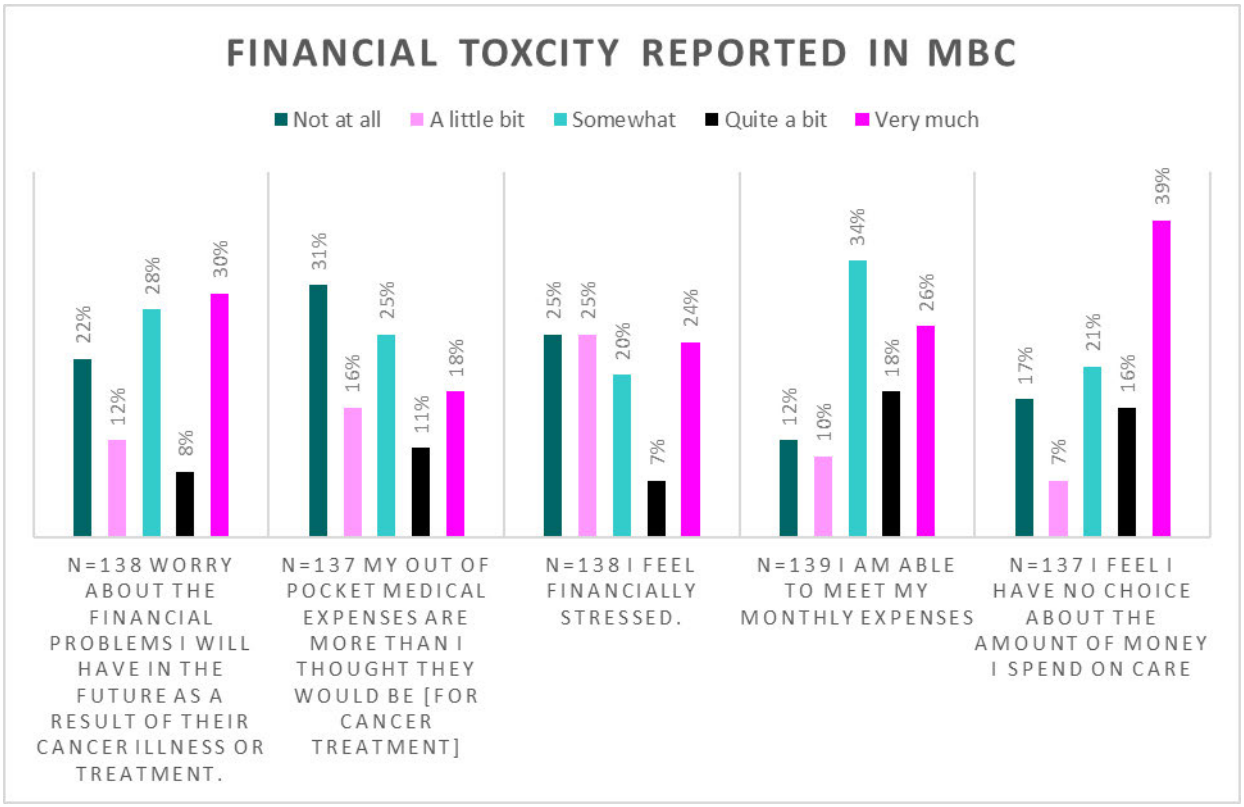
Living with chronic long-term breast cancer has been an achievement compared to 20 to 25 years ago with 5-year survival rates much higher. However, treatment is constant and ongoing with a majority of MBC patients without private 3rd party insurance making the financial burden of treatment, supportive therapies and compounded years of reduced income, a particular concern for today's HR+ MBC patient in Canada. Our 2023 survey included a focus on financial toxicity in the recurrent HR+ / HER2- MBC patient lived experience, with the inclusion of the COST-FACIT PRO[2] questionnaire and other financial-status questions. Within this long-term treated population, and their surviving caregivers left with a financial debt directly related to breast cancer diagnosis, there is financial vulnerability that should be factored into timely public funding decisions of new treatment access for recurrent MBC.

Figure 1: Reported financial strain as a result of HR+ / HER2- MBC is experienced by 43% of all survey responders, of whom 41% are caregivers.



Access to treatment in what is often a future of multi-recurrent HR+ / HER2- MBC should not add to financial toxicity for either MBC patient or surviving caregiver in Canada. As demonstrated in Figure 1, 43% (58 / 136 surveyed) of all responders reported having financial strain because of MBC, **41% (19 / 46 surveyed) of caregiver respondents reported having ongoing financial hardship** related to breast cancer either from living on single income, reduced retirement funds and/or medical costs **after their loved one has passed**.

Figure 2: The impact of MBC disease on financial burden for patients and their caregivers



As shown in Figure 2, over half of the 137 respondents (54%, n= 74) felt that their out-of-pocket medical expenses are more than expected with ratings of 'Very much' (18%), 'Quite a bit' (11%) or 'Somewhat' (25%).

Of n=138 respondents, 66% (n=91) indicated that they worry about financial problems in the future because of their cancer illness or treatment. 76% (n=105) feel some degree of financial stress related to their MBC.

Of n=139 respondents, 56% (n=78) report they are 'Somewhat' (34%), 'A little bit' (10%) or 'Not at all' (11%) able to meet their monthly expenses. Even of those patients and caregivers that had responded to low concerns about financial toxicity, more had indicated that they felt they had no choice about the amount of money spent on care.

These patient-reported financial toxicity outcomes demonstrate a high vulnerability in this chronic population who feel required to pay out of pocket medical expenses over the long-term. We would put the case forward that compared to other tumor types, MBC patients are particularly financially vulnerable given that the majority have significant out-of-pocket costs when diagnosed in early stage, and then recur, requiring further medical expenses over a longer period of their lifetime, and that of the surviving caregiver.

When considering length of curative multi-disciplinary treatment for high-risk adjuvant breast cancer management, and then the added toll of recurrent therapy for metastatic disease, the HR+ / HER2- MBC population experiences some of the longest-term years of cancer-related costs and financial burden. Timely drug funding access will positively contribute to reducing financial stress in Canadians with HR+ / HER2- PIK3CA-mutated MBC.

5. Improved Outcomes

HR+ / HER2- MBC has become a chronic disease without any significant oral targeted treatment options for patients after recurrence using ET, when compared to multi-lines of targeted therapy for HER2+ MBC or other tumour types such as EGFR+ or ALK+ non-small cell lung cancer. The growing understanding of PIK3CA-mutated BC and poor outcomes, particularly in HR+/HER2- subtype is offering exciting advances in precision treatment that is meaningful to patients. The INAVO-120 study[3] adding targeted therapy inavolisib to standard palbociclib + ET in first line for PIK3CA-mutated HR+ / HER2- MBC offers a new breakthrough in breast cancer precision therapy that aligns with patient and clinician goals for management of metastatic disease to extend cancer control, survival and preserve quality living.

Our 2025 survey asked the target population about their goals in therapy after recurrence having received adjuvant ET. The reported results provide perspective from people with HR+/HER2- frontline MBC, with or without / unknown PIK3CA-mutation.

88% of all 36 target responders felt 'somewhat' (11%), 'quite' (44%) or 'very' (33%) strongly about preferring treatment that can be taken at home (I.e. not IV chemotherapy).

Of 36 responders, a sliding scale of efficacy and QOL compromise was surveyed that focused on frontline treatment goals from people with recurrent HR+/HER2- MBC. Overwhelmingly 97% felt a long recurrence-free period was critical to their goals for treatment (responses: 3% 'somewhat', 8% 'quite a bit', 86% 'very much'); while '92% felt 'somewhat' (3%), 'quite a bit' (8%) and 'very' (81%) strongly about treatment that extends life for as long as possible, suggesting quality living is important beyond longer survival.

When treatment extends life with side effects negatively impacting 25% of daily activities and time with loved ones, 89% (36 responders) remained 'somewhat' (14%), quite' (36%) and 'very' (39%) strongly about the acceptance and trade-offs between these treatment goals. These responders consistently reported that 78% of the majority accept the balance of longer recurrence-free survival even in the case of a side-effect impact tradeoff of 50% inability to perform daily activities and spend time with loved ones (25% 'somewhat', 22% 'quite a bit', 31% 'very' in favour of treatment meeting frontline goals).

These survey side-effect trade-off impact opinions acceptable at 25% and 50% when considering improved efficacy outcomes are reflective of INAVO-120 trial. The study prospectively evaluated quality of life with targeted triplet therapy using validated "Bother Score" with ~75% of study participants scoring very positively indication they were 'a little bit' or 'not at all' bothered by treatment-related side effects consistently through the duration of treatment.

People with lived experience, HR+ / HER2- MBC in frontline are in favour of rebiopsy and genomic testing to determine PIK3CA-mutation status. In addition, this target population is highly motivated to take cancer therapy when it meets their optimal treatment goals by extending cancer control and survival and providing at-home therapy that preserves quality living while delaying IV chemotherapy. INAVO-120 efficacy and quality of life study outcomes demonstrate this triplet combination meets the therapeutic goals of people with HR+ / HER2 MBC in the frontline setting, consistent across those with or without PIK3CA cancer mutation.

6. Experience With Drug Under Review

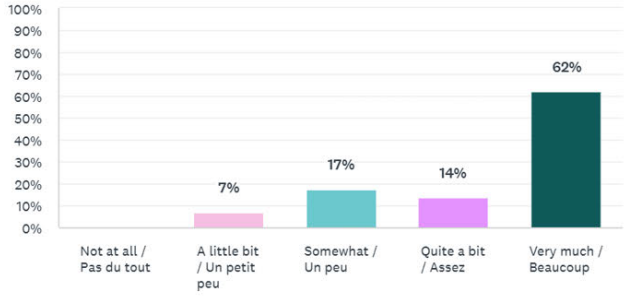
Our 2025 survey of target population for this treatment submission did not capture patients that have been participants on the INAVO-120 study. However, of the 5 people with HR+ / HER2- / PIK3CA-mutated MBC following adjuvant ET recurrence, our survey identified their goals for frontline therapy. Not knowing if people with identified PIK3CA-mutated HR+/HER2- MBC in frontline setting would respond differently in the survey than their counterparts with no knowledge of mutation status, the survey responses show strong alignment of treatment goals supporting inavolisib when added to palbociclib + ET among people with or without the knowledge of their cancer PIK3CA mutation status.

Across 33 target population respondents the survey specifically asked about how meaningful to them was extending cancer recurrence to 9 months or more and ~50% improvement over current treatment, reflective of the PFS outcomes in INAVO-120 trial. The subgroups, PIK3CA-mutated compared to PIK3CA unknown status, responded 'quite a bit' and 'very' strongly in favour of meeting their recurrence-free efficacy goals of frontline therapy, as shown in Figure 3.

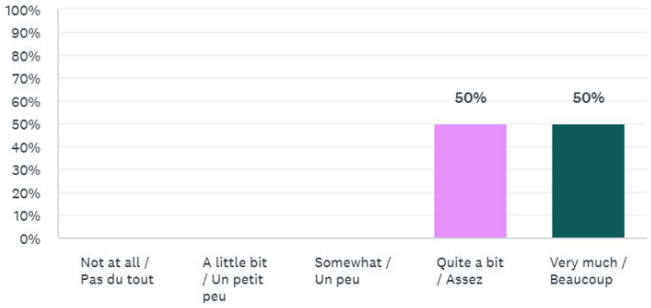
Figure 3: 33 responders, segmented based on PIK3CA known status, indicate >76% find the outcomes of the INAVO-120 study meets their treatment goals in frontline MBC.

Survey question "How likely are you to try a new treatment if it can make metastatic breast cancer stay in remission for at least 9 or more months, with about a 50% improvement over current treatment?"

Of 29 respondents with HR+/HER2- MBC, 76% majority feel 'somewhat', 'quite a bit' and most felt 'very' strongly about accepting a new treatment that demonstrated ~50% improvement over current treatment that provide 9 or more months delay of recurrence.



4 respondents with PIK3CA-mutated, HR+/HER2- MBC feel 'quite a bit' and 'very' strongly about accepting a new treatment that demonstrated ~50% improvement over current treatment that provide 9 or more months delay of recurrence.

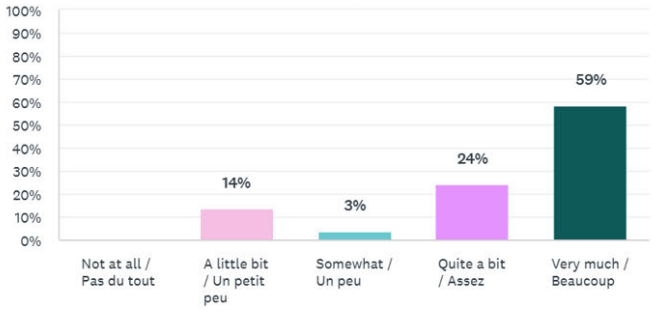


Across 33 target responders, the survey asked how realistic it would be to take long-term treatment, up to 2-years per >25% of responding INAVO-120 study participants at this landmark timepoint, with 2 oral agents and 1 monthly shot (injection). Responders reflected a very strong majority that the triplet combination given in this format would be 'quite a bit' and 'very' realistic to remain compliant, as shown in Figure 4.

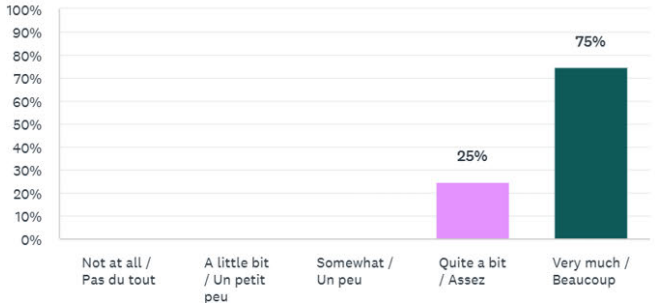
Figure 4: 33 responders, segmented based on PIK3CA known status, indicate >83% would be able to adhere to this triplet therapy.

Survey question: "How realistic is your ability to take 2 oral medications on a daily basis and 1 shot (injection) on a monthly basis for up to 2 years?"

Of 29 respondents with HR+/HER2- MBC 83% feel 'quite a bit' and 'very' strongly about adhering to triplet treatment regimen of oral agents and a monthly injection ('shot') over a long-term.



4 respondents with PIK3CA-mutated, HR+/HER2- MBC feel 'quite a bit' and 'very' strongly about adhering to triplet treatment regimen of oral agents and a monthly injection ('shot') over a long-term.

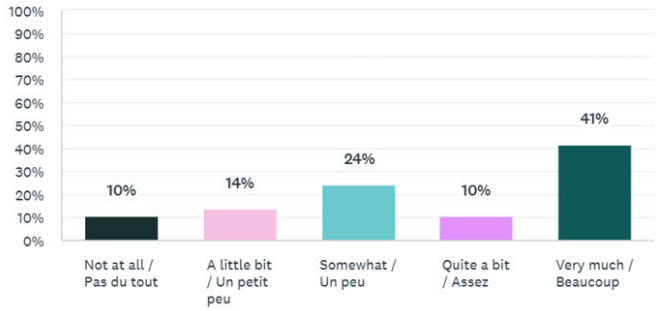


In addition, all 33 target respondents shared their frontline treatment goals to questions about specific high rates of two side effects reported with taking inavolisib + palbociclib + ET therapy, and their compromise to accept hyperglycemia and diarrhea as a trade-off for better recurrence-free survival outcomes. Consistent responses of 75% or higher, regardless of known PIK3CA status were reported as 'somewhat', quite a bit' and 'very' strongly that hyperglycemia (described like type 2 diabetes) and diarrhea are acceptable with standard management using oral antihyperglycemic and antidiarrheal agents, as shown in Figures 5 and 6.

Figure 5: 33 responders, segmented based on PIK3CA known status, indicate >75% would accept managing hyperglycemia treatment side effect with oral antihyperglycemic agents when considering improved efficacy outcomes.

Survey Question "How willing are you to try this new treatment, which might be 50% better than the current one, even if it causes high blood sugar like type 2 diabetes that can be managed effectively with diabetes pills?"

Of 29 respondents with HR+/HER2- MBC, 75% are willing ('somewhat', 'quite a bit' and most felt 'very') to accept hyperglycemia treatment side effect that can effectively be managed by oral agents for diabetes



4 respondents with PIK3CA-mutated, HR+/HER2- MBC feel 'somewhat' and 'very' strongly about accepting hyperglycemia treatment side effect that can effectively be managed by oral agents for diabetes

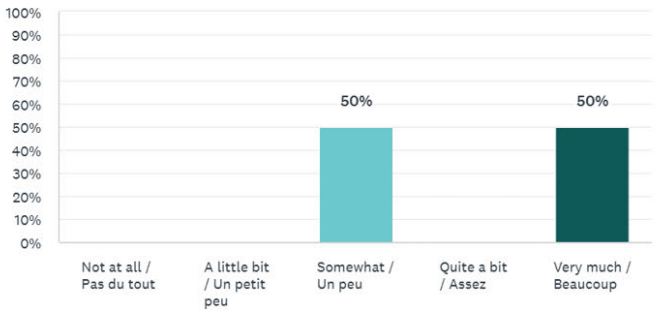
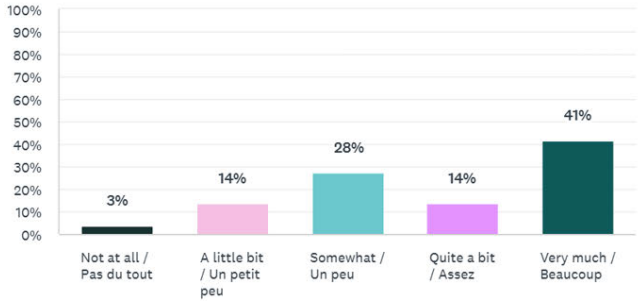


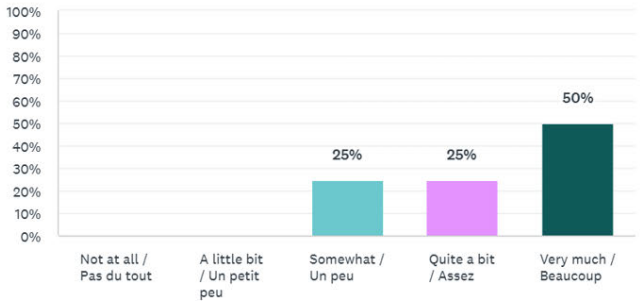
Figure 6: 33 responders, segmented based on PIK3CA known status, indicate >83% would accept managing diarrhea treatment side effect with oral antidiarrheal agents when considering improved efficacy outcomes.

Survey Question "How willing are you to try this new treatment, which might be 50% better than the current one, even if it causes diarrhea that can be managed effectively with diarrhea pills for most people?"

Of 29 respondents with HR+/HER2- MBC, 83% are willing ('somewhat', 'quite a bit' and most felt 'very') to accept diarrhea treatment side effect that can effectively be managed by oral agents



4 respondents with PIK3CA-mutated, HR+/HER2- MBC feel 'somewhat', 'quite a bit' and 'very' strongly about accepting diarrhea treatment side effect that can effectively be managed by oral agents



People with lived experience potentially eligible for frontline MBC targeted treatment with inavolisib, share frontline treatment goals with >50% improvement in recurrence-free efficacy, side-effect profile and quality living that have been demonstrated in the INAVO-120 trial. Targeted inavolisib added to well-established CDK4/6 inhibitor + ET therapy, would not compromise long-term adherence of 2 oral drugs + monthly injection.

7. Companion Diagnostic Test

With the breakthrough survival evidence of novel targeted therapy inavolisib for people with HR+/HER2- and PIK3CA-mutated MBC, BCC and MPSG advocate for public funded, equitable access of upfront routine and timely multigene molecular testing as standard of care in Canada.

With more than 30 molecular subclasses of breast cancer reported[4], comprehensive somatic testing informs precision clinical decisions for commercialized on or off-label gene-target therapeutics and equitable access to clinical trials with novel treatments. Therefore BCC - MPSG strongly align with the Canadian[5] (2023) and International clinical guideline recommendations from ASCO[6] (2022) and ESMO[7] (2021) that genomic somatic testing be adopted in HR+/HER2- MBC as standard of care using next generation sequencing with a

multigene panel. Furthermore, we support the recommendations for Canada's "readiness" to provide optimal comprehensive genomic testing[8] (2023).

8. Anything Else?

We note the definition of ET resistance in the Health Canada Product Monograph as those "whose disease progressed during or within 12 months of completing adjuvant endocrine therapy and who have not received prior systemic therapy for locally advanced or metastatic disease" (p25 ITOVEBI PM[9]). This definition does not include the full INAVO-120 study eligiblity with primary relapse while on the first 2 years of adjuvant ET, as noted in the US Product Insert (section 14.1 ITOVEBI PI[10]). In the rare occasion this clinical scenario could occur, we strongly advocate to include both primary and secondary definitions of ET resistance from the INAVO-120 study criteria to prevent a public funding scenario where patients are caught in an un-intended limited eligibility criteria for funded access to inavolisib added to standard palbociclib + ET.

The results of INAVO-120 trial using novel inavolisib with established standard palbociclib + ET is a significant advance in precision medicine with extended and meaningful survival that BCC – MPSG are very eager for Canadians with frontline HR+ / HER2- / PIK3CA-mutated MBC to have timely and equitable access all provinces.

To Summarize Top 5 Points for This BCC-MPSG Input on Inavolisib:

1. There is a significant unmet need for frontline targeted therapy in people with HR+ / HER2- PIK3CA-mutated MBC

2. Financial toxicity of people facing MBC is significant, and timely equitable access to novel Inavolisib will support relief to this population from this additional cancer toxicity in Canada

3. This population's cancer treatment goals for recurrence-free extended survival, positive quality of life with low treatment side effect "bother scores", and manageable side effect profile strongly align with the evidence outcomes from INAVO-120 clinical trial

4. Funding eligibility should include the full intent to treat study population that included definitions of both primary and secondary endocrine resistance in the adjuvant setting, as per the INAVO-120 eligibility criteria

5. This population is agreeable to rebiopsy and genomic testing for tumour alterations at initial recurrence following endocrine resistance given in the adjuvant setting

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Appendix: Patient Group Conflict of Interest Declaration

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 outside help used.**
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 outside help used.**
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 Canada with AstraZeneca Canada				x
BCC – Roche 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: **March 3, 2025**

CADTH

CADTH Reimbursement Review
Patient Input

Name of the Drug and Indication	Inavolisib (Itovebi) in combination with palbociclib and fulvestrant is indicated for the treatment of adult patients with PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, following recurrence on or within 12 months of completing adjuvant endocrine treatment.
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

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. Information Gathering

Information for this submission was collected via:

Excerpt from Past Submissions: In 2021, CBCN provided CDA-AMC with input on alpelisib (Piqray) for the treatment of HR-positive, HER2-negative metastatic breast cancer (project number PC0247-000). A copy of this input is reattached herein.

Key Informant Interviews: CBCN was not able to speak with patients taking inavolisib (Itovebi) for the treatment of HR-positive, HER2-negative metastatic breast cancer. Instead, an interview with someone taking alpelisib (Piqray) is included as part of the excerpt from our 2021 input (project number PC0247-000).

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

CBCN's 2022 Triple Negative Breast Cancer Patient Survey: Please see the Disease Experience section for 2022 Survey findings relevant for this submission.

Information for this submission was collected via:

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

Patient Respondents Profile:

180 metastatic, breast cancer patients responded to the survey in English and French.

In this submission, CBCN specifically utilizes the data provided by 90 Canadian, metastatic, hormone receptor (HR)-positive, HER2-negative breast cancer patients who responded to our survey.

The respondents all identified as female and primarily (58) spoke English as a first-language, with 16 speaking French as a first language, and 5 respondents selecting other as their first language (split between Hungarian, Russian, German, Dutch and Serbo-Croatian), with 10 respondents undeclared. The majority of respondents were from Ontario (33) and 16 from Quebec, British Columbia (7), Alberta (7), Saskatchewan (6), (4) from Manitoba, , 1 from Nova Scotia, 1 from New Brunswick, and 1 from Newfoundland and Labrador. The remainder did not specify their province of residence.

Most of the respondents (31) were between the ages of 40-49 when diagnosed,
21 respondents were in the 50-59 age range, 15 were between 60-69 years of age and 14 were between 30-39 years, 3 were between 20-29, and the remainder were undisclosed.

Most respondents were in a relationship (60), while 16 declared themselves as single, and the rest did not specify their relationship status. Most of the patients (60) had children, with the majority (39) with children 20 years or older, 17 had children between the ages of 13-19, 14 had children between 6-12 years of age, 5 had children 2-5 years of age, and 1 had children below 1 year.

CBCN's 2012 Metastatic Breast Cancer Patient and Caregiver Survey Report: An online survey, conducted in collaboration with ReThink Breast Cancer, was distributed to patients living with metastatic breast cancer and their caregivers. No patients surveyed had experience with the treatment under review. Survey questions comprised of a combination of scoring options and free form commentary. Patients were contacted through the membership databases of CBCN and other patient organizations.

- 71 patients participated in the survey
- 16 caregivers participated in the survey

Key informant interviews: Phone interviews were conducted in May 2021 with a metastatic breast cancer patient living with hormone receptor-positive, HER2-negative, PIK3CA- mutated breast cancer and had direct experience with the treatment under review.

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

3. Disease Experience

Metastatic breast cancer is the spread of cancerous cell growth to areas of the body other than where the cancer first formed, and is often more severe. It is most commonly spread to the bones, but can include the lungs, liver, brain and skin. Current treatment options for metastatic breast cancer are only effective at prolonging progression-free disease, and most cases of advanced disease will progress and symptoms will worsen. Patients with a diagnosis of metastatic breast cancer understand the limitations of current treatment options and seek to live their remaining months and years with the best possible quality of life that they can achieve.

Patients with hormone-receptor positive breast, HER2 negative breast cancer make up approximately 70 percent of breast cancer cases. Endocrine therapy-including the use of cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitors- are the standard treatment for patients with HR-positive, HER2 negative, advanced breast cancer. However, resistance to endocrine-based therapies remains a challenge. [1]

Approximately 40 percent of patients living with HR-positive, HER2-negative breast cancer have the PIK3CA mutated gene. These mutations are often associated with more aggressive tumour growth, resistance to endocrine treatment and a poor overall prognosis. [2]

The Physical Impact of Metastatic Breast Cancer

How the disease presents itself through symptoms, how it progresses, and how it is experienced varies by patient, but many effects of metastatic breast cancer represent a significant or debilitating impact on their quality of life. In our 2012 Metastatic Breast Cancer Patient and Caregiver Survey (2012 Survey), patients were asked what impact cancer-related symptoms had on their quality of life:

- 54% of patients reported that fatigue resulted in a significant or debilitating impact, and 40% reported some or moderate impact;
- 39% of patients reported that insomnia resulted in a significant or debilitating impact, and 46% reported some or moderate impact;
- 37% of patients reported that pain resulted in a significant or debilitating impact, and 44% reported some or moderate impact.

These results were further reinforced in our 2017 Metastatic Breast Cancer Patient Survey (2017 Survey).

The Social Impact of Metastatic Breast Cancer

The impact of this disease spreads across all aspects of a patient's life, restricting an individual's employment and career, ability to care for children and dependents, and their ability to be social and meaningfully participate in their community. When asked in the 2012 Survey what kind of impact living with metastatic breast cancer has had on their quality of life:

---

[1] Veronica Wendy Setiawan, Kristine R. Monroe, Lynne R. Wilkens, Laurence N. Kolonel, Malcolm C. Pike, Brian E. Henderson, Breast Cancer Risk Factors Defined by Estrogen and Progesterone Receptor Status: The Multiethnic Cohort Study, *American Journal of Epidemiology*, Volume 169, Issue 10, 15 May 2009, Pages 1251–1259, https://doi.org/10.1093/aje/kwp036

[2] Lea Mollon, Alejandra Aguilar, Elizabeth Anderson, Joni Dean, Lisa Davis, Terri Warholak, AyalA. Aizer, Emma Platt, Aditya Bardiyand Derek Tang, Abstract 1207: A systematic literature review of the prevalence of PIK3CA mutations and mutation hotspots in HR+/HER2- metastatic breast cancer, Cancer Res July 1 2018 (78) (13 Supplement) 1207; **DOI:** 10.1158/1538-7445.AM2018-1207

- Among those who were employed, 71% of patients identified significant restrictions to their ability to work;
- Among those with children or dependents, 21% identified significant restrictions and 53% reported some or moderate restrictions to their caregiving responsibilities;
- 49% of patients identified significant restrictions and 38% identified some or moderate restrictions to their ability to exercise;
- 42% of patients identified significant restrictions and 42% identified some or moderate restrictions to their ability to pursue hobbies and personal interests;
- 41% of patients identified significant restrictions and 41% identified some or moderate restrictions to their ability to participate in social events and activities;
- 22% of patients identified significant restrictions and 52% identified some or moderate restrictions to their ability to spend time with loved ones.

Other experiences identified by patients included: guilt, the feeling of being a burden on caregivers, fear of death, poor body image, not knowing what functionality will be lost, fear of the impact of cancer and the loss of a parent on children, not knowing what will happen to children, the loss of support of loved ones, as well as marital stress/loss of fidelity and affection from husband.

4. Experiences With Currently Available Treatments

The Goals of Current Therapy

The goals of current treatment options for metastatic breast cancer include controlling the progression of the disease (extending life), and reducing cancer-related symptoms (extending or stabilising quality of life). Treatment options and effectiveness vary among type of cancer, location of cancer, and how symptoms are experienced.

For patients with advanced hormone-receptor positive, HER2-negative breast cancer initial treatment typically involves sequential use of multiple lines of endocrine-based therapy. Current front-line therapy is usually an aromatase inhibitor in combination with a CDK 4/6 inhibitor. If there is disease progression after this there is no specific standard of care therapy. Current clinical practice aims to maintain quality of life for as long as possible in patients with advanced cancer before switching to chemotherapy.

In our 2017 Survey, the majority of respondents experienced metastases to their bones, liver and lungs. Twelve percent of metastatic patients reported metastases to their brain while 20% reported metastases to other body parts-including ovaries, pancreas and scalp. Most of the HR-positive, HER2-negative, metastatic breast cancer patients (90) patients had or were receiving hormone therapy, 73 patients had surgery, 66 patients had been or were currently being treated with chemotherapy, and 63 patients had or were receiving radiation therapy.

Key Factors for Decision-Making Around Treatment

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

1. Effectiveness of the treatment – how well the treatment stabilized their disease and delayed progression of their disease.
2. Prolonging life without sacrificing quality of life – being able to maintain productive, active lives with minimal disruption to daily routines.

3. Side effect management – minimizing risk while stabilizing their disease.
4. Cost and accessibility of treatments – affordability and ease of accessing treatments.

Treatment efficacy:

When asked how important progression-free survival was in considering treatments, the HR-positive metastatic patients in our 2017 Survey revealed that efficacy of the treatment is critical to their decision-making. Fifty-six percent of them indicated that progression-free survival of less than 3 months was important or very important, 68% indicated that progression-free survival of 3-5 months was important or very important and 85% indicated that progression-free survival of 6 months or longer was important or very important. When asked about overall survival, 95% of the HR-positive metastatic patients indicated that overall survival was important or very important when considering treatment options.

Metastatic patients in our 2017 Study also spoke on the importance of effectiveness in their decision-making anecdotally:

> *"Effectiveness in patients similar to myself*" -Patient respondent

Effectiveness is most important and then all other things being equal - least side effects"-Patient respondent

> *"The most important factors for me are progression free survival and quality of life."* -Patient respondent
>
> *"Anything to prolong my survival and maintain quality of life."* -Patient respondent
>
> *"Survival is of upmost importance to me."* -Patient respondent

Quality of life:

Quality of life was routinely cited by patients as a key factor in making treatment decisions. In our 2017 Survey, 87% of the HR-positive metastatic breast cancer patients revealed that quality of life was important or very important to them when considering treatment options.

This concern was reiterated anecdotally:

> *"Quality of life as well as keeping progression at bay.* "-Patient respondent
>
> *"Always quality of life. If I am to suffer greatly then no that is not what I want.* "-Patient respondent
>
> *"How it will affect the quality of life I currently experiencing, truth is I will never be the person I was before Stage IV*"-Patient *respondent*
>
> *"Quality of Life is of primary importance*"-Patient respondent
>
> *"Quality of life is more important to me than quantity. I want what time I have left to be somewhat of a life. I don't want to spend the whole time being so sick that I am incapacitated*"-Patient respondent

"Mainly progression free survival and quality of life are the most important factors." - Patient respondent

"I want to live as long as possible with a good quality of life. "-Patient respondent

Patient willingness to tolerate treatment side effects:

In our 2012 Metastatic Patient and Caregiver Survey, the responses to what level of side effects and how much impact on one's quality of life would be worth extending progression-free disease by six months was shown to be determined at the personal level.

When asked to rate how much impact different symptoms of cancer and cancer treatment would be considered tolerable:

- Almost two-thirds of patients indicated that when it comes to fatigue, nausea, depression, problems with concentration, memory loss, diarrhea and insomnia, some or a moderate impact on one's quality of life would be considered acceptable, and approximately one quarter of patients indicated that a strong or debilitating impact would be considered acceptable.
- 70% of patients indicated that when it comes to pain, some or a moderate impact on one's quality of life would be considered acceptable, and 27% of patients indicated that a strong or debilitating impact would be considered acceptable.

Similar responses were also found in our 2017 Survey. The majority of HR-positive metastatic breast cancer respondents indicated that pain, fatigue, nausea, lack of concentration, diarrhea, insomnia, and hair loss were very acceptable or somewhat acceptable symptoms in exchange for 6 months or less of benefits from breast cancer treatment. The majority of HR-positive metastatic respondents indicated that depression as a symptom in exchange of 6 months or less of benefits from breast cancer treatment was somewhat acceptable (53% respondents) Similarly, the majority indicated the memory loss would be somewhat acceptable (61% of respondents) When it came to the symptom of vomiting, only 45 % of HR-positive metastatic respondents indicated that it would be somewhat acceptable.

These responses were also related anecdotally:

"Risks vs benefits. Some adverse side effects are worth the benefits for short term." - Patient respondent

"I can deal with pretty significant side effects if the outcome of treatment is optimistic" Patient respondent

The financial burden of treating and managing breast cancer:

The financial burden associated with living with advanced 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, metastatic breast cancer patients can incur substantial costs associated with treatment and disease management.

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

- 80% of breast cancer patients report a financial impact due to their illness.
- 44% of patients have used their savings, and 27% have taken on debt to cover costs.[3]

These findings were consistent with the responses in our 2012 Survey:

- Nearly one-third of patients indicated that the cost of medication, the cost of alternative treatments (i.e. massage, physiotherapy, etc.) to manage symptoms and side effects, and the time required to travel to treatment had a significant or debilitating impact on their quality of life.
- 24% of patients indicated that the costs associated with travel had a significant or debilitating impact on their quality of life, and 41% of patients indicated that it had some or moderate impact on their quality of life.

In our 2017 Survey, 52% of HR-positive, metastatic patients indicated that the cost of prescription medications had a significant or some impact on their treatment decision-making and quality of life.

Other financial barriers that metastatic breast cancer patients mentioned include: not qualifying for insurance at work, inability to change employers due to loss of insurance, and the prohibitive cost of new treatment options.

> *"Many of the next step treatments are very expensive [and not covered by government programs] and it is a HUGE struggle to get [coverage]. […] When dealing with an incurable disease the last thing you want to have to do is spend time on a letter writing campaign to argue about whether or not you should receive the drugs [recommended by your physician]. At about $1500.00 a week, I don't know many who can afford that."* - Patient respondent
>
> *"Always a concern as you never know if the next drug will be covered or how long it takes to get approval from private coverage. Many times it delays treatment and this weighs on one's mind"* -Patient respondent
>
> *"I feel that Canada is slow in getting access to premium drugs"* -Patient respondent
>
> *"When I turn 65 I will no longer have private insurance. I will not be able to afford the medication I currently take never mind any future medication that I may require."* -Patient respondent
>
> *"I worry that in the future, a drug that may work for me won't be accessible to me based on provincial formulary."* -Patient *respondent*
>
> "*It is expensive. Private insurance is working but not the answer."* -Patient respondent
>
> *"The lack of support is a Health Crisis - people are dying because the cost of treatment is not covered."* -Patient respondent

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

Patient Access to Local Resources and Supports During Treatment

When living with cancer, many patients experience significant barriers and challenges around availability of health care services and quality childcare in their community. In response to the 2012 Survey questions about the availability of supports such as childcare, transportation and alternative treatments in their community:

- Among patients with children or other dependents, 53% indicated that there is minimal or no access to appropriate care for their loved ones when they are experiencing debilitating symptoms related to their cancer, and 40% identified barriers to accessing quality care during cancer treatment.

Patient Willingness to Tolerate Risk

When asked in the 2012 Survey about their willingness to tolerate risk with a new treatment:

- 34% of respondents were willing to accept serious risk with treatment if it would control the disease
- 45% of respondents were willing to accept some risk with treatment
- 21% of respondents were very concerned and felt less comfortable with serious risks with treatment

Need for Personal Choice

What was revealed in the responses to the open ended question, and which was confirmed in the key informant interviews, is that it is imperative that women with metastatic breast cancer have access to, and the option of what drugs they take. Most patients are well aware of the adverse effects of treatment up front and they want to make a personal choice that works for them. Metastatic breast cancer patients expressed the need for personal choice and autonomy in our 2012 Survey as well as in the 2017 Survey:

> *"I think patients (ESPECIALLY young patients) should be given more decision making power in terms of access to radical treatments to control disease. […] With two small I am determined to access any treatment that can extend my life and I hate struggling with doctors for this access."* – 2012 Survey
>
> *"I believe that I would prefer to tolerate severe restrictions in the quality of my life, if it meant that I would be able to have a longer period without progression."* – 2012 Survey
>
> *"It would be nice to have more choices and more information about them. I was lucky to get on a clinical trial perhaps because my oncologist was a research oncologist and involved in many. While I knew friend and acquaintances that had Stage IV BC and never informed of clinical trials, and sadly several did not survive the disease."* – 2017 Survey
>
> *"Accessibility to new drugs- not limiting choices."* – 2017 Survey
>
> *"Complete access to drug treatment choices and trials."* – 2017 Survey

Value to Patients

The value to patients of extending the time that their cancer is progression-free cannot be overestimated. Patients living with metastatic breast cancer are aware that their advanced disease will progress with worsening symptoms until death, and embrace opportunities to try new treatments, even if benefits may be as little as a six month extension of progression-free disease. It is also very important for patients to have good quality of life when receiving treatment for metastatic disease. Patients that we speak to on a regular basis acknowledge the importance to have the energy to attend their children's activities and to spend time with family and friends.

5. Experience With Drug Under Review

Patient Profile:

CBCN connected with a patient from the United States with experience on the treatment:

Patient 1- is a 42 year old woman, diagnosed at age 38 with de novo metastatic breast cancer, HR+, HER2-, ductal and lobular carcinoma in March 2017. She has both the ATM germline mutation and PIK3CA mutation. She has previously been treated with four cycles of Adriamycin and Cytoxane, followed by two years of Palbociclib (Ibrance) and letrozole. She has been on Alpelisib as of August 2019.

The Impact of the Treatment on the Disease

The patient expressed her gratitude at having access to this treatment. Patient 1 noted her personal satisfaction with the treatment, it's impact on her metastatic disease and noted her oncologists confidence in using the therapy.

> *"Piqray is actually keeping the cancer under control even better than Ibrance did…. We looked at a couple of other things, my doctor and I, but because I had the mutation, the whole idea of precision medicine and focusing on the weak spots in the cancer specifically, that was why my doctor felt like it would be the best way to go."* Patient 1
>
> *"It's been more effective than anything else I've been on. So my tumour markers came down precipitously in the very first month. And they fluctuate, but we could see a change after the very first PET scan, significantly. Mets that had remained active for years on Ibrance were gone."*
>
> *"When I was diagnosed, I had a super high disease load. So I went from so much disease to stability on Ibrance, but there was still a lot of active mets. And now I have one active mets. So it really was effective on the mets."*

Assessing Risks Associated with the Treatment

The patient discussed the adjustment period she had with the treatment. She experienced hyperglycemia, nausea and fatigue and how she has been able to manage these side effects. While the overall tolerability of her side effects fluctuated, she ranked her quality of life on Piqray as mid-range once she adjusted to the medication.

"I think there's always a learning curve, and I feel that the Piqray learning curve was longer for me than it was for Ibrance. And now that it's been two years since I've been on it, I have a much better handle on it now. "

"I'm one of the administrators of a support group on Facebook of everyone who is on Piqray, and we have people in the group who were on the original trial. So it is a drug that people seem to be able to stay on for a good amount of time, despite the side effects and some of the difficulty in managing them. "

"*But outside of the hyperglycemia, pretty intense fatigue. For the hyperglycemia, I'm on Jardiance, and that's kept the hyperglycemia under control. I do get a fair bit of nausea as well, and I've got a variety of medications that I take at different times of the day to keep the nausea under control. The fatigue: I drink a lot of coffee, and I've had to adjust my activity levels. The fatigue has been something that has been a side effect of every medication I've been on, so I feel that that's a side effect that I've become a little bit more able to handle. "*

"Going on Piqray, [my quality of life] definitely dipped below a five and was around a four. I would say that I've clawed my way back to that six area after being on it for a few months and getting used to the side effects."

"The change has definitely affected my productivity. Not destroyed it, but it's taken a hit. I've had to step back from some things that I was doing because of the fatigue."

Patient 1 noted that the side effect profile of the treatment was ultimately worth it for her if it could continue to control her cancer as it has.

"I have to say that if the medication is going to be effective in controlling the cancer, there are not many side effects that would be completely unacceptable. At this point in my cancer treatment, the hyperglycemia was not something that I was excited about, but I've been able to manage it. So again, I'm just not sure that any side effects would be categorically unacceptable because my goal is to have the cancer be under control or dead as much as possible. Having the side effects be something that can be managed—like fatigue is something that I can manage—that's acceptable to me."

Alternatives To The Treatment

The patient noted that she was continuing to monitor other options for managing her metastatic disease.

"My doctor and I have been watching the PARP inhibitors Lynparza That was definitely an option."

"Trying out a different CDK4/6 inhibitor. I was only on Ibrance, and so there's still Kisqali and Verzenio available. Xeloda was one of the other ones that my doctor talked about. Those are all still available in my arsenal for later."

She also *elaborated* on the value of having access to Piqray, and to a precision oncology therapy beyond the standard therapies available for metastatic hormone-receptor positive breast cancer.

> *"It means that I have another option. it means that if my body doesn't respond to something else, Piqray is an option. Having something that targets a mutation, having something that targets something that is specific to my cancer makes it more likely that my cancer will respond. And that's the goal all the way around."*

The Social and Financial Impact of the Treatment

As the patient accessed the medication in the United States she did not discuss the financial impact of the treatment but she did specifically address what having access to Piqray meant to her and her family.

> *"I think the biggest thing is having options that are specific to mutations equals longer lives for people with terminal cancer, and I think that that's really important."*

6. Companion Diagnostic Test

At this time, PIK3CA mutation testing is only available through select clinical testing programs and is not implemented routinely in breast cancer care in Canada.

Accessing testing and treatment is of great importance for hormone-receptor-positive breast cancer patients with a PIK3CA mutation. It is imperative that all HR-positive, HER2-negative metastatic/advanced breast cancer patients who could benefit from this therapy are being identified and offered genomic profiling to assess their eligibility for treatment with Piqray. It is critical that access to adequate oncogenomic testing does not create a barrier for access to effective therapies for metastatic patients.

7. Anything Else?

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

We note that Piqray, as a precision oncology therapeutic, treats cancer patients based on the presence of a specific tumour biomarker. We hope that CADTH will consider continuing to engage the manufacturer and other stakeholders to develop novel approaches to support translation into models of assessment for potential value in clinical practice in Canada.

Funding this type of molecularly targeted therapeutic would provide an important therapeutic option for metastatic and advanced breast cancer patients whose tumors test positive for a PIK3CA-mutation and are in need of further treatment options.

3. Disease Experience

CBCN's 2022 Triple Negative Breast Cancer Patient Survey (HR-positive, HER2-negative metastatic breast cancer)

Introduction

The following information was collected via CBCN's 2022 Triple Negative Breast Cancer Patient Survey. The 2022 Survey conducted by the Canadian Breast Cancer Network was distributed to patients living with breast cancer. Survey questions comprised of a combination of scoring options and free form commentary. Patients were contacted through the membership databases of CBCN and other patient organizations. 981 people completed the English-only survey. Below, we will share the responses from the 30 people with HR-positive, HER2-negative metastatic breast cancer (mBC) who completed this survey.

Demographic information

Figure 1 – 3 show the province of residence, first language, and age at the time of the survey for HR-positive, HER2-negative metastatic respondents, respectively.

Figure 1 shows that most respondents resided in Ontario (33.33%), followed by British Columbia (16.67%) and Alberta (13.33%). Saskatchewan (10.00%) and Newfoundland (10.00%) had moderate representation. New Brunswick (6.67%) and Quebec (6.67%) accounted for a smaller proportion of respondents. Nova Scotia (3.33%) had the lowest representation.

Figure 1: Province of Residence (%)

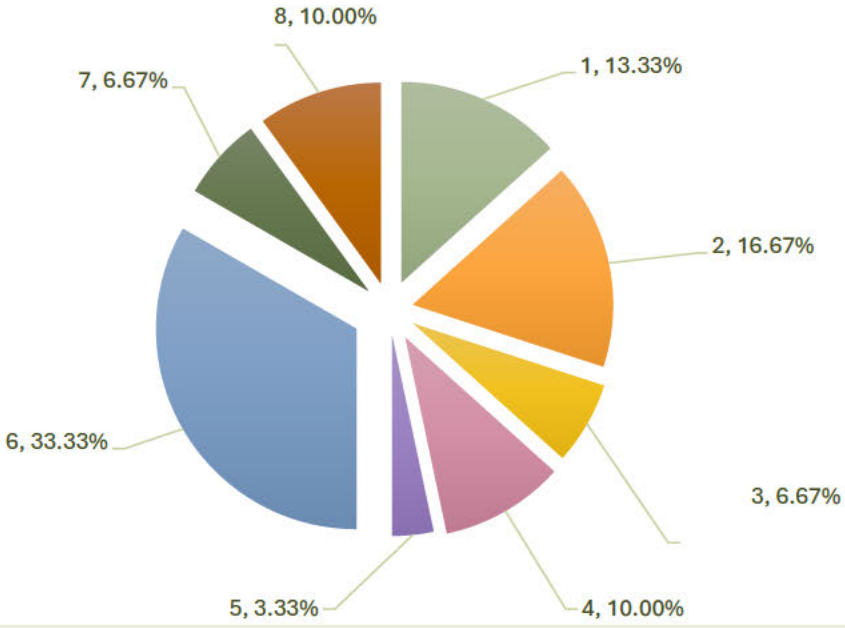


Figure 2 shows respondents' first language. Most respondents reported English (83.33%) as their first language. French (6.66%) was the next most common, followed by a language other than French or English (10%).

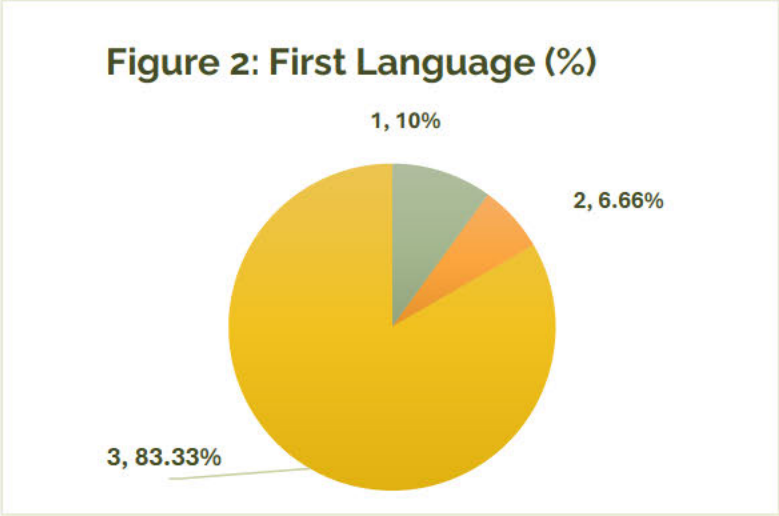
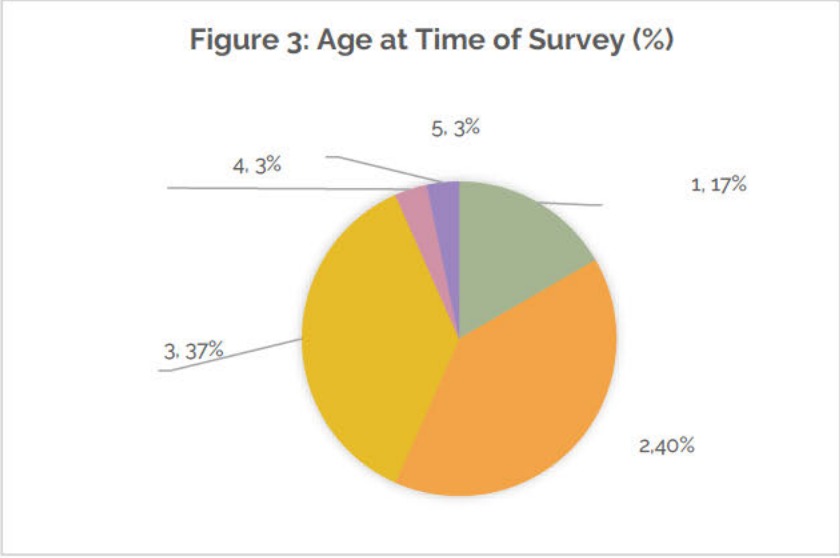


Figure 3 shows respondents' age at the time of the survey. The largest proportion of respondents were between 51-60 years old (40.00%), followed by those aged 61-70 (36.66%). Respondents aged 40-50 accounted for 16.66%, while 3.33% were older than 70. None of the respondents were younger than 40, and an additional 3.33% did not provide a response.

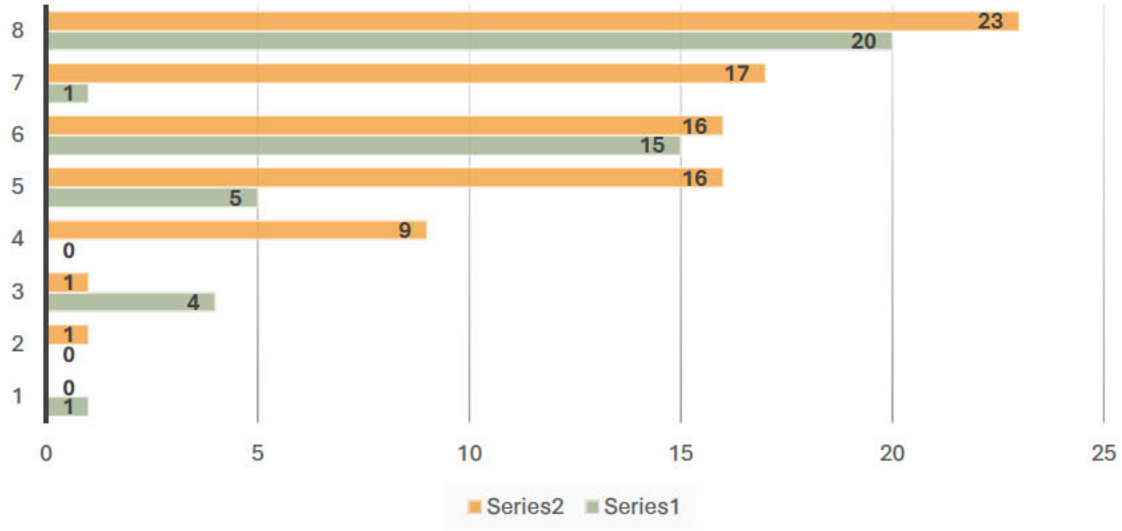


The Goals of Current Therapy

In our 2022 Survey, respondents were asked "Which of the following treatments are you CURRENTLY receiving to treat your breast cancer?" and "Which of the following treatments have you received in the PAST to treat your breast cancer?" Respondents chose all applicable selections between the following eight options: Surgery; Radiation; Chemotherapy; Hormone therapy (tamoxifen, aromatase inhibitor, etc.); Biologic or targeted therapy (trastuzumab, pertuzumab, palbociclib, ribociclib, abemaciclib, sacituzumab govitecan, etc.); Immunotherapy (pembrolizumab, atezolizumab); I have completed all treatments; and Other (please specify).

Figure 4 shows past and current treatments. Past treatments included hormone therapy (23), surgery (17), biologic/targeted therapy (16), chemotherapy (16), and radiation (9). Fewer respondents had received other treatments (1) and immunotherapy (1). Current treatments included hormone therapy (20), biologic/targeted therapy (15), and chemotherapy (5). A small number were receiving other treatments (4) and surgery (1). One respondent had completed all treatments at the time of the survey.

Figure 4: Current and past treatments used by respondants (HR-positive, HER2-negative mBC)



Key Factors for Decision-Making Around Treatment

In our 2022 Survey, we asked about the most important factors in treatment decision making, whether respondents were included in the decision-making process, comfort level in participating in treatment decisions, and topics of interest to respondents. Figure 5 – 8 present these responses, respectively.

Respondents answered the question "When making treatment decisions, what are the most important considerations (please list in order of importance, with 1 being the MOST important)." The five options were: Efficacy - how well a therapy works to treat my cancer; Quality of Life - how manageable the side effects are from my treatment, and what impact do they have on my quality of life; Work - whether I'm able to continue to work through treatment; Caregiving - whether I'm able to continue my caregiving roles through treatment; and Cost - that I don't have to pay out of pocket for the treatment.

Figure 5 shows that efficacy was the most important factor in treatment decision-making for 55.17% of respondents, with 37.93% considering it somewhat important. Quality of life was also highly important, with 35.71% ranking it as the most important and 42.86% as somewhat important. Work was ranked as medium importance by 41.38%, and care giving was ranked as less important to 40.63% of respondents. Cost was ranked as the least important factor by 34.48%, but still held importance for others, with 6.90% each considering it very important, or somewhat important.

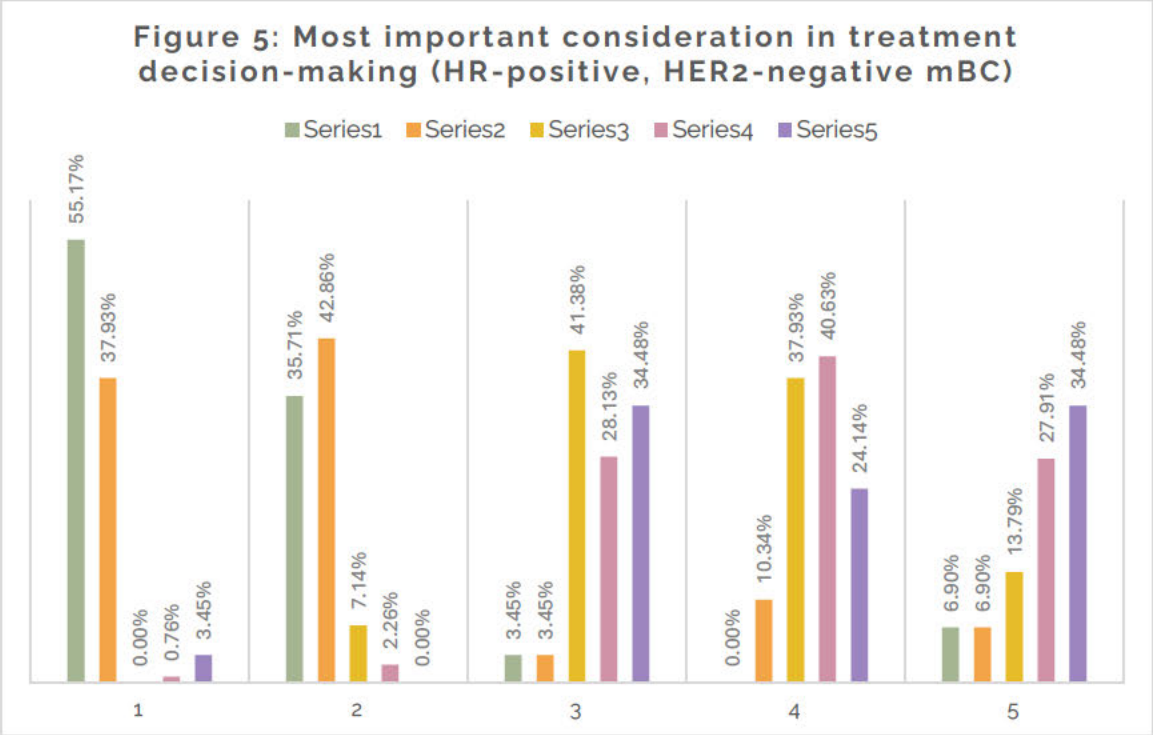


Figure 6 present responses to the questions; "Were you included in making decisions about your treatment?" Most respondents (75.86%) were included in treatment decisions, while 13.79% were not, and 10.34% did not recall.

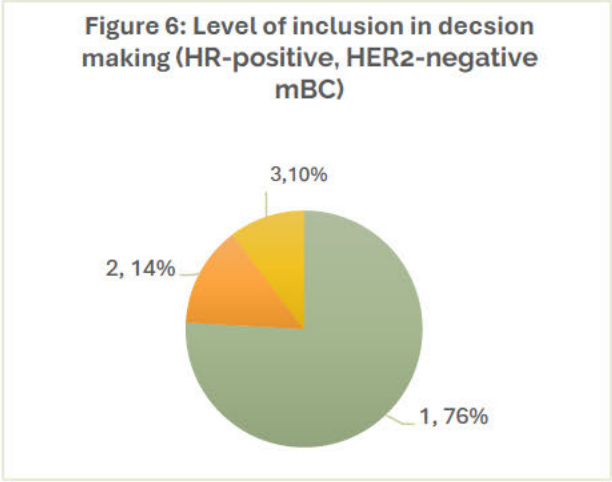
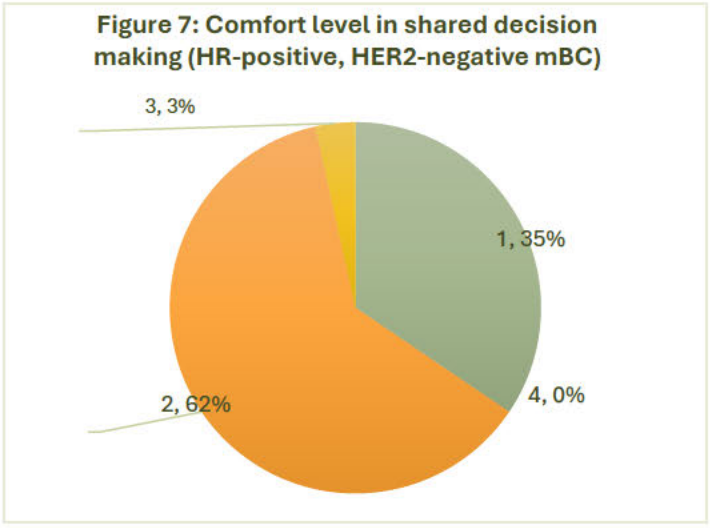


Figure 7 presents responses to the question "What was your comfort level in participating in making treatment decisions?" Most respondents felt very (34.48%) or somewhat (62.07%) comfortable, while 3.45% were not comfortable. No respondents were uninterested. Together, Figure 6 and Figure 7 show that most patients felt both included in the decision-making process, and comfortable making treatment decisions

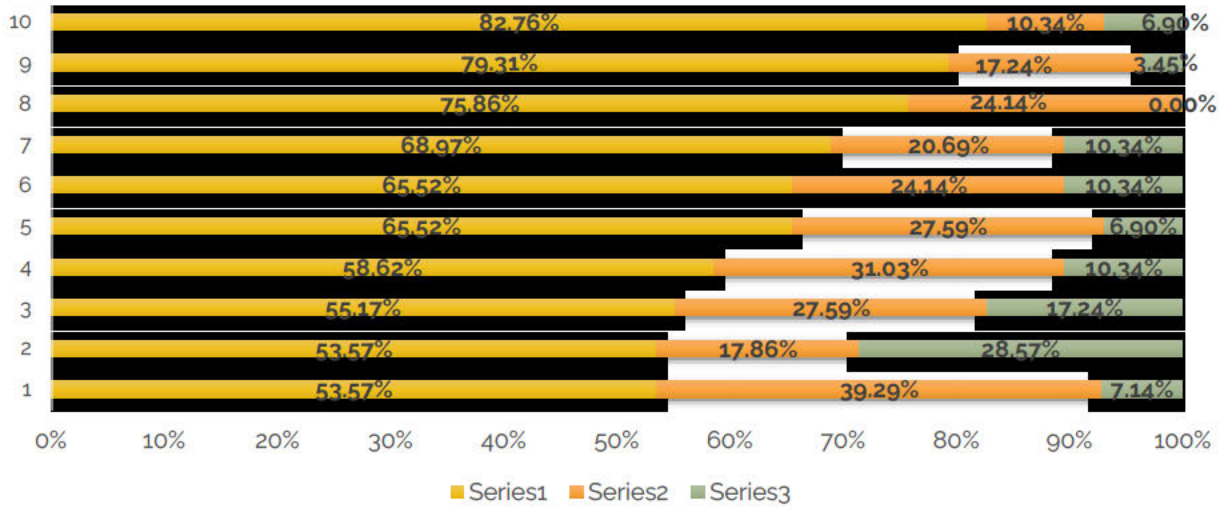


We asked respondents to indicate how interested they were in 31 different topics related to breast cancer at the time of taking the survey. Figure 8 shows the topics that at least 50% of HR-positive, HER2- negative metastatic respondents rated as "very interested." Respondents could

select “very interested”, “somewhat interested”, or “not interested” for each of these 31 topics. These results show the value patients place on each one of these topics, and by inference how each of these topics may relate to choice and decision making in treatment.

Figure 8 shows respondents prioritized topics related to treatment and research, with current breast cancer treatment options (82.76%), new treatments and the latest research (79.31%), and symptoms and side effect management (75.86%) ranking highest. Research and lifestyle factors were also key, including nutrition and exercise (68.97%), clinical trials/research studies (65.52%), and communicating with your doctor and healthcare team (65.52%). Additional areas of interest were managing the cognitive effects of treatment (58.62%), emotional and social support (55.17%), complementary and holistic health care (53.57%), and genetic and genomic testing (53.57%). These results demonstrate the value patients place on these topics and, by inference, their potential influence on treatment choices and decision-making.

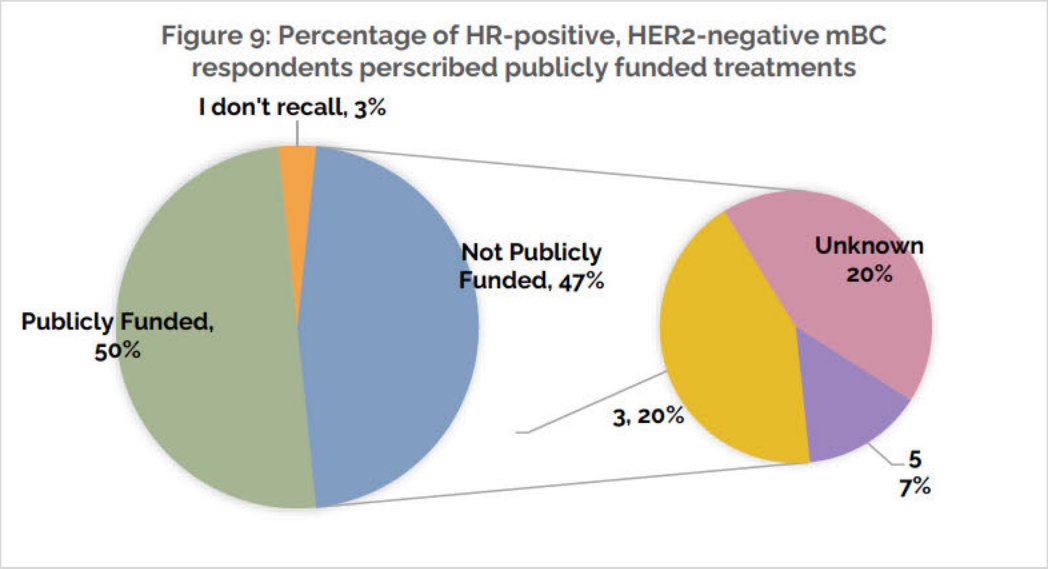
Figure 8: Topics of Interst to at least 50% of HR-positive, HER2-negative mBC respondants



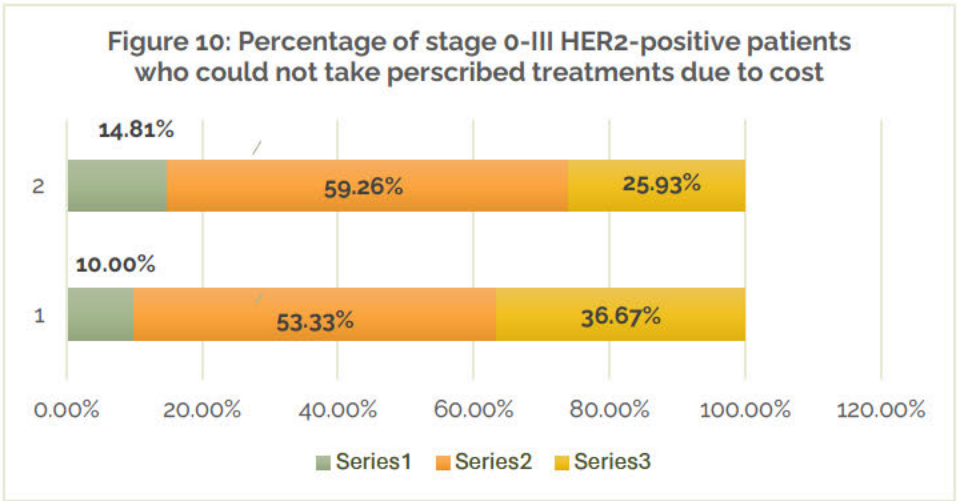
Cost and accessibility of treatments:

In our 2022 Survey, we asked about how prescribed treatments were funded, and whether the funding source affected their ability to take prescribed treatments. Respondents were asked “Were there medications prescribed to TREAT your cancer that were NOT covered by the public health care system,” and “Did the cost of the TREATMENT or SUPPORT (used to manage the side effects of treatment, not to treat the cancer) medications prevent you from taking them?”

Figure 9 shows that among stage 0-III, HER2-positive respondents, 50.00% were prescribed publicly funded treatments, while 46.66% were prescribed treatments that were not publicly funded. The non-publicly funded treatments included palbociclib (Ibrance) (either as a monotherapy, or in combination with fulvestrant, ribociclib, denosumab, or an unknown treatment) (20.00%), unknown treatments (20.00%), and other treatments (6.66%). An additional 3.33% of respondents did not recall whether their treatment was funded publicly or not.



Public funding can impact a person's ability to access treatment. Figure 10 shows that among stage 0-III, HER2-positive patients, 10.00% reported that cost prevented them from taking their prescribed treatment medication, 53.33% reported that cost did not prevent them from taking treatment medication, and 36.67% indicated that it was not applicable. For support medication, 14.81% reported that cost prevented them from taking their prescribed medication, 59.26% reported that cost did not prevent them from taking it, and 25.93% indicated that it was not applicable.



4. Experiences with Drug Under Review

CBCN was not able to speak with patients taking inavolisib (Itovebi) for the treatment of HR-positive, HER2-negative metastatic breast cancer. Instead, an interview with someone taking alpelisib (Piqray) is included above as part of the excerpt from our 2021 input (project number PC0247-000).

Improved progression free survival continues to represent an unmet need for people with HR-positive, HER2-negative metastatic breast cancer. Patients taking inavolisib had a median progression-free survival of 15.0 months, compared to 7.3 months for those in the placebo group. This indicates that inavolisib significantly delayed disease progression. Regarding side effects, severe (grade 3 or 4) neutropenia occurred in about 80% of patients in both groups. Severe hyperglycemia, stomatitis (mouth inflammation), and diarrhea were reported in 5.6%, 5.6%, and 3.7% of inavolisib patients, respectively, but none in the placebo group[4].

We also note the continued need for people with breast cancer to have choice in their treatments. As expressed by Patient 1 above, people with metastatic breast cancer highly value access to treatments which provide them with additional options, target their cancer specifically, and result in longer life. Patient 1 shared:

> *"[Access to Piqray] means that I have another option. It means that if my body doesn't respond to something else, Piqray is an option. Having something that targets a mutation, having something that targets something that is specific to my cancer makes it more likely that my cancer will respond. And that's the goal all the way around"*
>
> *"I think the biggest thing is having options that are specific to mutations equals longer lives for people with terminal cancer, and I think that that's really important."*

5. Companion Diagnostic Test

As stated above in the excerpt from CBCN's 2021 input on alpelisib (Piqray) (project number PC0247-000), PIK3CA mutation testing is not part of the standard of breast cancer care in Canada, therefore there is inequitable access to this testing across Canada. It is imperative that individuals diagnosed with HR-positive, HER2-negative metastatic breast cancer have access to PIK3CA mutation testing which can inform the most appropriate treatment for their care.

[4] https://www.nejm.org/doi/full/10.1056/NEJMoa2404625

6. Anything Else?

While there have been improvements to genomic testing infrastructure in Canada in recent years, access remains varied across the country[5]. This raises concerns about equitable access to testing, and by extension, to inavolisib. HR-positive breast cancer patients with a PIK3CA mutation consider access to testing and treatment of great importance. It is imperative that all HR-positive, HER2-negative metastatic/advanced breast cancer patients who could benefit from this therapy are being identified and offered genomic profiling to assess their eligibility for treatment. It is critical that access to adequate oncogenomic testing does not create a barrier for access to effective therapies for metastatic patients.

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 did connect with the manufacturer, Hoffmann-La Roche Limited, to learn about results from the 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.

[5] https://www.mdpi.com/1718-7729/30/6/408

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

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: February 27, 2025

CADTH

CADTH Reimbursement Review
Patient Input Template

Name of Drug: Itovebi (inavolisib)
Indication: Inavolisib in combination with a CDK4/6 inhibitor and fulvestrant for the treatment of endocrine resistant, PIK3CA-mutated, HR-positive, HER2-negative, locally advanced or metastatic breast cancer, following recurrence on or after completing adjuvant endocrine therapy.
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 hundreds of patients that have shared their stories on our blog; the 700 patients that participate in our virtual support groups each year; the 2,100 members of our private peer-support network; and the 44,000 people that have joined our Instagram community. We listen, learn, engage and have conversations in all these spaces.

Rethink also benefits from regular knowledge exchange with our Scientific Advisory Committee, which includes some of the leading clinical scientists in Canada who treat breast cancer.

For this submission, we have drawn on our observations and insights gathered through programming and meetings with breast cancer patients as described above. We have also drawn on the results from an online survey with 78 patients living with metastatic breast cancer (MBC) conducted by Rethink Breast Cancer to document the lived experience of patients and caregivers. Patients completed the survey between September 2018 and April 2019.

In addition, we drew on insights from interviews conducted in February 2025 with one person who is living with metastatic breast cancer and who has experience taking inavolisib to treat their disease.

3. Disease Experience

Most people in the Rethink community are diagnosed at a younger age. When young 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 take on a young person's life is devastating and traumatic.

Fear of recurrence is a reality for our community and for good reason. Despite improvements made with early detection and treatment for early-stage breast cancer, there's approximately a 20-30% chance that early breast cancer will metastasize. Moreover, 5-10% of newly diagnosed breast cancers are metastatic. There is currently no cure for metastatic breast cancer and patients' goal with treatment is to live as well as they can for as long as they can. Patients with metastatic HR+/HER2- cancers survive 4 to 5 years on average.

Processing this reality of a life-limiting diagnosis is extremely difficult, especially for the young patients in our community and the emotional impacts on quality of life cannot be understated. The physical and psychosocial challenges of metastatic breast cancer negatively impact both the patients and their loved ones who are often their caregivers. Most people with metastatic breast cancer have widespread disease, with metastasis to bone being the most common. Lung, liver, lymph nodes and skin are also commonly involved; while metastasis to the brain is less common for hormone positive MBC patients, it can happen too. Symptoms of hormone positive MBC depend on the sites of the metastasis and include fatigue, shortness of breath for lung metastasis, pain, and bone fractures for bone metastasis as well as nausea, headache and of course challenges doing normal daily activity. The challenges and uncertainty of living with MBC affects both the patients and their loved ones who support and help care for them.

4. Experiences With Currently Available Treatments

For people with HR+/HER2-negative MBC the current standard of care for first line therapy is a CDK4/6 inhibitor in combination with an aromatase inhibitor or fulvestrant. There are currently no treatments that are reimbursed for those who have this type of MBC along with a PIK3CA mutation who have recurred within 12 months of being treated for early-stage breast cancer.

This very niche and small patient population has two indicators that contribute to a poor prognosis, a PIK3CA mutation and endocrine resistance.

Chemotherapy is also another treatment used for this type and stage of breast cancer; however, chemotherapies are given sequentially usually with diminishing responses with each line of chemotherapy. Although initial lines of chemotherapy may provide a few months of progression free survival, this decreases substantially with later lines.

Metastatic breast cancer patients in our community go to great lengths to avoid standard chemotherapy and they are hit hard both emotionally and physically when it does come to that. In our community, we see a rapid decline once patients progress to having only standard chemotherapies as remaining options.

"While your tumour is responding to endocrine therapy, you tend to be able to remain longer on the treatment and stable. Then when it starts to progress, and you need to go into chemo because you don't have anything else, it's just faster, you know, and things go down so quickly."
– [redacted] MBC patient

Patients on standard chemo have a lot of difficulty managing their illnesses. Hospital appointments increase and they become mostly housebound managing side-effects of treatment.

"On weekly IV chemo, your normal life pretty much ends. It requires two visits per week for either blood work or for the chemo. The rest of the week is managing side effects of nausea, fatigue, pain, worsening neuropathy. And that's with me being in the cohort of people who 'tolerates well.'"
– [redacted] MBC patient

"My year on chemotherapy was a full-time job dealing with suppressed neutrophil counts that caused countless treatment delays and quality of life compromising side effects. When I was offered the chance to rely entirely on a newer therapy, the results were game changing and allowed me to get back to my active and scheduled lifestyle as it once had been. Knowing that a cutting-edge treatment option like Trodelvy may be available to me when/if I need it outside of standard of care shelf-life chemotherapies, in the precious time to come, is what helps me stay present and positive as I navigate life with this incurable diagnosis. Everyone deserves a shot at what works best for them and the more therapies available to us are key. Stage 4 needs so much more."
– [redacted], MBC patient, diagnosed de novo

"My biggest concern with fear of progression, is that my subtype changes from triple positive to any other subtype. So of course, the more treatments that are available that are effective and not chemo are important to me. I already did loads of chemo because my targeted therapy had to go on pause because of the damage to my heart. It was not fun knowing that I could be left on chemo if the cardiotoxicity didn't improve."
– [redacted], MBC patient, diagnosed de novo while pregnant

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. It's important that patients have a clear understanding of trade-offs and are well prepared for common side-effects of a given treatment.

When it comes to therapy for metastatic breast cancer, the primary improvement patients seek is to extend their life beyond what is expected with currently publicly available treatments. Patients also value progression free survival as disease progression often comes with symptoms that impact their quality of life.

As [redacted], a hormone positive, MBC patient from our community explains, when the stakes are so high, even a few extra months of survival matter. She explains:

"…those months could be the difference that lets me see my son start kindergarten; they could be the ones that give me time to get him off diapers before it all falls on dad; Or they could be the first time he says I Love You. While a few months are short on time they are bursting with possibility. Life happens in moments after all. Every scan matters.
Only, it's not simply a matter of days, it's also a matter of quality days. It's hard to make memories suffering the side effects of chemo on the couch. It's impossible to keep up with a toddler while managing the debilitating fatigue. An additional line of treatment that allows me quality time with my family is welcomed with open grateful arms…It's not easy for anyone to estimate the value of an extra day of life, but in my case, it could also mean my two-year old has one more day with mom. I'll give him every day I can."

In Rethink's 2018-2019 MBC survey, patients rated controlling disease and extending life expectancy as the most important outcomes for treatment. This suggests that patients value long-term health outcomes over immediate concerns like reducing symptoms or managing side effects. See the full survey results, along with methodology in Appendix A. Comments from the MBC patients surveyed included:

- "Symptom management and shrinking the cancer is the most important thing. Living well is the next most important thing."
- "Keeping me alive for my kids"
- "I want to live, LIVE, and enjoy my life for many more years and not be so afraid.

6. Experience With Drug Under Review

Rethink interviewed one patient who had experience with Inavolisib.

Patient 1: [redacted]

I was first diagnosed with HR-positive early-stage breast cancer in 2004. I was later diagnosed with metastatic breast cancer in 2010. My metastatic breast cancer was HR-positive, HER2-negative, we have since learned that it's actually HER2-low, but at the time of my diagnosis we were not aware of HER2-low. At the time of this interview, I have been living with metastatic breast cancer for 15 years and am currently on my 15th line of treatment. I have lived in Toronto, Calgary and Ottawa during this time and have travelled to different cities in Canada and the US to access various clinical trials.

While being treated for metastatic breast cancer I continued to work up until 2020, which was through 10 lines of treatment.

I accessed Inavolisib through a phase 1 clinical trial in Toronto in 2018, which I travelled to from Calgary in order access. This treatment worked for me for 18 months, and I was well enough to work during this time, and also fly back and forth to Toronto every 6 weeks for the required testing. I experienced hypoglycemia as a result of this treatment, which was managed through metformin and also through adapting a ketogenic diet for 6 months. My energy level was good while I was on this treatment, I was able to continue to participate in this trial. Given that this was my 7th line of treatment, this addressed an unmet need for me in terms of treatment options.

7. Companion Diagnostic Test

PIK3CA testing is required to access this therapy, this testing is currently accessible across Canada, but timely access and coverage varies from province to province and can also differentiate between institutions. Timely and equitable testing would need to be addressed to ensure that eligible patients are identified in a timely manner to allow for informed decision making.

8. Anything Else?

As our health system strives to provide personalized care to cancer patients, it's important that therapies with proven efficacy in specific patient populations are available to those patients who could benefit. Inavolisib is for a very niche patient population, but it's an important treatment option for this high-risk population who can benefit from this additional therapy being added to their treatment regime.

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
Lilly 2024			x	
Lilly 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: February 28, 2025

APPENDIX A: MBC Patient Survey Results

Information for this report was gathered through an online survey published in English and circulated through communications from Rethink Breast Cancer as well as the Rethink Network and other partner organizations. Messages were also posted on Facebook and Twitter as well as the Breastcancer.org, Cancer Connection and Cancer Survivors Network online discussion forums. 78 metastatic breast patients completed the survey between September 2018 and April 2019.

Rethink Breast Cancer asked respondents to evaluate the importance of different outcomes for their breast cancer treatment on a scale of 1 (not important) to 5 (very important). All the listed outcomes were considered important with no average scores lower than 4.4. However, controlling disease and extending life expectancy were rated as the most important results suggesting that patient values prioritize long-term health outcomes over immediate concerns like reducing symptoms or managing side effects.

Importance of outcome	1 - not important	2	3	4	5 — very important	Average
Controlling disease progression	0.00% 0	0.00% 0	0.00% 0	2.60% 2	97.40% 75	4.97 77
Reducing symptoms	1.30% 1	0.00% 0	12.99% 10	19.48% 15	66.23% 51	4.49 77
Maintaining quality of life	0.00% 0	0.00% 0	1.30% 1	12.99% 10	85.71% 66	4.84 77
Managing side effects	1.30% 1	1.30% 1	12.99% 10	19.48% 15	64.94% 50	4.45 77
Achieving NED (no evidence of disease)	1.32% 1	1.32% 1	1.32% 1	6.58% 5	89.47% 68	4.82 76
Extending life expectancy	0.00% 0	0.00% 0	0.00% 0	2.63% 2	97.37% 74	4.97 76

Comments included:

- Symptoms and shrinking the cancer is the most important thing. Living well is the next most important thing.
- Keep me alive for my kids.
- I want to live, LIVE and enjoy my life for many more years and not be so afraid.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0382-000
Generic Drug Name (Brand Name): Inavolisib (Itovebi)
Indication:
Manufacturer Requested Reimbursement Criteria[1]:
Inavolisib in combination with a CDK4/6 inhibitor and fulvestrant for the treatment of adult patients with PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, following recurrence on or after completing adjuvant endocrine treatment.

Indications:
Inavolisib in combination with palbociclib and fulvestrant is indicated for the treatment of adult patients with PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, following recurrence on or within 12 months of completing adjuvant endocrine treatment.

Name of Clinician Group: Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee ("OH (CCO) Breast DAC")

Author of Submission: Dr. Andrea Eisen and members of the OH (CCO) Breast DAC

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 via teleconference meetings and emails.

3. Current Treatments and Treatment Goals

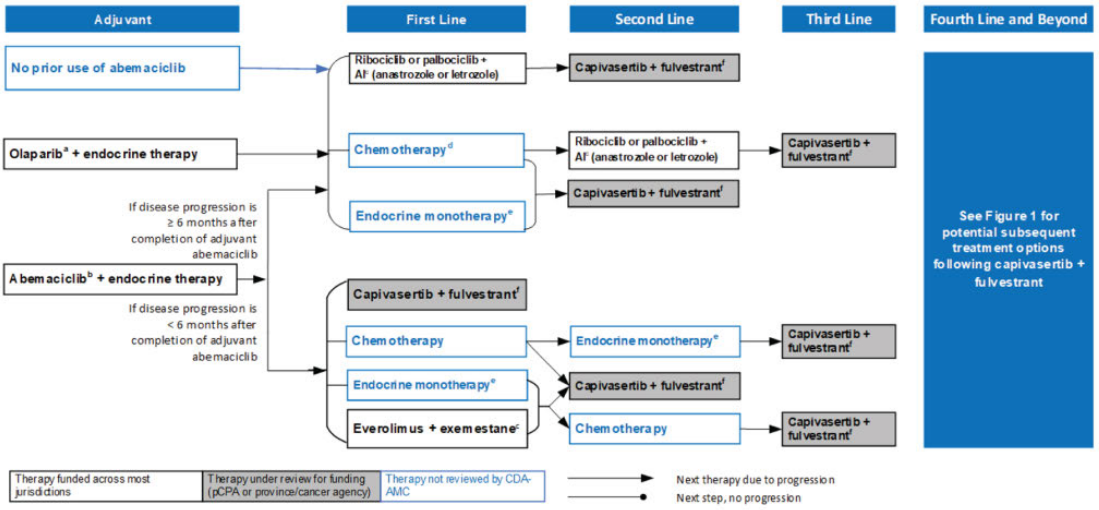
- Currently, access is available to PIK3CA drugs in 2L setting (capiversatib + fulvestrant) after CDK4/6 inhibitor + AI. This request is for combination instead of sequential use.

- INAVO120 was done in patients with early relapse and the reimbursement criteria requested removed the following wording “within 12 months of completing adjuvant endocrine treatment” and making this request more generalized. OH (CCO) Breast DAC does not support the removal of this eligibility criteria. The relevant patient group would be patients relapsing early on endocrine monotherapy (1.9% patients had prior CDK4/6i). Based on trial data, it would be difficult to extrapolate on how useful this combination is in patients treated with prior CDK4/6i.

- There is significant toxicity – 24% of patients had SAEs and 3.7% of patients had fatal AEs.

PH0053-HRPositive-HER2-Breast-Cancer_Provisional Funding Algorithm

Figure 2: Provisional Funding Algorithm Diagram for Additional Treatment Options for HR-Positive, HER2-Negative Breast Cancer, With Inclusion of HER2-Low, With *PIK3CA, AKT1,* or *PTEN* Alterations



AI = aromatase inhibitor; CDA-AMC = Canada’s Drug Agency; HER2 = human epidermal growth factor 2; HR = hormone receptor; pCPA = pan-Canadian Pharmaceutical Alliance.

[a]Olaparib adjuvant therapy is for patients with a deleterious or suspected deleterious germline *BRCA* mutation whose disease has been treated with neoadjuvant or adjuvant chemotherapy. Patients must have confirmation of germline *BRCA* mutation before olaparib treatment is initiated.

[b]Abemaciclib should be reimbursed for a maximum of 2 years (150 mg orally twice daily).

[c]In some jurisdictions, aromatase inhibitors may also include exemestane. Funding for everolimus plus exemestane may vary by province or cancer agency.

[d]Chemotherapy might be the first choice if visceral crisis is suspected; after adequate response, consider other choices.

[e]Patients with HR-positive breast cancer should have received at least 1 endocrine therapy and no longer be considered for endocrine therapy.

[f]Capivasertib plus fulvestrant is indicated for patients with 1 or more *PIK3CA*, *AKT1*, or *PTEN* alterations. Patients must have received at least 1 line of hormone therapy in the metastatic setting or have disease that progressed on adjuvant hormone therapy or within 12 months of adjuvant hormone therapy. Capivasertib plus fulvestrant should not be initiated in patients who have disease that progressed on prior therapy with fulvestrant, received more than 2 lines of hormone therapy, or received more than 1 line of chemotherapy in the metastatic setting.

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.

Advanced breast cancer is not curable and additional better treatments are needed. This study was enriched for patients with poor prognosis as they selected with early relapsed on endocrine therapy (i.e., endocrine resistant patients). Currently patients with PIK3CA mutation do have access to targeted therapy in 2L setting.

This study enrolled <2% patients who received adjuvant CDK4/6 inhibitors. Generalizability to this subset is uncertain.

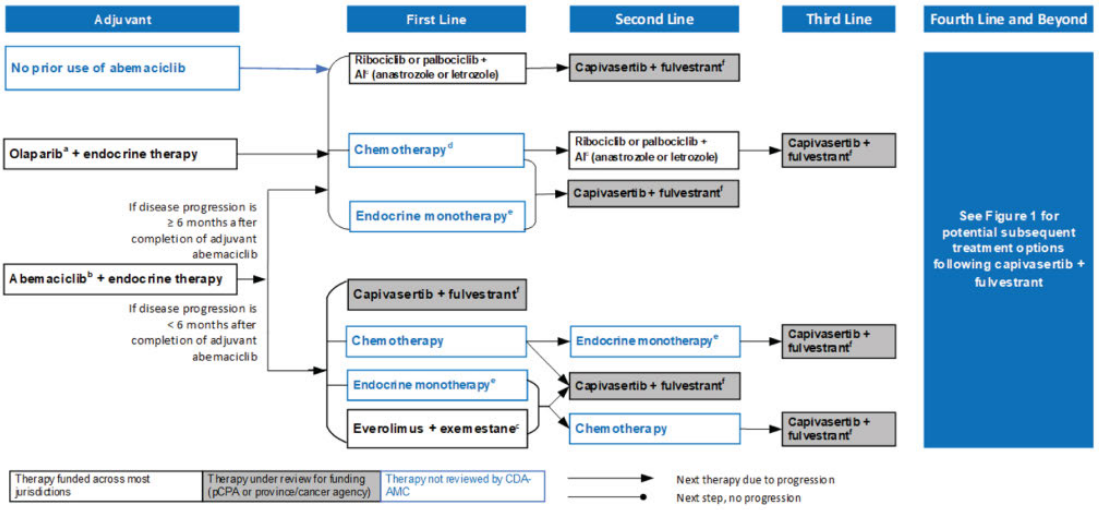
5. Place in Therapy

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

- Place in therapy – First line setting
- The requested combination would displace 2L capivasertib in patients who did not receive adjuvant CDK4/6 inhibitor
- The requested combination would possibly be an alternative to 1L capivasertib in patients who received adjuvant CDK4/6 inhibitor
    - The study was done with palbociclib; the request is generalized to any CDK4/6 inhibitors
    - Early relapse criterion should be maintained
    - Patients who relapsed early while on CDK4/6 inhibitor should not receive this combination – very few patients had adjuvant CDK4/6 inhibitor on the study
    - Significant toxicity with this combination

PH0053-HRPositive-HER2-Breast-Cancer_Provisional Funding Algorithm

Figure 2: Provisional Funding Algorithm Diagram for Additional Treatment Options for HR-Positive, HER2-Negative Breast Cancer, With Inclusion of HER2-Low, With *PIK3CA, AKT1,* or *PTEN* Alterations



AI = aromatase inhibitor; CDA-AMC = Canada's Drug Agency; HER2 = human epidermal growth factor 2; HR = hormone receptor; pCPA = pan-Canadian Pharmaceutical Alliance.

[a]Olaparib adjuvant therapy is for patients with a deleterious or suspected deleterious germline *BRCA* mutation whose disease has been treated with neoadjuvant or adjuvant chemotherapy. Patients must have confirmation of germline *BRCA* mutation before olaparib treatment is initiated.

[b]Abemaciclib should be reimbursed for a maximum of 2 years (150 mg orally twice daily).

[c]In some jurisdictions, aromatase inhibitors may also include exemestane. Funding for everolimus plus exemestane may vary by province or cancer agency.

[d]Chemotherapy might be the first choice if visceral crisis is suspected; after adequate response, consider other choices.

[e]Patients with HR-positive breast cancer should have received at least 1 endocrine therapy and no longer be considered for endocrine therapy.

[f]Capivasertib plus fulvestrant is indicated for patients with 1 or more *PIK3CA*, *AKT1*, or *PTEN* alterations. Patients must have received at least 1 line of hormone therapy in the metastatic setting or have disease that progressed on adjuvant hormone therapy or within 12 months of adjuvant hormone therapy. Capivasertib plus fulvestrant should not be initiated in patients who have disease that progressed on prior therapy with fulvestrant, received more than 2 lines of hormone therapy, or received more than 1 line of chemotherapy in the metastatic setting.

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?

Most suitable – patients with early relapse on endocrine therapy (i.e., endocrine resistant patients) if they meet the inclusion/exclusion criteria for the study. The Breast DAC does not support removing the early relapse criterion.

The DAC is concerned about the toxicity of this regimen, and notes that there were deaths due to toxicity, which is very unusual for a first line endocrine based therapy.

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?

As per standard clinical practice for treatment response and toxicity.

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

These patients will require frequent visits for disease and toxicity monitoring.

Discontinuation based on disease progression or toxicity.

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]?

Outpatient treatment. These patients will require frequent visits for disease and toxicity monitoring.

6. Additional Information

This study uses palbociclib in combination with inavolisib. In clinical practice, ribociclib is used more commonly in Ontario.

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) PDRP provided 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 <u>each clinician</u> 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 DAC
Date: 28-02-2025

☒ **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**
Add company name				
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 2

Name: Dr. Olexiy Aseyev
Position: Member, OH (CCO) Breast DAC
Date: 28-02-2025

☒ 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**
Add company name				
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 3

Name: Dr. Orit Freedman
Position: Member, OH (CCO) Breast DAC
Date: 28-02-2025

☒ 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

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 4

Name: Dr. Haider Samawi
Position: Member, OH (CCO) Breast DAC
Date: 28-02-2025

☒ 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

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			
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 5

Name: Dr. Ronita Lee
Position: Member, OH (CCO) Breast DAC
Date: 28-02-2025

☒ 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

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

Add company name				
Add or remove rows as required				

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

HTA Reimbursement Review
Clinician Group Input Template

Clinician Group Input

CDA Project Number: PC0382-000
Generic Drug Name (Brand Name): Inavolisib (Itovebi)
Indication: Inavolisib in combination with palbociclib and fulvestrant is indicated for the treatment of adult patients with endocrine-resistant, *PIK3CA*-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, following recurrence on or after completing adjuvant endocrine treatment.
Name of Clinician Group: REAL Alliance
Author of Submission: Dr. Sandeep Sehdev

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 and academic oncologists across Canada and Breast Cancer Canada, a patient organization. Formed in December 2023 in recognition of the need for a national voice to support evidence-based and equitable breast cancer management. REAL Alliance publishes national clinical consensus recommendations, routinely updated, to guide timely health policy and funding decisions, and to support knowledge translation and clinical adoption to ensure optimal outcomes for breast cancer patients across all provinces and territories in Canada.

2. Information Gathering

Our members engaged in virtual discussions and exchanged perspectives via email to formulate clinical recommendations for the use of inavolisib in patients with endocrine-resistant, HR+/HER2- metastatic breast cancer (MBC) with *PIK3CA* mutations. These recommendations represent a synthesis of our clinical expertise, informed by an extensive review of the literature, pivotal data from clinical trials, and the latest insights from global oncology congresses.

Our collective input is designed to provide a nuanced and evidence-based assessment, in order to guide the CDA in considering the therapeutic value of inavolisib within the broader context of need, benefit and patient values. This recommendation reflects not only scientific rigor but also our deep commitment to enhancing patient outcomes. With decades of combined experience in managing breast cancer, our group brings a comprehensive and compassionate perspective to the evaluation of new treatments like inavolisib.

3. Current Treatments and Treatment Goals

HR+/HER2- advanced or metastatic breast cancer with PIK3CA mutation

Breast cancer continues to be one of the most commonly diagnosed cancers among women in Canada, with approximately 70% of cases classified as HR+/HER2- [1,2]. Up to 40% of these breast cancers exhibit activating mutations in the *PIK3CA* gene, resulting in

hyperactivation of the PI3K pathway [3–5]. Tumours with *PIK3CA* mutations are associated with a poorer prognosis in the metastatic setting [6–8]. These mutations are also associated with endocrine therapy resistance [9,10].

Thus, *PIK3CA* mutation is now being recognized as an important actionable target with unique prognostic and therapeutic implications.

While targeted treatments like alpelisib and capivasertib are designed to target the PI3K pathway, current data primarily support their use in combination with endocrine therapy (ET) in the second-line setting following disease progression on CDK4/6 inhibitors used as first-line therapy [8,11].

The primary goals of systemic treatment for metastatic breast cancer, for both patients and clinicians, are to extend progression-free survival (PFS) and overall survival (OS) while minimizing treatment-related adverse events (AEs). Additionally, the convenience of oral, at-home therapy and the ability to delay chemotherapy are important outcomes of upfront treatment. These factors help ensure that patients can maintain their quality of life without compromising efficacy.

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 HR+/HER2-/PIK3CA-mutant variant have poor outcomes with current standard care

Despite the efficacy of current systemic therapies, managing *PIK3CA*-mutant breast cancer remains a significant challenge. In HR+/HER2- metastatic breast cancer, the presence of the *PIK3CA* mutation is associated with worse clinical outcomes, even when treated with the current standard therapy of CDK4/6 inhibitors and endocrine therapy (ET) [12]. Resistance mechanisms within the PI3K pathway are multifaceted, involving incomplete pathway inhibition, reactivation of signaling downstream of *PIK3CA* mutations, and the activation of alternative survival pathways [13]. The PI3K signaling network is highly complex, with numerous feedback loops and crosstalk with other pathways, which can drive resistance to PI3K inhibitors [13]. Although combining PI3K inhibitors with fulvestrant has shown some benefit, resistance to PI3K inhibitors in this context persists.

Recent research identifies CDK4/6 inhibitors as potent sensitizers of resistant cell lines, potentially overcoming resistance and enhancing therapeutic efficacy when combined with PI3K inhibitors [14,15]. This has led to increasing support for incorporating PI3K inhibitors, such as inavolisib, into first-line treatment alongside CDK4/6 inhibitors and ET to improve PFS in patients with HR+/HER2-, *PIK3CA*-mutant breast cancer [15]. The FDA has acknowledged the benefits of this combination, leading to the ORBIS approval of inavolisib with palbociclib and ET for use in this patient population.[16]. This approval represents a significant advancement in personalized treatment strategies, aiming to improve outcomes for patients with the dual challenges of rapid recurrence of HR+ disease and *PIK3CA* variants. Clinically, we agree that inavolisib holds significant promise for this patient population, offering a targeted treatment option for a challenging breast cancer sub-type.

5. Place in Therapy

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

The INAVO120 trial is the first phase 3 randomized study to explore the combination of inavolisib, a targeted agent for *PIK3CA*-mutated cancers, with palbociclib, a CDK4/6 inhibitor, and ET, in the first line setting in patients with HR+/HER2- metastatic breast cancer. The trial eligibility included those with a): primary endocrine resistance, defined as relapse while on the first 2 years of adjuvant ET; b) secondary endocrine resistance, defined as relapse while on adjuvant ET after at least 2 years OR relapse within 12 months of completing adjuvant ET with either an aromatase inhibitor or tamoxifen. In all cases, the treatment setting was first-line treatment for advanced disease [15].

The INAVO120 trial was founded on robust preclinical data demonstrating the potential efficacy of this combination. The results from INAVO120 revealed significant benefit in a high-risk population with historically poor outcomes and limited treatment options. As a result, this regimen would replace the current standard regimen of fulvestrant with CDK4/6 inhibition alone in this patient group. In the trial, patients treated with inavolisib, palbociclib, and fulvestrant experienced a significant improvement in PFS compared to those receiving CDK4/6 inhibitors and ET alone. At 21 months, the median PFS was 15.0 months for the combination group versus 7.3 months for the control group (HR=0.43; 95% CI: 0.32-0.59; P<0.001), a 7.7-month gain. For patients with aggressive disease driven by a *PIK3CA* mutation, this improvement is clinically meaningful. Additional key endpoints included PFS2 (time from randomization to the end or discontinuation of the next-line treatment or death from any cause) and time from randomization to first subsequent chemotherapy. The median PFS2 was 24 months for the combination group compared to 15 months for the control group (HR=0.54; 95% CI: 0.38-0.77), while time to first subsequent chemotherapy was not yet evaluable for the combination group and 15 months for the control group (HR=0.54; 95% CI: 0.37-0.78) [15]. The PFS2 results highlight that after standard front-line therapy (CDK4/6 inhibitor + ET), subsequent lines of treatment were not able to "make up" the difference in progression-free survival afforded by the triplet regimen.

Demonstrating OS benefits in metastatic HR+ breast cancer remains challenging, making PFS a globally recognized endpoint for regulatory and funding decisions, particularly when the magnitude of benefit is this pronounced. It is notable that inavolisib manufacturer recently announced a statistically significant OS improvement for the triplet therapy in a press release [17]. We look forward to seeing the full OS data presented at an upcoming academic congress to better assess its clinical impact.

The incidence of AEs, including grade 3 or 4 neutropenia and hyperglycemia, occurred early at initiation of treatment and was manageable, with discontinuation occurring in only 6.8% of patients in the inavolisib group. Importantly, inavolisib did not lead to the high incidence of diarrhea often associated with other PI3K inhibitors, and any rash was easily managed, suggesting a manageable safety profile relative to existing treatments [15]. Use of standard oral antihyperglycemic agents, such as metformin, are effective in managing most patients who develop low grade hyperglycemia. Moreover, positive quality of life data from the INAVO120 trial demonstrated that the overall treatment "bother" from AEs was moderate or less for both arms indicating that inavolisib does not contribute additional treatment burden for patients on this triplet therapy.

Although the combination of inavolisib with more potent CDK4/6 inhibitors, like ribociclib and abemaciclib, might conceptually offer better efficacy, trials are still ongoing. Adding inavolisib to the CDK4/6 inhibitor palbociclib and ET fits well into current practice in the first-line setting and palbociclib would be less likely to cause overlapping hepatic or gastrointestinal toxicity. The INAVO120 protocol has a predictable and manageable safety profile, requiring management of what is typical for PI3K inhibitors, CDK4/6 inhibitors, and ET.

Based on the positive outcomes of the INAVO120 trial, we recommend that inavolisib, in combination with palbociclib and ET, be made available as a first line treatment option for patients with HR+/HER2- advanced or metastatic breast cancer with *PIK3CA* mutations meeting the eligibility criteria for the trial. This recommendation aligns with ORBIS approval and underscores the potential of inavolisib to improve outcomes in this challenging patient population, beyond CDK4/6i + ET therapy.

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 the combination of inavolisib, palbociclib, and ET as a first-line treatment for all patients with HR+/HER2- locally advanced or metastatic breast cancer harboring a *PIK3CA* mutation following recurrence in any of the following clinical scenarios:

- a) recurrence in the setting of primary endocrine resistance, defined as relapse while on the first 2 years of adjuvant ET;
- b) recurrence in the setting of secondary endocrine resistance, defined as relapse while on adjuvant ET after at least 2 years OR relapse within 12 months of completing adjuvant ET with either an aromatase inhibitor or tamoxifen;
- c) recurrence within 12 to 18 months of completing adjuvant ET to allow for flexibility given the delays that occur in everyday practice due to access to diagnostics, staging, and specialists.

Patients without *PIK3CA* pathway abnormalities, those with contraindications to inavolisib (such as severe, poorly controlled diabetes mellitus) or any of the drugs in the combination, or individuals unable to undergo appropriate monitoring may be less suitable candidates. Close clinical follow-up is essential, particularly during the initial months of treatment, with regular blood work, adherence assessments, and proactive toxicity management. AEs can be effectively managed with early intervention, including dose adjustments and standard supportive care.

Although hyperglycemia is a common AE of PI3K inhibitors, this was expected and managed with oral antihyperglycemics in the INAVO120 trial **[15]**. In practice, careful selection of patients with normal or near-normal hemoglobin A1c levels should be and can be easily adopted as standard practice for patients prescribed PI3K inhibitor therapy. **Patients with pre-existing uncontrolled type II diabetes or those at risk of glucose intolerance** should be evaluated for inavolisib therapy on an individual basis and have their blood sugar levels closely monitored during inavolisib treatment. **Patients with well-controlled type 2 diabetes** may be suitable however require more frequent monitoring and treatment adjustments. Current health systems can integrate this follow-up monitoring by using models that involve pharmacists, nurses, and self-monitoring glucose devices, as needed, without adding extra burden to clinical workflows. **Patients with type 1 diabetes** would not be suitable for inavolisib therapy.

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?

Response assessments would be conducted using clinical assessments (history, physical examination), periodic restaging scans and blood tests at standard frequencies, but more often when needed in the setting of worsening symptoms. Usually, scans are done about every three months and the INAVO120 regimen would not increase the burden of required diagnostic imaging.

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

The combination of inavolisib, palbociclib, and ET should be discontinued upon confirmed disease progression per RECIST criteria or if persistent, refractory toxicity occurs despite dose modifications, as outlined in the product monograph. Treatment should also be stopped in cases of any grade 4 toxicity or if the patient experiences intolerance, with the decision made through shared decision-making.

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?

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

6. Additional Information

To note, the INAVO120 study included a small sample size of male HR+/HER2-/*PIK3CA*-mutated patients with breast cancer recurrence. Both male and female patients should be eligible for the triplet therapy in standard frontline practice [15]. There is no scientific justification to exclude male patients based on available evidence.

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DECLARATIONS:
NOTE – All the Clinicians (REAL NUCLEUS and additional opt-in, should be listed and COI's included in the submission)

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			

Declaration for Dr. Nathaniel Bouganim

Name: Nathaniel Bouganim

Position:

Date: 2024 02 20

☒ **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 Nathaniel Bouganim

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		
Knight	X			
Gilead	X			
McGill University	X			
Pfizer	X			

Declaration for Dr. Jeffrey Cao

Name: Jeffrey Cao

Position: Provincial Breast Tumour Team Lead, Alberta Health Services Cancer Care Alberta

Date: February 26, 2025

☒ **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 Jeffrey Cao

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Oncology Education	X			
Novartis		X		
Gilead	X			
Union Oncology Centre	X			
Pfizer		X		
La Roche-Posay			X	
AstraZeneca	X			
Daiichi-Sankyo	X			
Merck		X		
Breast Cancer Canada	X			
Canadian Breast Cancer Conference	X			
Canadian Breast Cancer Symposium	X			

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 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 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 Dr. Kara Laing

Name: Kara Laing

Position: Medical Oncologist

Date: 27-Feb-2025

☒ **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 Kara Laing

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		
Taro	X			
Pfizer	X			
Eli Lilly	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 Dr. Callista Phillips

Name: Dr. Callista Phillips

Position: **Medical Oncologist JBH cancer clinic Burlington and JCC Hamilton**

Date: **Feb 25/25**

☒ 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 Callista Phillips

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	Yes	No	No	No
Astra Zeneca	Yes	No	No	No
Lilly	Yes	No	No	No
Merck	Yes	No	No	No
Bayer	Yes	No	No	No
EMD Seronoi	Yes	No	No	No
Gilead Science	Yes	No	No	No

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 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

	Check appropriate dollar range*			
Company	**$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			