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Endocrine +/- Surgical Therapy for Elderly women with Mammary cancer

Submission date 14/03/2007	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 30/04/2007	**Overall study status** Stopped	
Last Edited 16/10/2012	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
UI06/7672 and 112984

Study information

Scientific Title

Acronym
ESTEeM

Study objectives
That Primary Endocrine Therapy (PET) with Arimidex is non-inferior to surgery plus adjuvant Arimidex therapy in terms of overall survival.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval has been received from the Central Manchester Research Ethics Committee on the 12th Decemeber 2006 (ref: 06/Q1407/250).

Study design
Randomised multicentre controlled open label prospective parallel group two-armed non-inferiority clinical trial with equal randomisation

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Breast cancer

Interventions
Please note that as of 08/01/2010 the record status was updated to 'Stopped' due to problems with recruitment and funding being withdrawn. The exact date of closure was 5th November 2009.

Arimidex alone arm:
The standard therapeutic dose of Arimidex (1 mg orally, once daily) will be given until five years post-randomisation and whilst the disease remains responsive (i.e., absence of metastatic disease and absence of new primary breast cancer), there is continued clinically beneficial response of the primary tumour, and the patient tolerates therapy.

Surgery plus Arimidex arm:
Women will be offered a choice of surgery appropriate to their preferences, the extent of their disease and their fitness for anaesthesia. In all cases ALL palpable disease MUST be excised with a clear margin. Failure to achieve a clear margin will necessitate further surgery to re-excise the involved margins unless the patient has become unfit or refuses.

The standard therapeutic dose of Arimidex (1 mg orally, once daily) will be given until five years post-randomisation or until local/regional disease recurrence, new primary breast cancer, metastatic disease or drug intolerance develops. Arimidex therapy is to start within four weeks of the final date of surgery.

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Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Arimidex

Primary outcome measure
To compare surgery plus Arimidex with Arimidex alone (PET) in older women with ER positive breast cancer in terms of overall survival in order to determine whether Arimidex alone provides anti-cancer efficacy which is not inferior to surgery plus adjuvant Arimidex therapy. Overall survival will be measured from the time of randomisation to the date of death from any cause.

Secondary outcome measures
To compare surgery plus Arimidex with Arimidex alone (PET) in older women with ER positive breast cancer in terms of:
1. Quality of Life (QoL), in order to determine whether Arimidex alone is superior to surgery plus Arimidex in terms of QoL: quality of life data will be recorded at baseline, at an early post-randomisation visit (six weeks post randomisation on the Arimidex alone arm and two weeks post-surgery on the Surgery plus Arimidex arm) and at four monthly time points up to 24 months and then annually to five years post randomisation:
a. Functional Assessment of Cancer Therapy for Breast cancer and Endocrine Sub-scale (FACT-B+ES) will be completed at all of the above time points and at progression or recurrence/new breast primary/metastatic disease
b. A Mini Mental State Examination (MMSE) and an Instrumental Activities of Daily Living (IADL) questionnaire will be completed at baseline

c. An Activities of Daily Living (ADL) questionnaire will be completed at baseline, at the early post-randomisation visit and at the four month visit
d. A Geriatric Depression Score questionnaire will be completed at all visits up to 24 months
e. A Patient Perceptions Questionnaire will be given at baseline, 12 months and at progression or local/regional recurrence
2. Breast cancer specific survival: breast cancer specific survival will be measured from the time of randomisation to the date of death related to breast cancer
3. Failure-free survival: failure-free survival is measured from the time of randomisation to the date of first investigation of either local or regional disease recurrence (for patients in the Surgery plus Arimidex arm), disease progression (for patients in the Arimidex alone arm), metastatic disease, or death from any cause, whichever date is the earliest
4. Local disease control, as secondary outcome measures to assess non-inferior anti-cancer efficacy of Arimidex alone: treatment response for patients randomised to Arimidex alone will be categorised as either clinically beneficial (which will include complete response, partial response, or static disease) or Progressive Disease (PD), according to Response Evaluation Criteria in Solid Tumours (RECIST) criteria. Progressive disease will be classed as failure of local disease control. Duration of local disease control is defined as the time from randomisation to PD/local recurrence/regional recurrence in the axilla
5. Health economic assessment: the health economics assessment using the EuroQoL (EQ-5D) instrument will be completed at the early post-randomisation visit, 4, 8, 12, 16, 20 and 24 months post-randomisation, and yearly thereafter until five years post-randomisation and at progression or recurrence/new breast primary/metastatic disease

Contralateral breast cancer rates, treatment related adverse events and skeletal related events will also be summarised.

Overall study start date
30/04/2007

Completion date
29/04/2010

Reason abandoned (if study stopped)
Lack of funding/sponsorship and Participant recruitment issue

Eligibility

Key inclusion criteria
1. Female patients equal to or over 75 years of age*
2. Primary operable (TNM categories: T1, T2, T3, N0, N1, M0) invasive breast cancer (core biopsy or diagnostic incision biopsy proven)
3. Suitable for surgery. This may include local or general anaesthesia, and must remove all clinically palpable disease with clear pathological margins. Axillary staging for the clinically un-involved axilla will depend on local protocols and patient tolerance
4. Moderate or strongly oEstrogen Receptor (ER) positive, i.e. H score greater than or equal to 100 or Allred score greater than or equal to five
5. Ability to give informed consent
6. Written informed consent
7. Willing to complete the questionnaires for the additional trial evaluations
8. Able to start trial treatment within four weeks of randomisation

* The inclusion criteria do not restrict for health status as we wish to leave flexibility for surgeons around the country to offer trial participation to those women for whom they feel PET is a reasonable option. This will give Surgeons discretion to select patients according to their own current practice and also give us a breadth of patient fitness levels, which will enable discrimination of those who are and are not suitable for PET on analysis.

Participant type(s)
Patient

Age group
Senior

Sex
Female

Target number of participants
1200

Key exclusion criteria
1. Disease unsuitable for surgery, e.g., locally advanced or metastatic disease, extreme physical frailty precluding adequate surgery under either local or general anaesthesia
2. Multifocal or bilateral invasive breast cancer
3. Previous invasive breast cancer
4. Previous or concurrent anti-oestrogen therapy for breast cancer
5. Previous solid cancers other than breast in the last ten years (except in the case of completely excised basal cell carcinoma/nonmelanomatous skin malignancy)
6. Inability to comply with study procedures
7. History of severe renal impairment (creatinine clearance less than 20 ml/min)
8. History of moderate or severe hepatic disease (transaminases greater than 3 x Upper Limit of Normal [ULN] or bilirubin greater than 1.5 x ULN)
9. Known hypersensitivity to anastrozole or to any of the following excipients: Lactose Monohydrate, Povidone, Sodium Starch Glycollate, Magnesium Stearate, Hypromellose, Macrogol 300, or Titanium Dioxide
10. Concurrent Hormone Replacement Therapy (HRT) or therapy with any other oestrogen containing preparation
11. Hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption

The presence of osteoporosis at baseline is NOT an exclusion criteria.

Date of first enrolment
30/04/2007

Date of final enrolment
29/04/2010

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Academic Surgical Oncology Unit
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Sponsor information

Organisation
The University of Sheffield (UK)

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Sponsor type
University/education

Website
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ROR
https://ror.org/05krs5044

Funder(s)

Funder type
Industry

Funder Name
Cancer Research UK (UK) (ref: C20169/A7251)

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

Funder Name
Astra Zeneca (UK) (ref: D5392L00021)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration