Non-invasive monitoring of breast cancer therapy using circulating tumor DNA from peripheral blood

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

Summary

ID

NL-OMON43952

Source
ToetsingOnline

Brief title
NAVIGATOR

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
ER-positive breast cancer, Metastatic breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: gesponsord door een farmaceutisch bedrijf,Merck Serono

Intervention

Keyword: Blood, ctDNA, Metastatic breast cancer, Non-invasive monitoring

Outcome measures

Primary outcome

The primary end point is to detect a difference in progression-free survival (PFS) between patients with and without detectable ESR1 mutations in their plasma.

Secondary outcome

Secondary, exploratory end points are to identify mutations emerging in ctDNA during treatment and associated with progression to AI and/or everolimus and exemestane treatment, to identify genetic markers in ctDNA explaining how initially responding tumors escape drug sensitivity, and to compare the DNA mutational landscape between primary tumors, metastatic lesions, if available, and matching ctDNA at start and during treatment for metastatic disease.

Study description

Background summary

The efficacy of endocrine treatment in patients with estrogen receptor (ER) positive metastatic breast cancer (MBC) is limited due to the presence of intrinsic endocrine resistance as well as the occurrence of acquired therapy resistance in initially responding patients. Important mechanisms whereby resistance develops are mutations in the ESR1 gene and activation of parallel signaling pathways. We hypothesize that evaluating the mutational status of a set of pre-specified genes involved in endocrine resistance in the peripheral blood of MBC patients may detect failure to endocrine treatment at an early stage. If confirmed, this will improve our insight into mechanisms underlying treatment failure, would allow to discontinue ineffective treatment earlier than based on routine radiological assessments, thereby sparing patients from toxicity and reducing costs, and lastly, would allow to explore switching to

other (combination) treatments based on the detected emerging mutations.

Study objective

The primary objective of this clinical study is to identify whether activating mutations in ESR1 detected in circulating tumor DNA (ctDNA) in peripheral blood are associated with resistance to endocrine therapy in patients with ER-positive, human epidermal growth factor receptor 2 (HER2)-negative MBC. Further aims are to obtain detailed molecular information on emerging (in)activating mutations in driver genes by targeted next generation sequencing (NGS) of ctDNA from plasma taken before and during two subsequent treatment lines and to determine which of the collected genetic information will be informative to predict and monitor disease progression and to eventually guide the choice of therapies. Also, the mutational landscapes of primary tumors and metastatic lesions,

Study design

This concerns a prospective longitudinal study.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: the burden for patients participating to this study is limited. Only one blood tube of 10 mL will be drawn every twelve weeks, preferentially in combination with a routine blood draw and out-patient visit. The risk of participation are negligible, since only blood draws per venipuncture are asked. Participation to this study will not directly benefit the patient herself, but may provide information to improve endocrine treatments for patients with ER-positive, HER2-negative MBC in the near future.

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
• Postmenopausal status, being defined as:
- Age >=60 years
- Age <60 years and last menstruation >=1 year ago when not treated with chemotherapy and/or endocrine treatment in the meantime
- Age <60 years and postmenopausal luteinizing hormone (LH), follicle stimulating hormone (FSH), and plasma estradiol levels
- Surgical or radiation-induced sterilization
• Histologically or cytologically confirmed diagnosis of metastatic breast cancer
• Histological confirmation of ER-positive (>10% of the tumor cells ER-positive), HER2-negative disease (1+ staining or 2+ non-amplified), preferentially of the primary tumor, but otherwise of a biopsied metastatic/recurrent site
• Radiologically evaluable disease according to RECIST version 1.1
• Willingness and capacity to follow the protocol specified visits for blood sampling for the total duration of the study
• Capacity of understanding and signing the informed consent brochure prior to the blood samplin

Exclusion criteria

• Prior treatment in the metastatic setting with any AI
• For the second part of blood sampling during everolimus/exemestane: other hormonal treatment in between the AI and combination everolimus/exemestane line. Chemotherapy to contain rapidly progressing before starting everolimus/exemestane is allowed.
• A secondary malignancy currently present or curatively treated within the last five years

before registration, except for non-melanoma skin cancer, cervical carcinoma in situ, or bladder cancer in situ.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-02-2017
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO

Date:	12-05-2016
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	NL53978.078.15