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An Open-label, Randomized Study Comparing 3 Years Tamoxifen Versus 3 Years Letrozole as Continuation of Adjuvant Treatment of Postmenopausal Women with Estrogen Receptor (ER) Positive and/or Progesterone Receptor (PR) Positive Early Breast Cancer Who Already Completed 2 years Adjuvant Tamoxifen. A Large Thai Multicenter Study.

Submission date
20/09/2005

Recruitment status
No longer recruiting

Registration date
12/10/2005

Overall study status
Completed

Last Edited
24/09/2007

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Study website
https://www.lotus-f.net/portal

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CFEM345DTH01

Study information

Scientific Title

Acronym
LOTUS trial

Study objectives
Letrozole is more effective than tamoxifen in first line treatment of metastatic breast cancer. In advanced disease, letrozole has been associated with significantly more tumor regression than anastrozole, especially in patients with unknown ER status. Letrozole has also been shown to be more effective than tamoxifen in the neoadjuvant treatment of breast cancer. Recently, anastrozole has been shown to induce a reduction in the rate of relapse as compared with tamoxifen in the adjuvant setting. Extended adjuvant therapy with letrozole after 5 years tamoxifen has been demonstrated to reduce the risk of recurrence and to improve significantly the diseasefree survival of postmenopausal women with early breast cancer. International studies are investigating the effect of letrozole compared to tamoxifen in the adjuvant treatment of early breast cancer patients. Few Asian patients are included. A large number of early breast cancer patients in Thailand are currently being treated with tamoxifen as adjuvant treatment.
It is not yet clear whether aromatase inhibitor can replace tamoxifen as adjuvant treatment for early breast cancer. Sequence and timing of tamoxifen and aromatase inhibitor treatment in adjuvant treatment still needs to be determined as well.
The goals of this study are the following:
1. To determine whether the replacement, as adjuvant therapy, of tamoxifen by letrozole for the last 3 years of a standard 5 year treatment period can reduce the risk of treatment failure in early breast cancer patients
2. To conduct this study in a Thai population
3. To compare the 2 treatments in terms of safety and tolerability

Approximately 1000 patients from up to 15 centers across Thailand will be enrolled into this study. The patient population will include postmenopausal women with resected Stage I, II, or

IIIa, ER+ and/or PR+ breast cancer who have received 2 years of adjuvant tamoxifen and who have no clinical or radiological evidence of recurrent or metastatic disease before randomization. Pre-menopausal women who are/become amenorrheic due to either chemotherapy or Luteinizing Hormone Releasing Hormone (LHRH) use may participate in the study. Patients must have undergone complete tumor resection and margins of the resected specimen must be microscopically free of tumor.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Open-label, Randomized Study

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
ER positive and/or PR positive early breast cancer

Interventions
After providing consent, patients will be screened for eligibility.
Eligible patients will be registered at any time up to 2 years (+/- 3 months) of tamoxifen treatment. Tamoxifen treatment had to be started at a dose of 20 mg/day for 2 years. After that, patients event-free will be randomly assigned to continue receiving tamoxifen for an additional 3 years or receiving letrozole 2.5 mg/day for 3 years.
After completion of treatment, patients should be followed up for study end points for 3 years.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome measure

Compare these treatment regimens in terms of disease free survival (DFS)

Secondary outcome measures
1. Compare these treatment regimens in terms of overall survival (OS)
2. Compare these treatment regimens in terms of safety and tolerability in the Thai patient population

Overall study start date
01/01/2005

Completion date
31/12/2012

Eligibility

Key inclusion criteria
1. Patients with stage I, II or IIIa adenocarcinoma of the breast at diagnosis. Patients with breast cancer whose tumor has been completely removed macroscopically and margins of the resected tumor have been microscopically free of tumor. If appropriate, additional local (e.g. radiotherapy) and/or systemic (i.e. adjuvant chemotherapy) treatments are allowed.
2. Postmenopausal status defined by one of the following:
a. Age ≥55 years with cessation of menses
b. Age <55 but no spontaneous menses for at least 1 year
c. Age <55 and spontaneous menses within the past 1 year, but currently amenorrheic (e.g. spontaneous, or secondary to hysterectomy), and with postmenopausal gonadotrophin levels (luteinizing hormone and follicle stimulating hormone levels >40 IU/l) or postmenopausal estradiol levels (<5 ng/dl) or according to the definition of 'postmenopausal range' for the laboratory involved
d. Bilateral oophorectomy
3. Patients whose tumors are either ER+ and/or PR+ (defined as ER and/or PR ≥10 fmol/mg cytosol protein; or ≥10% of the tumor cells positive by immunohistochemical evaluation)
4. Under tamoxifen therapy for 2 years before randomization
5. At randomization, patients must have no clinical or radiological evidence of distant metastasis, and no other concomitant malignancy (confirmed by mammography, chest X-ray or computed tomography [CT] scan, bone scan and liver US)
6. Eastern Cooperative Oncology Group (ECOG) performance status of 02
7. No prior treatment with letrozole
8. Patients must be accessible for follow-up
9. Signed written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants

1000

Key exclusion criteria
1. Patients with any clinical or radiological evidence of distant spread of their disease at any point before randomization
2. Patients with other non-malignant systemic diseases including uncontrolled infections, uncontrolled type 2 diabetes mellitus, uncontrolled thyroid dysfunction, cardiovascular, renal, hepatic, and lung diseases which would prevent prolonged follow-up. Patients with previous history of thrombosis or thromboembolism can be included only if medically suitable. Patients with a known history of human immunodeficiency virus (HIV) are excluded.
3. Total serum calcium >2.75 mmol/l (11.0 mg/dl)
4. White Blood Cell Count (WBC) <3.0 x 10^9/l or granulocytes <1.5 x 10^9/l, platelets <100 x 10^9/l
5. Aspartate amino transferase (AST)/serum glutamic oxaloacetic transaminase (SGOT) and/or alanine amino transferase (ALT)/serum glutamic pyruvic transaminase (SGPT) >3 upper limit of normal (ULN) in combination with other laboratory and clinical abnormalities indicating liver insufficiency to a degree that precludes dosing with letrozole (Child-Pugh grade C)
6. Patients with abnormal renal function as defined by a serum creatinine ≥3 mg/dl (265.2 mmol /l)
7. Previous history of fracture within 2 years
8. Patients treated with other systemic investigational drug(s) and/or device(s) within the past 30 days
9. History of non-compliance to medical regimens and patients who are considered potentially unreliable
10. Mental illness that precludes the patient from giving informed consent

Date of first enrolment
01/01/2005

Date of final enrolment
31/12/2012

Locations

Countries of recruitment
Thailand

Study participating centre
Department of Radiology
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Sponsor information

Organisation

Thai Breast Cancer Study Group (Thailand)

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Sponsor type
Other

Website
http://www.chulacancer.net

Funder(s)

Funder type
Industry

Funder Name
Partially sponsored by Novartis Thailand

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