Early monitoring of trastuzumab +/- pertuzumab therapy with 18F-choline PET/CT in patients with advanced disease breastcancer.

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In this pilotstudy we are planning to investigate in a relatively low number of patients if [18F]-choline uptake will decrease after 2 to 3 weeks of trastuzumab +/- pertuzumab therapy in morphologically responding patients (as noted after 12 weeks...

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

Summary

ID

NL-OMON39351

Source
ToetsingOnline

Brief title
Trastuzumab +/- pertuzumab PET/CT pilotstudy.

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
advanced disease breastcancer, Breastcancer with distant metastases

Research involving
Human

Sponsors and support

Primary sponsor: Catharina-ziekenhuis

Source(s) of monetary or material Support: Deelnemende ziekenhuizen (overhead).,VU Cyclotron BV te Amsterdam

Intervention

Keyword: 18F-choline PET/CT, Breastcancer, Therapymonitoring, Trastuzumab

Outcome measures

Primary outcome

To measure changes in [18F]-choline uptake in targetlesions after 2 to 3 weeks of trastuzumab +/- pertuzumab (and docetaxel) treatment and relate these changes to the morphological response on CT after 12 weeks of therapy.

Primary endpoint:

Per category of morphological response on CT after 12 weeks of therapy (RECIST 1.1 criteria for CR, PR, SD and PD) a mean and 95% confidence interval will be computed for the corresponding changes in [18F]-choline uptake after 2 tot 3 weeks of therapy (4 groups). The categories CR+PR and SD+PD will then be taken together as responders and non-responders, respectively. For both responders and non-responders a mean and 95% confidence interval will be computed as well (2 groups). In addition it will be investigated if there is a significant difference between these two groups.

Secondary outcome

Investigate if a cutoff value can be determined for the decrease in [18F]-choline uptake after 2 tot 3 weeks of therapy that can discriminate responding patients from the non-responding ones.

Secondary endpoint:

Determination of a cutoff value for the decrease in [18F]-choline uptake after

2 tot 3 weeks of therapy that can discriminate responding patients from the

non-responding ones.

Study description

Background summary

Trastuzumab (Herceptin) +/- pertuzumab (Perjeta) in combination with docetaxel (Taxotere) is being used in the treatment of HER2/neu receptor positive advanced disease breastcancer. At present patients treated with trastuzumab +/- pertuzumab are monitored using conventional morphological techniques, i.e. CT-scans. Routinely, the first follow-up CT-scan is performed after twelve weeks of therapy and compared to the initial pre-therapy scan. According to morphological RECIST criteria targetlesions do or do not respond to therapy. In the case of a non-responder alternative strategies need to be considered. In the meantime these patients have been treated with an ineffective therapy, causing serious side effects. Most important side effect of trastuzumab and pertuzumab is potential cardiotoxicity. Taking into consering these potentially serious side effects, earlier follow-up than at 3 months seems to be mandatory. This is where nuclear medicine comes into play with functional techniques rather than morphological. PET/CT is a hibrid technique that combines both a functional and a morphological approach and is expected to allow monitoring as early as after 2 or 3 weeks of trastuzumab +/- pertuzumab therapy .

[11C]-choline is a radiotracer of choline phospholipid metabolism in cell membranes. Choline is an essential amino acid needed for the synthesis of cell membrane phospholipids, and has both anabolic and katabolic pathways. Normally these pathways are in balance, but in rapidly dividing cancer cells the anabolic pathway is dominant, being the solid base for [11C]-choline PET/CT imaging. There is good uptake of [11C]-choline in HER2/neu receptor positive breast cancer lesions, that seems to decrease in patients responding clinically to trastuzumab therapy. This seems to make [11C]-choline an ideal radiotracer for the early response monitoring of trastuzumab and pertuzumab therapy in these patients.

The use of the short lived [11C] label demands for PET/CT facilities in close proximity to the cyclotron that is producing the radiotracer. The longer lived [18F] label allows transportation to sites more remote from the producing cyclotron, and is at present commercially available and being used in the

routine staging and restaging of patients with prostate cancer. Application in breast cancer patients has been anecdotal so far, but seems possible because biodistribution of [18F]-choline and [11C]-choline is nearly identical.

Because of this anecdotal experience with [18F]-choline in breast cancer patients, we are planning to perform a pilotstudy in a relatively low number of patients in order to investigate if [18F]-choline uptake will decrease after 2 to 3 weeks of trastuzumab +/- pertuzumab therapy in morphologically responding patients (as noted after 12 weeks on a CT-scan). In addition, we would like to sort out if responders can thus be discriminated from non-responders. The results of this pilotstudy will be used to design a definite study involving a sufficient number of patients in order to determine a cutoff value for the decrease in [18F]-choline uptake that can discriminate responding from non-responding patients.

Study objective

In this pilotstudy we are planning to investigate in a relatively low number of patients if [18F]-choline uptake will decrease after 2 to 3 weeks of trastuzumab +/- pertuzumab therapy in morphologically responding patients (as noted after 12 weeks on a CT-scan). In addition, we would like to sort out if responders can thus be discriminated from non-responders.

Study design

The study design is that of a prospective pilotstudy that can suit the routine diagnostic and therapeutic work-up of patients with HER2/neu receptor positive advanced disease breast cancer. Patients will have an initial [18F]-choline PET/CT study (PET/CT study No. 1) that will be repeated after 2 to 3 weeks of trastuzumab +/- pertuzumab (and docetaxel) therapy (PET/CT study No. 2). The initial [18F]-choline PET/CT study can be combined with a contrast enhanced diagnostic CT when there is a high suspicion upon distant metastases. Of course all patients will be evaluated and treated according to existing criteria.

A total number of 20 evaluable patients that will have completed the entire research protocol is anticipated. Taking into account premature withdrawal of patients from the study, we anticipate a total number of 45 PET/CT studies in approximately 23 patients. From historical data on the incidence of HER2/neu receptor positive advanced disease breast cancer in the participating hospitals we can estimate the total duration of the pilotstudy to be one to one and a half years. The participating hospitals are the Bronovo hospital in The Hague, the Reinier de Graaf hospital in Delft, the Catharina hospital in Eindhoven and the NKI/AVL in Amsterdam. We are planning to restart the pilotstudy in november 2013.

Study burden and risks

The burden associated with participation comprises of two additional studies for which Brovono patients will have to travel to Delft where an intravenous access is to be instituted. Patients from Eindhoven and Amsterdam can have their studies done in their respective hospitals. When there is a high suspicion upon distant metastases, the initial [18F]-choline PET/CT study can be combined with a contrast enhanced diagnostic CT for which an intravenous access is mandatory as well.
The radiotracer [18F]-choline, that will be used in both PET/CT studies, will be administered in very low tracer amounts that probably will not cause any adverse side effects.
However PET/CT studies do have a radiation burden. In the literature an effective equivalent dose of approximately 10 mSv was reported for [18F]-choline PET studies (no CT). In this study dating from 2002 less sensitive PET scanners were being used than nowadays. Using present modern PET/CT scanners a dose reduction of approximately 60% can be achieved, enabling an effective equivalent dose of 4 mSv per study and 8 mSv for a study including a low dose CT (PET/CT). In case of both an initial and follow-up PET/CT scan, the total effective equivalent dose administered extra to the patients is 16 mSv. For comparison: the radiation burden of a contrast enhanced diagnostic CT is 8 to 20 mSv per scan, depending on the protocol being used. The extra radiation burden of 16 mSv may lead to an increased risk for developing a second tumor in the participating patients. However, the latency time of such an effect is probably much longer than the average life expectancy of these patients.

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

Her2/neu receptor positive breastcancer with new distant metastases, qualifying for initial regular therapy with trastuzumab, docetaxel and pertuzumab (facultatively)
At least 18 years old and
Mentally competent

Exclusion criteria

Younger than 18 years old
Mentally incompetent
Pregnancy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-04-2014
Enrollment:	23

Type:	Actual

Ethics review

Approved WMO Date:	31-05-2012
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	05-04-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	11-11-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL38411.098.12