Phenotyping CYP2D6 in frail elderly by a 13C-dextromethorphan breath test

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	General system disorders NEC
Study type	Interventional

Summary

ID

NL-OMON36834

Source
ToetsingOnline

Brief title
frailty study

Condition

- General system disorders NEC

Synonym
CYP2D6 metabolism, frailty

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: adelingsfonds Klinische Farmacie en Toxicologie

Intervention

Keyword: breath test, CYP2D6, elderly, frailty

Outcome measures

Primary outcome

The main parameters obtained in the determination of CYP2D6 clinical phenotype

by 13C-DM-BT.

Parameters concerning CYP2D6 clinical phenotype which are collected::

- DOB values on t=0-120

- AUCDOB0-120

- Cumulative percentage of dose recovery (cPDR)

Secondary outcome

- sex

- race

- age

- length

- body weight

- body mass index (BMI)

- smoking status

- use of concomitant medication

- concomitant disease

- parameters on frailty: walking speed, grip strength, weight loss, energy

expenditure,

- Mini mental state examination (MMSE), questionnaire on all-day-living (ADL)

and mood (HADS-1)

Study description

Background summary

Older people display considerable variability in efficacy and adverse effects of medicines. A person*s response to medication depends on the pharmacokinetic and pharmacodynamic properties of a specific drug in a specific patient.
The pharmacokinetics and pharmacodynamics of a drug are in turn influenced by pathological and clinical factors associated with comorbidity, concomitant use of drugs, and age-related changes in organ function. Frailty is a clinical phenotype that is associated with adverse health outcomes and is characterized by an excessive reduction of lean body mass, sarcopenia, chronic under-nourishment, reduced function, and poor endurance . Frailty is likely to increase the age-related heterogeneity in the pharmacokinetics and pharmacodynamics of drugs.CYP2D6 is the most important isozyme in the metabolism of a variety of drugs such as betablockers, antipsychotics (like haloperidol) most selective serotonin reuptake inhibitors (SSRIs), and antitumour agents like tamoxifen and gefitinib.
To date, no phenotype studies have been reported on CYP2D6 activity and frailty.

Study objective

-The primary objective is to compare the CYP2D6 phenotype, determined by DM-BT in frail and non-frail elderly (by using Fried definition).
-The secondary objective is to correlate individual parameters of frailty (e.g. grip strength) with CYP2D6 phenotype, determined by a 13C-dextromethorphan breath test (DM-BT)

Study design

Pharmacokinetic intervention study

Intervention

Assesment of CYP2D6 phenotype by 13C-dextromethorphan breath test

Study burden and risks

Adverse events to dextromethorfan are mostly very mild and selden occur to happen. Dextromethorfan has been registered in the Netherlands (over the

counter status).

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

Inclusion Criteria
* Men and women aged 70-85 years
* Body-mass index between 20 and 30 kg/m2

Exclusion criteria

Exclusion Criteria

* Presence of acute illness
* Presence of metastasized cancer
* CYP2D6 poor metabolizer genotype
* 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 cirrhosis
* Stage III renal insufficiency defined by a MDRD of < 30 mL/min
* Use of medication known to slow gastric emptying or gastrointestinal motility (within 24 hours of the breath test). The use of medication inhibiting CYP2D6 and/or mono-amine oxidase (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):	11-02-2013
Enrollment:	42
Type:	Actual

Ethics review

Approved WMO

Date:	05-02-2013

Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	18-03-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	17-07-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL41905.058.12