Netherlands Cohort Study on Acute HIV Infection

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

Summary

ID

NL-OMON53114

Source
ToetsingOnline

Brief title
NOVA study

Condition

- Viral infectious disorders

Synonym
acute HIV infection

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: AIDS fonds (toekenningsnummer 2013169) en Amsterdam diner foundation 2013 (dit is een non-profit fundraiser ten behoeve van HIV onderzoek en behandeling).,BMS functional cure grant

Intervention

Keyword: acute HIV infection, immune response, treatment, viral reservoir

Outcome measures

Primary outcome

- the cell associated viral reservoir size (total integrated HIV DNA, 2LTR circles, single copy RNA, cell associated RNA, viral outgrowth and inducible RNA) in peripheral blood, lymph node and GALT and viral load in CSF during the three to five years after initiation of cART.

- the functional properties of the HIV-specific CD8+ T cell, B cell and T follicular helper cell response during the three years after initiation of cART.

- immune activation parameters (type I interferons, IFN*, IL-6, IL-10, IL-15, IL18, IL-22, sCD14, CRP, TGF*, IL-1, IL8, sCD163, IP-10) during the three years after initiation of cART.

Secondary outcome

- the replication competent viral reservoir (as described in methods section, paragraph 8.3.2) in peripheral blood, lymph nodes, GALT and CSF during the three years after initiation of cART.

Study description

Background summary

There is renewed interest in finding a cure for HIV infection. Recent studies show that in a select group of individuals the initiation of combination anti-retoviral therapy (cART) during the early phase of infection results in long-term absence of viremia following treatment interruption after prolonged treatment. These patients are described as having achieved a *post-treatment viral remission*. It is unclear why this is only seen in a subset of

individuals. However, an important factor associated with post-treatment viral control appears to be the early limitation of viral reservoir formation. There are many unsolved issues regarding the question which virological and immunological factors determine which individuals achieve a *post-treatment viral remission*. First studies suggest that the early reduction of viral reservoir size and potential accompanying preservation of immune function may be important factors. Furthermore, patients that initiate cART during acute infection are potential candidates for additional therapeutic strategies, such as latency reversing agents (LRAs) or therapeutic vaccination.

Study objective

The primary objective of the NOVA study is the establishment of a prospective cohort study of patients that initiate cART during the acute infection phase. The secondary objective is to characterize the viro-immunological factors that correlate with achievement of *post-treatment viral remission* for several years in these patients.

Study design

Prospective cohort study. Patients diagnosed with an acute HIV infection (AHI) are offered immediate standard first-line cART. In consenting patients, at several time points samples will be obtained to analyze the size and characteristics of the viral reservoir and the accompanying immune function. Three groups are assembled based on the preparedness of individual patients to participate in the extensiveness of sampling. Patients that accept early treatment and follow-up but decline additional blood and tissue sampling (lymph node, GALT and cerebral spinal fluid (CSF)) are included in group 1 (*standard*) and only routine diagnostic procedures are performed. Patients willing to undergo, in addition to routine monitoring, leukapheresis and blood sampling for PBMC and virological analyses are included in group 2 (*less-invasive*). In group 3 (*extended*) additional tissue and CSF sampling will be performed for the proposed viro-immunological analyses.
This set up allows to guide the duration of cART based on viro-immunological parameters and to adjust cART in case better cART strategies may become available in future. Furthermore, based on the available data that show preservation of immunity and reduction in viral reservoir size, the AHI patients that start therapy early may have better responses to future cure strategies such as therapeutic vaccination or LRAs.

Study burden and risks

Offering treatment in early HIV infection is currently recommended in clinical guidelines for treatment of HIV infection. This recommendation is based on studies showing improvement of markers of disease progression, decrease of severity of acute disease, lowering of the viral setpoint (associated with

disease progression) and a reduction in size of the viral reservoir. The burden and risks associated with study participation are related to tissue sampling: lymph node excision biopsy, sigmoid biopsies, lumbar puncture at three and leukapheresis at two timepoints during the study (week 0 (baseline), week 24 and week 156 (3 years)). The risks of sampling are considered minimal (see also section on *sampling*). These study procedures are necessary to answer the question underlying the research proposal that aim to characterize the determinants of "post-treatment viral control", under which the most important are the immune response and viral reservoir in blood, lymph node, gut associated tissue and cerebral spinal fluid. In order to minimize burden associated with study visits, we aim to combine visits for routine clinical care with routine clinical visits.

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

In order to be eligible to participate in this study, a subject must meet the following criteria:
-Written informed consent to store samples and perform genetic testing.
-Separate written informed consent for invasive sampling procedures: leukapheresis, sigmoidoscopy with biopsies, lymph node biopsy or excision biopsy and lumbar puncture, to store samples and perform genetic testing. - Age >= 18 years
- An acute HIV-1 infection, defined according to the modified Fiebig stages I-IV, as described in the previous paragraph (HIV-1 RNA positive and 4th generation ELISA negative or HIV-1 RNA positive and 4th generation HIV ELISA positive with indeterminate Western Blot). Patients in Fiebig stage V and VI will only be included if they have a documented negative HIV test 6 months prior to the (first) positive test.
-Female subjects should be willing to use adequate contraception.

Chronic control group:
-Written informed consent to store samples and perform genetic testing
-Separate written informed consent for sampling procedure: leukapheresis (or large blood draw), and/or lymph node excision biopsy, with storage of samples
-Age >= 18 years
-ART initiated in the chronic infection phase and chronic HIV-infection as confirmed by Western Blot (p31 positive)
-Three to 5 years on ART with undetectable viral load and no more than two consecutive blips of >100 HIV RNA copies per mL of plasma in the year before enrollment

Elite control group:
-Written informed consent to store samples and perform genetic testing
-Separate written informed consent for sampling procedure: leukapheresis (or large blood draw), and/or lymph node excision biopsy, with storage of samples
-Age >= 18 years
-Natural control of HIV infection, defined as having 3 undetectable HIV-1 RNA measurements >12 months upon diagnosis or 90% of HIV-1 RNA measurements undetectable >10 years.

Exclusion criteria

-Contraindication for proposed cART regimen (e.g. impaired renal function) for participants enrolled with an acute HIV infection
-Mental disorder that in the view of the investigator would interfere with adherence to the treatment or the study procedures, or the decision to participate in the study.

-Immunosuppressive medication or other diseases associated with immunodeficiency.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-08-2015
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO Date:	26-03-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-07-2015
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-11-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-03-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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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	NCT05728996
CCMO	NL51613.018.14