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Breast Cancer - anti-progestin prevention study 1

Submission date 01/07/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 01/07/2015	**Overall study status** Completed	
Last Edited 23/10/2018	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-of-ulipristal-acetate-to-prevent-breast-cancer-bc-apps1

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT02408770

Secondary identifying numbers
19209

Study information

Scientific Title
A pilot prevention study of the effects of the anti-progestin Ulipristal acetate (UA) on surrogate markers of breast cancer risk

Study objectives
1.4 million women worldwide are diagnosed with invasive breast cancer (BC) each year and over a third die from their disease. Uptake and adherence to licensed chemo-preventative agents, tamoxifen and raloxifene, is low due in part to their adverse toxicity profiles. There is an urgent need for effective, well tolerated and safe breast cancer chemo-preventative agents. Endogenous progesterone induces proliferation of the normal mammary stem/progenitor cell population and exogenous progesterone is well known to increases the risk of postmenopausal breast cancer. Taken together these data suggest antagonism of PgR signaling may be a fruitful approach in the prevention of BC. Ulipristal acetate (UA) is a well-tolerated anti-progestin already licensed for the treatment of benign uterine fibroids. This project will, for the first time, determine the effects of the PgR antagonist UA on the normal breast in women at increased risk of BC and correlate molecular with imaging (MRI) effects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
UK National Research Ethics Service: North West – Greater Manchester South Committee, provisional approval 18/06/2015, ref: 15/NW/0478

Study design
Non-randomised; Interventional; Design type: Prevention

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Malignant neoplasm of breast

Interventions
1. Treatment: Ulipristal acetate 5mg daily for 12 weeks
2. Vacuum assisted breast biopsies before and on treatment
3. Imaging, MRI and USS elastography before and on treatment

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Ulipristal acetate

Primary outcome measure
The change in the proliferation of normal breast epithelium, assessed by Ki67, from baseline to 3 months on treatment with ulipristal acetate

Secondary outcome measures
1. The changes in expression of individual genes and key pathways induced by UA therapy at baseline and after 3 months of therapy
2. The change in tissue stiffness and collagen organisation induced by UA therapy at baseline and after 3 months of therapy
3. The changes in key stem cell and PgR target proteins induced by UA therapy at baseline and after 3 months of therapy
4. The proportion and type of clonogenic cells in the breast following treatment with UA at baseline and after 3 months of therapy
5. MRI imaging biomarkers of anti-progestin (UA) activity at baseline and after 3 months of therapy
6. The side effect profile of UA in this patient population at baseline and then monthly to 4 months

Overall study start date
01/01/2014

Completion date
30/06/2019

Eligibility

Key inclusion criteria
1. Premenopausal females aged between 25 and 45 years
2. Regular menses defined as date of onset of last menstrual period +/- 3 days of expected
3. Known BRCA1 or BRCA2 mutation or moderate to high risk of developing BC defined as >17% lifetime risk from age 20 or >3% risk between 40-50 years
4. Ovulatory menstrual cycles defined as serum progesterone =15nmol 7 days prior to expected onset of menses
5. eGFR = 40mls/min/1.73m2 in view of requirement for gadolinium contrast MRI scans
6. Willing and able to provide informed consent to undergo all trial procedures

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 30; UK Sample Size: 30

Key exclusion criteria
1. Personal history of breast, uterine, cervical or ovarian cancer
2. Breast feeding within the last 3 months
3. Pregnant or planning for pregnancy in the next 6 months. Pregnancy must be excluded with serum ßhCG <5nmol during screening.
4. Known hypersensitivity to radiological contrast media or to ulipristal acetate or any of its excipients (microcrystalline cellulose, mannitol, croscarmellose sodium, talc, magnesium stearate)
5. Current treatment with:
5.1. Anti-estrogens (e.g. tamoxifen or raloxifene), GnRH analogue therapy (e.g. goserelin or buserelin) or hormonal contraceptives including androgens such as cyproterone acetate. Such treatments must have been stopped for at least6 months and regular menstrual cycles resumed
5.2. Corticosteroids at any dose, these must have been stopped for at least 1 month with low likelihood that retreatment will be required
5.3. Antiplatelet or anticoagulant therapy – must have been stopped for at least 7 days and clotting be at satisfactory levels
5.4. Moderate or potent inhibitors of CYP3A4
5.5. Potent inducers of CYP3A4
6. APTT and PT outside the normal institutional ranges. Hb <100g/l and platelet count <150x109 /l
7. Serum creatinine, bilirubin, ALT, ALP or LDH >1,5xULN
8. Contraindications to MRI, such as intracranial aneurysm clips, implanted electrical devices and intra-ocular metallic foreign bodies
9. Co-morbidity that would put the patient at increased risk such as recognised bleeding diathesis, moderate to severe hepatic impairment, moderate or severe renal impairment (eGFR <40 ml/min/1.73m2), severe asthma not adequately controlled with corticosteroids (note steroid usage precludes trial entry)
10. Prior breast enhancement/augmentation surgery
11. Genital bleeding of unknown aetiology

Date of first enrolment
01/09/2015

Date of final enrolment
31/08/2016

Locations

Countries of recruitment

England

United Kingdom

Study participating centre
University Hospital of South Manchester
Genesis Prevention Centre
Wythenshawe Hospital
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Sponsor information

Organisation
University Hospital of South Manchester

Sponsor details
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Charity

Funder Name
Breast Cancer Campaign

Alternative Name(s)

Funding Body Type

Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No