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A study to assess the effects of enobosarm on early breast cancer

Submission date 23/01/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 26/01/2017	**Overall study status** Completed	
Last Edited 09/01/2023	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-enobosarm-for-women-with-early-breast-cancer-emerald

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2016-000543-13

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
31856

Study information

Scientific Title
A window of opportunity study to assess the biological effects of enobosarm in oestrogen receptor positive, androgen receptor positive early breast cancer

Acronym
EMERALD

Study objectives
The aim of this study is to determine the effect of enobosarm, a selective androgen receptor modulator, using a "window of opportunity study" in women with early breast cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West – Haydock Research Ethics Committee, 28/12/2016, ref: 16/NW/0807

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

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
Specialty: Cancer, Primary sub-specialty: Breast Cancer; UKCRC code/ Disease: Cancer/ Malignant neoplasm of breast

Interventions
Current interventions as of 24/09/2018:
Patients are screened, consented and then randomised onto the trial using the LCTUs TARDIS (Treatment Allocation RanDomIsation System) which for EMERALD uses randomly permuted blocks based on stratified lists to a ratio of 3:1 (treatment : standard of care).

Treatment arm: Patients will take 9 mg of enobosarm capsules orally every day for 14 (+4) days, before pre-scheduled surgery/research core biopsy (within 24 hours of last dose). Patients will be followed up for 14 days after surgery/research core biopsy for adverse events. Blood (20 ml or about 4 teaspoons) will be taken at the Baseline Visit (Day 1) and the Tissue Collection Visit (Day 14). The sample from the core biopsy (FFPE block) will be requested to measure Ki67 at baseline and a sample (FFPE block) will be taken from the surgical specimen/research core biopsy specimen.

Standard care arm: Patients will have their pre-scheduled surgery/research core biopsy as planned after 14 (+4) days. Blood (20 ml or about 4 teaspoons) will be taken at the Baseline Visit (Day 1) and the Tissue Collection Visit (Day 14). The sample from the core biopsy (FFPE block) will be requested to measure Ki67 at baseline and a sample (FFPE block) will be taken from the surgical specimen/research core biopsy specimen.

Previous interventions:
Patients are screened, consented and then randomised onto the trial using the LCTUs TARDIS (Treatment Allocation RanDomIsation System) which for EMERALD uses randomly permuted blocks based on stratified lists to a ratio of 3:1 (treatment : standard of care).

Treatment arm: Patients will take 9mg of enobosarm capsules orally every day for 14(+4) days, before pre-scheduled surgery (within 24 hours of last dose). Patients will be followed up for 14 days after surgery for adverse events. Blood (20ml or about 4 teaspoons) will be taken at the baseline visit (Day 1), the mid-treatment visit (Day 7) and the surgery visit (Day 14). The sample from the core biopsy (FFPE block) will be requested to measure Ki67 at baseline and a sample (FFPE block) will be taken from the surgical specimen.

Standard care arm: Patients will have their pre-scheduled surgery as planned after 14 (+4) days. Blood (20ml or about 4 teaspoons) will be taken at the baseline visit (Day 1), the mid-treatment visit (Day 7) and the surgery visit (Day 14). The sample from the core biopsy (FFPE block) will be requested to measure Ki67 at baseline and a sample (FFPE block) will be taken from the surgical specimen.

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Current primary outcome measure as of 24/09/2018:
Change in the proliferation marker Ki67 (% positive tumour cells) determined by tissue immunohistochemistry at baseline and 2 weeks.

Previous primary outcome measure:
Reduction in the proliferation marker Ki67 (% positive tumour cells) determined by tissue immunohistochemistry at baseline and 2 weeks.

Secondary outcome measures
Current secondary outcome measures as of 24/09/2018:
1. Amount of cleaved caspase 3 determined by tissue immunohistochemistry at baseline and two weeks
2. Expression of PSA, Gross Cystic Disease Fluid Proteins (GCDFP)-24 &-15; PgR, GREB1 by tissue immunohistochemistry at baseline and two weeks
3. Amount in serum levels of circulating steroidogenic hormones oestradiol, oestrone, oestrone sulfate, androstenedione, follicle stimulating hormone, luteinizing hormone, DHT, progesterone, sex hormone binding globulin (SHBG) and total testosterone in blood determined by blood assay at baseline and two weeks; free testosterone to be derived from SHBG and total testosterone
4. Amount in serum levels of PSA and steroidogenic hormones determined by blood assay at baseline and two weeks

Previous secondary outcome measures:
1. Amount of cleaved caspase 3 determined by tissue immunohistochemistry at baseline and two weeks
2. Expression of PSA, Gross Cystic Disease Fluid Proteins (GCDFP)-24 &-15; PgR, GREB1 by tissue immunohistochemistry at baseline and two weeks
3. Amount in plasma levels of circulating steroidogenic hormones oestradiol, oestrone, oestrone sulfate, androstenedione, follicle stimulating hormone, luteinizing hormone, DHT, progesterone, sex hormone binding globulin (SHBG) and total testosterone in blood determined by blood assay at baseline and two weeks; free testosterone to be derived from SHBG and total testosterone
4. Amount in plasma levels of PSA and steroidogenic hormones determined by blood assay at baseline and two weeks

Overall study start date
11/12/2015

Completion date
31/05/2019

Eligibility

Key inclusion criteria

Current inclusion criteria as of 24/09/2018:
1. Females 16 years of age or older
2. Histologically confirmed ER positive breast cancer (Allred ≥3)
3. AnR positive breast cancer (defined as ≥10% nuclear AnR staining by immunohistochemistry)
4. Any HER2 status
5. Tumour measuring ≥14 mm in longest diameter by ultrasound (US) examination, MRI or mammogram
6. Postmenopausal as defined by one of the following criteria:
6.1. Women ≥55 years of age with an intact uterus and amenorrhoea ≥12 months at the time of diagnosis (or documented or current FSH and oestradiol levels within the postmenopausal range (as per local institutional/laboratory standard))
6.2. Prior bilateral oophorectomy
6.3. Documented or current FSH and oestradiol levels within the postmenopausal range (as per local institutional/laboratory standard) in women aged <55 years or in women who have had a hysterectomy with intact ovaries
7. Eastern Cooperative Oncology Group (ECOG) performance status 0, 1 or 2
8. 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 ≤2.5 ULN and ALP ≤2.5 ULN
9. Acceptable risk of bleeding (e.g. bleeding diathesis, warfarin) as assessed by the PI (if the PI is unsure the CI will make the final decision)
10. Written informed consent
11. Able to comply with treatment and follow up

Previous inclusion criteria:
1. Females 16 years of age or older
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3. AnR positive breast cancer (defined as ≥10% nuclear AnR staining by immunohistochemistry)
4. Any HER2 status
5. Tumour measuring ≥14mm in longest diameter by ultrasound (US) examination, MRI or mammogram
6. Postmenopausal as defined by one of the following criteria:
6.1. Amenorrhoea >12 months at the time of diagnosis and an intact uterus, with FSH and oestradiol in the postmenopausal ranges
6.2. Prior bilateral oophorectomy
6.3. FSH and oestradiol levels within the postmenopausal range (as per local practice) in women aged <55 years who have undergone hysterectomy
7. Eastern Cooperative Oncology Group (ECOG) performance status 0, 1 or 2
8. 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 ≤2.5 ULN and ALP ≤2.5 ULN
9. Acceptable risk of bleeding (e.g. bleeding diathesis, warfarin) as assessed by the PI (and where the PI is unsure the CI)
10. Written informed consent
11. Able to comply with treatment and follow up

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned Sample Size: 147; UK Sample Size: 147

Key exclusion criteria
Current exclusion criteria as of 24/09/2018:
1. Inoperable breast cancer
2. Males
3. Inflammatory tumours
4. Evidence of metastatic disease
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. Prior endocrine therapy of chemotherapy for breast cancer
7. Concomitant use (defined as use within 12 weeks prior to entry) of HRT or any other oestrogen-containing medication or supplement (including vaginal oestrogens and phytoestrogens)
8. Previous use of oestrogen implants within the last 12 weeks
9. Uncontrolled abnormalities of serum potassium, sodium, calcium or magnesium levels
10. Evidence of uncontrolled active infection
11. 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
12. Participation in a clinical trial of an IMP in the last 30 days

Previous inclusion criteria:
1. Inoperable breast cancer
2. Inflammatory tumours
3. Evidence of metastatic disease
4. 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)
5. Evidence of bleeding diathesis
6. Prior endocrine therapy of chemotherapy for breast cancer
7. Concomitant use (defined as use within 12 weeks prior to entry) of HRT or any other oestrogen-containing medication or supplement (including vaginal oestrogens and phytoestrogens)
8. Previous use of oestrogen implants at ANY time
9. Uncontrolled abnormalities of serum potassium, sodium, calcium or magnesium levels
10. Evidence of uncontrolled active infection
11. 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
12. Participation in a clinical trial of an IMP in the last 30 days

Date of first enrolment
01/03/2017

Date of final enrolment
28/02/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cancer Research UK Liverpool Cancer Trials Unit
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Study participating centre
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Study participating centre
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M8 5RB

Study participating centre
Clatterbridge Hospital
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CH63 4JY

Study participating centre
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

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

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
30/11/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request following the process laid out on the LCTU website here or LCTU.org.uk > About the LCTU > Data Sharing.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 6.0	17/05/2021	09/01/2023	No	No
HRA research summary			28/06/2023	No	No