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Palbociclib for HR Positive / HER2-negative Isolated Locoregional Recurrence of Breast Cancer (POLAR)

E ETOP IBCSG Partners Foundation

Status and phase

Active, not recruiting Phase 3

Conditions

Breast Cancer Recurrent

Treatments

Drug: Standard endocrine therapy

Drug: Palbociclib 125mg

Study type

Interventional

Funder types

NETWORK Industry

Identifiers

NCT03820830

WI239003 (Other Identifier)

2018-003553-19 (EudraCT Number)

BIG 18-02 (Other Identifier)

IBCSG 59-19

Take notes

View 53 locations

Contact trial

Timeline

Last updated: Mar 07, 2025

Start date
Aug 27, 2019 • 5 years ago

Today
Mar 21, 2025

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Sponsors of this trial

Lead Sponsor

E ETOP IBCSG Partners Foundation

Collaborating Sponsor

Pfizer

Details and patient eligibility

About

POLAR is a phase III clinical trial, which will test the safety and efficacy of an investigational combination of drugs to learn whether the combination of drugs works for a specific cancer. Palbociclib (Ibrance®) is the name of the investigational agent, which is assessed together with standard anti-hormone therapy in this study. Palbociclib is used to treat patients with hormone receptor-positive / HER2-negative breast cancer which has spread beyond the original tumor and/or to other organs.

During this study, anti-hormone therapy will consist of either a selective estrogen receptor modulator (such as tamoxifen) or an aromatase inhibitor (anastrozole, letrozole, exemestane) or fulvestrant (Faslodex®). Premenopausal women and men may also receive a drug called an LHRH (luteinizing hormone-releasing hormone) agonist by injection.

It is standard of care for people with hormone receptor positive breast cancer to take anti-hormone therapy. The study doctor will determine the type of standard anti-hormone therapy that will be given during this trial.

The purpose of the POLAR study is to compare the effect of using 3 years of palbociclib in combination with standard anti-hormone therapy with standard anti-hormone therapy alone and to evaluate the time until the breast cancer returns, if it does return.

Full description

Local or regional recurrence of breast cancer after mastectomy or lumpectomy indicates a poor prognosis, and accompanies or precedes distant metastasis in a high proportion of patients. Patients with isolated locoregional recurrences (ILRR), without evidence of distant metastasis hold a substantial risk of developing subsequent distant metastasis, with 5-year survival probabilities ranging between 45% and 80% after locoregional recurrence. These outcomes show the powerful negative prognostic importance of ILRR events and the need for treatments beyond surgical removal of the ILRR.

Adjuvant chemotherapy and endocrine therapies reduce the risk of relapse and death in patients with primary breast cancer. However, few data are available to inform the recommendation of systemic treatment for locoregional recurrence.

The International Breast Cancer Studies Group carried out the CALOR trial, Chemotherapy as Adjuvant for Locally Recurrent breast cancer (IBCSG 27-02 / BIG 1-02 / NSABP B-37), in collaboration with the Breast International Group (BIG) and the National Surgical Adjuvant Breast and Bowel Project (NSABP), to establish whether chemotherapy improves the

CALOR results strongly suggest that tailoring treatment according to the disease characteristics of the recurrent lesion, in this case ILRR, provides a better indication of the possible responsiveness to treatment than relying on the characteristics of the primary tumor.

Palbociclib has been granted FDA approval in the U.S. for the treatment of HR-positive/HER2-negative advanced breast cancer in combination with the hormonal treatments letrozole and fulvestrant given the unprecedented results in terms of efficacy of two pivotal clinical trials (PALOMA-2 and PALOMA-3). Palbociclib and other CDK4/6 inhibitors have also shown a good toxicity profile and therefore are ideal candidates for combination with hormonal therapy. CDK4/6 pathway activation is a well-known mechanism of resistance to endocrine therapy, indeed CDK4/6 inhibitors have shown activity in cellular models of acquired resistance to endocrine therapies.

The reason for prolonged duration of palbociclib in the adjuvant setting (2 years) comes from the evidence of preclinical studies where cell senescence was investigated as an appealing mechanism of cell death and was indeed observed in vitro after exposure of breast cancer cells and tumors to a combination of endocrine therapy and palbociclib. It is therefore hypothesized that the longer patients receive combined treatment with palbociclib and an antiestrogen, the more likely they may derive prolonged clinical benefit.

Based on the results of the CALOR trial and on strong evidence of activity of the combination of CDK4/6 inhibitors and endocrine therapy, the hypothesis of the POLAR trial is that the CDK4/6 inhibitor palbociclib in combination with endocrine therapy may be active as adjuvant therapy in patients with HR-positive/HER2-negative resected isolated locoregional recurrence of breast cancer.

Hide

Enrollment	**Sex**
405 patients	All
Ages	**Volunteers**
18+ years old	No Healthy Volunteers

Inclusion criteria

1. Histologically confirmed invasive breast cancer, defined as first proven ipsilateral local and/or regional recurrence of a primary invasive breast cancer in at least one of these sites:
    - breast;
    - the chest wall including mastectomy scar and/or skin;
    - axillary or internal mammary lymph nodes.
2. Completion of locoregional therapy:
    - completion of gross excision of recurrence within 6 months prior to randomization;
    - completion of radiotherapy (if given) more than 2 weeks prior to randomization
3. Negative or microscopically involved margins

amplified).Tumor with HER2 status 2+ by IHC must also be negative (not amplified) by ISH/FISH

8.-10. Normal hematological, renal, and liver function 11. The patient agrees to make tumor (diagnostic core biopsy or surgical specimen of ipsilateral isolated locoregional recurrence) available for submission for central pathology review 12. Patients must either be planned to initiate, or have already started, endocrine therapy for ipsilateral isolated locoregional recurrence 13.) Written Informed Consent prior to randomization

Exclusion criteria

1. Recurrence of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules) not surgically removable
2. Evidence of distant metastasis as based on conventional staging examinations (physical, chest X-ray or CT, abdominal ultrasound or CT, bone scintigraphy or FDG-PET-CT).
3. Bilateral synchronous or metachronous invasive breast cancer (in situ carcinoma of the contralateral breast is allowed)
4. Inflammatory breast cancer
5. Patients with a history of malignancy, other than invasive breast cancer, with the following exceptions:
    - Patients diagnosed, treated and disease-free for at least 5 years and deemed by the investigator to be at low risk for recurrence of that malignancy are eligible.
    - Patients with the following malignancies are eligible, even if diagnosed and treated within the past 5 years: ductal carcinoma in situ of the breast; cervical cancer in situ; thyroid cancer in situ; non-metastatic, non-melanomatous skin cancers.
6. Previous treatment with palbociclib or any other CDK 4/6 inhibitors
7. Previous or planned chemotherapy or planned radiotherapy for the ipsilateral isolated locoregional recurrence (radiotherapy is allowed, but must be completed more than 2 weeks prior to randomization)
8. Concurrent disease or condition that would make the patient inappropriate for study participation or any serious medical disorder that would interfere with the patient's safety
9. Pregnant or lactating women; lactation has to stop before randomization
10. Patients with psychiatric illness/social situations that would limit compliance with study requirements
11. Contraindications or known hypersensitivity to the palbociclib or excipients
12. History of extensive disseminated/bilateral or known presence of interstitial fibrosis or interstitial lung disease, including a history of pneumonitis, hypersensitivity pneumonitis, interstitial pneumonia, obliterative bronchiolitis, and pulmonary fibrosis. A history of prior radiation pneumonitis is not considered an exclusion criterion.

Trial design

Interventional model

Parallel Assignment

Masking

None (Open label)

405 participants in 2 patient groups

Palbociclib plus standard endocrine therapy

Experimental group

Description:
Palbociclib 125 mg/day tablet taken orally for 21 days, followed by 7 days rest for 3 years from randomization, plus standard endocrine therapy for at least 3 years from randomization.

Treatment:
Drug: Palbociclib 125mg
Drug: Standard endocrine therapy

Standard endocrine therapy

Active comparator group

Description:
Aromatase inhibitor (anastrozole or exemestane or letrozole) oral daily tablet, or Selective Estrogen Receptor Modulator (SERM) such as tamoxifen oral daily tablet or fulvestrant (Faslodex) injection once every 2 weeks for 3 doses then every month. Premenopausal women and men may also receive an LHRH (luteinizing hormone-releasing hormone) agonist by injection. Standard endocrine therapy will be given for at least 3 years from randomization.

Treatment:
Drug: Standard endocrine therapy

Trial contacts and locations 53

All locations

A **ASST Papa Giovanni XXIII | Ospedale di Bergamo - SC Malattie Endocrine-Diabetologia**
Veeva-enabled site

PIAZZA OMS 1, BERGAMO, Bergamo 24127

Enrolling

L **Luzerner Kantonsspital | Luzern - Cardiology Department**
Veeva-enabled site

Ospedale S. Stefano
Prato, Italy

Institut Bergonie
Bordeaux, France, 33076

Institut Claudius Regaud
Toulouse, France, 31100

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Central trial contact

Holly Shaw; Adriana Karausch

Contact trial

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Enrolling

Breast Cancer Recurrent

Salt Lake City, Utah, United States

Breast Cancer Recurrence - the Accuracy of Dual-time PET/CT
Odense University Hospital

Odense, Funen, Denmark

Data sourced from clinicaltrials.gov