ISRCTN15621797 https://doi.org/10.1186/ISRCTN15621797

A pre-surgery trial looking at the effect of combining megestrol acetate with letrozole or letrozole alone for postmenopausal patients with early, oestrogen receptor positive breast cancer

Submission date 02/05/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 26/05/2017	**Overall study status** Completed	
Last Edited 16/10/2024	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-megestrol-acetate-and-letrozole-for-women-with-breast-cancer-pioneer

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Type(s)
Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT03306472

Clinical Trials Information System (CTIS)
2016-003752-79

Protocol serial number
33915

Study information

Scientific Title
Randomised Phase II clinical trial PIONEER: A Pre-operative wIndOw study of letrozole plus PR agonist (megestrol acetate) versus letrozole aloNE in post-menopausal patients with ER-positive breast cancer

Acronym
PIONEER

Study objectives
The aim of this study is to investigate the effect of combining megestrol acetate (a progesterone receptor activator) and letrozole (an anti-oestrogen, and standard endocrine therapy for post-menopausal women), in patients with newly diagnosed, untreated, ER-positive, HER2-negative, invasive primary breast cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Newcastle & North Tyneside 1 Research Ethics Committee, 24/05/2017, ref: 17/NE/0113

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment, Screening, Drug, Surgery

Study type(s)
Treatment

Health condition(s) or problem(s) studied
ER-positive breast cancer in post-menopausal patients

Interventions
Patients will be randomised to one of three study arms.

Arm A: Participants receive oral letrozole (2.5 mg) alone daily for 15 days (this may be extended up to 19 days to accommodate the surgery date).
Arm B: Participants receive oral letrozole 2.5mg plus megestrol acetate 40 mg daily for 15 days (this may be extended up to 19 days to accommodate the surgery date).
Arm C: Participants receive oral letrozole 2.5mg plus megestrol acetate 160mg daily for 15 days (this may be extended up to 19 days to accommodate the surgery date).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Letrozole, megestrol acetate

Primary outcome(s)
Change in tumour proliferation is measured using Ki67 immuno-histochemical (IHC) assessment between pre-treatment (baseline) and post-treatment tumour samples (Day 15).

Key secondary outcome(s)
1. Change in tumour apoptosis is measured using Caspase 3 IHC assessment between pre-treatment (baseline) and post-treatment tumour samples (Day 15)
2. Changes in the expression of Androgen Receptor (AR) and Progesterone Receptor (PR) are measured using IHC assessment between pre-treatment (baseline) and post-treatment tumour samples (Day 15)
3. Change in proliferation by Aurora Kinase A (IHC) between baseline and Day 15 (+≤4 Days)
4. Change in tumour proliferation is also measured using Aurora Kinase A IHC assessment between pre-treatment (baseline) and post-treatment tumour samples (Day 15).
5. The absolute value of the Ki67 IHC assessment post-treatment (Day 15) is also recorded.
6. Safety of the trial treatments is assessed based on the incidence of serious adverse events and adverse events of all grades throughout the trial, grading is assessed using CTCAE criteria.

Exploratory Outcomes:
1. Transcription factor mapping of the Oestrogen Receptor (ER) will be assessed using ChIP-sequencing
2. The differences in response to treatments within the METABRIC-defined subtypes of ER-positive breast cancer will be assessed

Completion date
30/11/2022

Eligibility

Key inclusion criteria
1. Histologically confirmed breast adenocarcinoma
2. Postmenopausal women, defined as having experienced:
2.1. 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. ≥50 years, history of vasomotor symptoms) or
2.2. Six months of spontaneous amenorrhea with serum FSH levels > 40 mIU/mL and estradiol < 20 pg/mL or
2.3. Surgical bilateral oophorectomy (with or without hysterectomy) at least six weeks ago.
3. Core biopsy confirmation of ER positive (Allred≥3) and HER2 negative invasive carcinoma on core biopsy, >=T1c, either cN0 or N+
4. Patients whose cancers have been deemed to be operable by the MDT
5. Surgery planned within the next 2-6 weeks
6. ECOG performance status of 0, 1 or 2
7. Adequate Liver, Renal and Bone marrow function, defined as:

7.1. Adequate liver function where bilirubin is ≤1.5 x ULN
7.2. Adequate renal function with estimated creatinine clearance of ≥60 ml/min
7.3. Adequate bone marrow function with ANC ≥1.0 x 10(9)/L and Platelet count ≥100 x 10(9)/L
8. Written informed consent to participate in the trial and to donation of tissue

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria
1. History of hormone replacement therapy in the last 6 months
2. Previous treatment with tamoxifen or an aromatase inhibitor in the last 6 months
3. Known hypersensitivity or contraindications to aromatase inhibitors or megestrol acetate
4. Known allergy to lactose
5. Known to have a progestogen-containing intrauterine system in situ, unless removed prior to randomisation
6. Known metastatic disease on presentation
7. Recurrent breast cancer (patients with a new primary invasive breast cancer will be eligible to participate)
8. Serious concomitant disorders that would compromise the safety of the patient or compromise the patient's ability to complete the study, at the discretion of the investigator
9. Treatment with an investigational drug within 4 weeks before randomization
10. Inability to swallow orally administered medication and patients with gastrointestinal disorders likely to interfere with absorption of the trial medication
11. Inability to give informed consent

Date of first enrolment
01/07/2017

Date of final enrolment
31/10/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

Cambridge University Hospitals NHS Foundation Trust
Addenbrooke's Hospital
Cambridge Biomedical Campus
Hills Road
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CB2 0QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Research organisation

Funder Name
Het Anti-Kankerfonds - Le Fonds Anti-Cancer

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		15/10/2024	16/10/2024	No	No
HRA research summary			28/06/2023	No	No