Bioequivalence study in healthy volunteers of a new paediatric formulation of valacyclovir used for prophylaxis and treatment of VZV and HSV infections in children, phase I (VALID I)

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

Summary

ID

NL-OMON39942

Source
ToetsingOnline

Brief title
VALID I

Condition

- Viral infectious disorders

Synonym
chicken pox, herpes infection

Research involving

Human

Sponsors and support

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

Intervention

Keyword: bioequivalence, paediatric formulation, pharmacokinetics, valacyclovir oral solution

Outcome measures

Primary outcome

Pharmacokinetic parameters of valacyclovir

Secondary outcome

amount and severity of adverse events

Study description

Background summary

Herpes infections in immunocompromised patient cause longer periods of clinical symptoms and viral shedding, increased severity and more frequent episodes of reactivation. This may leed to dissemination, hepatitis, post herpetic neuralgia, bacterial super infection, pneumonitis, encephalitis and death. Valacyclovir is an oral prodrug of acyclovir, with at least equal efficacy and a similar safety profile as intravenous aciclovir and therefore less expensive and more convenient. However, in immunocompromised children practical problems exist with adult-dose tablets. A formulation with acceptable palatability, good pharmaceutical quality and possibility of flexible dosing is needed. A new paediatric formulation (oral solution) has been developed to fullfill those needs. To ensure comparable in vivo efficacy, the bioequivalence of this formulation versus valacyclovir tablets will be investigated in healthy adults, according to the EMA guidelines for bioequivalence.

Study objective

In this trial will be investigated if a new formulation of valacyclovir, e.g. oral solution, is bioequivalent to valacyclovir tablets. This comparison will

be made by determining pharmacokinetic parameters (AUC0-*, Cmax, and tmax) of both formulations in healthy adult volunteers.
Next to this, the safety profile of a single dose of valacyclovir oral solution will be determined by monitoring adverse events.

Study design

Open label, two-period, single dose, crossover, single centre, randomized phase-I trial.
Group A will receive a single dose of valacyclovir tablet 500 mg (Zelitrex®) on day 1. After a wash-out period of 7 days, the subjects will receive a single dose of valacyclovir oral solution (20 mg/mL) equal to valacyclovir 500 mg (25 mL) on day 8.
Group B will receive a single dose of valacyclovir oral solution (20 mg/mL) equal to valacyclovir 500 mg (25 mL). After a wash-out period of 7 days, the subjects will receive a single dose of valacyclovir tablet 500 mg (Zelitrex®) on day 8.
Subjects will be randomly divided into two treatment groups.

Intervention

Administration of a single dose of valacyclovir 500 mg on two days.

Study burden and risks

The subjects are healthy volunteers. This treatment will not be of benefit to their health. The subject need to be present at the trial location during 2 days. The trial period (excluding screening) encompasses 8 days. The cannula used to draw blood may cause inconvenience or pain at the insertion site. Blood will be drawn through a venous punction (at screening) and through the cannula (on trial days).
In this trial a low dose of valayclovir is used and therefore the risk on adverse events is minimized, but not excluded. Possible side effects of valacyclovir include headache (>=10%), nausea, vomiting, diarrhea, dizziness, rash, pruritis (>=1% and <10%), leucopenia, thrombocytopenia, hallucinations, mental confusion, diminished consciousness, agitation, tremor, dyspnoea, abdominal discomfort, urticaria, kidney pain (>=0,1% and <1%), anaphylaxis, ataxia, dysarthria, convulsions, encephalopathy, coma, psychotic symptoms, reversible increase in liver enzymes and bilirubin, angioedema, impaired renal function and acute renal failure (>=0,01% and <0,1%).
The single-dose nature of this trial minimizes the development of drug resistance.

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 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 has signed 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 the first dose. Results of biochemistry, haematology and urinalysis testing should be within the laboratory's reference ranges (see Appendix A). 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 re-corded.

6. Subject has a normal blood pressure and pulse rate, according to the investigator's judgement.
7. Female subject is either not of childbearing potential, defined as postmenopausal for at least 1 year or is of childbearing potential with adequate contraception (e.g. hysterectomy, bilateral tubal ligation, (nonhormonal) intrauterine device, total abstinence, double barrier methods, vasectomized partner).

Exclusion criteria

1. Documented history of sensitivity/idiosyncrasy to medicinal products or excipients.
2. Positive HIV, hepatitis B or C test.
3. Therapy with any drug (for two weeks preceding dosing), except for acetaminophen.
4. Relevant history or presence of pulmonary disorders (especially COPD), cardiovascular disor-ders, neurological disorders (especially seizures and migraine), gastro-intestinal disorders, renal and hepatic disorders, hormonal disorders (especially diabetes mellitus), coagulation disorders.
5. Relevant history or current condition that might interfere with drug absorption, distribution, metabolism or excretion.
6. History of or current abuse of drugs, alcohol or solvents.
7. Inability to understand the nature and extent of the trial and the procedures required.
8. Participation in a drug trial within 60 days prior to the first dose.
9. Donation of blood within 60 days prior to the first dose.
10. Febrile illness within 3 days before the first dose.
11. Pregnant female (as confirmed by an HCG test performed less than 4 weeks before the first dose) or breast-feeding female.

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):	08-05-2013
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n.v.t.
Generic name:	valacyclovir
Product type:	Medicine
Brand name:	Zelitrex
Generic name:	valacyclovir
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-04-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-12-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-01-2015
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
EudraCT	EUCTR2011-005077-22-NL
CCMO	NL39308.091.12