Pharmacokinetic and safety pilotstudy of RAltegravir and atazanavir in a once DAily dose regimen in HIV-1 in-fected patients (PRADA)

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Primary: To compare the pharmacokinetics of raltegravir 400 mg twice daily vs. ralte-gravir 800 mg once daily (QD) by intrasubject comparison. Secondary: To determine the efficacy of an antiretroviral regimen consisting of raltegravir 800mg QD,...

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

Summary

ID

NL-OMON33412

Source
ToetsingOnline

Brief title
PRADA

Condition

- Viral infectious disorders

Synonym
HIV, human immunodeficiency virus

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Atazanavir, HIV, pharmacokinetics, Raltegravir

Outcome measures

Primary outcome

comparison of raltegravir pharmacokinetics (AUC, Cmax and Cmin) after 2 weeks

of 400mg BID dosing versus 2 weeks of 800mg QD dosing.

Secondary outcome

viral load (efficacy), adverse events (safety).

Study description

Background summary

Anti-HIV-medication has to be used for life. Therefore it is of importance to simplify the therapy as much as possible by reducing the dose frequency to once daily dosing. Once daily dosing improves the quality of life and will increase treatment compliance, reducing the risk on resistance to the drugs taken (virological failure).

Study objective

Primary:
To compare the pharmacokinetics of raltegravir 400 mg twice daily vs. ralte-gravir 800 mg once daily (QD) by intrasubject comparison.
Secondary:
To determine the efficacy of an antiretroviral regimen consisting of raltegravir 800mg QD, atazanavir 600mg QD and lamivudine 300mg or emtricitabine 200mg QD in HIV-infected patients
To determine the safety of combined use of raltegravir and atazanavir QD in HIV- infected patients

Study design

the trial will be conducted in 20 HIV-patients. The duration of the trial is 8 weeks, devided in two periods of four weeks each.

Treatment in the first period of 4 weeks:
-600 mg atazanavir QD
-400 mg raltegravir BID
-300 mg lamivudine QD or 200 mg emtricitabine QD

Blood concentrations of raltegravir and atazanavir will be determined after 2 weeks of treatment.

Evaluation at week 4: decision taken based on viral load and atazanavir blood concentrations. After this evaluation the second period of 4 weeks will start.

Treatment in the second period of 4 weeks:
-600 mg atazanavir QD
-800 mg raltegravir QD
-300 mg lamivudine QD or 200 mg emtricitabine QD

Blood concentrations of raltegravir and atazanavir will be determined in week 6 of the trial (after 2 weeks of treatment).

Intervention

The treatment of patients will be adapted according to the schedule above. There will be two days of blood sampling for pharmacokinetics.

Study burden and risks

Adverse events of the antiretroviral drugs. There is a chance that the HIV virus will not be suppressed effectively. This will be monitored by regular determination of viral load and atazanavir concentrations in the blood. If the therapy is not effective the therapy will be adapted or the previous treatment will be resumed.

The needles used for blood collection could inflict nuisance or pain at the place of insertion. Blood collection will be done by qualified personnel.

The patients will come to the unit during two days on which blood sampling will take place. The amount of blood collected during the study is small (approximately 172 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

1. HIV-infected as documented by positive HIV antibody test and confirmed by Western Blot.
2. Subject is at least 18 years of age at the day of screening.
3. Subject is able and willing to sign the Informed Consent Form prior to screening evaluations.
4. HIV-1 RNA < 40 copies/mL for at least 6 months on antiretroviral therapy.
5. Subject has no history of previous virological failure or documented resistance mutations.

Exclusion criteria

1. History of sensitivity/idiosyncrasy to the drug or chemically related compounds or excipients, which may be employed in the trial.
2. Relevant history or current condition that might interfere with drug absorption, distribution, metabolism or excretion.
3. Inability to understand the nature and extent of the trial and the procedures re-quired.
4. Pregnant female (as confirmed by an HCG test performed less than 3 weeks before the first dose) or breast-feeding female.
5. Abnormal serum transminases determined as levels being > 5 times upper limit of normal

(see Appendix A for normal ranges of clinical laboratory values).
6. Concomitant use of medications that interfere with raltegravir or atazanavir pharmacokinetics: rifampicin, irinotecan, midazolam, triazolam, ergotamine, dihydroergotamine, cisapride, pimozide, lovastain, simvastatin, indinavir, proton pump inhibitors, H2 receptor antagonists, St. john*s wort, Ginkgo Biloba, didanosine, tenofovir, efavirenz, nevirapine, antacids, clarithromycin, phenytoin, phenobarbital, carbamazepine.
7. Active hepatobiliary or hepatic disease (including chronic hepatitis B infection).
8. Alcohol abuse.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2009
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	isentress
Generic name:	raltegravir
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	reyataz

Generic name:	atazanavir
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-05-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-07-2009
Application type:	First submission
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
EudraCT	EUCTR2008-008556-16-NL
CCMO	NL27841.091.09