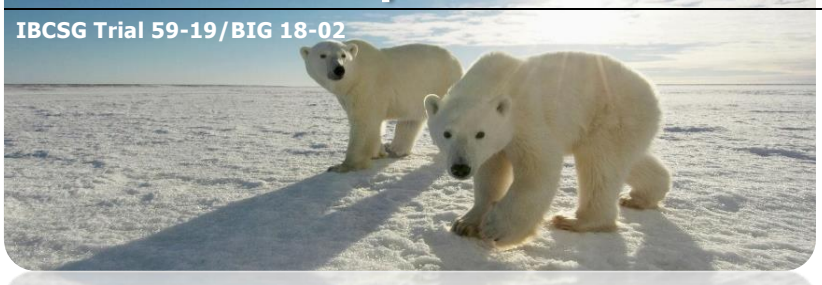
POLAR Express



IBCSG Trial 59-19/BIG 18-02

March 2022 Volume 3, Issue 1

Welcome!

Welcome to the next edition of the POLAR Express! Thank you for your continued work on this important trial. In this issue, we will provide you with an update on the current status of the POLAR Trial, discuss the importance of data submission, and answer some of the most frequently asked questions.

Of Special Interest

Current Accrual: 162

Accrual Goal: 400

No. of Centers Activated: 50

28-March-2022

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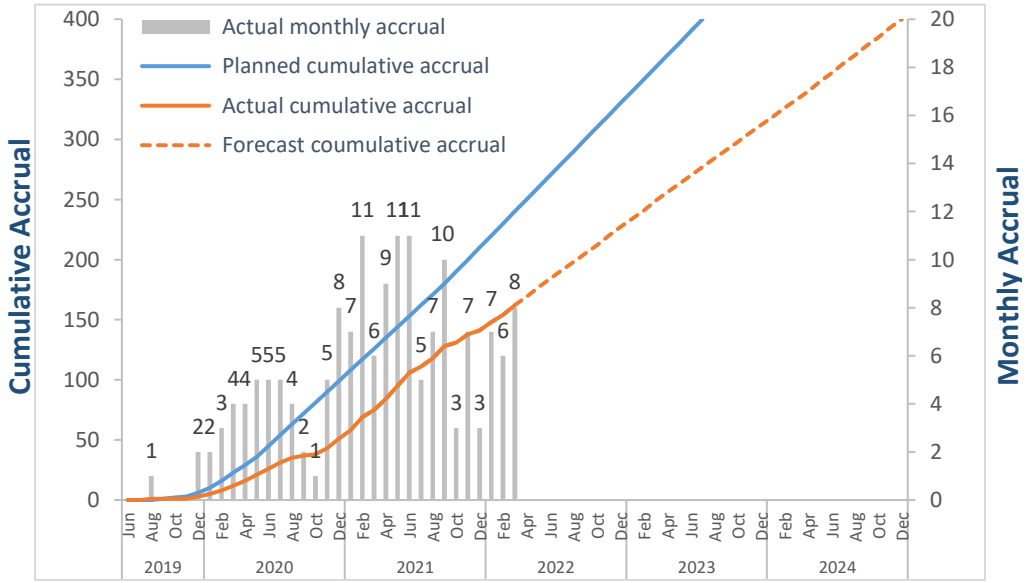
Accrual and Activation Update

We are pleased to announce the POLAR Trial is now nearing the completion of activation and it is currently activated in 50 of the 51 planned Centers. 38 Centers have enrolled one or more patients. Thank you for your hard work in reaching this point!

As of February 2022, POLAR reached another milestone, enrolling the 150th patient. This milestone is a great achievement and reflects the excellent effort of the Centers. As of 28 March 2022, the current accrual is 162 patients. With the help and commitment of the Centers, we are optimistic that we will soon reach the 50% accrual milestone of 200 patients. Thank you for your work and dedication to the POLAR Trial!

Target Sample Size: 400

Planned vs Actual Accrual (as of 28 March 2022)



Importance of Baseline Forms to Complete Patient Inclusion Criteria Review

An important step to accomplish a successful trial analysis is to have all patients' inclusion criteria reviewed in an accurate and timely manner. Patient inclusion criteria compliance is defined by our Medical Review Team after reviewing the baseline forms, which include the Confirmation of Randomization (A Form), History (H Form) and Pathology Reports/ Hormone Receptor and HER2 results. These forms contain key data required to assess patient inclusion in the trial.

Pathology and tumor information have special importance for patient inclusion criteria review purposes. Without them, patient inclusion/exclusion review cannot be accomplished. Our Medical Review Team closely compares the information reported in the baseline forms with the Pathology and Hormone Receptor Reports to ensure that all the aspects of patient inclusion criteria are accurate and correctly documented. This is a task that requires a significant amount of time and we need to have all the baseline forms and reports available in a timely manner.

If baseline key data or procedures are missed, oftentimes it means that the trial inclusion criteria is not met for the patient. For the POLAR Trial, examples of this include: pregnancy test not done, ECOG assessment not performed, and appropriate radiotherapy (if applicable) completion timelines not met.

Another significant piece of data that need special attention when completing, is the data entered in the IBCSG Registration/Randomization System when randomizing the patient. It is extremely important that POLAR stratification factors questions are correctly answered when randomizing the patient in the system. These questions are in reference to planned ET for the patient for the ILRR, patient gender and menopausal status. The information reported at randomization is also verified with the data reported in Question 6, "Planned Endocrine Therapy for the ILRR" and Question 7, "Gender and Menopausal status" on the Confirmation of Randomization Form (59-A Form). Stratification factor variables are used for analysis, so paying special attention to minimize errors when completing the randomization questions and the A Form is crucial.

Please put forth your best effort in submitting these forms, reports and data as soon as possible. Feel free to ask all questions you may have, as we are here to help you with any inquiries or concerns.

Importance of Up-to-Date Trial Data

The reporting of accurate and up-to-date data is a critical component in the success of clinical trials, which leads to generation of high-quality, reliable, and statistically sound data for analysis.

Only timely data submission would allow us to detect early on any potential safety concerns in the trial through our central monitoring and medical review activities as well as through the Data and Safety Monitoring Committee review. These review activities will not be efficient if we do not have timely data available.

Up-to-date data also helps to generate accurate reports and provides insight into the current status of the trial. For example, the Drug Supply Report is dependent on accurate and timely treatment data submission. This report is key for Center distribution and timely supply of the protocol treatment drugs. Lacking submission of data or reporting inaccurate data directly affects the patients' treatment information reported in the Drug Supply Report, which could create inefficient drug distribution for the patients.

Delaying data submission also impacts the trial monitoring visits. The Monitor will have to spend time trying to update the data rather than checking critical elements such as data submitted, source document verification, assisting the Center with query replies, answering protocol or data management questions, collecting updated documents, etc. This is an inefficient use of time and resources for all the parties involved during the Monitor's visit that could be used in a more productive way.

Data Management Tips

Once again our goal for this section of the POLAR Express is to prevent some of the most common issues we have encountered in POLAR Trial data management. We hope this helps to clarify data collection and lessen the number of queries, questions and concerns when entering data.

AE Form: When the patient experiences an adverse event and the question referring to it is answered as "Yes", please always complete the other sub-questions (e.g., "Is this an SAE?").

PV Form: Question 1 - Visit Date never should be the same as the Date of the Laboratory Investigations reported in Question 1 of the PALBO Form.

Remember that Visit Date should be the end of the Month Visit and the Laboratory Investigations should be done at the beginning of the Month Visit.

PALBO Form: Always report the lab tests units of measurement and record the ULN as requested in the form.

Question 10 of the PALBO Form "Date of final dose" should only be reported when Palbociclib is **permanently** discontinued.

NOTE: When data is not available for any reason, please mark the answer to the question as "Missing Value" in the missing value box by clicking on the green plus sign, select "missing value" and then clicking apply at the bottom.

If possible, please provide the reason of the missing value by clicking "Field" from the Toolbar and then "add reason for data value".

Frequently Asked Questions

Q: How should data be reported if a patient on Arm A stops taking palbociclib for any medical reason?

A: While this may not be an ideal scenario, if an Arm A patient stops taking palbociclib but continues with standard endocrine therapy, s/he remains in the POLAR Trial. According to protocol section 10:
Patients who have unacceptable toxicity from palbociclib should continue endocrine therapy wherever possible and continue in the 3-year protocol treatment phase.

The change in palbociclib treatment should be reflected on:

- The PV Form, Question 5 by entering "yes, change in treatment".
- PALBO Form, Question 7 by entering "permanently discontinued early." Please also enter the reason for discontinuation in Question 8, answer Question 9 if applicable and enter the date of the final dose in Question 10.
- The EoT Form should *not* be submitted since the patient is not ending all protocol therapy, but only palbociclib. The patient should continue the assessment schedule and clinic visits similar to the patients on Arm B (receiving ET only).
    - For future visits after the patient stops taking palbociclib, Question 5 of the PV Form should be "not applicable (never took/no longer taking)".

Frequently Asked Questions (continued)

Q: If an Arm A patient tests positive for COVID-19, can s/he continue taking palbociclib?

A: Yes, patients with COVID-19 infection, clinically stable, can continue taking palbociclib. If the patient is admitted to the hospital and unstable, palbociclib dose adjustments as per protocol are allowed. Please report the COVID-19 infection on the AE form, page 4 and enter an SAE as applicable.

Q: If a patient's breast cancer primary tumor was Hormone Receptors (HR) + positive and HER2+positive but subsequently, the patient had an ILRR (HR+ positive and HER2-negative), can the patient be included in the POLAR Trial?

A: According to the POLAR protocol only the recurrent tumor (ILRR) must be HER2-negative (0, 1+, and 2+ by IHC and/or ISH/FISH not amplified). Therefore, this patient can be included to POLAR Trial. Only the ILRR must be HR+ and HER2- and not the primary tumor.

Q: Can a patient undergo surgery for breast reconstruction while on POLAR Trial?
If this type of surgery is allowed, should the patient discontinue temporarily the study treatment?

A: In reference to concomitant therapy, Section 9.5 of the POLAR protocol (v2.0 26 June 2020) states:

- Radiotherapy and surgery are not permitted while patients are in the protocol treatment phase.

  Please note that this section refers to radiotherapy and surgery with a curative or adjuvant intent for the isolated local-regional recurrence of breast cancer. Such treatment is not permitted while patients are in the protocol treatment phase; this treatment is to be completed prior to trial randomization. It is not intended to exclude other types of surgery, such as reconstructive breast surgery. The Patient Information Sheet does not contain information that any surgery would be prohibited and that patients would have to choose between reconstructive breast surgery or trial participation. In the POLAR Trial, reconstructive breast surgery and surgeries without curative or adjuvant intent for the isolated local-regional recurrence of breast cancer are permitted, but IBCSG must be informed in advance of the type of surgery planned.

  To ensure safety while patients are receiving palbociclib (patients randomized to Arm A), the below instructions should be followed:
  - Blood counts should be within the normal range.
  - Any palbociclib-related toxicities should be resolved.
  - Palbociclib therapy should be interrupted for a maximum of 3 weeks.