A prospective cohort for ex vivo cure studies with chronic HIV infected patients in the Netherlands: The CHRONO project

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Primary objectives: 1. To develop a prospective cohort in the Netherlands of chronic HIV infected patients with in-depth reservoir characterization for future cure interventions.2. To study the evolution of the HIV reservoir and immune host...

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

Summary

ID

NL-OMON49028

Source
ToetsingOnline

Brief title
CHRONO

Condition

- Viral infectious disorders

Synonym
AIDS, HIV

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Gilead Sciences,Health Holland TKI-LSH;Aidsfonds

Intervention

Keyword: AIDS, ART, Cure, HIV

Outcome measures

Primary outcome

1. The evolution in reservoir size ex vivo as assessed as the number of cells expressing viral RNA and viral protein Gag (vRNA/prGag +/+) in HIV patients on cART at week 24 and 48 after treatment initiation.

Secondary outcome

1. The evolution in reservoir size ex vivo as assessed as the number of cells expressing viral RNA and viral protein Gag (vRNA/prGag +/+) in HIV patients on cART at week 24, 48 and 156, and later, after treatment initiation.

2. The evolution of cytotoxic T-lymphocyte responses and inflammatory environment (cell subpopulations, phenotypical cell characterization, pro-inflammatory cytokines), and its relation to the reservoir (endpoint 1.1 and 2.1) and viral load setpoints pre-cART.

3. Assessment of additive, synergistic, or antagonistic effects of (combinations of) established and novel LRA ex vivo as determined by increase in cellular HIV-RNA, protein production and cell decay.

4. Assessment of the underlying mechanisms to explain observed differences in reservoir size and LRA effects, e.g. chromatin accessibility, transcription factor binding, HIV promotor sequencing, or transcriptomics.

5. Differences in the reservoir size and activity, and immune responses (immune

activation, cytokines, T/B/NK cell phenotype and functionality) between the HIV subtypes.

6. Evaluation of clinical parameters with reservoir size, activity and host immune responses, including sex, ethnicity, INSTI pharmacokinetics, and HIV clinical characteristics (CD4+T-cell and HIVRNA pre-cART, comedication, HIV center for disease control (CDC) A/B/C events)

7. Correlation between established and future assays of the reservoir*s size and activity.

Study description

Background summary

HIV cannot be cured with the current treatment armamentarium. A reservoir of latently HIV infected long lived CD4+T-cells is present in patients with HIV that are not affected by antiretroviral therapy. The evolution of this reservoir after therapy initiation is ill understood, as are the potential strategies to eradicate this reservoir. This study aims to anticipate on future HIV cure strategies by building a cohort to study ex vivo the reservoirs of HIV patients, the obstacles to cure HIV, and new therapeutic compounds and strategies.

Study objective

Primary objectives:
1. To develop a prospective cohort in the Netherlands of chronic HIV infected patients with in-depth reservoir characterization for future cure interventions.
2. To study the evolution of the HIV reservoir and immune host responses over time during antiretroviral therapy.
Secondary objectives:
1. To explore established and putative new interventions aimed at curing HIV.
2. To explore differences in reservoir size, activity and host responses, and their relation with clinical characteristics, between patients with different dominant HIV subtypes and sexes.
3. To compare and validate new reservoir assays with current established assays.

Study design

Prospective non-interventional cohort study

Study burden and risks

There are no expected benefits for participants in this study. A potential future benefit can be that insights from this study can provide an advantageous position to participate in future cure intervention studies where the kind of measurements done in this study are very likely necessary to take into account for participation. The potential risk of participation in this study is the development of an adverse reaction on the blood obtainment. The main adverse reactions related to leukapheresis are haematomas, a slight increased risk on infection (e.g. flebitis) and vasovagal complaints or collapse. 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 symptomatic anaemia as stated in the exclusion criteria and hemoglobulin levels are routinely monitored during the procedure. The patients will be able to contact the investigators if any AE will occur. Another risk is that unexpected results occur from routine lab measurements, e.g. sex hormones, that warrant work-up. As internists who treat the patients, we are trained and proficient in the work-up and treatment of laboratory abnormalities of the measured variables, including hormonal disturbances that are measured for the aim of this study. In case of exceptional findings, internist-endocrinologist are direct colleagues within the internal medicine section and there is a 24/7 consultant internist-endocrinologist on call who can immediately be reached by the internist-infectious diseases specialists should the clinical profile or laboratory results necessitate this. The study cannot be done with another group since participants need to be infected with HIV and have a medical indication to start cART.

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

Adult chronic HIV infected patients of >=18 years of age who initiate antiretroviral therapy in routine care.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
1. Inability to place venous catheters to draw blood.
2. Major comorbidities:
a. Severe symptomatic anemia or recent symptomatic cardiovascular event (unstable angina pectoris, decompensated heart failure, myocardial infarction).
b. The inability to participate due to any other relevant 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:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-05-2021
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO

Date:	25-09-2020
Application type:	First submission
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	NCT04888754
CCMO	NL72765.078.20