Pharmacogenetics of drug-induced liver injury

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The principal aim of this project is to identify genetic biomarkers involved in susceptibility for drug-induced liver injury in a set of candidate genes (genes relevant to metabolism of drugs and immune system genes).The results of this study will...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hepatic and hepatobiliary disorders
Study type	Observational invasive

Summary

ID

NL-OMON38286

Source
ToetsingOnline

Brief title
DILI

Condition

- Hepatic and hepatobiliary disorders

Synonym
drug-induced liver injury

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ASAT innovation program;initiatief van het ministerie van VWS. Projectbudget bestaat uit overheidsgeld en subsidies van een aantal farmaceutische bedrijven. Sinds oktober 2010 door het Serious Adverse Events Consortium.,Eli Lilly,GlaxoSmithKline,Pfizer,Roche

Intervention

Keyword: Adverse drug-reaction, Drug-induced liver injury, Pharmacogenetics

Outcome measures

Primary outcome

Variations in metabolic and immune genes between patients with drug-induced liver injury and controls with no liver injury will be studied. Other variables are patient characteristics like age and weight, alcohol and (recreational) drug use.

Secondary outcome

None

Study description

Background summary

A wide variety of drugs can cause liver injury. Only a small proportion of patients develop liver injury during treatment with commonly used medicines, but the severity of the adverse drug reaction has been one of the main reasons for withdrawal of drugs from the market. It is difficult to identify people who are likely to suffer liver injury. Genetic susceptibility may be an important risk factor for drug-induced liver injury. It would be of considerable benefit if a test could be developed that could identify high risk patients.

Study objective

The principal aim of this project is to identify genetic biomarkers involved in susceptibility for drug-induced liver injury in a set of candidate genes (genes relevant to metabolism of drugs and immune system genes).
The results of this study will contribute to:
1. The ability to identify high risk-patients
2. Reduce the number of patients developing drug-induced liver injury
3. The establishment of a biobank, which will provide material for future pharmacogenetic, proteomics and metabolomics studies

Study design

Case control study
Blood will be obtained from cases of drug-induced liver injury (DILI) and DNA will be isolated. Genes relevant to DILI will be studied and compared with the genetic profile of selected controls from existing databases.

Study burden and risks

Patients will donate once blood (17 ml) and urine and fill out a short questionnaire concerning their lifestyle (10 min maximum). Patients will have minor discomfort and risks will be minimal.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
3015 CE Rotterdam
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
3015 CE Rotterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

age >=18
an ALT > 5 x upper limit of normal (ULN) (or AST when ALT is unavailable)
or an ALP > 2 x ULN (especially when associated with 5'-nucleotidase or gamma-glutamyl transpeptidase elevations and when there is no bony cause for rise in ALP)
or an ALT > 3 x ULN plus bilirubin > 2 x ULN

Exclusion criteria

see inclusion criteria

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-02-2011
Enrollment:	325
Type:	Actual

Ethics review

Approved WMO Date:	19-02-2010
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-10-2012
Application type:	Amendment
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
CCMO	NL29097.078.09