StatHIV trial.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23117

Source
Nationaal Trial Register

Brief title
StatHIV trial

Health condition

HIV infection
Immune activation

Sponsors and support

Primary sponsor: Stichting Research Interne Geneeskunde, OLVG, Amsterdam, the Netherlands
Source(s) of monetary or material Support: Stichting Research Interne Geneeskunde, OLVG, Amsterdam, the Netherlands

Intervention

Outcome measures

Primary outcome

Primary Objective: To investigate the effect of rosuvastatin 20 mg qd on subsequent immune activation markers in treatment-naïve HIV-patients:

Circulating LPS (LAL assay), TLR mRNA expression in whole blood, circulating IL-6, D-dimer,

hsCRP, CD38 and HLA-DR expression on lymphocytes, and microparticles and endogenous thrombin potential as indicators of endothelial damage.

Secondary outcome

Secondary Objective: To investigate the effect of rosuvastatin 20 mg qd on HIV viral load, CD4 cell count, total cholesterol and cholesterol subfractions, ApoB/ApoA1 ratio, CK, liver enzymes, renal function, and complete blood count as well as on markers of quality of life measured with the EuroQol-6D questionnaire in treatment-naïve HIV-patients throughout the study period.

Study description

Background summary

Despite the success of highly active antiretroviral therapy (HAART), life expectancy of HIV patients still lags behind the general population. Excess morbidity and mortality may be attributed to several factors. Persistent immune activation has recently been implicated in the observed increase in non-AIDS defining morbidity such as cardiovascular disease and non-AIDS defining malignancies. Early in HIV infection the gut mucosal barrier is irreparably damaged leading to bacterial translocation and persistent immune activation through activation of Toll-like receptors (TLRs) by intestinal bacteria and bacterial products. It has been postulated that early intervention in this process of immune activation may postpone the indication of starting HAART and may decrease morbidity and mortality in HIV patients. Recognition of bacteria and bacterial products by TLRs, and subsequent signal transduction, is crucial in the process of immune activation. Apart from their cholesterol-lowering properties, statins have shown anti-inflammatory effects, and two recent studies found that statins have an inhibitory effect on the TLR-mediated inflammatory response. The present randomized placebo-controlled trial aims at investigating the effect of rosuvastatin on immune activation markers in treatment-naïve HIV patients.

Study objective

HIV-induced immune activation through intestinal bacterial translocation can be modulated by statins.

Study design

Throughout the study, patients will have regularly scheduled visits at the clinic every 4 weeks. At those visits there will be collection of blood samples, assessments of symptoms, physical examinations, and questionnaires to complete. Primary laboratory investigations include circulating LPS (LAL assay), whole blood TLRmRNA expression, TLR4 polymorphisms (Asp299Gly and Thr399Ile), circulating IL-6, D-dimer, hsCRP, CD38 and HLA-DR expression on lymphocytes, and microparticles and endogenous thrombin potential. Secondary laboratory

investigations comprise HIV-viral load, CD4 cell count, total cholesterol and cholesterol subfractions, ApoB/ApoA1 ratio, CK, liver enzymes, renal function, and complete blood count.

Blood is drawn for baseline measurement on day –28 and day –1 before the start of the study medication. After the start of the study medication, blood is drawn on days 28, 56, 84, 112, 140 and 168 (weeks 4, 8, 12, 16, 20 and 24).

Intervention

This is a double blind, randomized, placebo-controlled therapeutic intervention study with a cross-over design.

The patients will be assigned to random groups: One receives rosuvastatin 20 mg daily, and the other receives placebo. Patients remain in their treatment groups for 8 weeks. After 8 weeks all patients, in both study groups, will be required to discontinue all study-related medications for 4 weeks. After that period, patients receiving placebo will take rosuvastatin, and vice versa. The study will proceed for another 8 weeks, followed by a period of stopping study-related medications and patients being observed for 4 weeks.

Throughout the study, patients will have regularly scheduled visits at the clinic every 4 weeks. At those visits there will be collection of blood samples, assessments of symptoms, physical examinations, and questionnaires to complete.

To obtain reliable reference values for the experimental laboratory investigations, ten healthy, age and sex-matched volunteers will be asked to donate blood samples twice for all the parameters investigated in the patients. The patients will be asked to provide such a healthy volunteer, for instance an HIV-negative partner or friend.

Contacts

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Eligibility criteria

Inclusion criteria

1. Adults 18 years of age or older;

2. HIV-1 infection, as documented by a licensed ELISA test kit and confirmed by a Western blot assay;

3. No evidence of acute HIV infection. For the purposes of this study acute HIV infection will be defined as presence of a detectable HIV-1 viral RNA in the presence of a non reactive HIV-1 or HIV-2 antibody assay or an indeterminate western blot;

4. Treatment naïve, i.e. no current of previous use of HAART;

5. Willingness to use a method of contraception during the study period. Adequate methods of birth control include: condoms, male or female, with or without a spermicide; diaphragm or cervical cap with spermicide; intrauterine device; any of the methods that require a prescription (such as contraceptive pills or patch, Norplant, Depo-Provera, and others) or a male partner who has previously undergone a vasectomy;

6. Willingness to have blood drawn;

7. Non known allergy or contraindication to rosuvastatin use;

8. Ability to understand and willingness to sign the informed consent;

9. Willingness to have blood stored for future phenotyping and genotyping;

10. CD4 cell count greater than 350 cells/ml;

11. Two viral loads that average greater than 1000 copies/ml within a 4 week period;

12. Liver function tests (AST or ALT) not greater than 1.5 times the upper limit of normal. Evidence of active hepatitis B or C will not be considered an exclusion criterion if the liver function tests are within normal limits;

13. Creatine phosphokinase elevations (CK) not greater than 3 times the upper limit of normal (ULN) on two sequential determinations and, in the opinion of the investigator, without clear association with exercise;

14. Laboratory values:

A. Absolute neutrophil count (ANC) greater than or equal to 1000/mm3;

B. Hemoglobin greater than or equal to 7.5 mmol/L;

C. Platelet count greater than or equal to 100,000/mm3;

D. Creatinine less than or equal to 2 x ULN;

E. Serum amylase and lipase less than or equal to 1.25 x ULN.

15. Negative serum pregnancy test at randomization.

Exclusion criteria

1. Pregnancy or breast feeding;

2. Active drug use or alcohol abuse/dependence, which in the opinion of the investigators will interfere with the patient's ability to participate in the study;

3. Serious illness requiring systemic treatment and/or hospitalization within 30 days of entry;

4. Evidence of active opportunistic infections or neoplasms that require chemotherapy during the study period;

5. Allergy or hypersensitivity to rosuvastatin or any of its components;

6. History of myositis or rhabdomyolysis with use of any statins;

7. History of inflammatory muscle disease such as poly- or dermatomyositis;

8. Concomitant use of fibric acid derivatives or other lipid lowering agents including statins and ezetimibe;

9. Concomitant use of drugs that have significant interactions with rosuvastatin;

10. Concomitant use of St. Johns wort;

11. Concomitant use of Valproic acid;

12. Patients who are on concurrent immunomodulatory agents;

13. Serum LDL cholesterol less than 1.0 mmol/L;

14. Vaccinations within 6 weeks of study entry.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2010
Enrollment:	40
Type:	Anticipated

Ethics review

Positive opinion

Date:	01-06-2010
Application type:	First submission

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
NTR-new	NL2224
NTR-old	NTR2349
Other	CWOO / EudraCT number : 2009-011 / 2010-019781-85 ;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A