Ex vivo activation characterization and targeting of the latent HIV infected reservoir to cure HIV

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1. Ex vivo stimulation of HIV genome expression in latently infected peripheral blood mononuclear cells (PBMC's) from patients on cART using new and established compounds.2. To characterize latently HIV-1 infected peripheral blood mononuclear...

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

Summary

ID

NL-OMON54790

Source
ToetsingOnline

Brief title
EX VIVO

Condition

- Viral infectious disorders

Synonym
Latent HIV infection

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,AIDSfonds;Erasmus MC beurs MRACE

Intervention

Keyword: Eradication, HIV, Reservoir

Outcome measures

Primary outcome

The following endpoints refer to in vitro experiments:

1. Descriptive analysis of latently infected HIV sub-populations of PBMC*s, by use of flow cytometry.

2. Quantify increases transcription related factors before and after the addition of HIV expression modulating agents.

3. To quantify the virologic response of latent HIV infected reservoir to treatment by HIV expression modulating agents.

4. To explore potential biomarkers of the size of the HIV reservoir. These include cytokines (IFNg, IL1beta, IL2, IL4, IL6, IL8, IL10, IL-12p70, IL13, TNFalfa etc), HLA phenotyping (HLA B27 and B57), amount of HIV specific broadly neutralizing antibodies, SOMAscan (proteomics) level of HIV specific CTL activation and CD4+ T cel responses.

5. Prospective clinical cohort

6. Differences in HIV reservoir, shock and kill strategies, and immunity between different HIV clinical phenotypes

Secondary outcome

Not applicable

Study description

Background summary

Combined antiretroviral therapy (c-ART) effectively controls viral replication but does not affect cells in which the human immunodeficiency virus (HIV) is latently present. c-ART is not curative, therefore, and is a lifelong therapy. Finding a way to eradicate HIV from the pool of HIV infected resting memory CD4+T cells could lead to a definitive cure for HIV, as these cells harbour replication competent, transcriptionally latent HIV virus.

Recent research has given new insight in mechanisms to purge HIV from the body. In the light of these findings we identified and tested new compounds that could stimulate HIV genome expression in a preclinical-clinical drug pipeline. Identifying potent activators of HIV transcription in vitro could help reaching an optimal medical solution towards HIV latency.

Study objective

1. Ex vivo stimulation of HIV genome expression in latently infected peripheral blood mononuclear cells (PBMC's) from patients on cART using new and established compounds.
2. To characterize latently HIV-1 infected peripheral blood mononuclear cells (PBMC*s) ex vivo before and after addition of new and established compounds (alone and in combination).
3. To characterize potential predictive biomarkers of the size of the latent HIV-1 reservoir.
4. Setup prospective cohort for HIV cure research.

Study design

This is an invasive observational research with no intervention on patients. In vitro experiments are performed on patient derived material.

Study burden and risks

The potential risk of participation in this study is the development of an adverse reaction on the blood obtainment. In the leukapheresis procedure, two 2.5 cm venous catheters will be inserted in the patient*s elbows (one in each) to drain whole blood to the leukapheresis machine. This is a well-defined routine procedure performed by highly skilled personnel and which takes some 3-5 hours. In short, the machine will isolate peripheral blood mononuclear cells from blood based on weight and granularity. Erythrocyte and plasma fraction will be given back to the patient. The main adverse reactions related to leukapheresis are haematomas, a slight increased risk on infection (e.g. flebitis) and vasovagal complaints or collaps. The leukapheresis procedure might cause a slight decrease in total erythrocytes due to cell lysis in the machine. Although the occurrence of leukapheresis induced anaemia is unlikely,

we will exclude patients with pre-existent anaemia. The risks associated with standard phlebotomy are minimal. The follow up phlebotomies or leucapheresis will be done during routine follow up and routine blood sampling for a maximum of 4 years. No extra visits are required. The maximum amount of blood is equal to the amount that can be drawn at 1 standard blood donation (500mL) and the total amount stays well below the acceptable amount by the blood bank over this 4 year period.

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

1. Age 18 years or older.
2. Confirmed HIV infectie

Exclusion criteria

1. Inability to place 2.5 cm venous catheter or perform phlebotomy
2. Major comorbidities:
A. Severe symptomatic anemia
B. Recent symptomatic cardiovascular event.
3. The inability to participate due to any other relevant medical, social, environmental, psychological, factors or according to the HIV treating physician*s judgement.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-09-2013
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	11-02-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-04-2016
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-07-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-06-2023
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
ClinicalTrials.gov	NCT05215704
CCMO	NL42819.078.12