Cardiac sympathetic innervation imaging in patients with trastuzumab induced cardiotoxicity

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational non invasive

Summary

ID

NL-OMON34705

Source
ToetsingOnline

Brief title
CARIT

Condition

- Heart failures
- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Trastuzumab induced cardiotoxicity

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 123I-MIBG scintigraphy, Cardiac neuroadenergic system, Cardiotoxicity, Trastuzumab

Outcome measures

Primary outcome

The primary objective of this pilot study is to assess the neuroadrenergic

system in patients with cardiac toxicity due to trastuzumab in order to reveal

the pathofysiological mechanisms of trastuzumab induced cardiotoxicity

Secondary outcome

The secondary objective of this study is, in case of a positive tendens of

abnormal I-MIBG scans in patients with declined LEVFs, to set up a prospective

randomized controlled trial for patients with trastuzumab induced cardiotoxiciy

in the future.

Study description

Background summary

Trastuzumab is a humanized monoclonal antibody directed against the human epidermal growth factor receptor-2 (HER-2), also known as ErbB-2 or NEU, and inhibits HER2-mediated malignant transformation. Amplification or overexpression of HER-2 is seen in approximately 25% of invasive breast cancers and is associated with a more aggressive form of cancer with an unfavorable prognosis. However, cardiac toxicity is an important side effect of trastuzumab therapy, which can manifest as symptomatic congestive heart failure (CHF) or asymptomatic left ventricular ejection fraction (LVEF) decline. A higher incidence of cardiotoxicity is seen in combination with high cummulative doses of antracyclines, a common used type of cytotoxic drugs in breast cancer. Cardiotoxicity due to trastuzumab differs from caardiotoxicty caused by antracyclines. The pathofysiology of trastuzumab induced cardiotoxicity is currently unknown. A hypotheses is that ,by blocking the HER-2 receptor, signaling of the sympatovagal controle systems of the heart is impaired. According to the interim analysis of the CARIT study, in the first three

patients, a scintigraphic evidence of cardiac sympathetic dysfunction was observed. This is the reason for submitting this amendment where we extend the patient population to include trastuzumab-treated breast cancer patients who did not develop a significant reduction of the LVEF as a control group.

Study objective

We intend to study the effect of trastuzumab on the cardiac neuronal activity in patients with HER-2 positive breast cancer by using iodine-123 meta-iodobenzylguanidine (123I-MIBG) and cardiac imaging. 123I-MIBG, an analogue of the false neurotransmitter guanithidine, localizes in adrenergic nerve terminals.

Study design

Retrospective, diagnostic, blinded, single center observationial/ diagnostic pilot study

Study burden and risks

Unfortunately, the MUGA scan and I-MIBG scan cannot be done on the same day. So the patient has to come to the LUMC twice. Both scans are well approved and standard of care for certain indication. The MUGA scan is commonly used as a diagnostic test for analysing the LVEF in patient, every 3 months during therapy with trastuzumab and for many other indications. The scan takes about 45 minutes, the patient has to lay still which can be a burden. The radiofarmaceuticals are well aproved, the radiation dose is low and not toxic. The I MIBG scan is wel known for it's use in pateintes with heart failure. The scan takes 45 minutes and has to be repeated after 4 hours. For this scan the radiation exposure is low.

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

•Adult patients with confirmed HER-2 positive breast cancer (immunohistochemistry score 3 or fluorescence in-situ hybridization positive) who have completed local regional therapy and treatment with trastuzumab or are still on treatment with trastuzumab.
•Permanent LVEF <=50% after treatment with trastuzumab, and/or
•A permanent relative decrease of >=10% from baseline measured by means of echocardiography or MUGA scan and confirmed after 3 weeks after/during treatment with trastuzumab, and/or
•Symptomatic congestive heart failure defined as NYHA class III/IV
•Age 18-80 years.
•Signed informed consent
•WHO 0-2
Amendement: Add control group: patients without a permanent relative decrease of >=10% from baseline measured by means of echocardiography or MUGA scan and confirmed after 3 weeks after/during treatment with trastuzumab, and/or symptomatic congestive heart failure defined as NYHA class III/IV

Exclusion criteria

•Pre-existing cardiac disease such as heart failure, ischemic and valvular heart disease, arrhythmia or poorly controlled hypertension.
•Concomitant inflammatory disease.
•Pregnancy/beast feeding.
•Allergy against radiopharmaceutical (99m Tc-based tracer) for MUGA scan.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-07-2010
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	Technetium 99m-pertechnetate en 123-I-MIBG
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	12-05-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL31280.058.10