Zirconium-89 Trastuzumab tracer uptake in metastatic breast cancer: A pilot study.

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Primary Objectives:Use 89Zr-Trastuzumab to characterise the in vivo biodistribution using PET imaging in the primary tumour and distant metastases.Comparie the uptake in patients with Her2/neu positive breast cancer to patients with HER2/neu...

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

Summary

ID

NL-OMON41895

Source
ToetsingOnline

Brief title
Zirconium-89 Trastuzumab tracer for metastatic breast cancer patients

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
HER2 positive or -negative metastatic breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Afdeling Nucleaire Geneeskunde;NKI-AVL

Intervention

Keyword: Breast cancer, HER2/neu, PET/CT, Zirconium

Outcome measures

Primary outcome

Describe and quantify the 89Zirconium-Trastuzumab biodistribution in all patients in terms of dose per volume (MBq/ml), percentage of injected dose per volume tissue (%ID/ml) and Standardised Uptake Values (SUVs) based on the PET/CT. This work will provide an insight into the tracer accumulation in malignant and normal tissues with respect to mean accumulation and the variation in accumulation patterns. Hence, this project will be used as a pilot for a future larger study or, depending on the results, may serve as a validation for the clinical application of this technique.

Secondary outcome

A description of the relation between uptake patterns on 18F-FDG and 89Zr-Trastuzumab PET/CT will be provided. Additionally, the variation serum HER2 and Trastuzumab concentrations will be related to the Zr-89 Trastuzumab accumulation in the normal liver tissue and tumour lesions. These data again will provide mean and variation values in Her2/neu positive and negative tumours.

Study description

Background summary

For patients with HER2/neu overexpressing or amplificated breast cancer, Trastuzumab is the most import key of treatment. If we can visualise the amount

of 90-Zirconium-Trastuzumab tracer that binds the primary tumour, we could in the future possibly predict the effectiveness of Trastuzumab therapy.

If discant metastases are present, the Trastuzumab therapy is meant to bind to all the lesions to achieve an optimal treatment. The problem exists that commonly used diagnostic modalities cannot discriminate between different primary tumour or metastatis subtypes without a biopsy. If the distant metastasis present is near an important organ or greater artery (aorta), it can be a challenge or even life-threatning to attempt a biopsy. Therefore lesions sometimes are left unclassified before treatment.

With the 89-Zirconium-Trastuzumab tracer it is possible to visualise on PET/CT images which lesions binds the tracer and where it can be expected that the treatment will be effective. If there are lesions present where the tracer doesn't bind a different treatment can be chosen (chemotherapy, resection of radiotherapy).

Study objective

Primary Objectives:
Use 89Zr-Trastuzumab to characterise the in vivo biodistribution using PET imaging in the primary tumour and distant metastases.
Comparie the uptake in patients with Her2/neu positive breast cancer to patients with HER2/neu negative breast cancer.

Secondary Objectives:
Compare the 89Zirconium tracer uptake within the primary tumour and metastases with lesions visualised on the 18F-FDG PET/ CT.
Relate circulating HER2/neu (serum HER2) concentration to 89Zr-Trastuzumab uptake in the tumour.

Study design

Patients with stadium II/III breast cancer with discant metastases visible on 18F-FDG PET/CT will be asked to participate in this study. A total of 12 patients will be included (8 with and 4 without HER2/neu amplification or overexpression).

Two hours before administration of of het tracer veneus blood samples will be taken for the measurement of circulating Trastuzumab after administration of a preparation dose Trastuzumab (50 mg intravenously). A total dose of 37 MBq 89-Zirconium-Trastuzumab will be administered.

On the fourth day after adminstration of the tracer, a new venous bloodsample will be taken for the measurement of circulating tracer directly followed by a PET/CT acquisition in hanging prone- and in supine position, followed by a

prone position acquisition on a dedicated breast PET (MAMMI PET). On the sixth day the venous blood sample will be followed solely by a PET/CT acquisition in supine position.
On the Zirconium PET/CT the tracer accumulation will be quantified in all lesions and in normal tissue (e.g. liver, blood pool and kidneys).

Study burden and risks

The participation in this study is not associated with significant risk for the patient or personnel.

The participating patients will acquire a total dose of 20 mSv after the single administration of 37 MBq 89-Zirconium-Trastuzumab and the two low-dose (PET/)CT's. The radiation dose is comparable to 2 abdominal contrast enhanced CT scans or 3 FDG PET/CT scan acquisitions.

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

Histological confirmed breast cancer (8 with and 4 without HER2/neu overexpression or amplification), with a primary tumour and at least 1 distant metastatic lesion.;Recent diagnostic 18F-FDG PET/CT (less than 1 month old) made at the NKI-AvL.

Exclusion criteria

A medical condition (e.g. Li-Fraumeni) that would place the patient at unusual risk for development of new malignancies due to radiation.
Concurrent use of investigational drug with unknown biodistribution.
Present pregnancy, or the patient refuses to use an adequate contraception method if pre-menopausal.
Known allergy for murine proteins (present in Trastuzumab).

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2014
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	89-Ziconium-Trastuzumab

Generic name:	Zr89 Trastuzumab
Product type:	Medicine
Brand name:	Herceptin-DM1
Generic name:	Trastuzumab-DM1
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	30-09-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	02-02-2015
Application type:	First submission
Review commission:	METC NedMec

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	EUCTR2014-002800-25-NL
CCMO	NL49980.031.14