Genetics in Efavirenz Metabolism, the GEM study

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To find an explanation for the abnormal blood levels of efavirenz. With the main research question: Are variations in genetic markers, e.g. CYP2B6 (subtype *6, *7 and *18), for the metabolism of efavirenz, an explanation for the abnormal...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON32907

Source
ToetsingOnline

Brief title
the GEM study

Condition

- Immunodeficiency syndromes

Synonym
DNA make-up, Genetic marker

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Centrum Haaglanden
Source(s) of monetary or material Support: eigen afdeling

Intervention

Keyword: efavirenz, genetic marker, metabolism

Outcome measures

Primary outcome

Difference in variation of genetic markers, for example CYP2B6 (subtype *6, *7

and *18), in the metabolism of efavirenz, between case and control population.

Secondary outcome

Demography of participants

Study description

Background summary

Summary Genetics in Efavirenz Metabolism, the GEM study:

In the standard treatment of the HIV infected patients of the Medical Centre Haaglanden, location Westeinde and the HAGA teaching hospital, location Leyweg, therapeutic drug monitoring for HIV medication, like efavirenz, is standard. During therapeutic drug monitoring, some patients drew our attention. These patient showed high drug levels whilst using normal efavirenz dosage. This observation has led to the development of a study to find an explanation for this phenomenon.

Efavirenz is a Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI), that is commonly used as first line treatment in Highly Active Anti Retroviral Therapy (HAART). This to prevent progression of the HIV infection. Efavirenz has a defined therapeutical range of 1 * 4 mg/l. A drug level over 4mg/l is associated with side effects. A drug level under 1mg/l is associated with a higher change of therapeutic failure.

Efavirenz is metabolised in the liver, by CYP2B6 enzyme. In CYP2B6 various Single Nucleotide Polymorphisms (SNP) are described, that possibly affect the capacity of the CYP2B6 enzyme to metabolise efavirenz. Variations in CYP2B6 could be an explanation as to why some patients have abnormal drug levels of efavirenz.

These findings have led to the development of the following research questions:

Are variations in genetic markers, e.g. CYP2B6 (subtype *6, *7 and *18), for the metabolism of efavirenz, an explanation for the abnormal pharmacokinetics in the HIV population of the participating hospitals?

Is it possible to connect the variations in genetic markers to specific population characteristics?

The study is a pilot study, designed an a multi-centre explorative case-control study.

Study objective

To find an explanation for the abnormal blood levels of efavirenz. With the main research question: Are variations in genetic markers, e.g. CYP2B6 (subtype *6, *7 and *18), for the metabolism of efavirenz, an explanation for the abnormal pharmacokinetics in the HIV population of the participating hospitals?

Study design

Pilot study, designed as a multi-centre explorativ case-control study

Study burden and risks

An extra bloodsample (4ml) is taken from the participant. This bloodsample will be taken on the same moment that the routine bloodsample for therapy control is collected. Because these bloodsamples are beeing collected at the same moment, there will be no additional risk/burden for the participant.

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

All patients who are being treated with efavirenz and are monitord in the participating hospitals

Exclusion criteria

HIV infected patients that do not use efavirenz

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2009

Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	19-11-2008
Application type:	First submission
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	NL24524.098.08