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A trial looking at progesterone to treat early breast cancer in premenopausal women

Submission date 04/09/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 07/09/2017	**Overall study status** Completed	
Last Edited 11/10/2023	**Condition category** Cancer	

Plain English summary of protocol
See https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-electrocautery-ablation-to-prevent-lung-cancer-earl (added 08/01/2021)

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2017-001521-41

Integrated Research Application System (IRAS)
225455

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 35420, IRAS 225455

Study information

Scientific Title
A window of opportunity study to assess the biological effects of progesterone in premenopausal ER-positive, PgR-positive early breast cancer

Acronym
PEARL

Study objectives
The aim of the study is to evaluate the effects of two-weeks preoperative therapy with micronised progesterone alongside tamoxifen in premenopausal women with ER-positive, PgR-positive early breast cancer.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 11/09/2017, North West - Greater Manchester South Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 (0)207 104 8002; gmsouth.rec@hra.nhs.uk), ref: 17/NW/0460

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

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Cancer, Primary sub-specialty: Breast Cancer; UKCRC code/ Disease: Cancer/ Malignant neoplasm of breast

Interventions
Patients are randomised 1:1 to either Tamoxifen plus micronised progesterone (therapeutic arm) or Tamoxifen alone (control arm). All participants take 100mg of Tamoxifen orally on Day 1, followed by 20mg of Tamoxifen orally, once daily from Day 2 until their scheduled breast surgery. Patients on the therapeutic arm also take 300mg micronised progesterone (Utrogestan) orally, once daily from Day 1 until their scheduled breast surgery. Surgery is scheduled for Day 14-18, so patients will receive study treatment for 14-18 days.

Following surgery, patients return 28 days later and the following procedures will be carried out at this visit:
1. Haematology and biochemistry

2. Adverse event review and recording
3. Translational blood sample collection

Adverse events will be reported until 28 days post treatment.

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
Changes in tumour cell proliferation will be measured using the Ki67 proliferation index at baseline (Day 0) and at surgery (Day 14-18).

Key secondary outcome(s))
1. Changes in the pro-aptoptic marker cleaved caspase 3 are measured using tissue immunohistochemistry at baseline (Day 0) and at surgery (Day 14-18)*
2. Changes in ER, PgR, FoxA1, Cyclin D1, RANKL protein and mRNA expression are measured using tissue immunohistochemistry at baseline (Day 0) and at surgery (Day 14-18)*
3. Changes in circulating steroidogenic hormones are measured by analysis of blood samples at baseline and surgery (Day 14-18)
4. Pharmacokinetics of tamoxifen and N-desymethyltamoxifen (DMT) will be measured by mass spectrometry at Mid-treatment (Day 7) and surgery (Day 14-18)
5. Safety and tolerability of progesterone plus tamoxifen will be measured by the following –
5.1. Occurrence of grade 3+toxicity as classified by NCI-CTCAE v4.03 throughout the treatment period until 28 days post treatment.
5.2. Occurrence of adverse events throughout the treatment period until 28 days post treatment.
5.3. Occurrence of withdrawal from trial treatment due to toxicity throughout the treatment period until 28 days post treatment.
5.4. Experience of delay to scheduled surgery.

Completion date
23/06/2019

Eligibility

Key inclusion criteria
1. Women 16-49 years of age
2. Newly diagnosed histologically confirmed breast cancer
3. Premenopausal as defined by: gonadotrophin levels (luteinizing hormone and follicle stimulating hormone) and estradiol levels within the local laboratory’s reference range for premenopausal females
4. Ability to provide menstrual cycle information
5. ER positive (Allred ≥3)
6. PgR positive (Allred ≥3)
7. HER2 negative (IHC 1+ or 2+ and HER2/CEP17 ratio of <2)
8. Tumour measuring ≥14mm in longest diameter by ultrasound (US)/mammogram examination
9. Eastern Cooperative Oncology Group (ECOG) performance status 0, 1 or 2
10. Adequate bone marrow function defined by Hb≥10 g/dl, WBC≥3.0 x109 , PLT≥100 x109 /L.

11. Adequate renal function defined by a serum creatinine ≤1.5 x ULN. Adequate liver function defined by total bilirubin ≤ 1.5 ULN (patients with Gilbert's syndrome exempted), either ALT or AST ≤1.5 ULN and ALP ≤1.5 ULN
12. Written informed consent, able to comply with treatment and follow-up
13. Currently using adequate contraception, and willing to continue use of this for the duration of the trial. Also willing to use a form of adequate contraception for one year following end of treatment (the type of contraception can be changed following the end of the trial). Adequate contraception is defined as either:
13.1. Total abstinence: When this is in line with the preferred and usual lifestyle of the subject. Periodic absence (e.g. calendar, ovulation, symptothermal, postovulation methods) and withdrawal are not acceptable methods of contraception.
13.2. Sterlisation: have had surgical tubal ligation at least six weeks before taking study treatment.
13.3. Male partner sterilization (with the appropriate postvasectomy documentation of the absence of sperm in the ejaculate). For female study subjects, the vasectomized male partner should be the sole partner for that patient.
13.4. Placement of a copper intrauterine device (IUD)
13.5. Barrier methods of contraception: Condom or Occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/vaginal suppository
Note: Hormonal contraceptive methods (e.g. oral, injected and implanted) are not permitted.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Upper age limit
49 years

Sex
Female

Total final enrolment
7

Key exclusion criteria
1. Inoperable breast cancer
2. Inflammatory tumours
3. Evidence of metastatic disease
4. Prior endocrine therapy or chemotherapy for breast cancer
5. Any history of invasive malignancy within 5 years of starting study treatment (other than adequately treated basal cell carcinoma or squamous cell carcinoma of the skin and cervical carcinoma in situ)
6. Concomitant use (defined as use within 12 weeks prior to entry) of OCP or any other

oestrogen-containing medication or supplement
7. Concomitant use of any of the prohibited medications listed in Section 9.6.2
8. History of thromboembolic disease
9. Known carrier of genetic defects predisposing to thromboembolic disorders
10. Any medical condition that would prevent the use of low molecular weight heparin for venous thromboembolism prophylaxis
11. Uncontrolled abnormalities of serum potassium, sodium, calcium or magnesium levels
12. Evidence of bleeding diathesis
13. Evidence of uncontrolled active infection
14. Evidence of significant medical condition or laboratory finding which, in the opinion of the investigator, makes it undesirable for the patient to participate in the trial
15. Pregnant or lactating women

Date of first enrolment
18/06/2018

Date of final enrolment
23/12/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Liverpool University Hospital
Royal Liverpool and Broadgreen University Hospitals NHS Trust
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Wythenshawe Hospital
University Hospital of South Manchester NHS Foundation Trust
Southmoor Road
Wythenshaw
Manchester
United Kingdom
M23 9LT

Study participating centre

New Cross Hospital
The Royal Wolverhampton NHS Trust
Wolverhampton Road
Heath Town
West Midlands
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Arrowe Park Hospital
Wirral University Teaching Hospital NHS Foundation Trust
Arrowe Park Road
Wirral
Merseyide
Upton
United Kingdom
CH49 5PE

Study participating centre
Macclesfield Distrcit General Hospital
East Cheshire NHS Trust
Victoria Road
Cheshire
Macclesfield
United Kingdom
SK10 3BL

Study participating centre
North Manchester General Hospital
Pennine Acute Hospitals NHS Trust
Delaunays Road
Crumpsall
Manchester
United Kingdom
M8 5RB

Study participating centre
North Manchester General Hospital
Pennine Acute Hospitals NHS Trust
Delaunays Road
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M8 5RB

Study participating centre
Guy's Hospital
Guy's and St Thomas' NHS Foundation Trust
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
The Countess of Chester Health Park
Countess of Chester Hospital Foundation Trust
Cheshire
Chester
United Kingdom
CH2 1UL

Study participating centre
The Royal Bolton Hospital
Bolton NHS Foundation Trust
Minerva Road
Farnworth
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United Kingdom
BL4 0JR

Study participating centre
St James's University Hospital
Derby Teaching Hospitals NHS Foundation Trust
Beckett Street
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LS9 7TF

Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets analysed during the conduct of the PEARL study will be available upon request from the trial Chief Investigator, Professor Carlo Palmieri, c.palmieri@liv.ac.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Other unpublished results	Final Analysis Report version 1.0	06/10/2023	11/10/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes