A Modified Case Control Study To Identify Pharmacogenomic Factors Associated With Hepatocellular Injury Following Exposure To Lapaquistat Acetate

Published: 16-07-2009
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To examine the genetic contribution to the mechanism of lapaquistat acetate induced hepatic abnormalities.

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

Summary

ID

NL-OMON32955

Source
ToetsingOnline

Brief title
PG Factors, Hepatocellular Injury, Lapaquistat Acetate

Condition

- Hepatic and hepatobiliary disorders

Synonym
Hepatocellular Injury (liver disturbance)

Research involving
Human

Sponsors and support

Primary sponsor: PRA Belgium BVBA
Source(s) of monetary or material Support: Takeda,Takeda Global R&D

Intervention

Keyword: Hepatocellular Injury, Lapaquistat Acetate, Pharmacogenomic Factors

Outcome measures

Primary outcome

• Whole genome scanning using the Illumina 1M chip. The Illumina 1M chip can measure about 1,000,000 single-nucleotide polymorphisms (SNPs) and 14,000 copy number variation regions.

• Whole genome scanning using the Affymetrix 500K array chip. The Affymetrix 500K array can measure about 500,000 SNPs.

• Candidate gene scanning using the Affymetrix Drug Metabolizing Enzymes and Transporter (DMET) array. The Affymetrix DMETTM Plus chip can measure 1936 drug disposition markers in 225 genes that have been associated with drug absorption, distribution, metabolism, and excretion.

Secondary outcome

NVT

Study description

Background summary

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Study objective

To examine the genetic contribution to the mechanism of lapaquistat acetate induced hepatic abnormalities.

Study design

This is a modified case control study to identify pharmacogenomic factors

associated with hepatocellular injury following exposure to lapaquistat acetate.

The DNA profile of subjects that experienced significant biochemical hepatic derangement following exposure to lapaquistat acetate will be compared with the DNA profiles of a population of pregenotyped untreated control subjects from a public database to investigate the association of hepatocellular injury with genetic polymorphism. If data from the subjects exposed to lapaquistat acetate indicates that there is a genetic marker of interest, the stored DNA from non-exposed subjects will be assayed to further investigate the signal.

Each subject will sign the informed consent document prior to undergoing the study-related procedure. One 10 mL samle of whole blood will be collected from each subject. Extracted DNA will be analyzed using a whole genome scan approach as well as a candidate gene approach.

Study burden and risks

NVT

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

Subjects that experienced marked ALT increases (>=5×ULN or concurrent elevation of ALT >=3×ULN and bilirubin >=2×ULN) during the original lapaquistat acetate development program.

Exclusion criteria

Not applicable.

Study design

Design

Study phase:	3
Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-09-2009
Enrollment:	1
Type:	Actual

Ethics review

Approved WMO Date:	16-07-2009
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	03-08-2009
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	09-12-2009
Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (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	ID
EudraCT	EUCTR2008-006906-41-NL
CCMO	NL27672.003.09