The influence of Raltegravir (MK_0518) on the pharmacokinetics of single-dose Lamotrigine in healthy male subjects (GRANOLA)

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In vitro data indicate that raltegravir is not a substrate of UGT1A4 or UGT2B7, but there is no evidence that raltegravir itself does not influence metabolism of other agents mediated by either UGT1A4 or UGT2B7.

Ethical review	Approved WMO
Status	Pending
Health condition type	Immunodeficiency syndromes
Study type	Interventional

Summary

ID

NL-OMON32367

Source
ToetsingOnline

Brief title
GRANOLA study

Condition

- Immunodeficiency syndromes
- Viral infectious disorders

Synonym
HIV infections

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Merck

Intervention

Keyword: HIV integrase inhibitor, interaction, pharmacokinetics, raltegravir

Outcome measures

Primary outcome

To determine the effect of raltegravir on the pharmacokinetics of single-dose

lamotrigine determined by intrasubject comparison.

Secondary outcome

To determine the effect of single-dose lamotrigine on the pharmacokinetics of

raltegravir when compared to historical controls

To evaluate the safety of combined use of single-dose lamotrigine and

ralte-gravir

Study description

Background summary

Raltegravir is a newly developed HIV integrase inhibitor. Raltegravir has been tested in both treatment-naïve and -experienced patients and appears to have an excellent risk/benefit ratio. Raltegravir is not a substrate of CYP450, but it is metabolized by glucuronidation via UGT1A1.

Lamotrigine (Lamictal®) is an anticonvulsant drug. It can be used for the treatment of epilepsy of HIV-infected patients. Furthermore, lamotrigine is used for the treatment of neuropathic pain. Lamotrigine appears to be one of the few effective agents for HIV-associated neuropathic pain.
Recent in vitro work suggests that UGT1A4 and UGT2B7 are the main isozymes of UGT responsible for glucuronidation of lamotrigine; hence lamotrigine can be considered as a mixed UGT1A4/2B7 probe to evaluate potential drug interactions.

Study objective

In vitro data indicate that raltegravir is not a substrate of UGT1A4 or UGT2B7, but there is no evidence that raltegravir itself does not influence metabolism of other agents mediated by either UGT1A4 or UGT2B7.

Study design

open-label gerandomiseerd, cross-over single-centre, fase IV multiple-dose trial

Intervention

During this study, which lasts 34 days in total, subjects have to take Raltegravir twice daily during five consecutive days. During two days of the 34 study days Lamotrigine is taken once daily.
During the study 254ml blood is taken from each subject.
- screening (4 weeks before start of the trial): 19 ml
- group A # day 1: 14ml, day 2: 14ml, day 4: 79ml, day 5: 7ml, day 6: 14ml, day 29: 7ml, day 32: 79ml, day 33: 7ml day 34: 14ml
- group B # day 1; 7ml, day 4: 79ml, day 5: 7 ml, day 6: 14ml, day 29: 14ml, day 30: 14ml, day 32: 79ml, day 33: 7ml, day 34: 14ml

Study burden and risks

The side effects of raltegravir can be: dizziness, headache, tiredness.
The side effects of lamotrigine can be: rash, headache, double vision, misty eyes, tiredness, nausea, dizziness, irritation,sleepyness, sleeplesness, The needles that are used for bloodtake may cause discomfort or pain at the place of injection.
The risks of participation are relatively small. Raltegravir tablets are taken during 5 consecutive days. The side effects are mild. The Lamotrigine medication is taken on two days in the early morning of an admission day; those days the subject is under medical attention of the research centre. In the ELLA study (CMOnr 2005/314) a single dose Lamotrigine was very well tolerated.

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

- men in the age of 18- 55 years
- does not smoke more than 10 cigarettes, 2 cigars or 2 pipes
- has a Quetelet Index between 18 - 30 kg/m2
- willing and able to sign informed consent
- in a good health age-appropriate
- heeft een normale bloeddruk en pols

Exclusion criteria

- sensitivity to medicinal products
- HIV positive
- hepatitis B or C positive
- therapy with any drug, except for paracetamol
- relevant history or presence of pulmonary disorders, cardiovascular disorders, neurological disorders, gastro-intestinal disorders, renal- or hepatic disorders, hormonal disorders especially diabetes mellitus, coagulation disorders
- history or current abuse of drugs, alcohol or solvents.
- inability to understand the nature and extent of the trial and the procedures required
- participation in a drug trial within 60 days prior to the first dose
- donation of blood within 60 days prior to the first dose

- 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:	Pending
Start date (anticipated):	01-03-2008
Enrollment:	24
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	n.a.
Generic name:	Raltegravir

Ethics review

Approved WMO

Date:	08-11-2007
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	27-03-2008
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	EUCTR2007-005405-21-NL
CCMO	NL20016.091.07