TEAM II A randomised, multicentre, prospective, phase III trial investigating TEAM IIa: Neoadjuvant hormonal therapy with exemestane for three versus six months.
and / or
TEAM IIb: The efficacy and safety of the addition of ibandronate to adjuvant hormonal therapy in postmenopausal women with hormone receptor positive early breast cancer.

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TEAM IIa: Six months of neoadjuvant therapy with exemestane is superior to three months with respect to the rate of downsizing in postmenopausal women with ER positive (> 50% of tumour cells positive) primary breast cancer. TEAM IIb: Adjuvant...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON27856

Bron
NTR

Verkorte titel
TEAM II

Aandoening

Breast Cancer, Neoadjuvant hormonal therapy, Aromatase inhibitor, Adjuvant therapy, Bisphosphonates

Ondersteuning

Primaire sponsor: TEAM II Study Group
Overige ondersteuning: Pfizer, Roche Nederland BV, Leiden University Medical Centre

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

TEAM IIa

BACKGROUND:
Clinical trials in patients with hormone receptor positive breast cancer have shown that neoadjuvant hormonal therapy accomplished relevant clinical and ultrasound response rates resulting in an improved rate of breast conserving surgery. Aromatase inhibitors are superior to tamoxifen in this setting. However, the optimal duration of neoadjuvant hormonal therapy has never been investigated in a phase III trial. Moreover, at present it is unknown who will benefit from neoadjuvant exemestane.

INTERVENTION:
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.

PRIMARY OBJECTIVE:

Objective response rate (immediately prior to surgery) of the primary breast tumour, assessed by palpation

SIDE STUDIES:

* Translational research

TEAM IIb

BACKGROUND:
Clinical trials have shown that bisphosphonates reduce the rate of skeletal related events and the incidence of new bone metastases in breast cancer patients with bone metastases. Two trials in patients with early breast cancer suggest that the bisphosphonate clodronate might prevent or delay bone metastases. One other trial produced conflicting results. At present, the value of adjuvant bisphosphonates is unclear. It is assumed that more potent bisphosphonates, such as ibandronate, may have greater potential to prevent bone metastases.

INTERVENTION:
Patients will be randomised (1:1) to receive hormonal treatment with or without oral ibandronate (50 mg once daily) for three years. Hormonal treatment will be according most recent NABON guideline. Exemestane will be used as aromatase inhibitor.

PRIMARY OBJECTIVE:
Three years disease free survival.

SIDE STUDIES:

* Translational research

* Life style study

Doel van het onderzoek

TEAM IIa: Six months of neoadjuvant therapy with exemestane is superior to three months with respect to the rate of downsizing in postmenopausal women with ER positive (> 50% of tumour cells positive) primary breast cancer.

TEAM IIb: Adjuvant systemic therapy combined with oral ibandronate results in an improved 3-years disease free survival compared to adjuvant systemic therapy without ibandronate in postmenopausal women with hormone receptor positive primary breast cancer.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

Leiden University Medical Center (LUMC),
Department of Surgical Oncology,
P.O. Box 9600
C.J.H. Velde, van de
Leiden 2300 RC
The Netherlands
+31 (0)71 5262309

Wetenschappelijk

Leiden University Medical Center (LUMC),
Department of Surgical Oncology,
P.O. Box 9600
C.J.H. Velde, van de
Leiden 2300 RC
The Netherlands
+31 (0)71 5262309

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

TEAM IIa:

1. Female patients with histologically, by core needle biopsy-proven, invasive

adenocarcinoma of the breast.

2. Any tumour with a size >= 2 cm (except cT4d = inflammatory breast cancer).

3. Indication to receive adjuvant hormonal therapy according to most recent NABON guideline.

4. ER expression > 50% (PgR either positive or negative).

5. Postmenopausal women; postmenopausal defined as:

5.1 Age >= 50 and amenorrhoea for > 1 year.

5.2 Bilateral surgical oophorectomy and no HRT (any age is acceptable).

5.3 Age < 50 with natural amenorrhoea >1 year at breast cancer diagnosis (and uterus in situ).

5.4 Postmenopausal due to chemotherapy will be excluded.

5.5 In case of doubt about menopausal status, assessment of FSH, LH and estradiol has to be performed to define the menopausal status.

6. WHO performance status 0 or 1.

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 ICH/GCP and local IRB guidelines.

TEAM IIb:

1. Histological confirmed invasive adenocarcinoma of the breast.

2. Stage I-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 >= 10% and/or PgR >= 10%).

7. Known HER2 status.

8. Adequate renal- and hepatic function as assessed by laboratory testing within four weeks prior to enrolment.

8.1 Renal function;
Creatinine <= 120 µmol/L.
If limit values, the calculated creatinine clearance should be >= 30 mL/min with the Cockcroft and Gault-formula.

8.2 Hepatic function;
Total bilirubin <= 1.5 UNL

ASAT (SGOT) and ALAT (SGPT) <= 2.5 UNL

Alkaline Phosphatase <= 2.5 UNL

9. Postmenopausal women;postmenopausal defined as:

9.1 Age >= 50 and amenorrhoea for > 1 year.

9.2 Bilateral surgical oophorectomy and no HRT (any age is acceptable).

9.3 Age < 50 with natural amenorrhoea >1 year at breast cancer diagnosis (and uterus in situ).

9.4 Postmenopausal due to chemotherapy will be excluded.

9.5 In case of doubt about the menopausal status, assessment of FSH, LH and estradiol has to be performed to define the menopausal status.

10. WHO performance status 0 or 1.

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.

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

TEAM IIa:

1. M1 disease by clinical examination according to the NABON guideline.

2. Multicentric breast cancer (including 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 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 >= 1 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 4 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 5 weeks after final surgery or after end of adjuvant chemotherapy.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel

Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-10-2006
Aantal proefpersonen:	2478
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	27-09-2006
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL774
NTR-old	NTR785
Ander register	: BOOG 2006-04
ISRCTN	ISRCTN17633610

Resultaten

Samenvatting resultaten
N/A