ISRCTN18026884 https://doi.org/10.1186/ISRCTN18026884

Palbociclib combined with aromatase inhibitors for the treatment of breast cancer

Submission date
29/01/2023

Recruitment status
No longer recruiting

Registration date
11/02/2023

Overall study status
Completed

Last Edited
10/02/2023

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Neoadjuvant chemotherapy is chemotherapy that a person with cancer receives before their primary course of treatment. It is an important treatment for locally advanced breast cancer and findings from the pathological efficacy evaluation can also provide an accurate reference for guiding postoperative adjuvant treatment (used after primary treatment to lessen the chance of the cancer coming back). With the continuous development and maturity of new adjuvant treatment, neoadjuvant chemotherapy has become the main preoperative systemic treatment applied to locally advanced breast cancer.
For patients with hormone receptor positive (HR+) breast cancer who are insensitive to neoadjuvant chemotherapy, sequential neoadjuvant endocrine therapy is also an option, but clinicians still have concerns about the treatment onset time and duration of neoadjuvant endocrine therapy. Furthermore, clinical difficulties in the treatment of patients with locally advanced HR+/HER2- breast cancer who are insensitive to neoadjuvant chemotherapy require guidance on how to choose an appropriate follow-up treatment to achieve the goal of phase reduction or breast conservation. This study aims to evaluate the application of neoadjuvant endocrine therapy combined with the CDK4/6 inhibitor palbociclib to enhance neoadjuvant endocrine therapy, provide survival benefits, and improve quality of life.

Who can participate?
Female patients aged over 18 years with invasive breast cancer who are postmenopausal or premenopausal and reach the menopausal standard after suppression of ovarian function

What does the study involve?
General information and clinical diagnosis data of patients, including basic information, tumor-related imaging information, and pathological information will be collected. Patients will be followed up once every 2 months and treatment-related information will be recorded. Treatment-related adverse reactions will be recorded once per treatment cycle. Patients will receive palbociclib treatment combined with endocrine therapy for four to six cycles (28 days being one cycle). The timing of any surgical intervention will be determined according to the results of the imaging evaluation.

What are the possible benefits and risks of participating?
If a patient participates in this study, the researchers will regularly assess their condition and fully inform them. During the clinical trial, the patient will be provided with a routine examination and will be followed up using WeChat, and the patient's examination process will be simplified.
The common adverse reactions (incidence of 10% or more) of palbociclib treatment include leukopenia, fatigue, anemia, upper respiratory tract infection, nausea, stomatitis, alopecia, diarrhea, thrombocytopenia, loss of appetite, vomiting, peripheral neuropathy, and epistaxis. Mild adverse reactions will not receive specific treatment, especially if they are tolerated by patients and only symptomatic support will be provided. Symptomatic treatment will be administered to all patients for clinical symptoms (such as nausea, vomiting, and joint pain) and adverse reactions (such as infection, leukopenia, and thrombocytopenia).

When is the study starting and how long is it expected to run for?
September 2022 to December 2023

Who is funding the study?
There are no funders for the study.

Who is the main contact?
Fan Yao, yaofancmu@sina.com

Contact information

Type(s)
Principal investigator

Contact name
Prof Fan Yao

ORCID ID
https://orcid.org/0000-0001-8689-0291

Contact details
No.155, Nanjing North Street
Heping District
Shenyang
China
110001
+86 (0)13998373748
yaofancmu@sina.com

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Palbociclib combined with aromatase inhibitors for the treatment of locally advanced HR+HER2- breast cancer insensitive to neoadjuvant chemotherapy: a prospective, single-arm, Phase II clinical trial

Study objectives
This study assumes that four to six cycles of palbociclib treatment combined with endocrine therapy can completely or partially improve disease conditions in patients with locally advanced HR+HER2- breast cancer who have received two cycles of neoadjuvant chemotherapy and have stable or progressive disease status.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/09/2022, Medical Scientific Research Ethics Committee of The First Hospital of China Medical University (No. 155, Nanjing Street, Heping District, Shenyang 110000, Liaoning Province, China; +86 (0)24 83282837; email: not provided), ref: 2022]2022-360-2

Study design
Prospective open single-arm Phase II clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Breast cancer

Interventions
At the start date of the trial, patients who meet the eligibility criteria will begin to be enrolled in this study. General information and clinical diagnosis data of patients, including basic information, tumor-related imaging information, pathological information (ER and/or PR status, and Ki67 expression) will be collected. Patients will be followed up once every 2 months, and treatment-related information will be recorded. Written informed consent will be obtained from each patient. Treatment-related adverse reactions will be recorded once every cycle. Patients will receive palbociclib treatment combined with endocrine therapy for four to six cycles (28 days being one cycle). Operation timing will be determined based on the results of the imaging evaluation.

Piperacillin (28 days as a treatment cycle, oral piperacillin at 125 mg/d for 3 consecutive weeks, followed by piperacillin withdrawal for 1 week)
Aromatase inhibitors (endocrine therapy)

Exemestane (25 mg/tablet, one tablet per day, once daily, oral use)
Letrozole (2.5 mg/tablet, one tablet per day, once daily, oral use)
Anatriazole (1 mg/tablet, one tablet per day, once daily, oral use)

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Piperacillin, exemestane, letrozole, anatriazole

Primary outcome(s)
Objective response rate (ORR) is defined as the proportion of patients with a complete response (CR) or a partial response (PR) to treatment among the total number of patients enrolled, i.e., ORR = CR + PR / total number of patients ×100%. ORR will be evaluated at 4 to 6 months after initiating palbociclib treatment combined with endocrine therapy.

Key secondary outcome(s))
1. Pathologic complete response (pCR): pCR is defined as no residual in situ or invasive tumor in the breast or axillary nodes. pCR will be evaluated on the day of operation.
2. Disease-free survival (DFS): DFS is defined as the time from tumor resection to distant relapse or invasive contralateral breast cancer, which is used to determine patient survival. DFS will be evaluated from the time of surgery to tumor recurrence or metastasis.
3. Overall survival (OS): OS is defined as the time from randomization (starting point for survival analysis) to death. A small increase in improvement in OS is considered a clinically meaningful benefit. OS will be evaluated at the time from randomization to death.
4. Tumor resection rate: Tumor resection rate refers to the percentage of the number of patients who undergo cancer resection among the total number of patients. The cancer resection rate will be evaluated immediately after tumor resection.
5. Postoperative pathological evaluation using the Miller–Payne grading system and the Residual Cancer Burden index:
5.1. The Miller–Payne grading system is a five-grade classification method. It is used to grade the proportion of tumor cell reduction after treatment relative to that before treatment. Grade 1: no reduction in overall cellularity; grade 2: up to 30% reduction in cellularity; grade 3: 30%–90% reduction in cellularity; grade 4: marked disappearance of more than 90% of cellularity; grade 5: no invasive malignant cells identifiable in sections from the site of the tumor.
5.2. The Residual Cancer Burden index is an indicator used to judge the prognosis of four subtypes of breast cancer. It is also closely related to prognosis in patients subjected to long-term follow-up. The Residual Cancer Burden index will be evaluated immediately after tumor resection.
6. Incidence of adverse reactions = number of patients with adverse reactions / total number of patients × 100%. The incidence of adverse reactions will be determined from the beginning to the end of palbociclib treatment combined with endocrine therapy.

Completion date
01/12/2023

Eligibility

Key inclusion criteria
1. Age >18 years (note: there is no upper age limit for the onset of breast cancer, and older patients are more intolerant of chemotherapy)
2. Postmenopausal female patients; or premenopausal female patients who meet the menopausal standard after ovarian function suppression (OFS)*
3. Before neoadjuvant chemotherapy, a needle biopsy of the breast will be performed to confirm the diagnosis of invasive breast cancer. In addition, immunohistochemistry will indicate ER-positive (ER expression ≥ 50%), progesterone receptor (PR)-positive or negative, and HER2-negative luminal type breast cancer
4. Patients who have not received any breast cancer-related treatment prior to admission
5. Patients with newly confirmed breast cancer who have received two cycles of neoadjuvant chemotherapy (the neoadjuvant chemotherapy protocol will be determined according to patient condition) and are insensitive to neoadjuvant chemotherapy
6. Availability of complete clinical pathological data

* Menopausal women will be considered if one or more of the following conditions are met:
1. Women who have undergone bilateral oophorectomy
2. Age ≥60 years
3. Age <60 years: For patients who have natural menopause ≥12 months, levels of follicle-stimulating hormone and estradiol within the postmenopausal range without receiving chemotherapy, tamoxifen, toremifene, or ovarian castration; for patients who are taking tamoxifen or toremifene, levels of follicle-stimulating hormone and estradiol levels should reach those of postmenopausal levels.
Chemotherapy insensitivity: according to the efficacy evaluation criteria for solid tumors, chemotherapy insensitivity is considered when progressive disease (PD) or stable disease (SD) is established after two cycles of neoadjuvant chemotherapy.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Patients who have received surgery, radiotherapy and endocrine therapy related to breast cancer in the past
2. Bilateral breast cancer: bilateral primary breast cancer and bilateral metastatic breast cancer. Generally, bilateral breast cancer refers to bilateral primary breast cancer; or inflammatory breast cancer: The first symptoms of primary inflammatory breast cancer are breast enlargement, skin redness and firmness, and pain. The typical clinical manifestations of primary inflammatory breast cancer are diffuse breast enlargement, skin congestion, and edema (orange peel skin) in 1/3 or more areas of the breast, and obvious palpable boundaries in the areas of

congestion and edema. The boundaries of tumors are often unclear by palpation. The clinical manifestations are also accompanied by erysipelas such as edge or stripe pigmentation, an increase in skin temperature and tenderness. Some patients have skin ulcers caused by local tumor collapse, which is often secondary to locally advanced breast cancer.
3. Patients complicated by other malignant tumors or having a history of other malignant tumors
4. Patients with distant metastasis at initial diagnosis
5. Patients with breast cancer, which will not be histopathologically confirmed
6. Patients who have immune system disease, blood system disease, or mental disease before chemotherapy
7. Before chemotherapy, patients have severe dysfunction of important organs such as the heart, liver, or kidney

Date of first enrolment
30/01/2023

Date of final enrolment
01/03/2023

Locations

Countries of recruitment
China

Study participating centre
First Hospital of China Medical University
No. 155, Nanjing Street
Heping District
Shenyang
China
110001

Sponsor information

Organisation
First Hospital of China Medical University

ROR
https://ror.org/04wjghj95

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
First Hospital of China Medical University

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes