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

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

Contact name
Prof Alastair Thompson

Contact details
Professor of Surgical Oncology
University of Dundee
Ninewells Hospital & Medical School
Dundee
United Kingdom
DD1 9SY
+44 (0)1382 633936
a.m.thompson@dundee.ac.uk

Additional identifiers

ClinicalTrials.gov (NCT)
NCT00553410

Clinical Trials Information System (CTIS)
2007-001370-88

Protocol serial number
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

Primary study design
Interventional

Study design
Randomised controlled phase III trial

Study type(s)
Treatment

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(s)
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.

Key secondary outcome(s)
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.

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

Healthy volunteers allowed
No

Age group
Other

Sex
Female

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
United Kingdom

Scotland

Australia

Belgium

Chile

Denmark

Germany

Hungary

Italy

New Zealand

Peru

South Africa

Sweden

Switzerland

Study participating centre
University of Dundee
Dundee
United Kingdom
DD1 9SY

Sponsor information

Organisation
European Institute of Oncology (IEO) (Italy)

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

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?
Results article	results	01/01/2018	10/09/2019	Yes	No
Basic results			10/09/2019	No	No
Plain English results			27/07/2022	No	Yes