

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

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<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Breast neoplasms malignant and unspecified (incl nipple)
<b>Study type</b>	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**

### **Public**

Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80  
Rotterdam 3015 CN  
NL

### **Scientific**

Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80  
Rotterdam 3015 CN

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Elderly (65 years and older)

### Inclusion criteria

- Age  $\geq 18$  years
- Postmenopausal status, being defined as:
  - Age  $\geq 60$  years
  - Age  $< 60$  years and last menstruation  $\geq 1$  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 sampling

### 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

CCMO

### ID

NL53978.078.15