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Evaluating the biological and clinical effects of the combination of palbociclib with letrozole as neoadjuvant therapy in post-menopausal women with primary breast cancer

Submission date
08/01/2015

Registration date
09/01/2015

Last Edited
27/11/2025

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-palbociclib-and-letrozole-before-breast-cancer-surgery-pallet

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2014-000887-16

ClinicalTrials.gov (NCT)
NCT01889680

Protocol serial number

ICR-CTSU/2014/10044

Study information

Scientific Title
A phase II randomised study evaluating the biological and clinical effects of the combination of palbociclib with letrozole as neoadjuvant therapy in post-menopausal women with ER+ primary breast cancer

Acronym
PALLET

Study objectives
PALLET will evaluate whether adding palbociclib to standard hormone therapy with letrozole is better than using letrozole alone at treating breast cancer before surgery.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London-Fulham REC, 01/09/2014, ref. 14/ LO/ 1291

Study design
Randomized; Interventional

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Post-menopausal patients with ER+ and HER2- primary breast cancer

Interventions
1. Palbociclib is an unlicensed drug that is a 125-mg capsule that should be administered orally. The treatment schedule is 3 weeks on, 1 week off.
2. Letrozole is a 2.5-mg tablet that will be administered orally on a daily basis. Both drugs will be taken for up to 14 weeks, depending on treatment arm. Patients will be followed up for 1 year after date of randomisation.

Added 27/11/2025:
Additional Data Linkage Information:
Participants from this trial will also be included in the INTERACT project which will link to their data held by NHS England. For more information, please see the INTERACT website: https://www.icr.ac.uk/interact.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Palbociclib, letrozole

Primary outcome(s)
1. Change in the proliferation marker Ki67 (% positive tumour cells) as tested by IHC from baseline to after 14 weeks treatment with letrozole with or without palbociclib
2. Clinical response as measured by ultrasound according to ECOG criteria after 14 weeks treatment with letrozole with or without palbociclib

Key secondary outcome(s))
1. Effect of palbociclib on Ki67 after 2 weeks and the added effect of letrozole from weeks 2-14 (within group)
2. Effect of letrozole on Ki67 after 2 weeks and the added effect of palbociclib from weeks 2-14 (within group)
3. pCR rates after letrozole with or without 14 weeks palbociclib
4. PEPI score after letrozole with or without 14 weeks palbociclib
5. Assessment of safety and tolerability
6. Changes between surgical intent at baseline, surgical intent after 14 weeks and actual surgery received after treatment with letrozole with or without palbociclib (added 01/11/2016)

Completion date
03/03/2020

Eligibility

Key inclusion criteria
1. Postmenopausal women defined as:
1.1. Age 56 or older with no spontaneous menses for at least 12 months prior to study entry
1.2. Age 55 or younger with no menses for at least 12 months prior to study entry (e.g., spontaneous or secondary to hysterectomy) and with a documented oestradiol level in the postmenopausal range according to local institutional/laboratory standard
1.3. Age ≥16 with documented bilateral oophorectomy
2. Operable ER+ HER2- invasive early breast cancer suitable for neoadjuvant AI treatment. ER positivity is defined as an Allred score of 3 (or equivalent) [sentence added 01/11/2016]. HER2 negativity will be defined as per the 2013 ASCO/CAP guidelines as follows:
2.1. IHC 1+ as defined by incomplete membrane staining that is faint/barely perceptible and within >10% of the invasive tumour cells
2.2. IHC 0 as defined by no staining observed or membrane staining that is incomplete and is faint/barely perceptible and within ≤10% of the invasive tumour cells
2.3. ISH negative based on:
2.3.1. Single-probe average HER2 copy number <4.0 signals/cell
2.3.2. Dual-probe HER2/CEP17 ratio <2.0 with an average HER2 copy number <4.0 signals/cell
3. No medical contra-indication to palbociclib (as defined according to latest version of Investigator Brochure)
4. A tumour with an ultrasound size of at least 2.0cm
5. No evidence of metastatic spread by standard assessment according to local guidelines
6. ECOG performance status of 0 or 1
7. Adequate organ function including:

7.1.Haemoglobin ≥10g/dL (90g/L)
7.2. ANC ≥ 1,500/ mm³ (> 1.5 x 109/L)
7.3. Platelets ≥ 100,000/mm³ (> 100 x 109/L)
7.4. AST and/or ALT 1.5 x upper normal limits (ULN)
7.5 Alkaline phosphatase 1.5 x ULN
7.6. Total serum bilirubin ULN unless the patient has a bilirubin elevation > ULN to 1.5 x ULN due to Gilbert's disease or similar syndrome involving slow conjugation of bilirubin
7.7. Serum creatinine ≤ 1.25 x ULN or estimated creatinine clearance < 60 mL/min (as calculated using the method standard for the institution)
7.8. No severe and relevant co-morbidity that would affect a patients participation in the study
7.9. INR must be within normal limits of the local laboratory ranges
8. Written informed consent to participate in the trial and to donation of tissue and blood samples
9. Patients must have the ability to swallow oral medication

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Premenopausal or perimenopausal women
2. Inflammatory/inoperable breast cancer
3. HER2 positive
4. Concurrent use (defined as use within 4 weeks prior to baseline tissue sample being taken) of HRT or any other oestrogen-containing medication (including vaginal oestrogens)
5. Prior endocrine therapy for breast cancer
6. Any invasive malignancy within previous 5 years (other than basal cell carcinoma or cervical carcinoma in situ)
7. Bilateral invasive disease (added 01/11/2016)
8. Any severe coincident medical disease, including seizure disorder requiring medication
9. Diagnosis by FNA alone or excisional biopsy or lumpectomy performed prior to study entry
10. Surgical axillary staging procedure prior to study procedure (with the exception of FNA or core biopsy)
11. Definitive clinical or radiologic evidence of metastatic disease
12. History of ipsilateral invasive breast cancer regardless of treatment or ipsilateral DCIS treated with radiotherapy or contralateral invasive breast cancer at any time
13. New York Hearth Association classification of level III or IV heart disease
14. Any treatment, including radiotherapy, chemotherapy, and/or targeted therapy, administered for the currently diagnosed breast cancer prior to study entry
15. Patients on established CYP3A inhibitors/inducers

16. QTc >480 msec or a family or personal history of long or short QT syndrome, Brugada syndrome or know history of QTc prolongation, or Torsade de Pointes (TdP)
17. Active Hepatitis B or Hepatitis C with abnormal liver function tests
18. HIV positive patients receiving antivirals

Date of first enrolment
23/02/2015

Date of final enrolment
08/03/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
ICR Clinical Trials and Statistics Unit
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Sponsor information

Organisation
The Institute for Cancer Research

ROR
https://ror.org/043jzw605

Funder(s)

Funder type
Industry

Funder Name
Pfizer UK

Alternative Name(s)

Pfizer Ltd, Pfizer Limited

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from PALLET-icrctsu@icr.ac.uk.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	20/01/2019	26/02/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results				No	Yes
Protocol file	version 2.1	24/11/2015	16/01/2023	No	No