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TEAM II: a randomised, multicentre, prospective, phase III trial investigating neoadjuvant hormonal therapy with exemestane for three versus six months (TEAM IIa) and/or the efficacy and safety of the addition of ibandronate to adjuvant hormonal therapy in post-menopausal women with hormone receptor positive early breast cancer (TEAM IIb)

Submission date
28/12/2006

Recruitment status
No longer recruiting

Registration date
28/12/2006

Overall study status
Completed

Last Edited
13/11/2008

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
http://www.ikcnet.nl

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
BOOG 2006-04; NTR785

Study information

Scientific Title

Acronym
TEAM II

Study objectives
TEAM IIa: Six months of neoadjuvant therapy with exemestane is superior to three months with respect to the rate of downsizing in post-menopausal women with oestrogen receptor (ER) positive (more than 50% of tumour cells positive) primary breast cancer.

TEAM IIb: Adjuvant systemic therapy combined with oral ibandronate results in an improved three-years disease free survival compared to adjuvant systemic therapy without ibandronate in post-menopausal women with hormone receptor positive primary breast cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Received from the Protocol Reviewing committee of the Netherlands Cancer Institute/Antoni van Leeuwenhoek Ziekenhuis (Protocol Toetsingscommissie van het Nederlands Kanker Insitituut/Antoni van Leeuwenhoek Ziekenhuis) on the 28th September 2006 (4th amendment) (ref: PTC06.1431/M06TM2).

Study design
Multicentre, randomised, active controlled, parallel group trial

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

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

Interventions
TEAM IIa:
Patients will be randomised (1:1) between three versus six months of neoadjuvant therapy with exemestane (25 mg once daily). After surgery, patients may be randomised in the adjuvant part of the study (TEAM IIb) if the adjuvant inclusion criteria are met.

TEAM IIb:
Patients will be randomised (1:1) to oral ibandronate (50 mg once daily) for three years added to standard adjuvant systemic treatment or to standard adjuvant systemic therapy only. Hormonal treatment will be according to the most recent NABON guideline. Exemestane will be used as aromatase inhibitor.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Exemestane, ibandronate

Primary outcome measure
TEAM IIa:
Objective response rate (immediately prior to surgery) of the primary breast tumour, assessed by palpation, which is preferably performed by the same person.

TEAM IIb:
Three years disease free survival.

Secondary outcome measures
TEAM IIa:
1. Objective response rate of the breast tumour by mammography (Response Evaluation Criteria in Solid Tumors [RECIST])
2. Objective response rate of the breast tumour assessed by ultrasound (RECIST)
3. Objective response rate of the breast tumour assessed by magnetic resonance imaging (MRI) (RECIST)
4. Objective response rate of the regional lymph nodes assessed by ultrasound (RECIST)
5. Pathological complete response rate of primary breast cancer

6. Pathological complete response rate of eventually positive lymph nodes
7. Number of patients who required a mastectomy before neoadjuvant therapy and for whom breast conserving surgery became feasible after neoadjuvant therapy (independent of actual surgical treatment received)
8. Number of patients who required a mastectomy before neoadjuvant therapy and who received breast conserving surgery after neoadjuvant therapy
9. Determination of predictive factors able to predict clinical and pathological response
10. Collection of tumour samples for translational research to improve diagnostics and treatment of breast cancer

TEAM IIb:
1. Time to and rate of bone metastases as first occurrence, in patients treated with these regimens
2. Time to and rate of bone metastases, per se, in patients treated with these regimens
3. Time to and rate of visceral and other distant metastases in patients treated with these regimens
4. Time to and rate of local- and locoregional recurrences in patients treated with these regimens
5. Time to and rate of contralateral breast cancer in patients treated with these regimens
6. Five years disease free survival
7. Overall survival (all cause mortality and breast cancer specific mortality) in patients treated with these regimens
8. Safety and toxicity of ibandronate in patients treated with this bisphosphonate
9. Specific prognostic indicators for the development of bone metastases and factors that are able to predict specific benefit from ibandronate treatment in these patients using tissue micro-array and other modern techniques

Overall study start date
01/10/2006

Completion date
01/10/2010

Eligibility

Key inclusion criteria
TEAM IIa:
1. Female patients with histologically, by core needle biopsy-proven, invasive adenocarcinoma of the breast
2. Any tumour with a size more than or equal to 2 cm (except cT4d = inflammatory breast cancer)
3. Indication to receive adjuvant hormonal therapy according to most recent Nationaal Borstkanker Overleg Nederland (NABON) guideline
4. ER expression more than 50% (progesterone receptor [PgR] either positive or negative)
5. Post-menopausal women: post-menopausal defined as:
5.1. Age more than or equal to 50 and amenorrhoea for more than one year
5.2. Bilateral surgical oophorectomy and no hormone replacement therapy (HRT) (any age is acceptable)
5.3. Age less than 50 with natural amenorrhoea more than one year at breast cancer diagnosis (and uterus in situ)
5.4. Post-menopausal due to chemotherapy will be excluded
5.5. In case of doubt about menopausal status, assessment of follicle stimulating hormone (FSH), luteinising hormone (LH) and oestradiol has to be performed to define the menopausal status

6. World Health Organization (WHO) performance status zero or one
7. Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule
8. Accessible for follow-up for the duration of the trial
9. Before randomisation, patients must be capable of understanding the trial and give written informed consent according to International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use/Good Clinical Practice (ICH /GCP) and local Institutional Review Board (IRB) guidelines

TEAM IIb:
1. Histological confirmed invasive adenocarcinoma of the breast
2. Stage I to III breast cancer
3. Completed adequate surgical treatment
4. (Neo)adjuvant chemotherapy, radiotherapy and/or trastuzumab are allowed
5. Indication to receive adjuvant hormonal therapy according to most recent NABON guideline
6. ER and/or PgR receptor positive (ER expression more than or equal to 10% and/or PgR more than or equal to 10%)
7. Known human epidermal growth factor receptor 2 (HER2) status
8. Adequate renal- and hepatic function as assessed by laboratory testing within four weeks prior to enrolment:
8.1. Renal function: creatinine less than or equal to 120 µmol/L. If limit values, the calculated creatinine clearance should be more than or equal to 30 mL/min with the Cockcroft and Gault-formula
8.2. Hepatic function: total bilirubin less than or equal to 1.5 x upper normal limit (UNL); aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase [SGOT]) and alanine transaminase (ALT) (serum glutamic pyruvic transaminase [SGPT]) less than or equal to 2.5 x UNL; alkaline phosphatase less than or equal to 2.5 x UNL
9. Post-menopausal women: post-menopausal defined as:
9.1. Age more than or equal to 50 and amenorrhoea for more than one year
9.2. Bilateral surgical oophorectomy and no HRT (any age is acceptable)
9.3. Age less than 50 with natural amenorrhoea more than one year at breast cancer diagnosis (and uterus in situ)
9.4. Post-menopausal due to chemotherapy will be excluded
9.5. In case of doubt about the menopausal status, assessment of FSH, LH and oestradiol has to be performed to define the menopausal status
10. WHO performance status zero or one
11. Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule
12. Accessible for follow-up for the duration of the trial
13. Before randomisation, patients must be capable of understanding the trial and give written informed consent according to ICH/GCP, and local IRB guidelines

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
2478

Key exclusion criteria
TEAM IIa:
1. M1 disease by clinical examination according to the NABON guideline
2. Multicentric breast cancer (including carcinoma in situ [CIS])
3. Bilateral breast cancer (including CIS)
4. cT4d tumour (inflammatory breast cancer)
5. Hormone replacement therapy during the last 12 months
6. One of the following diseases:
6.1. Uncontrolled cardiac disease
6.2. Psychiatric disorders preventing proper informed consent
6.3. Concomitant malignancies within the last five years, except for adequately treated carcinoma in situ of the uterine cervix or basal squamous cell carcinoma of the skin
6.4. Prior invasive breast cancer or CIS within the last 15 years
6.5. Other serious illnesses that may interfere with subject compliance, adequate informed consent or determination of causality of adverse events
7. Concurrent participation in another clinical study that may interfere with the results of the trial involving investigational agents within thirty days of treatment from this study, unless this is agreed by the Study Coordinators
8. More than three weeks after date of histological biopsy of primary breast cancer

TEAM IIb:
1. M1 disease by clinical examination according to the NABON guideline
2. Bilateral invasive breast cancer (including CIS)
3. Patients having shown progressive disease in TEAM IIa (preoperative hormonal treatment with exemestane)
4. One of the following diseases:
4.1. Uncontrolled cardiac disease
4.2. Psychiatric disorders preventing proper informed consent
4.3. Patients with untreated oesophagitis, gastric ulcers or irritable bowel disease (IBD)
4.4. Concomitant malignancies within the last five years, except for adequately treated carcinoma in situ of the uterine cervix or basal squamous cell carcinoma of the skin
4.5. Prior invasive breast cancer and/or CIS within the last 15 years
4.6. Other serious illnesses that may interfere with subject compliance, adequate informed consent or determination of causality of adverse events
5. History of disease with influence on bone metabolism, including:
5.1. Pagets disease of the bone
5.2. Primary hyperparathyroidism (patients cured by surgery may be included if interval more than or equal to one year)
6. Hormone replacement therapy during the last 12 months
7. Current active dental problems including dental abscess or infection of the jawbone (maxilla or mandible), or a current or prior diagnosis of osteonecrosis of the jaw requiring maxillo-facial surgery
8. Recent (within four weeks of study entry) or planned dental or jaw surgery (e.g. extraction, implants). Recent dental fillings, teeth scaling and polishing or minor gingival surgery do not exclude the patient
9. Concurrent participation in another clinical study that may interfere with the results of the

trial involving investigational agents within thirty days of treatment from this study, unless this is agreed by the Study Coordinators
10. More than five weeks after final surgery or after end of adjuvant chemotherapy

Date of first enrolment
01/10/2006

Date of final enrolment
01/10/2010

Locations

Countries of recruitment
Netherlands

Study participating centre
Leiden University Medical Centre (LUMC)
Leiden
Netherlands
2300 RC

Sponsor information

Organisation
TEAM II Study Group (The Netherlands)

Sponsor details
-
Alkmaar
Netherlands
-

Sponsor type
Other

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Leiden University Medical Centre (LUMC) (The Netherlands)

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