Switch from a NNRTI or PI-based regimen to a RAltegravir-based regimen in virologically suppressed HIV-infected patients: effects on Platelet reactivity, platelet-monocyte aggregation and the Inflammatory anD thrombotic state of monocytes

Published: 20-01-2015
Last updated: 18-07-2024

Investigate whether switch from a non-nucleoside reverse transcriptase inhibitor (NNRTI)- or protease inhibitor (PI)-based regimen to a raltegravir-based regimen results in reduced platelet reactivity, reduced platelet-leukocyte aggregate formation...

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

Summary

ID

NL-OMON42115

Source
ToetsingOnline

Brief title
RAPID-study

Condition

- Viral infectious disorders

Synonym
human immunodeficiency virus (HIV)

Research involving
Human

Sponsors and support

Primary sponsor: Radboudumc
Source(s) of monetary or material Support: Merck Sharp & Dohme (MSD),MSD Pharmaceuticals

Intervention

Keyword: HIV, Integrase inhibitor, platelets, Raltegravir

Outcome measures

Primary outcome

1. Platelet reactivity: platelet expression of the platelet activation marker

CD62P (P-selectin) and activated fibrinogen receptor (αIIbβ3) upon stimulation

with different platelet agonists. 2. Platelet-leukocyte aggregates (eg. PMA).

3. Proportion of CD14+CD16 ++(bright) monocytes compared to CD14+CD16- and

activation state of monocytes (CD11b expression) and lymphocytes (CD38+ HLA-DR+

CD8+ T cells). 4. Soluble (plasma) markers of platelet and monocyte

activation.

Secondary outcome

Investigate whether switch to raltegravir is associated with:

a) reduced activation status of monocytes and of CD4 and CD8 lymphocytes

b) reduced expression of CCR5 on monocytes and CD4+ T-lymphocytes

c) reduced plasma levels of inflammatory markers (eg. hs-CRP, several cytokines)

d) epigenetic changes (eg. Histone methylation)

e) altered IL-32 expression and splicing

Study description

Background summary

Cardiovascular disease (CVD) has emerged as a leading cause of morbidity and mortality in HIV-infected individuals. The precise mechanisms underlying this increased cardiovascular risk remain to be elucidated . Platelet hyperreactivity and increased platelet-monocyte aggregation (PMA) are found in HIV-infected patients and may contribute to the excess cardiovascular risk as platelets play a key role in the onset and progression of atherosclerosis and in acute cardiovascular events. In addition, HIV-infected individuals frequently suffer from persistent immune activation and inflammation. In a cross-sectional study we recently showed that individuals using a regimen containing the integrase inhibitor raltegravir have reduced platelet hyperreactivity and PMA compared to other antiretroviral regimens. Other recent studies showed that raltegravir is associated with decreased immune activation. Due to the inherent limitations of cross sectional studies, we aim to expand our findings in an intervention study.

Study objective

Investigate whether switch from a non-nucleoside reverse transcriptase inhibitor (NNRTI)- or protease inhibitor (PI)-based regimen to a raltegravir-based regimen results in reduced platelet reactivity, reduced platelet-leukocyte aggregate formation and pro-inflammatory status of monocytes.

Study design

Investigator initiated, single-center, open-label, randomized controlled trial in HIV-infected patients using a NNRTI- or PI-based regimen

Intervention

Participants will be randomized (1:1) to continue the same ART regimen (*Continuation group*) or to switch their NNRTI or PI to raltegravir (*Switch group*) during 10 weeks.

Study burden and risks

Raltegravir is a registered drug for both naïve and treatment experienced HIV-infected patients. There is extensive clinical experience with this drug and it has a good safety profile with few side effects. A raltegravir-based regimen is one of the recommended first line treatment option for HIV-infected individuals. A possible burden is that raltegravir should be taken twice daily,

whereas some regimens are taken once daily. Participation in this study involves three extra visits and three extra venipunctures with a total amount of blood taken for the whole study of approximately 160 mL.

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

•Documented HIV-infection
•Age >= 18 years
•On stable antiretroviral therapy (ART) for >= 6 months at screening
•Undetectable plasma HIV viral load (<50 copies/mL) for at least 6 months
•CD4 cell count > 300 cells/mm3 at last measurement
•Current ART regimen at screening consisting of a backbone of two NRTI*s (either TDF/FTC or ABC/3TC) with either a NNRTI (EFV or RPV) or a boosted PI (DRV/r, ATZ/r or LPV/r) and on this

regimen for > 3 months
•If female and of childbearing potential using effective birth control methods

Exclusion criteria

•Use of platelet function inhibitors, such as aspirin and ADP receptor antagonists
•Known hypersensitivity to raltegravir or any other component of the formulation
•Using any concomitant therapy disallowed as per SPC for the study drug
•Signs of symptoms of an active (opportunistic) infection other than HIV
•Active hepatitis B or C
•Estimated glomerular filtration rate (by MDRD) <50 ml/min
•History of suspected or proven virologic failure since ART initiation (HIV-1 RNA *blips* less than 500 copies per milliliter with subsequent resuppression are allowed)
•Known genotypic resistance to any current ART component
•In females, pregnancy or breast feeding

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-03-2015
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	20-01-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-07-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NCT02383355
CCMO	NL50681.091.14