The effect of Trastuzumab treatment on B-cell kinase activities assessed by microarray derived phosphorylation profiles.

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

Summary

ID

NL-OMON30106

Source
ToetsingOnline

Brief title
Trastuzumab and HER kinase profiling.

Condition

- Breast disorders

Synonym
Breast cancer, metastatic breast cancer.

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis

Source(s) of monetary or material Support: farmacologische research gelden (4e geldstroom)

Intervention

Keyword: HER-receptor., kinase, microarray, trastuzumab

Outcome measures

Primary outcome

Primary endpoint of this study is to obtain peptide phosphorylation profiles of

patients treated with trastuzumab.

Secondary outcome

Secondary endpoints of this study are to correlate the generated

phosphorylation profiles as well as metabolic and proteomic changes following

trastuzumab treatment to trastuzumab pharmacokinetics .

Study description

Background summary

Cancer is associated with activation and deactivation of a wide range of proteins. With the development of the peptide microarray system by Pamgene, it is possible to measure the phosphorylation of a wide variety of peptide substrates, and thus kinase enzyme activities, at once. Using a phosphopeptide capture assay, the SELDI-TOF MS technology can also be applied in generating a protein phosphorylation profile. These protein phosphorylation profiles can tell us more about the signalling pathways involved in cancer progression.

Study objective

Objectives to explore: :
1-whether kinase activities can be detected in lymphocytes derived from cancer patients, using a peptide array or a phosphopeptide capture SELDI-TOF MS assay.
2-how many cells are needed for the generation of a kinase activity profile by a peptide array and SELDI-TOF MS assay.
3-whether an (indirect) effect of patient treatment with trastuzumab, targeting Her2/Neu/ErbB2 (receptor tyrosine kinase), is detectable by changes in the

phosphorylation profile from lysates of lymphocytes sampled before and after patient treatment, using a peptide array or using a phosphopeptide capture SELDI-TOF MS assay.
4-Whether changes in kinase profile can be correlated with the exposure to trastuzumab in plasma.
5-Whether changes in the SELDI-TOF MS protein profiles of PMBC lysates and serum are correlated with patient exposure to trastuzumab.
6-Whether changes in the kinase profile are correlated with changes in the SELDI-TOF MS protein profiles of PBMC lysates or serum.
7-Whether changes in kinase activity are correlated with metabolic changes in urine.

Study design

In total, thirty (30) patients will be included. Fifteen (15) patients who will be treated with trastuzumab will be asked to donate blood and urine samples at predefined timepoints during the first 4 cycles of treatment in order to determine kinase activities in white blood cells and to quantitate trastuzumab levels in serum and determine metabolites in urine. Fifteen patients whose treatment is discontinued will be asked to donate blood samples at predefined timepoints over a period of 8 weeks in order to construct a elimination curve of trastuzumab. These patients must have completed at least 4 months of trastuzumab treatment.

Intervention

Local hospital procedures for dosage and administration of trastuzumab will be followed. Dose modifications because of developed toxicities are left to the discretion of the responsible oncologist. Discontinuation of treatment is left to the discretion of the responsible oncologist.

Study burden and risks

The study procedures in this study include the collection of blood as well as of urine samples. Participants of this study might get a bruise due to drawing of blood samples.

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

Patients who will be treated with trastuzumab in their best interest as single agent or in combination with chemo- or hormonal therapy (15 patients), or who are about to discontinue treatment with trastuzumab (15 patients for elimination curve), Age >18 years, written informed consent prior to participation in the trial, Able and willing to undergo blood and urine sampling.

Exclusion criteria

The common exclusion criteria regarding trastuzumab treatment will be followed, and left to the discretion of the treating physician.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-12-2006
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	14-09-2006
Application type:	First submission
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
CCMO	NL12950.031.06