A phase IV, randomized, open label, cross-over, intervention trial to investigate the effect of the switch of protease inhibitors to raltegravir on endothelial function, chronic inflammation, immune activation and HIV replication below 50 copies/ml

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1. To assess the effect of the switch from protease inhibitors to raltegravir on endothelial function. 2. To assess the effect of the intervention mentioned above on markers of endothelial function; immune activation; chronic inflammation; and, on...

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

Summary

ID

NL-OMON39957

Source
ToetsingOnline

Brief title
RASSTER

Condition

- Viral infectious disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym

hart- en vaatziekten, HIV

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: subsidie van Merck Sharp & Dohme Ltd.

Intervention

Keyword: Endothelial function, HIV, Raltegravir

Outcome measures

Primary outcome

Change in flow-mediated dilatation (FMD) of the brachial artery after 8 weeks

of raltegravir treatment (compared to treatment with protease inhibitors).

Secondary outcome

-Change in endothelial function measured by EndoPAT

-change in markers of endothelial function

-change in markers of chronic inflammation

-change in markers of immune activation

-change in plasma HIV-RNA below 50 copies/ml

Study description

Background summary

Lopinavir-ritonavir (LPV/r) and atazanavir/ritonavir (ATZ/r) are widespread antiretroviral drugs belonging to the class of protease inhibitors (PIs). PIs are associated with an increased risk of myocardial infarction. However, data is available suggesting that increased levels of plasma lipids are not the sole explanation for this observation. We hypothesize that treatment with LPV/r or ATZ/r leads to a decrease of endothelial function as well, thus explaining the increased risk of myocardial infarction besides increased plasma lipids.

Raltegravir is a registered antiretroviral drug with no known cardiovascular side effects. We hypothesize that switching of LPV/r or ATZ/r to raltegravir in HIV-infected patients with suppressed plasma viral load (<50 copies/ml) will lead to an improvement of endothelial function.

Study objective

1. To assess the effect of the switch from protease inhibitors to raltegravir on endothelial function.
2. To assess the effect of the intervention mentioned above on markers of endothelial function; immune activation; chronic inflammation; and, on plasma HIV-RNA below the cut-off of 50 copies/ml.

Study design

Phase IV, randomised, open label, cross-over, intervention trial.

Intervention

Randomisation into two arms: A and B. In arm A, LPV/r or ATZ/r will be switched to raltegravir, while study subjects in arm B will continue their LPV/r or ATZ/r-containing regimen. After 8 weeks, cross-over of the study arms will be performed. Subjects in arm A will then switch back to LPV/r or ATZ/r, while subjects in arm B will then switch to raltegravir. The total duration of the study is 16 weeks. Raltegravir has to be taken twice daily.

Study burden and risks

Study duration is 16 weeks, consisting of 8 visits. Assuming HIV-infected patients are monitored every three months, there will be approximately 6 extra visits. Endothelial function will be measured by FMD three times (non-invasively, combined), each visit blood will be drawn for assessment of the level of chronic inflammation, immune activation and virological studies. Complete physical examination will be performed at screening visit. Vital parameters and weight measurement will be performed on every visit. There seems low risk when participating in this study, since the study medication is approved and registered, currently known side effects of raltegravir are minimal, duration of treatment with study medication is short (8 weeks) and patients will be monitored frequently. With this study we hope to gain more insight into the mechanism of increased risk of myocardial infarction in patients treated with protease inhibitors.

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

-Age >= 18 years
-HIV-1 infection
-Treatment with antiretroviral regimen containing lopinavir/ritonavir or atazanavir/ritonavir for at least the previous 3 months
-No other protease inhibitors besides lopinavir-ritonavir or atazanavir/ritonavir in antiretroviral regimen
-Subjects must have a minimum period of viral suppression (plasma HIV-RNA <50 copies/ml) of 6 months
-Subjects will not have a history of virological failure on antiretroviral therapy
-Results of previous resistance testing allowing replacement of lopinavir-ritonavir or atazanavir/ritonavir by raltegravir
-CD4+ cell count > 200 cells/µL

-Signed informed consent

Exclusion criteria

-Pregnancy
-Breastfeeding
-Raltegravir hypersensitivity
-Treatment of underlying malignancy
-Renal insufficiency requiring dialysis
-Acute or decompensated chronic hepatitis (Child-Pugh score C)
-Modification of antiretroviral regimen in the previous 3 months

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-02-2012
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Isentress
Generic name:	raltegravir

Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-11-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-11-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	21-02-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	21-03-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-10-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	11-02-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-03-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	06-05-2014
Application type:	Amendment
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
EudraCT	EUCTR2011-003298-26-NL
CCMO	NL37593.041.11