

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	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 20/12/2005	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 02/09/2024	Condition category Cancer	<input type="checkbox"/> Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

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

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Other

Participant information sheet

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 measure

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 docetaxel-containing 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.

Secondary outcome measures

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

Overall study start date

01/10/2004

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 RNA later 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 $\geq 1.5 \times 10^9/L$;

12.1.2. Platelets $\geq 100 \times 10^9/L$;

12.1.3. Hemoglobin $\geq 6.0 \text{ mmol/L}$;

12.2. Hepatic function:

12.2.1. Total bilirubin $\leq 16 \text{ } \mu\text{mol/L}$;

12.2.2. ASAT (SGOT) and ALAT (SGPT) $\leq 1.5 \text{ UNL}$;

12.2.3. Alkaline phosphatase $\leq 2.5 \text{ UNL}$;

12.3. Renal function:

12.3.1. Creatinine $\leq 120 \text{ } \mu\text{mol/L}$;

12.3.2. If limit values, the calculated creatinine clearance should be $\geq 60 \text{ mL/min}$.

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 RNA later 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 Nabholz (1) age <65 years was required)

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

Hematology:

i. Neutrophils $>1.5 \times 10^9/l$

ii. Platelets $>100 \times 10^9/l$

iii. Hemoglobin $>6.0 \text{ mmol/l}$

Hepatic function:

i. Total bilirubin $<16 \text{ } \mu\text{mol/L}$

ii. ASAT (SGOT) and ALAT (SGPT) $<1.5 \text{ UNL}$

iii. Alkaline phosphatase $<2.5 \text{ UNL}$

Renal function:

i. Creatinine $<120 \text{ } \mu\text{mol/l}$

ii. If limit values, the calculated creatinine clearance should be $>60 \text{ ml/min}$

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Female

Target number of participants

600

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, ipsilateral ductal carcinoma in-situ (DCIS) of the breast,

6.3 Lobular 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)

Sponsor details

Plesmanlaan 121

Amsterdam

Netherlands

1066 CX

+31 (0)20 5129111

y.rhemrev@nki.nl

Sponsor type

Hospital/treatment centre

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

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

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	results	27/11/2017	16/01/2019	Yes	No
Results article	results	01/10/2018	16/01/2019	Yes	No
Results article		29/06/2024	02/09/2024	Yes	No