BReast cancer Ex vivo Anthracycline Sensitivity Test (BREAST) study;Using ex vivo drug sensitivity tests to optimize breast cancer therapy in the future

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To determine the concordance between the ex vivo anthracycline sensitivity test and in vivo response to anthracycline-based NAC. Also, optimal cut-off values for the ex vivo anthracycline sensitivity assay are determined to carefully predict in vivo...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Observational invasive

Summary

ID

NL-OMON43367

Source
ToetsingOnline

Brief title
BREAST study

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Interne Oncologie

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: anthracyclines, breast cancer, neoadjuvant, sensitivity

Outcome measures

Primary outcome

The primary end point is the concordance between the ex vivo anthracycline sensitivity test and the in vivo response to anthracycline-based NAC on MRI. To this end, the degree of agreement between the ex vivo anthracycline sensitivity test on BrC biopsies and the in vivo radiological response (by MRI) to anthracycline-based NAC is assessed. The radiological response by MRI is based on the percentage change in tumor size comparing baseline with size measurements after 3-4 courses of anthracycline-based chemotherapy. Good response is defined as >50% decrease intermediate response as <=50% decrease and <=20% increase and poor response as >20% progression according to RECIST , after 3-4 courses of anthracycline containing NAC. In our ex vivo sensitivity assay (based on morphology, proliferation and apoptosis), tumors can be classified as either resistant, intermediate or highly sensitive to anthracyclines. Concordance between ex vivo and in vivo response is met when a) resistant tumors by ex vivo assay show poor response by MRI, b) highly sensitive tumors show good response, or c) intermediate sensitive tumors show intermediate response after 3-4 courses after anthracyclines-containing NAC.

Secondary outcome

1) Explore whether the use of different cut-off values for the ex vivo anthracycline sensitivity assay could even better predict the in vivo

anthracycline response.

2) Decipher the underlying molecular mechanisms of highly anthracycline

sensitive/ resistant tumors.

3) Develop tumor organoids from a small part of the tumor biopsy.

Study description

Background summary

Neo-adjuvant chemotherapy (NAC) for primary breast cancer (BrC) without detectable distant metastases has decreased development of distant metastases by 20-35%, depending on age. Although this is an impressive improvement, 65-80% of BrC patients are treated without any benefit of (N)AC. Moreover, these chemotherapeutics can lead to severe short and long term side effects, which negatively affect quality of life. Currently, selection of patients for NAC depends on age at BrC diagnosis and tumor characteristics (e.g. size, grade and receptor- and nodal status). To overcome the burden of overtreatment, preselection of patients with micro-metastases on the one hand, and better predictive markers for treatment efficacy on the other, are of the utmost importance. In this study, we focus on the latter by further developing a predictive ex vivo drug sensitivity assay. Recently, culture conditions for tissue slices of various tumors, including BrC, were optimized and they remain vital ex vivo for at least one week. The anthracycline sensitivity assay, that relies on proliferation, apoptosis and morphology, was developed on a set of 23 breast tumors that were not treated with NAC before surgical resection. Here, we propose to take the next step towards personalized medicine, exploring the predictive value of this assay by linking the anthracycline sensitivity test results to in vivo response after neoadjuvant anthracycline-based chemotherapy.

Study objective

To determine the concordance between the ex vivo anthracycline sensitivity test and in vivo response to anthracycline-based NAC. Also, optimal cut-off values for the ex vivo anthracycline sensitivity assay are determined to carefully predict in vivo anthracycline response.

Study design

Pilot study

Study burden and risks

Burden for the patient will be minimal, since primary breast tumors are generally easily approachable for biopsy and there is a lot of experience with this procedure. During participation in this study, only one biopsy of the primary tumor is planned. Expected but confined side effects are mild pain and hematoma.

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

• Age >18 years
• WHO performance status 0 or 1
• Planned treatment with anthracycline-based NAC (either 3 courses of FEC or 4 courses of AC)
• Written informed consent

Exclusion criteria

• Planned treatment with TAC (taxanes concomitant with anthracyclines) courses
• Current therapeutical use of anti-coagulant (coumarin derivates, warfarin, heparin or low molecular weight heparin [LMWH]) whereby a short interruption of drug use is not allowed. LMWH use in a prophylactic dose is allowed
• Any psychological condition potentially hampering compliance with the study protocol

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-02-2017
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	09-11-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL58869.078.16