Identification and characterization of the latent HIV-infected reservoir in long-term anti-retroviral therapy (ART) suppressed patients

Published: 16-06-2016
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To identify and quantify the HIV reservoir in T-cell subsets of patients who have been on ART for almost 20 years.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON43932

Source
ToetsingOnline

Brief title
Identification of the latent HIV-reservoir

Condition

- Viral infectious disorders

Synonym
HIV-infection, infection with human immunodeficiency virus

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: AIDS fonds

Intervention

Keyword: cure, HIV, persistence, reservoir

Outcome measures

Primary outcome

Aim 1) Identify and quantify the HIV reservoir in T-cell subsets after almost 20 years of effective ART.

* Amount of viral DNA in T-cell subsets.

* Amount of 2-LTR circles in T-cell subsets.

* Amount of intracellular viral RNA in T-cell subsets.

* Amount of extracellular viral RNA in plasma.

Aim 2) Determine the characteristics of the different cell subsets with respect to immunological markers and viral quasi species.

* Sequencing of viral RNA in plasma.

* Sequencing of viral DNA in T-cell subsets.

* Sequencing of HIV DNA integration sites in T-cell subsets.

* Amount of soluble cell-activation markers in plasma.

* Amount of cell-activation markers in T-cell subsets and other cells such as CD8+ T-cells, monocytes and NK cells.

Aim 3) Determine the reactivation potential of the latently infected T-cell subsets.

* Amount of intra- and extracellular viral RNA before and after stimulation of different CD4+ T-cell subsets by anti-latency compounds.

* Amount of intra- and extracellular cell activation markers before and after

stimulation by anti-latency compounds.

Secondary outcome

Not applicable.

Study description

Background summary

Currently available antiretroviral therapy (ART) can successfully suppress HIV replication. However, HIV can persist as an integrated provirus in latently infected cells and conventional treatment lacks the ability to clear this reservoir. This reservoir fuels viral rebound following treatment failure or interruption and is the major obstacle towards eradication of HIV. The major cellular HIV reservoir during long-term treatment is the CD4+ T-cell. Recently, this cell population was found to be highly heterogeneous consisting of several distinct subsets with specific characteristics that may differentially impact the long-term in vivo persistence. In the UMC Utrecht, we have a unique cohort of well-characterized patients who were among the first to initiate effective ART and who delivered a large blood draw in 2005. It is of major interest to determine the evolution of the viral reservoir using the data available from this earlier blood draw and longitudinally investigate in which cell subsets HIV resides after almost 20 years of effective ART. Knowing where and how HIV persists in long-term treated patients is pivotal for the development of strategies aimed at eradicating the latent reservoir and ultimately, HIV cure.

Study objective

To identify and quantify the HIV reservoir in T-cell subsets of patients who have been on ART for almost 20 years.

Study design

Cohort study with a single blood draw procedure.

Study burden and risks

The intended participants are eight HIV-infected UMC Utrecht patients and part of the CHEESE cohort. The patients in the CHEESE cohort were among the first HIV patients in the Netherlands on effective ART (1997), and the intended

subset of eight patients has previously (2005) donated a large blood draw (METC-04017). At that time-point, after 8 years of effective therapy, HIV DNA could still be detected in these patients. Now, 10 years later, we would like to re-approach these patients to donate a large blood draw, which will allow us to longitudinally assess in more detail if and in which T-cell subsets HIV can reside. The blood-draw procedure will take place at a designated room at the outpatient clinic (dagbehandeling). The one-time procedure bears little risk but discomforts associated with large volume blood draws may occur such as dizziness, headache, nausea, sweating, hyperventilation, fainting and fatigue.

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

The intended participants are eight HIV-infected UMC Utrecht patients and part of the

CHEESE cohort. The patients in the CHEESE cohort were among the first HIV patients in the Netherlands on effective ART (1997), and the intended subset of eight patients has previously (2005) donated a large blood draw (METC-04017). At that time-point, after 8 years of effective therapy, HIV DNA could still be detected in these patients. Now, 10 years later, we would like to re-approach these patients to donate a large blood draw, which will allow us to longitudinally assess in more detail if and in which T-cell subsets HIV can reside.

Exclusion criteria

Unability to undergo a large blood draw in the opinion of the treating physician.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-11-2016
Enrollment:	8
Type:	Actual

Ethics review

Approved WMO

Date:	16-06-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL55494.041.16