Microarray Analysis in breast cancer to Tailor Adjuvant Drugs Or Regimens, a randomized phase III study.

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To define gene expression profiles that can predict a disease-free survival (DFS) advantage for either dose dense therapy, or docetaxel—containing chemotherapy.

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

Samenvatting

ID

NL-OMON23149

Bron
NTR

Verkorte titel
MATADOR, BOOG 2005-02, CKTO 2004-04

Aandoening

Primary operable breast cancer

Ondersteuning

Primaire sponsor: Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital
Overige ondersteuning: CKTO (KWF Kankerbestrijding - Dutch Cancer Society)
Research grant Sanofi-Aventis
Research grant Amgen

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To define gene expression profiles that can predict a disease-free survival (DFS) advantage for either dose dense therapy, or docetaxel—containing chemotherapy.

Toelichting onderzoek

Achtergrond van het onderzoek

Results of a recent randomized trial comparing dose-dense chemotherapy (2 –weekly schedule with growth factor support) with a conventional 3-weekly schedule show that dose density improves both disease free and overall survival (Citron et al. J Clin Oncol 2003; 21:1431-1439).
Martin et al. recently published first results of the TAC-FAC trial (Martin et al. N Engl J Med 2005; 352:2302-2313). Replacement of 5-FU by docetaxel leads to improvement of disease free survival and overall survival.

So far, no discriminating factors have been identified in prospective adjuvant trials that can predict who benefits most from a docetaxel containing regimen. Besides it is unclear for whom 4 cycles of chemotherapy are sufficient, and who needs 6 cycles. The number of cycles is especially interesting in the light of chemotherapy risks.
This started as a randomized multicenter study with a 2 x 2 factorial design to assess the two factors of ACdd vs. TAC, and 4 vs. 6 chemotherapy courses in relation to gene expression profiles of primary tumors. In a later amendment (February 2006) randomization to the treatment arms containing four cycles of treatment was discontinued because new data became available in favour of 6 treatment cycles. Patients will be randomized to 6x ACdd versus 6x TAC.

Patients will be stratified according to treatment center, menopausal status (pre vs. post), hormone receptor status (ER and/or PR+ vs. both negative), nodal status (pN0, pN1(sn), N1-3 vs. N4+), tumor size (T1 vs. T2 vs. T3), and sequence of radiotherapy/chemotherapy. At a later stage all pathology data will be revised centrally.

Doel van het onderzoek

To define gene expression profiles that can predict a disease-free survival (DFS) advantage for either dose dense therapy, or docetaxel—containing chemotherapy.

Onderzoeksproduct en/of interventie

Randomization:

To one of the treatment arms (6 cycles TAC or AC dd).

ACdd:

Doxorubicin 60 mg/m2 i.v. bolus and cyclophosphamide 600 mg/m2 i.v. bolus on day 1 every 2 weeks.

TAC:

Doxorubicin 50 mg/m² as an i.v. bolus on day 1, followed by cyclophosphamide 500 mg/m2 as i.v. bolus and, after 1 hour, docetaxel 75 mg/m² as 1 hour i.v. infusion on day 1 every 3 weeks.

Both Arms:

1. Prophylactic pegfilgrastim 6 mg s.c. given 1 day after completion of administration of each chemotherapy cycle;

2. Radiotherapy, if indicated;

3. Endocrine treatment for at least 5 years, (according to the most recent Dutch national guidelines)starting 1 to 6 weeks after radiotherapy or 3 to 6 weeks after chemotherapy for patients with positive estrogen and/or progesterone receptors.

HER2 positive patients:

For HER2 positive patients we recommend to treat these patients outside the context of this study. Only in case of an increased risk of cardiotoxicity, the HERA study schedule is an alternative, in which case patients could participate in the MATADOR study.

Both Arms:

For HER2 positive patients with increased risk of cardiotoxicity, who are going to receive trastuzumab according to the schedule of the HERA study, trastuzumab should be given for 52 weeks, and should start within 7 weeks from day 1 of the last chemotherapy cycle or within 6 weeks from the end of adjuvant radiotherapy, whichever is last.

Contactpersonen

Publiek

Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital,
Departments of Molecular Biology and Medical Oncology,
Plesmanlaan 121

S.C. Linn
Plesmanlaan 121
Amsterdam 1066 CX
The Netherlands
+31 (0)20 5122951

Wetenschappelijk

Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital,
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The Netherlands
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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Women with pT1-T3, pN0-3b, M0 adenocarcinoma of the breast (TNM classification 2002). Women with a macrometastasis in the sentinel node, who did not receive an axillary dissection (pN1(sn)), are only eligible if radiotherapy of the axilla is included in the treatment plan (for instance experimental arm AMAROS study);

2. Known HER2 and estrogen receptor status;

3. Frozen tumor tissue available (or tumor tissue sent in RNAlater to NKI-AVL);

4. Primary surgery (defined as date of last surgical intervention) < 6 weeks before randomisation, or radiotherapy < 5 weeks before randomisation;

5. Good performance status (WHO < 1);

6. Normal hematology, normal renal and liver function tests (see below);

7. No history of heart failure;

8. Patients of childbearing potential must implement adequate non-hormonal contraceptive measures during study treatment (chemotherapy and hormonal therapy);

9. No conditions that may compromise follow-up;

10. Informed consent;

11. At least 18 years old and able to undergo intensive chemotherapy (in the study of Martin et al. employing the TAC regimen (1d) age < 65 years was required);

12. Laboratory requirements: (within 14 days prior to registration):

Hematology:

Neutrophils ≥ 1.5 109/L;

Platelets ≥ 100 109/L;

Hemoglobin ≥6.0 mmol/L.

Hepatic function:

Total bilirubin ≤ 16 umol/L;

ASAT (SGOT) and ALAT (SGPT) ≤ 1.5 UNL;

Alkaline phosphatase ≤ 2.5 UNL.

Renal function:

Creatinine ≤ 120 µmol/L;

If limit values, the calculated creatinine clearance should be ≥ 60 mL/min.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Prior systemic anticancer therapy for any cancer (immunotherapy, hormonal therapy, chemotherapy);

2. Prior radiation therapy for breast cancer;

3. HER2 positive breast cancer (except for patients who are going to be treated according to HERA study (1c)(see also ‘Dosage regimens’ p 8-9);

4. Pregnant, or lactating patients;

5. Pre-existing motor or sensory neurotoxicity of a severity > grade 2 by NCI criteria;

6. Other serious illness or medical condition:

A. Congestive heart failure or unstable angina pectoris, previous history of myocardial infarction within 1 year from study entry, uncontrolled hypertension or high-risk uncontrolled arrhythmias;

B. History of significant neurological or psychiatric disorders including psychotic disorders, dementia or seizures that would prohibit the understanding and giving of informed consent;

C. Active uncontrolled infection.

7. Past history of invasive breast cancer or past or current history of neoplasm other than breast carcinoma, except for:

A. Curatively treated non-melanoma skin cancer;

B. In situ carcinoma of the cervix;

C. Ipsilateral ductal carcinoma in-situ (DCIS) of the breast;

D. Lobular carcinoma in-situ (LCIS) of the breast.

8. Concurrent treatment with other experimental drugs. Participation in another clinical trial with any investigational not marketed drug within 30 days prior to study entry;

9. Male patients.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel

Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-10-2004
Aantal proefpersonen:	660
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	09-09-2005
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	NL248
NTR-old	NTR286
Ander register	: N/A
ISRCTN	ISRCTN61893718

Resultaten

Samenvatting resultaten
N/A