Studying the relationship between the CYP3A and CYP2D6 probe dextromethorphan and the pharmackinetics of tamoxifen.

Published: 14-04-2009
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To investigate the relationship fo the pharmacokineticsof the probe drug (dextromethorphan) and tamoxifen.

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

Summary

ID

NL-OMON33769

Source
ToetsingOnline

Brief title
Relationship between CYP3A and CYP2D6 probe and PK of tamoxifen

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: dextromethorphan, pharmacokinetics, tamoxifen

Outcome measures

Primary outcome

Pharmacokinetic sampling for tamoxifen and dextromethorphan.

The relationship between clearance of tamoxifen and of dextromethorphan.

Secondary outcome

The intra-patient variability in pharmacokinetics of tamoxifen and

dextromethorphan.

The effects of known polymorfismes in CYP2D6 and CYP3A and other relevant

medication metabolizing enzyms and transporters for the pharmacokinetics of

tamoxifen and dextromethorphan.

Study description

Background summary

Tamoxifen is frquently used in the treatment of breast cancer patients in adjuvant and metastasized setting. In comparison with cytostatics the side-effects of tamoxifen are less in number, but could be dose-limiting and potentially life-threathening (for example thrombolic complications, endometrial carcinoma). It is unpredictable at the start of treatment which patients will receive such side-effects. Hence, it is important to devellop good predictors.

After intake tamoxifen is metabolised by cytochrome P450 iso-enzymes (for example CYP2D6, CYP3A4, CYP3A5) in active metabolites, such as endoxifen. The formation of endoxifen is determinant for the effect and toxicity of tamoxifen. Recent studies have proven the inter-individual variability in pharmacokinetics of tamoxifen, leading up to different respons en toxicity profile between patients. The inter-individual variability can be influenced by many facotrs, including co-medication, life-style and genetic variation. Recently the relatiuonship between CYP2D6 polymorfismes and the pharamcokinetics, clinical

outcome and toxicity of tamoxifen has been proven. At this moment the use of genotyping for CYP2D6 is under investigation. However, the presence of other iso-enzymes such as CYP3A, responsible for the conversion of 90% of tamoxifen and life-style are not taken into account in this investigation. To adjust for these factors, a phenotype probe, which stimulates the metabolism of tamoxifen, would be hopefullly a beter prognostic marker for the pharmacokinetics of tamoxifen and possibly even for its therapeutic effect and toxicity.

Study objective

To investigate the relationship fo the pharmacokineticsof the probe drug (dextromethorphan) and tamoxifen.

Study design

Single center pharmacokinetics study to investigate the relationship between tamoxifen and dextromethorphan

Study burden and risks

Patients wil be admitted for one day for pharmacokinetic sampling.
Patients will be asked to keep record of a diary for monitoring of compliance of tamoxifen purpose.

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

Histological or cytological confirmed breast cancer
indication for treatment with monotherapy tamoxifen
18 years of age or older
written informed consent
adequate renal, hepatological and hematological lab results

Exclusion criteria

pregnant or lactating women
impossibility for oral intake medication
serious illness or instable medical condition
symptomatic central nervous system metastases
use of strong CYP3A and/or P-glycoprotein inhibiting and inducing medication/supplements

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):	15-06-2009
Enrollment:	37
Type:	Actual

Medical products/devices used

Product type:	Medicine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	14-04-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-06-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2008-006017-25-NL
CCMO	NL25016.078.09
Other	NLxxxxx.xxx.09