The effect of FOsamprenavir/Ritonavir on the pharmacokinetics of a single-dose of the antipsychotic agent olanZApine (FORZA)

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Primary objective: To evaluate the influence of fosamprenavir/ritonavir on single-dose pharmacokinetics of olanzapine in healthy volunteersSecondary objective: To evaluate the safety of fosamprenavir/ritonavir combined with single-dose olanzapine in...

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

Summary

ID

NL-OMON33257

Source
ToetsingOnline

Brief title
FORZA

Condition

- Viral infectious disorders
- Schizophrenia and other psychotic disorders

Synonym
HIV, psychosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: farmaceutische industrie,GlaxoSmithKline

Intervention

Keyword: HIV, interaction, pharmacokinetics, psychosis

Outcome measures

Primary outcome

The influence of fosamprenavir/ritonavir on single-dose pharmacokinetics of

olanzapine in healthy volunteers

Secondary outcome

The safety of fosamprenavir/ritonavir combined with single-dose olanzapine in

healthy volunteers

Study description

Background summary

Psychosis and other mental illnesses are commonly described in patients infected with the human immunodeficiency virus (HIV). The high rates of co-morbidity of mental illness and HIV can be partly explained by the risk behaviour of patients with mental illness. Furthermore, having an HIV-infection, places people at risk for developing psychoses.
When psychosis is present in HIV-infected people (either new-onset or existing psychosis), treatment with an antipsychotic agent is usually necessary. HIV-infected patients with new-onset psychosis generally respond well to antipsychotic medication, but are extra sensitive for their side-effects, especially extrapyridamal side effects (EPS) and tardive dyskinesia (TD) induced by conventional antipsychotics. Because of their favourable side-effect profile, atypical antipsychotic agents are preferable in HIV-infected people. Olanzapine could be an attractive antipsychotic in HIV/AIDS patients with schizophrenia. However, there is little experience with olanzapine in treating schizophrenia in HIV/AIDS patients. Further, olanzapine is metabolised by uridine diphosphate-glucuronosyltransferase (UGT) and CYP1A2, which puts it at risk for pharmacokinetic interactions with HIV-medication. Fosamprenavir is a

protease-inhibitor (PI) that is used to treat HIV-infection in combina-tion with ritonavir. Ritonavir has many influences on the diverse CYP-enzymes, among which CYP1A2 and UGT. Because olanzapine is a substrate for both UGT and CYP1A2, the pharmacokinetics of olanzapine might be influenced by low-dose ritonavir in combination with fosamprenavir.

Study objective

Primary objective:
To evaluate the influence of fosamprenavir/ritonavir on single-dose pharmacokinetics of olanzapine in healthy volunteers

Secondary objective:
To evaluate the safety of fosamprenavir/ritonavir combined with single-dose olanzapine in healthy volunteers

Study design

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

Intervention

Two groups are defined for treatment.

Group 1:
Day 1-16: Fosamprenavir/ritonavir 700/100 mg BD Day + olanzapine 15 mg single-dose on Day 13
Day 17-47:wash-out
Day 48: single-dose olanzapine 10 mg on Day 48

Group 2:
Day 13: single-dose olanzapine 10 mg
Day 14-35: wash-out
Day 36-52: fosamprenavir/ritonavir 700/100 BD + olanzapine single-dose 15 mg on Day 48

After the morning dosage on Day 13 and Day 48 a 96h pharmacokinetic curve (17 samples) will be performed

Study burden and risks

The needles used for blood sample collection may cause slight discomfort at the injection site.

The healthy volunteers may experience adverse events of the trial medication.

The risks for adverse events are minimalized by limiting the use of fosampravir/ritonavir to 16 days and limiting the use of olanzapine to 2 times a single-dose. Study subjects will be monitored almost every other day, and adverse events can be detected early. The information we will collect from this study outweighs the risks for toxicity in healthy volunteers.

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 of age at screening.
2. Subject has a Quetelet Index (Body Mass Index) of 18 to 30 kg/m2, extremes in- cluded.
3. Subject is able and willing to sign the Informed Consent Form prior to screening evaluations.
4. Subject is in good age-appropriate health condition as established by medical his-tory,

physical examination, electrocardiography, results of biochemistry, haema-tology and urinalysis testing within 4 weeks prior to the first dose. Results of bio-chemistry, 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.
5. Subject has a normal blood pressure and pulse rate, according to the Investiga-tor'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 be-fore the first dose) or breast-feeding female. Female subjects of childbearing po-tential without adequate contraception, 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), cardio-vascular disorders, neurological disorders (especially seizures and migraine), gas-tro-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 re-quired.
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
13. History of narrow-angle glaucoma

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):	16-12-2009
Enrollment:	24
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Norvir
Generic name:	ritonavir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Telzir
Generic name:	fosamprenavir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Zyprexa
Generic name:	olanzapine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	16-07-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-08-2009
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	EUCTR2009-009430-32-NL
CCMO	NL27936.091.09