Study of neo adjuvant chemotherapy in large and/or lymphenode positive breast cancer (stage IIB-III pT2> 3cm). Multicentre - phase II - trial.

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The main goal of neoadjuvant therapy should be a pathological complete response (pCR), because pCR more accurately predicts improved patient outcome and prolonged survival. In the present study, pathological response will be evaluated by The Miller...

Ethical review	Not approved
Status	Will not start
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Observational invasive

Summary

ID

NL-OMON30125

Source
ToetsingOnline

Brief title
Neoadjuvant chemotherapy in large and/or lymphenode positive breast cancer.

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breastcancer > 3 cm and/or metastatic disease of axilary lymfenodes

Research involving
Human

Sponsors and support

Primary sponsor: Catharina-ziekenhuis

Source(s) of monetary or material Support: opgenomen in standaard behandeling;geen extra geldstroom,Sanofi-aventis

Intervention

Keyword: breast cancer, locally advanced, lymphe node positive, Neoadjuvant chemotherapy

Outcome measures

Primary outcome

- To evaluate clinical and pathological response to neoadjuvant chemotherapy

- To evaluate the value of dynamic contrast-enhanced breast MRI in monitoring

and predicting response to neoadjuvant chemotherapy.

- To evaluate the value of circulating tumour cells in monitoring and

predicting reponse to neoadjuvant chemotherapy.

- To define gene expression profiles that can predict treatment response or

failure by microarray analysis.

Secondary outcome

- To determine disease-free and overall survival.

- To evaluate the use of radioactive labeled (125-I) seed as to localize tumour

prior to chemotherapy to enable - after surgical excision (conservation

therapy or mastectomy) pathological evaluation of tumour residue after

chemotherapy

Study description

Background summary

Docetaxel-based neoadjuvant chemotherapy is an effective alternative to surgery followed by adjuvant chemotherapy in both early and locally advanced breast cancer. Findings from randomized studies suggests that the sequential administration of docetaxel and anthracycline-based therapy may provide improved outcome versus the outcome with concomitant administration. Recently, the Dutch multidisciplinary guidelines for treatment of early breast cancer were updated and antracycline-based therapy consisting of FEC was defined as standard treament. Therefore, in the present study, eligible patients will be treated with sequential 4 cycles of docetaxel after 4 cycles of neoadjuvant FEC. In line with the data of Van Pelt and Buzdar, patients with HER-2 positive disease will be treated with 8 cycles of docetaxel in combination with trastuzumab. Trastuzumab and docetaxel will be administered in a 3-weekly schedule based on the data of Leyland-Jones.

Study objective

The main goal of neoadjuvant therapy should be a pathological complete response (pCR), because pCR more accurately predicts improved patient outcome and prolonged survival. In the present study, pathological response will be evaluated by The Miller and Payne and RECIST classification system (see appendix I). In addition clinical response to treatment will be evaluated by dynamic contrast-enhanced MRI of the effected breast. Breast MRI images will be correlated to the pathological information to determine whether this technique is able to accurately predict tumour response to neoadjuvant chemotherapy. Moreover, repetitive breast MRI images obtained before, during and after chemotherapy offers the ability to determine the optimal duration of preoperative therapy and to delineate the necessity to change the regimen in chemotherapy-resistant tumours

Study design

Multi centre, phase II - non randomised - study.

Study burden and risks

Neo adjuvant chemotherapy is indicated based on criteria also used for adjuvant chemotherapy. Advantages could be: - monitoring clinical respons and possibility of adjustment of treatment, - possibility of breast saving procedure after (nearly) complete respons of large breast tumours. This treatment is also made possible after placement of 125-I seed.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

•Women presenting with locally advanced stage IIB-III breast cancer pT2 > 3 cm, and/or clinically proven N+ disease. Exclusion cT4. (TNM classification 2002).
•No prior surgery other than biopsy and no prior chemotherapy or radiation therapy.
•Age > 18 years and age < 60 years.
•Karnofsky Performance status index > 80%
•Estrogen and/or progesterone receptor analysis performed on the primary tumour. Results must be known by the end of chemoptherapy in order to decide whether hormonal therapy is indicated.
•Her2/neu receptor analysis performed on the primary tumour.
•Adequate bone marrow (within 14 days prior to registration):WBC > 3.0 x 109/l, neutrophils > 1.5 x 109/l, platelets > 100 x 109/l, hemoglobin > 7 mmol/l.
•Adequate liver function (within 21 days prior to registration):bilirubin < 1 x upper limit of

normal (UNL) range, ALAT and/or ASAT < 2.5 x UNL, Alkaline Phosphatase < 5 x UNL.
•Adequate renal function (within 21 days prior to registration):Creatinine < 120 µmol/L; if limit values reached, the calculated creatinine clearance should be > 60 mL/min.
•No sign of metastatic disease on X-thorax, liver ultrasound or nuclear bone scan.
•Cardiac LVEF evaluation by ECHO or MUGA (within normal limits).
•Patients must be accessible for treatment and follow-up.
•Negative pregnancy test (urine or serum) within 7 days prior to registration for all women of childbearing potential.
•Having signed written informed consent according to the local Ethics Committee requirements.

Exclusion criteria

•Prior systemic anticancer therapy for any cancer (immunotherapy, hormonaltherapy, genetherapy, chemotherapy).
•Prior anthracycline-based or taxoid-containing therapy (paclitaxel, docetaxel) for any malignancy.
•Prior radiation therapy for breast cancer.
•Patients with advanced pulmonary disease.
•Peripheral neuropathy > grade 2 whatever the cause.
•Clinical evidence of CNS disease.
•Patients with a history of another malignancy (except basal cell skin carcinoma and carcinoma-in-situ of the uterine cervix) within 5 years of study entry.
•Pregnant or lactating women, or potentially fertile women not using adequate contraception.
•Clinically T4

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Endoxan
Generic name:	Cyclophosphamidum
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Farmorubicin
Generic name:	epirubicini hydrocloridum
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Fluorouracil - TEVA
Generic name:	fluoroucacilum
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Herceptin
Generic name:	trastuzumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	Docetaxelum
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-07-2006
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Not approved

Date:	11-07-2007
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2006-001206-89-NL
CCMO	NL11339.060.06