Prospective, randomized, pharmacological intervention study; evaluating the effect of the angiotensin II-receptor (AT1) blocker candesartan versus placebo in prevention of trastuzumab-associated cardiotoxicity in patients with primary breast cancer treated with trastuzumab

Published: 26-03-2007
Last updated: 11-05-2024

Primary objectives:1) To determine whether concurrent ATII-antagonist treatment can prevent trastuzumab-related cardiotoxicity, defined as a decline in LVEF of more than 15% or a decrease to an absolute value

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON34077

Source
ToetsingOnline

Brief title
Prospective intervention of candesartan

Condition

- Heart failures
- Miscellaneous and site unspecified neoplasms benign

Synonym
decrease of the left ventricular ejection fraction (LVEF)

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Astra Zeneca,bedrijven

Intervention

Keyword: angiotensin II-receptor (AT1) blocker, cardiotoxicity, prevention, trastuzumab

Outcome measures

Primary outcome

Left ventricular ejection fraction (LVEF)

Secondary outcome

- NT-proBNP en tropinin T analysis

- genotype analysis

- electrocardiogram

- cardiac questionnaire

- New York Heart Association (NYHA)

Study description

Background summary

The addition of trastuzumab to the standard adjuvant chemotherapy in HER2-positive breast cancer patients markedly improves treatment outcome. Cardiac dysfunction is an important side effect observed with the use of trastuzumab for the treatment of patients with HER2-positive breast cancer. In recent clinical trials evaluating the addition of trastuzumab to the adjuvant treatment of these patients, trastuzumab treatment had to be discontinued in approximately 20% due to the occurrence of a significant decrease in LVEF.

In a fraction of the patients trastuzumab was stopped before completion of the treatment. These patients with HER2 positive breast cancer are excluded from the best adjuvant systemic treatment at this moment. It is imperative in practice to follow the stringent criteria for eligibility and cardiac monitoring used by the HERA and NSABP B-31 trials. However, cardio-protective drugs and optimizing screening methods are important measurements to investigate. It is important to decrease the morbidity and mortality of trastuzumab treatment to enable optimal therapy with trastuzumab in the adjuvant setting, but also in patients with metastatic disease.

Study objective

Primary objectives:
1) To determine whether concurrent ATII-antagonist treatment can prevent trastuzumab-related cardiotoxicity, defined as a decline in LVEF of more than 15% or a decrease to an absolute value <45%

Secondary objectives:
1) To determine if *Brain Natriuretic Peptide* (NT-proBNP) and troponin T can be used as surrogate marker in the monitoring of trastuzumab-associated cardiotoxicity
2) To determine genetic variability in relevant genes such as the HER2 gene (by assessing single nucleotide polymorphisms [SNPs] in the kinase domain) and explore any correlations with trastuzumab induced cardiotoxicity
3) To determine the reversibility of a decrease in left ventricular ejection fraction (LVEF) associated with trastuzumab treatment

Study design

Prospective, randomized pharmacological intervention study

Intervention

Arm I : placebo
Arm II : AT1 blocker candesartan (32 mg/day; run in 16 mg during week 1)

Study burden and risks

Three bloodsamples and two MUGA scans more than in standard medical care.

There are no data about the preventive use of candesartan to protect against cardiotoxicity during treatment with trastuzumab.

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

cytologically or histologically confirmed primary breast cancer

Exclusion criteria

history of hypersensitivity for the study medication

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-06-2007
Enrollment:	160
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	atacand
Generic name:	candesartan
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	26-03-2007
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	26-11-2007
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	15-04-2008
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-09-2008
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	19-11-2008
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-06-2009
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-09-2010
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	EUCTR2006-001707-11-NL
CCMO	NL11334.031.07