

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

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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...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Breast disorders
<b>Study type</b>	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 an 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**

### **Public**

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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**

CCMO

**ID**

NL12950.031.06