ISRCTN31243262 https://doi.org/10.1186/ISRCTN31243262

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	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 09/01/2015	**Overall study status** Completed	
Last Edited 16/01/2023	**Condition category** Cancer	

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

Contact name
Ms Katie Goddard

Contact details
ICR Clinical Trials and Statistics Unit
15 Cotswold Road
Sutton
United Kingdom
SM2 5NG

Additional identifiers

EudraCT/CTIS number
2014-000887-16

IRAS number

ClinicalTrials.gov number
NCT01889680

Secondary identifying numbers
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
Randomised; Interventional

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
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

Secondary outcome measures
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)

Overall study start date
23/02/2015

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/ mm^3 (> 1.5 x 109/L)
7.3. Platelets ≥ 100,000/mm^3 (> 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

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 306; UK Sample Size: 150

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
England

United Kingdom

Study participating centre
ICR Clinical Trials and Statistics Unit
15 Cotswold Road
Sutton
United Kingdom
SM2 5NG

Sponsor information

Organisation
The Institute for Cancer Research

Sponsor details
Section of Clinical Trials
15 Cotswold Road
Sutton
England
United Kingdom
SM2 5NG

Sponsor type

Hospital/treatment centre

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

Publication and dissemination plan

Intention to publish date

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?
Plain English results				No	Yes
Results article	results	20/01/2019	26/02/2019	Yes	No
Protocol file	version 2.1	24/11/2015	16/01/2023	No	No