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

Submission date 20/12/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/12/2005	**Overall study status** Completed	
Last Edited 23/03/2026	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Study information

Scientific Title
Microarray Analysis in breast cancer to Taylor Adjuvant Drugs Or Regimens, a randomized phase III study

Acronym
MATADOR, BOOG 2005-02, CKTO 2004-04

Study objectives
Current study hypothesis as of 29/04/2013:
To define gene expression profiles that can predict a disease-free survival (DFS) advantage for either dose dense therapy, or docetaxel-containing chemotherapy.

Previous study hypothesis until 29/04/2013:
With microarray analysis of primary breast cancers of patients who participate in this study one can identify gene expression profiles that can predict a disease-free survival advantage for either dose dense therapy, docetaxel, and/or 6 versus 4 courses of chemotherapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Netherlands Cancer Institute, 15/03/2004, ref: EV04-87

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Other

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

Interventions
Current interventions as of 29/04/2013:
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:
- prophylactic pegfilgrastim 6 mg s.c. given 1 day after completion of administration of each chemotherapy cycle;
- Radiotherapy, if indicated;
- 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.

Previous interventions until 29/04/2013:
2 randomizations:
1. To one of the treatment arms (TAC or AC dd)
2. To 4 or 6 courses of chemotherapy (second randomization only open for patients with 1-3 positive axillary lymph nodes)

AC dd: doxorubicin 60 mg/m2 iv bolus and cyclophosphamide 600 mg/m2 iv bolus on day 1 every 2 weeks.
TAC: Docetaxel 75 mg/m2 1 hour i.v. infusion on day 1 in combination with doxorubicin 50 mg /m2 i.v. bolus and cyclophosphamide 500 mg/m2 i.v. bolus on day 1 every 3 weeks.

Both Arms:
1. Prophylactic pegfilgrastim 6 mg sc given 1 day after completion of administration of each chemotherapy cycle
2. Radiotherapy, if indicated
3. Endocrine treatment for 5 years, starting 1 to 6 weeks after radiotherapy or 3 to 6 weeks after chemotherapy for patients with positive estrogen and/or progesterone receptors.

Intervention Type
Mixed

Primary outcome(s)
Current primary outcomes as of 29/04/2013:
To define gene expression profiles that can predict a disease-free survival (DFS) advantage for either dose dense therapy, or docetaxelcontaining chemotherapy.

Previous primary outcomes until 29/04/2013:
To define gene expression profiles that can predict a disease-free survival advantage for either dose dense therapy, docetaxel, and/or 6 versus 4 courses of chemotherapy.

Key secondary outcome(s))
Current secondary outcome measures as of 29/04/2013:
Is docetaxel-doxorubicin-cyclophosphamide (TAC) better than doxorubicin-cyclophosphamide dose-dense (AC dd) concerning DFS, RFS, breast cancer specific survival and all cause survival?
Objectives of optional side studies:
1. To determine whether the proteomic profile of patients, with primary breast cancer, relates to patient demographic characteristics, tumor stage, tumor biologic characteristics or tumor genetic (micro-array) profile
2. To identify a proteomic pattern that positively or negatively predicts relapse according to the genetic profile of the primary tumor (micro-array analysis) in each treatment arm
3. To identify a proteomic pattern in follow-up serum samples that can predict for relapse

Previous secondary outcome measures until 29/04/2013:
1. Is TAC better than AC dd regarding disease free survival and overall survival?
2. Are 6 courses better than 4 regarding disease free survival and overall survival?

Objectives of optional side studies
1.To determine whether the proteomic profile of patients, with primary breast cancer, relates to patient demographic characteristics, tumor stage, tumor biologic characteristics or tumor genetic (micro-array) profile
2.To identify a proteomic pattern that positively or negatively predicts relapse according to the genetic profile of the primary tumor (micro-array analysis) in each treatment arm
3.To identify a proteomic pattern in follow-up serum samples that can predict for relapse

Completion date
19/11/2012

Eligibility

Key inclusion criteria
Current inclusion criteria as of 29/04/2013:
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)
12.1. Hematology:
12.1.1. Neutrophils ≥ 1.5 109/L;
12.1.2. Platelets ≥ 100 109/L;
12.1.3. Hemoglobin ≥6.0 mmol/L;
12.2. Hepatic function:
12.2.1. Total bilirubin ≤ 16 umol/L;
12.2.2. ASAT (SGOT) and ALAT (SGPT) ≤ 1.5 UNL;
12.2.3. Alkaline phosphatase ≤ 2.5 UNL;
12.3. Renal function:
12.3.1. Creatinine ≤ 120 µmol/L;
12.3.2. If limit values, the calculated creatinine clearance should be ≥ 60 mL/min.

Previous inclusion criteria until 29/04/2013:
1. Women with pT0-T3, pN 1-3b, 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. Frozen tumor tissue available (or tumor tissue sent in RNAlater to NKI-AVL)
3. Primary surgery <6 weeks before randomisation, or radiotherapy <5 weeks before randomisation
4. Good performance status; WHO <1
5. Normal hematology, normal renal and liver function tests (see below)
6. No history of heart failure
7. Patients of childbearing potential must implement adequate non-hormonal contraceptive measures during study treatment (chemotherapy and hormonal therapy)
8. No conditions that may compromise follow-up
9. Written Informed consent
10. Able to undergo intensive chemotherapy (in the study of Nabholtz (1) age <65 years was required)
11. Laboratory requirements: (within 14 days prior to registration)
Hematology:
i. Neutrophils >1.5 x 10^9/l
ii. Platelets >100 x 10^9/l
iii. Hemoglobin >6.0 mmol/l
Hepatic function:
i. Total bilirubin <16 µmol/L
ii. ASAT (SGOT) and ALAT (SGPT) <1.5 UNL
iii. Alkaline phosphatase <2.5 UNL
Renal function:
i. Creatinine <120 µmol/l
ii. If limit values, the calculated creatinine clearance should be >60 ml/min

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
Female

Total final enrolment
664

Key exclusion criteria

Current exclusion criteria as of 29/04/2013:
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)
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:
6.1. 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
6.2. History of significant neurological or psychiatric disorders including psychotic disorders, dementia or seizures that would prohibit the understanding and giving of informed consent
6.3. Active uncontrolled infection
7. Past history of invasive breast cancer or past or current history of neoplasm other than breast carcinoma, except for:
7.1. Curatively treated non-melanoma skin cancer
7.2. In situ carcinoma of the cervix
7.3. Ipsilateral ductal carcinoma in-situ (DCIS) of the breast
7.4. 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

Previous exclusion criteria until 29/04/2013:
1. Prior systemic anticancer therapy for any cancer (immunotherapy, hormonal therapy, chemotherapy)
2. Prior radiation therapy for breast cancer
3. Pregnant, or lactating patients
4. Pre-existing motor or sensory neurotoxicity of a severity > grade 2 by NCI criteria
5. Other serious illness or medical condition:
5.1 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
5.2 A history of significant neurological or psychiatric disorders including psychotic disorders, dementia or seizures that would prohibit the understanding and giving of informed consent
5.3 Active uncontrolled infection
6. Past or current history of neoplasm other than breast carcinoma, except for:
6.1 Curatively treated non-melanoma skin cancer
6.2 In situ carcinoma of the cervix, cipsilateral ductal carcinoma in-situ (DCIS) of the breast,
6.3 Llobular carcinoma in-situ (LCIS) of the breast
7. Concurrent treatment with other experimental drugs. Participation in another clinical trial with any investigational not marketed drug within 30 days prior to study entry.
8. Male patients

Date of first enrolment
01/10/2004

Date of final enrolment
19/11/2012

Locations

Countries of recruitment
Netherlands

Study participating centre
Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital
Amsterdam
Netherlands
1066 CX

Sponsor information

Organisation
Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI AVL)

ROR
https://ror.org/03xqtf034

Funder(s)

Funder type
Industry

Funder Name
Sanofi-Aventis

Funder Name
Amgen

Alternative Name(s)
Amgen Inc., Applied Molecular Genetics Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location

United States of America

Funder Name
Koningin Wilhelmina Fonds

Results and Publications

Individual participant data (IPD) sharing plan
The gene expression data will be available after publication. The patient level data have been submitted to the Early Breast Cancer Trialists's Group, also called the Oxford Overview. This database is not publicly available (https://www.ctsu.ox.ac.uk/research/ebctcg).

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		27/11/2017	16/01/2019	Yes	No
Results article		01/10/2018	16/01/2019	Yes	No
Results article		29/06/2024	02/09/2024	Yes	No
Results article		13/03/2026	23/03/2026	Yes	No