Amendment on the CYPTAM documentation study: effect of CYP2D6 genotype on pharmacokinetics and clinical outcome in tamoxifen treated breast cancer patients:;(P07.234 CYPTAM study)
Validation and optimization of 13C-dextrometorphan breath test (DM-BT) for CYP2D6 phenotyping

Published: 27-11-2007
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-To optimize DM-BT by addition of multiple breath sampling and improve it for use in clinical practice-To create a population based pharmacokinetic model based on DM-BT predicting endoxifen serum levels-To identify ideal single or two time points...

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

Summary

ID

NL-OMON38059

Source
ToetsingOnline

Brief title
CYPTAM second amendment

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Cambridge Isotopes Labarotories Inc.

Intervention

Keyword: breast cancer, pharmacokinetics, phenotyping, tamoxifen

Outcome measures

Primary outcome

Correlation between CYP2D6 phenotype (by 13C-dextromethorphan breath test) and

endoxifen serum levels.

Secondary outcome

none

Study description

Background summary

Results from the first amendemt of rtge CYPTAM documentation study have showm that 13C-dextrometorphan breath test is a good CYP2D6 phenotyping test in patients with breast cancer using tamoxifen in the adjuvant setting. CYP2D6 is an important enzyme involved in the conversion of tamoxifen into the active metabolite endoxifen. Recent literature suggest a treshold serum endoxifen level, above which the recurrence of breast cancer decreases. We found a good correlation between the CYP2D6 genotype and breath test results (i.e. CYP2D6 phenotype). However, we found a large intra- and interindividual variation in

breath tet results in patients with the same CYP2D6 genotype.
We hypothesize that this large variation might be due to large dextromethorphan pharmacokinetics in individuals and to breath test specifications.

Study objective

-To optimize DM-BT by addition of multiple breath sampling and improve it for use in clinical practice
-To create a population based pharmacokinetic model based on DM-BT predicting endoxifen serum levels
-To identify ideal single or two time points for breath collection post ingestion of 13C-DM by correlating DOB*s at specific timepoints with AUC0-240.
-To compare correlation of single sampling versus 9-point sampling DM-BT with endoxifen serum levels
-To determine intrapatient variability in DM-BT results
-To determine if the *ceiling effect* in clinical CY2D6 phenotype we have observed in patients with (het)EM genotype could be reversed by an increased dose of 50 mg of 13C-dextromethorphan

Study design

Second amendement on de CYPTAM study
In the Leiden University Medical Center, 6 patients recruited from the first amendment on the CYPTAM documentation study, will undergo a 13C-dextromethorphan breath test on 3 following days.
This study is an intervention study with the CYP2D6 phenotyping probe 13C-dextromethorphan.

Intervention

Patients included in the amendment will be given 50 mg 13-C dextromethorphan, prior to the breath test. Subjects are asked to breath in a plastic bag for 11 times during each breath test.
One sample of blood (10 cc) will be withdrawmn for determination of tamoxifen and metabolites.

Study burden and risks

Estimated side effects caused by the use of dextrometorphan will be limited and if present mild. The overall patient*s burden will be limited as only a vena puncture and a rapid breath test are required.

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

1. Pre- and postmenopausal women who have already been using tamoxifen as part of a standard adjuvant therapy for newly diagnosed breast cancer;2. Willing and able to give written informed consent ;3. Age >= 18 years;4. Women who have already been enrolled in the first amendment on the CYPTAM documentation study ((P.07.234): Addition of CYP2D6 phenotyping by a 13C-dextrometorphan breath test (DM-BT)) and are currently on tamoxifen therapy for at least two months.

Exclusion criteria

Inability or unwillingness to fast overnight prior to the study session.
Inability or willingness to abstain from drinking alcohol for 24 h prior to the DM-BT.

A diagnosis of pulmonary disease such as asthma or other respiratory disease associated with hypercapnia.
Existence of metabolic or gastrointestinal disorders which influence absorption and/or gastric emptying.
A demonstrated adverse reaction to previous dextromethorphan exposure.
Impaired hepatic function as defined by >= Grade 3 AST, alkaline phosphatase or total bilirubin or a history of liver chirrosis
Renal insufficiency
Use of medication known to slow gastric emptying or gastrointestinal motility within 24 hours of the breath test (known to slow gastric emptying or gastrointestinal motility •
The use of MAO inhibitors in the last two weeks
Use of dextrometorphan cough syrup/tablets within 24 hours of the breath test.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-02-2008
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	13-C-Dextromethorphan Cambridge Isotope Inc,
Generic name:	13-C-Dextrometorphan
Product type:	Medicine
Brand name:	Tamoxifen PCH
Generic name:	Tamoxifen
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-11-2007
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	02-05-2012
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	EUCTR2007-006270-28-NL

Register	ID
CCMO	NL20595.058.07