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SOLE: Study Of Letrozole Extension in post-menopausal women with breast cancer

Submission date	Recruitment status	[_] Prospectively registered
02/09/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
03/11/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
27/07/2022	Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-letrozole-after-hormone-therapy-early-breast-cancer-postmenopausal-women

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2007-001370-88

IRAS number

ClinicalTrials.gov number
NCT00553410

Secondary identifying numbers
IBCSG 35-07/BIG 1-07

Study information

Scientific Title
A phase III trial evaluating the role of continuous letrozole versus intermittent letrozole following 4 to 6 years of prior adjuvant endocrine therapy for post-menopausal women with hormone-receptor positive, node positive early stage breast cancer

Acronym
SOLE

Study objectives
In 2006, the standard duration of adjuvant endocrine therapy for breast cancer (either selective estrogen receptor modulators [SERMs] or aromatase inhibitor [AI]) is five years. Patients who receive extended adjuvant letrozole for five years following approximately five years of tamoxifen obtain further benefit compared with the five years of tamoxifen alone. Similarly, benefit has been demonstrated for switching from tamoxifen to an AI after 2 to 3 years of tamoxifen to complete five years of endocrine therapy, as well as initiating therapy with AI following surgery and administering the AI for five years.

Questions remain about the optimal duration and best schedule of AIs in the extended adjuvant setting. This trial tests the hypothesis that introducing 3-month treatment-free intervals during the course of five years of extended adjuvant letrozole will improve disease-free survival. This hypothesis is based on the theoretical principle that letrozole withdrawal for 3 months will permit some estrogenic stimulation which makes residual resistant disease susceptible to letrozole reintroduction.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled phase III trial

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
Breast cancer

Interventions
Arm A - Continuous letrozole 2.5 mg daily for 5 years
Arm B - Intermittent letrozole 2.5 mg daily for first 9 months of years 1 through 4, followed by 12 months in year 5

Intervention Type
Drug

Phase
Phase III

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

Primary outcome measure
Disease-free survival (DFS) is defined as the time from randomisation to local (including invasive recurrence restricted to the breast after breast conserving treatment), regional or distant relapse, contralateral breast cancer, appearance of a second (non-breast) malignancy, or death from any cause, whichever occurs first. Appearance of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) either in the ipsilateral or in the contralateral breast will not be considered as an event for DFS.

Event driven analyses - final analysis requires 647 events, interim analysis at 259 and 453 events.

Secondary outcome measures
1. Overall survival (OS) is defined as the time from randomisation to death from any cause
2. Distant disease-free survival (DDFS) is defined as the time from randomisation to any recurrent or metastatic disease in distant sites (i.e., other than the local mastectomy scar/chest wall/skin, the ipsilateral breast in case of breast conservation, or the ipsilateral axilla and internal mammary lymph nodes), second (non-breast) malignancy, or death from any cause, whichever occurs first
3. Breast cancer free interval (BCFI) is defined as the time from randomisation to local (including recurrence restricted to the breast after breast conserving treatment), regional, or distant relapse, or contralateral breast cancer. In calculating BCFI, second (non-breast) malignancies are ignored and deaths without cancer event are censored at the time of death as a competing event. Appearance of DCIS or LCIS either in the ipsilateral or in the contralateral breast is not considered a BCFI event, but should be recorded on the Follow-up Form (E)
4. Sites of first DFS failure
5. Second (non-breast) malignancies
6. Deaths without prior cancer event
7. Adverse events

Event driven analyses - final analysis requires 647 events, interim analysis at 259 and 453 events.

Overall study start date
01/11/2007

Completion date
31/12/2018

Eligibility

Key inclusion criteria
1. Patients must be post-menopausal; definitive confirmation of post-menopausal status is required
2. Patients must be accessible for follow-up
3. At diagnosis, patients must have had operable, non-inflammatory breast cancer
4. Patients must be clinically disease-free at randomisation
5. Patients must have had steroid hormone receptor positive tumours (oestrogen receptor [ER] and/or progesterone receptor [PgR]), determined by immunohistochemistry, after primary surgery and before commencement of prior endocrine therapy
6. Following primary surgery, eligible patients must have had evidence of lymph node involvement either in the axillary or internal mammary nodes, but not supraclavicular nodes
7. There must have been no evidence of recurrent disease or distant metastatic disease at any time prior to randomisation
8. Patients must have had proper local treatment including surgery with or without radiotherapy for primary breast cancer with no known clinical residual loco-regional disease
9. Patients must have clinically adequate hepatic function
10. Patients must have completed 4 to 6 years of prior adjuvant endocrine therapy with SERMs, AI or a sequential combination of both. When calculating 4 - 6 years, neoadjuvant endocrine therapy should not be included.
11. Patients must have stopped prior endocrine SERM/AI therapy, and must be randomized within 12 months (1 year) of the last dose of prior endocrine SERM/AI therapy
12. Patients may have received any type of prior adjuvant therapy, including but not limited to neoadjuvant chemotherapy, neoadjuvant endocrine therapy, adjuvant chemotherapy, trastuzumab, ovarian ablation, GnRH analogues, lapatinib
13. Patients must have stopped hormone replacement therapy (HRT), bisphosphonates (except for treatment of bone loss), or any investigational agent at randomisation
14. Pathology material from the primary tumour must be available for submission for central review as part of the quality control measures for this protocol
15. Written informed consent (IC) must be signed and dated by the patient and the investigator prior to randomisation
16. Written consent to pathology material submission, indicating the patient has been informed of and agrees to tissue material use, transfer and handling, must be signed and dated by the patient and the investigator prior to randomisation
17. Females, no defined age limits

Participant type(s)
Patient

Age group
Other

Sex
Female

Target number of participants
UK: 300; total International sample including UK: 4800; European economic area: 3500

Total final enrolment
4884

Key exclusion criteria
1. Patients who have had bilateral breast cancer
2. Patients who have had a bone fracture due to osteoporosis at any time during the 4-6 years of prior endocrine SERM/AI therapy
3. Patients who have had any previous or concomitant malignancy EXCEPT adequately treated: basal or squamous cell carcinoma of the skin, in situ carcinoma of the cervix or bladder, contra- or ipsilateral in situ breast carcinoma
4. Patients who have had any other non-malignant systemic diseases (cardiovascular, renal, lung, etc.) that would prevent prolonged follow-up
5. Patients with psychiatric, addictive, or any disorder which compromises compliance with protocol requirements

Date of first enrolment
01/11/2007

Date of final enrolment
08/10/2012

Locations

Countries of recruitment
Australia

Belgium

Chile

Denmark

Germany

Hungary

Italy

New Zealand

Peru

Scotland

South Africa

Sweden

Switzerland

United Kingdom

Study participating centre
University of Dundee
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Sponsor information

Organisation
European Institute of Oncology (IEO) (Italy)

Sponsor details
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Sponsor type
Research organisation

Website
http://www.ieo.it/inglese/index.asp

ROR
https://ror.org/02vr0ne26

Funder(s)

Funder type
Research organisation

Funder Name
International Breast Cancer Study Group (UK) - funding for UK arm of trial

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
31/12/2019

Individual participant data (IPD) sharing plan
The data sharing plans for the study are currently unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			10/09/2019	No	No
Results article	results	01/01/2018	10/09/2019	Yes	No
Plain English results			27/07/2022	No	Yes