[89Zr]trastuzumab PET/CT imaging of HER2 positive breast cancer for predicting pathologic complete response after neoadjuvant chemotherapy; a multicentre study

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In this feasibility study, we will validate the value of the preoperative [89Zr]trastuzumab PET/CT imaging to identify HER2 positive primary breast cancer and the possibility to predict pathological complete response.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast disorders
Study type	Observational non invasive

Summary

ID

NL-OMON50044

Source
ToetsingOnline

Brief title
[89Zr]trastuzumab PET/CT imaging of HER2 positive breast cancer

Condition

- Breast disorders

Synonym
Breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Europese Unie (ERC grant)

Intervention

Keyword: [89Zr] trastuzumab, HER2+ breast cancer, pCR, PET/CT imaging

Outcome measures

Primary outcome

To determine if HER2 positive primary breast cancer can be detected by

[89Zr]trastuzumab PET/CT imaging, using histopathological examination as the

gold standard, after neoadjuvant treatment.

- Assess the negative predictive value and sensitivity of [89Zr]trastuzumab

PET/CT imaging to detect HER2 positive primary breast cancer.

Secondary outcome

- Assess agreement between [89Zr]trastuzumab PET/CT-imaging signal in the tumor

and axilla, histopathologic evidence of tumor and HER2 expression.

- Assess the agreement between different imaging modalities ([89Zr]trastuzumab

PET/CT-scan, [18F]FDG-PET/CT and MRI).

Study description

Background summary

Currently, there is no adequate non-invasive diagnostic modality to assess treatment response after neoadjuvant therapy in breast cancer patients. To adequately predict histological complete response, further optimization of non-invasive imaging approaches for response monitoring is crucial. For patients with a complete response to neoadjuvant treatment non-operative treatment might be an option.

Approximately 20% of breast cancers have an overexpression of the human epidermal growth factor receptor 2 (HER2), which can be selectively targeted by the monoclonal antibody trastuzumab (Herceptin, Genentech, San Francisco, USA). By labelling trastuzumab with a radiotracer ([89Zr]trastuzumab) preoperative imaging using positron emission tomography (PET/CT) is possible.

Study objective

In this feasibility study, we will validate the value of the preoperative [89Zr]trastuzumab PET/CT imaging to identify HER2 positive primary breast cancer and the possibility to predict pathological complete response.

Study design

This pilot study is a phase II, multicenter study in HER2 positive breast cancer patients. This study will assess the feasibility of detection of HER2 positive breast cancer by preoperative [89Zr]trastuzumab PET/CT imaging of the primary tumor. For this study 20 patients with HER2 positive breast cancer will be included. All patients will undergo standard-of-care treatment, with additionally pre- and after neoadjuvant chemotherapy [89Zr]trastuzumab PET/CT imaging. All patients will receive 50 mg [89Zr]trastuzumab 4 days prior to the pre-neoadjuvant [89Zr]trastuzumab PET/CT scan and 4 days prior to the post-neoadjuvant [89Zr]trastuzumab PET/CT scan. The negative predictive value and sensitivity of HER2-targeting PET will be determined. Validation will take place by histopathologic assessment of tissue to determine the presence (or absence) of tumor tissue and immunohistochemically assessment for tumor HER2 expression.

Study burden and risks

The risk for the individual patients is the risk of the use of ionizing radiation, incidental PET findings and (so far unknown) possible adverse effects of [89Zr]trastuzumab. Interference with standard clinical care is not expected.

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

• Female patients aged 18 years or older.
• Confirmed diagnosis of HER2 positive primary breast cancer (confirmed by immunohistochemical staining of preoperative core-needle biopsy of tumor tissue; IHC with strong intensity 3+ or fluorescence in situ hybridization (FISH)) and eligible for breast cancer surgery.
• Tumor size >= 5 mm (0.5 cm) diameter according to anatomical imaging data.
• WHO performance score 0-2.
• Patients planned for neoadjuvant therapy.
• Female patients need to be either surgically sterile, post-menopausal or pre-menopausal and not pregnant. Pre-menopausal female patients who are not surgically sterile should also employ an effective method of birth control for at least one month post-dosing when it consists of a hormonal contraceptive method or IUD. For other contraceptive methods, premenopausal females who are not surgically sterile have to agree to use an effective method of contraception.
• Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial.
• Before patient registration, written informed consent must be given according to ICH/GCP, and national/local regulations.

Exclusion criteria

• Any condition that in the opinion of the investigator could potentially jeopardize the health status of the patient.
• Medical or psychiatric conditions that compromise the patient*s ability to give informed consent. Presence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule.
• Prior radiotherapy to the targeted breast.
• Breast prosthesis in the target breast.
• Unacceptable known (clinical significant) cardiovascular or pulmonary disease, renal or liver dysfunction.
• Known hypersensitivity to drugs comparative to trastuzumab or drugs in the same class (immunoglobulins), or any of their excipients or to any component of [89Zr]trastuzumab.
• Concomitant medication known to interact with trastuzumab.
• Inability to undergo PET/CT scanning (e.g. claustrophobia, weight limits or inability to tolerate lying for the duration of an PET/CT scan (~30 min)).

Study design

Design

Study phase:	2
Study type:	Observational non invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-06-2019
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	[89Zr]trastuzumab
Generic name:	[89Zr]trastuzumab

Ethics review

Approved WMO Date:	19-12-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	22-03-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	06-06-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	26-06-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	08-10-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	17-06-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	02-10-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	01-02-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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
EudraCT	EUCTR2018-004247-23-NL
CCMO	NL68188.058.18

Study results

Date completed: 01-01-2023

Actual enrolment: 7

Summary results
Trial ended prematurely