Investigation of the effects of switching to a high genetic barrier protease inhibitor based regimen on low level viremia, immune activation and neurocognitive performance in patients on antiviral therapy

Published: 04-06-2014
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Primary: to investigate the most importants determinants of the viral dynamics of low-level viremia. Secondary: to investigate the effects on immune activation, neurocognitive performance and periodontal status.

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

Summary

ID

NL-OMON44785

Source
ToetsingOnline

Brief title
LOWERIT

Condition

- Immunodeficiency syndromes
- Viral infectious disorders

Synonym
aids, HIV

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Janssen-Cilag,Janssen-Cilag BV

Intervention

Keyword: HIV, low level viremia, viral reservoirs

Outcome measures

Primary outcome

Evolution, as measured by genetic variation of viral clones at different time points. This outcome gives an indication if the low-level viremia is based on viral replication or production.

Secondary outcome

HIV-RNA-level, Immunological markers, neurocognitive performance, periodontal inflammation, HIV resistance associated mutations, Genetic compartmentalization of HIV (CSF-plasma and saliva-plasma comparison).

Study description

Background summary

HIV low-level viremia is a frequently observed clinical phenomenon and a possible risk for the development of drug resistance and virological failure [1]. The origin of low-level viremia is not known, but it is hypothesized that virus production or virus replication in cellular and anatomical reservoirs are involved. The viral activity related with low-level viremia may be associated with higher levels of immune activation, deterioration of neurocognitive performance and periodontitis. These are frequently observed problems in the HIV-infected population. Regarding management of HIV low level viremia, guidelines differ in their advices. Clinicians usually change the combination antiretroviral therapy (cART) to a regimen that contains a high genetic barrier

protease inhibitor (PI) to prevent the development of resistance mutations. The preferred choice is most often darunavir (DRV), boosted with ritonavir (DRV/r). By systematically studying the effects of starting a high genetic barrier drug we can safely obtain insights in the dynamics of low-level viremia and its etiology.

Study objective

Primary: to investigate the most importants determinants of the viral dynamics of low-level viremia.
Secondary: to investigate the effects on immune activation, neurocognitive performance and periodontal status.

Study design

An observational cohort-study of 48 weeks with subjects having low-level viremia that undergo a treatment change containing a high genetic barrier protease inhibitor.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The study will include 6 hospital visits. To a great extent it includes normal clinical practice regarding clinical history taking, physical examination, viral load assessment, CD4 count measurements, lumbar punctures (on indication) and safety controls in blood to monitor potential side-effects. The additional burden lies in: questionnaires (about adherence, depression and self-reported impairment in daily functioning), additional blood samples for virological, immunological and pharmacological analyses, 3 times a set of validated neurocognitive tests for 40 minutes and two (optional) periodontitis measurements.
Subjects will be informed about their personal neurocognitive test results after completion of the study at 48 weeks, unless there is a medical reason for intervention (e.g. depression). Out of ethical considerations, subjects with cognitive impairment at the end of the study will be offered a thorough neurocognitive investigation by a clinical neuropsychologist and offered a revalidation programme to cope with the impairment if deemed necessary or useful.

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

a. Using cART for at least 48 weeks, including 2 NRTIs + 1 NNRTI or 1 PI or 1INSTI
b. Low level viremia (2 or more HIV viral loads between 50-1000 cp/mL in a year, without Target Not Detected (TND) in between)
c. Viral load <200cp/mL at at least one measurement since starting cART
d. A planned therapy change of the PI or NNRTI to DRV/r

Exclusion criteria

a. Presence of known pol major IAS mutations for darunavir (I47V; I50V; I54M/L; L76V; I84V)
b. Signs of opportunistic infections
c. Major suspicion of inadequate therapy adherence
d. Severe depression at screening (BDI score >30)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-11-2014
Enrollment:	65
Type:	Actual

Ethics review

Approved WMO Date:	04-06-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	14-09-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-03-2017
Application type:	Amendment
Review commission:	METC NedMec

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	NL47035.041.13