Pharmacokinetic study of the HCV protease inhibitor bO-cePrevir and the HIV integrase inhibitor rALtegravir (OPAL)

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Primary objectiveTo determine the effect of steady state boceprevir on the pharmacokinetics (AUC0-12h, Cmax, C12h) of a single dose raltegravir.Secondary objectives:To determine the effect of a single dose raltegravir on the pharmacokinetics (AUC0-...

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

Summary

ID

NL-OMON36218

Source
ToetsingOnline

Brief title
OPAL

Condition

- Viral infectious disorders

Synonym
HIV; AIDS

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: farmaceutische industrie,Merck

Intervention

Keyword: boceprevir, hepatitis C, HIV, raltegravir

Outcome measures

Primary outcome

Pharmacokinetic parameters of raltegravir.

Secondary outcome

Pharmacokinetic parameters of boceprevir in comparison with historical

controls. Safety: adverse events en lab values.

Study description

Background summary

The prevalence of hepatitis C virus (HCV) in human immunodeficiency virus (HIV) infected patients ranges from ± 7 to 57% in Europe and North America1. Since the introduction of combination antiretroviral therapy (cART) the life expectancy of HIV infected patients has improved dramatically. Since then, hepatitis C has become one of the main causes of death among patients with stable HIV.

Combined use of boceprevir and raltegravir is not expected to give a major drug-drug interaction as raltegravir is not a CYP3A substrate and thus will not be affected by the strong inhibition of CYP3A by bo-ceprevir. Raltegravir is metabolized by UGT but boceprevir is not known to influence UGT. However, recent data indicate that raltegravir is a P-gp substrate and boceprevir is a substrate and a moderate inhibitor of P-gp in vitro.

Even when no drug interaction is expected, it may be recommended to collect sufficient evidence that this is the case as in many cases un-expected drug-drug interactions have been observed in the past.

Study objective

Primary objective
To determine the effect of steady state boceprevir on the pharmacokinetics

(AUC0-12h, Cmax, C12h) of a single dose raltegravir.

Secondary objectives:
To determine the effect of a single dose raltegravir on the pharmacokinetics (AUC0-8h, Cmax, C8h) of steady state boceprevir (by comparison with historical controls).

To study the safety of single-doses raltegravir combined with steady state boceprevir.

Study design

Open-label, 2-period, randomized, cross-over, single-centre, phase-I trial

Group A will receive a single dose of 400mg RTG on Day 10. After a washout period of at least two weeks they will take 800mg BOC TID (8 hours intervals) with food for 9 days (Day 29-37). On day 38 they will receive a single dose of 400mg RTG and two doses of 800mg BOC (one together with RTG and one dose 8 hours later).

Group B will take 800mg BOC TID (8 hours intervals) with food for 9 days (Day 1-9). On day 10 they will receive a single dose of 400mg RTG and two doses of 800mg BOC (one together with RTG and one dose 8 hours later). After a washout period of at least 4 weeks they will receive a single dose of 400mg RTG on Day 38.

The treatment group will be assigned at random.

On Days 10 and 38 a pharmacokinetic curve will be recorded.

Intervention

Dosing with raltegravir (two times a single dose of 400 mg) and boceprevir (9 days three times daily 800 mg and on day 10 two doses of 800 mg).

Study burden and risks

The study participants are healthy volunteers and will not benefit from the participation in this clinical trial.
They will visit the centre for short visits (1 hour) 5 times and stay for appr. 14 hours on two occasions. The duration of the entire trial (excluding screening period) is 38 days.
A total number of 30 times a blood sample will be taken; the total volume taken will be maximally 300mL.
During the days that blood samples will be collected for a pharmacokinetic curve an intravenous cannula will be inserted to facilitate blood sampling.

Boceprevir is a compound which is still in clinical research. A total of 377 healthy volunteers have been exposed to this drug already. The maximum dose given to healthy volunteers was 1200mg TID. The longest dosing period was 56 days.
Possible adverse events (in healthy volunteers) are: dysgeusia, anaemia, headache, nausea, vomiting and elevated liver transaminases.

Raltegravir has been marketed since 2007. Common side effects (affects 1 to 10 users in 100):
• trouble sleeping; abnormal dreams
• feeling dizzy; headache
• spinning sensation
• bloating; abdominal pain; diarrhoea; excessive gas in the stomach or bowel; feeling sick;
vomiting
• certain kinds of rash (more often when used in combination with darunavir)
• tiredness, unusual tiredness or weakness; fever
• increased liver blood tests; abnormal white blood cells; increased fat levels in blood; increased level of enzyme from salivary glands or pancreas.

Possible side effects of the combination of boceprevir and raltegravir are unknown.

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. Subject is at least 18 and not older than 55 years at screening.
2. Subject does not smoke more than 10 cigarettes, 2 cigars, or 2 pipes per day for at least 3 months prior to the first dosing
3. Subject has a Quetelet Index (Body Mass Index) of 18 to 30 kg/m2, extremes included.
4. Subject is able and willing to sign the Informed Consent Form prior to screening evaluations.
5. Subject is in good age-appropriate health condition as established by medical history, physical examination, electrocardiography, results of biochemistry, haematology and urinalysis testing within 4 weeks prior to Day 1. Results of biochemistry, haematology and urinalysis testing should be within the laboratory's reference ranges. If laboratory results are not within the reference ranges, the subject is included on condition that the Investigator judges that the deviations are not clinically relevant. This should be clearly recorded.
6. Subject has a normal blood pressure and pulse rate, according to the Investigator's judgement.

Exclusion criteria

1. Documented history of sensitivity/idiosyncrasy to medicinal products or excipients.
2. Positive HIV test.
3. Positive hepatitis B or C test.
4. Pregnant female (as confirmed by an HCG test performed less than 4 weeks before Day 1) or breast-feeding female. Female subjects of childbearing potential without adequate contracep-tion, e.g. hysterectomy, bilateral tubal ligation, (non-hormonal) intrauterine device, total abstinence, double barrier methods, or two years post-menopausal. They must agree to take precautions in order to prevent a pregnancy throughout the entire conduct of the trial.
5. Therapy with any drug (for two weeks preceding dosing), except for paracetamol.
6. Relevant history or presence of pulmonary disorders (especially COPD), cardiovascular disorders, neurological disorders (especially seizures and migraine), psychiatric disorders, gastro-intestinal disorders, renal and hepatic disorders, hormonal disorders (especially diabetes mellitus), coagulation disorders.
7. Relevant history or current condition that might interfere with drug absorption,

distribution, metabolism or excretion.
8. History of or current abuse of drugs, alcohol or solvents.
9. Inability to understand the nature and extent of the trial and the procedures required.
10. Participation in a drug trial within 60 days prior to the first dose.
11. Donation of blood within 60 days prior to the first dose.
12. Febrile illness within 3 days before the first dose.

Study design

Design

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):	13-09-2011
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Boceprevir (merknaam komt nog)
Generic name:	boceprevir
Product type:	Medicine
Brand name:	isentress
Generic name:	raltegravir
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-02-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-03-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-05-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-09-2011
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
EudraCT	EUCTR2010-024542-29-NL
CCMO	NL35464.091.11