Activity of trastuzumab based chemotherapy in metastatic breast cancer patients with HER2-negative primary tumor but HER2 positive circulating tumor cells

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

Summary

ID

NL-OMON46900

Source
ToetsingOnline

Brief title
CareMore-Trastuzumab

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
metastastic mammary cancer, metastatic breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Interne Oncologie
Source(s) of monetary or material Support: EU-FP7;CareMore;projectnumber 601760-2

Intervention

Keyword: circulating tumor cells, HER2, metastatic breast cancer, trastuzumab

Outcome measures

Primary outcome

The primary endpoint is progression free survival rate at 6 months (PFR6mth) in patients with HER2-negative primary tumor but at least one HER2-positive CTC, receiving trastuzumab/taxane-based chemotherapy.

Secondary outcome

Secondary endpoints are the association between 6 months PFR and PIK3CA mutation status, pHER2 expression and ER expression on CTC*s. In addition, the PIK3CA mutation status, HER2 and ER expression status will be re-evaluated on the primary tumor. Furthermore, CTC enumeration and characterization done following CellSearch procedures and CytoTrack procedures, respectively, will be compared. Lastly, it will be explored whether the % of HER2-positive CTCs correlates with response to trastuzumab/taxane-based chemotherapy.

Study description

Background summary

Today*s treatment of metastatic breast cancer is guided by characteristics of the primary tumor, while 90% of deaths due to breast cancer occur as a consequence of metastases. It is appreciated that tumor characteristics may differ between the primary tumor and the metastases. In addition, evidence is accumulating that there are patients with HER2-negative primary tumors who

respond to trastuzumab-based chemotherapy. One group of patients with HER2-negative primary tumors who might benefit from trastuzumab-based approaches is patients with HER2-positive circulating tumor cells (CTCs). CTCs are cancer cells present in the peripheral blood of patients with metastatic breast cancer and are thought to represent characteristics of the metastases. We hypothesize that patients with a HER2-negative primary tumor but with at least one HER2-positive CTC benefit from HER2 targeted treatment with trastuzumab.

Study objective

The primary objective is to determine if metastatic breast cancer patients with HER2-negative primary tumors but with at least one HER2-positive CTC benefit from trastuzumab-containing chemotherapy. Secondary objectives are to determine the impact of ER, phosphorylated HER2 (pHER2) and PIK3CA mutations in CTCs on the outcome of trastuzumab-based chemotherapy and to determine the PIK3CA mutation status, pHER2 and ER expression status on primary tumor tissue to compare with CTCs. Furthermore, two methods to enumerate and characterize CTCs will be compared.

Study design

Multi-center prospective intervention study

Intervention

1x20 mL of blood will be drawn to screen patients for the presence of HER2-positive CTCs. In patients with at least one HER2-positive CTC, an additional 60 mL of blood will be drawn for CTC characterization. These patients will be treated with trastuzumab starting in combination with docetaxel or paclitaxel at the following dose:
For the docetaxel-containing regimen: : Intravenous administration starts the first cycle at a dose of 8 mg/kg, lowering the dose to 6 mg/kg for the subsequent cycles, intravenously, every 3 weeks, continuing until disease progression. Subcutaneous administration is always 600mg, regardless of the body weight of the patient, given every 3 weeks, continuing until disease progression. This is combined with docetaxel at 100mg/m2 intravenously every 3 weeks, for a maximum of 6 cycles.
Fro the paclitaxel containing regimen: Intravenous administration starts the first week at a dose of 4mg/kg, lowering the dose to 2mg/kg for the subsequent weeks. Subcutaneous administration of 600mg given every 3 or 4 weeks, depending on a 3- or 4- weekly paclitaxel regimen, regardless of the body weight of the patient, continuing until disease progression. This is combined with weekly paclitaxel 80-90mg/m2 intravenously for a maximum of 12 administrations.

Study burden and risks

20 mL blood will be drawn for screening for CTC enumeration. The laboratory for Translational Tumor Immunology will report back whether the patient has HER2-positive CTCs or not within 4 days. These 4 days waiting time are not considered as a relevant delay of treatment. In case a patient has at least one HER2-positive CTC, an additional 60 mL blood for CTC characterization will be collected and patients will be treated with trastuzumab and docetaxel or paclitaxel, which is a well-known treatment with potential risks of toxicity.
All blood will be drawn during another blood draw that is already required for standard care.

Contacts

Public
Selecteer

Groene Hilledijk 301
Rotterdam 3075EA
NL
Scientific
Selecteer

Groene Hilledijk 301
Rotterdam 3075EA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Screening:

Female patient with metastatic breast cancer with HER2-negative primary tumor
Age >= 18 years old
WHO performance status <=2
Considered fit enough to receive trastuzumab/taxane-based chemotherapy by the treating physician
Able to understand and give written informed consent;Secondary inclusion criteria:
Female patient with metastatic breast cancer with HER2-negative primary tumors with the presence of at least one HER2-positive CTC
Adequate left-ventricular ejection fraction (LVEF) of at least 45%

Exclusion criteria

Previous chemotherapy for metastatic disease.
Adjuvant chemotherapy within 6 months prior to treatment start.
Hormonal antitumor treatment within one week prior to treatment start.
Symptomatic CNS metastases

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-03-2015
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Herceptin

Generic name:	Trastuzumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Taxol
Generic name:	Paclitaxel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	Docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-11-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-02-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-07-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-07-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-08-2016
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-02-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-08-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-09-2018
Application type:	Amendment
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

ID: 20549
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2014-004432-18-NL
CCMO	NL51298.078.14
OMON	NL-OMON20549

Study results

Date completed: 17-07-2023

Actual enrolment: 9

Summary results
Trial ended prematurely