Palatability testing of a new paediatric formulation of valacyclovir for the prophylaxis and treatment of VZV and HSV infections in children - VALID 0

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

Summary

ID

NL-OMON43617

Source
ToetsingOnline

Brief title
VALID-0: palatability testing

Condition

- Viral infectious disorders

Synonym
chickenpox, herpes

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum

Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: formulation, paediatric, palatability testing, valacyclovir oral solution

Outcome measures

Primary outcome

A 100 mm facial hedonic scale will be employed to indicate the palatability of each formulation.

Secondary outcome

For (one of) the parents a 100 mm facial hedonic scale will be employed to indicate the palatability of each formulation. They will also fill in a questionnaire to determine which of the formulations they think will have the preference of their child. Also, they have to fill in what basic taste they taste.

Study description

Background summary

In children acyclovir is used as prophylaxis and treatment of varicella zoster virus (VZV) and herpes simplex virus (HSV) infections. In adults, valacyclovir has replaced oral acyclovir in many clinical scenarios. Pharmacokinetic data support the use of oral valacyclovir in children, but practical problems with the adult tablets exist in children. For children, a formulation with acceptable palatability, good pharmaceutical quality, and possibility of flexible dosing is needed. This study is part of the VALID-project in which a new paediatric formulation of valacyclovir will be developed and evaluated. During the development phase palatability testing will be performed. The bioequivalence of the new paediatric formulation versus valacyclovir tablets will be investigated in a study in healthy adults. Subsequently the pharmacokinetics and safety of the new paediatric oral formulation will be determined in children receiving this drug as prophylaxis against VZV and HSV infections post stem cell transplantation. The VALID-project has been granted

by ZonMW within the *Priority Medicines for Children* Programme.

Study objective

Primary
To determine whether the palatability of a newly developed formulation of valacyclovir is non-inferior to administration of crushed and suspended tablets in children, is the primary objective of the second phase of the trial.
The primary objective of the first phase of the trial was to determine which of three newly developed formulations of valacyclovir is accepted best in children.
Secondary
To determine whether parents can predict the palatability preference of their child.
In the second phase of the trial a new secondary objective is to validate the results of the in vitro taste assessment.

Study design

Randomized, two-period, multi centre, cross-over study

Intervention

Three formulations will be tested. Each participant will taste 4 or 8 ml of each formulation containing 20-25 mg/ml valacyclovir.
Collection of 2 ml of saliva (voluntary) for research on genetics of taste.

Study burden and risks

The burden of this study is very low: a single dose, or less, exposure to pharmaceutical active substance. The substance has solely antiviral activity and therefore does not influence normal physiological processes in the human body.
The dose of valacyclovir in immunocompromised children for the treatment of VZV and HSV infection is 60-90 mg/kg daily, divided in two to three doses. The estimated bodyweight of a child of 4 years of age is 15-19 kg and for a child of 8 years of age 25-28 kg. The lowest single therapeutic dose would be 300 mg (15 kg * 20 mg/kg). For children 4-8 years of age the administered dose during the taste assessment (270 mg) is comparable to a single therapeutic dose and less than 1/3 of a total daily therapeutic dose for a child of 15 kg. For children 8-12 years of age the dose administered (540 mg) is comparable to a single therapeutic dose for a child of 27 kg, and 1/3 or less of a total daily therapeutic dose.
The taste assessment will be performed combined with a regular visit to the outpatient clinic. Subjects don*t have to come to the hospital separately to participate in this study.

The taste assessment will be performed directly after a regular visit to the outpatient clinic. Subjects don*t have to come to the hospital separately to participate in this study.

Adverse events of prolonged use of valacyclovir include: headache (>=10%), nausea, vomiting, diarrhea, dizziness, rash, pruritis, photosensibilisation (>=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%).
During the taste assessment, subjects will receive a dose of valacyclovir that is equal to a single therapeutic dose, or less, depending on body weight (see 6.3). It is not expected that drug resistance to valacyclovir or acyclovir will develop.
The excipients that are used in the formulations, are commonly used in extemporaneously prepared products by pharmacists.

Contacts

Public
Selecteer

Geert Grooteplein-Zuid 10
Nijmegen 6525 GA
NL
Scientific
Selecteer

Geert Grooteplein-Zuid 10
Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

1. Subject is at least 4 years of age.
2. Subject is capable of performing the taste assessment, according to the investigator*s judgement.
3. The child is willing to participate in the taste assessment.
4. Signed informed consent by the legal guardian for participation of the child and if the parent also wants to participate: signed informed consent for their own participation, prior to start of the study.

Exclusion criteria

1. Documented history of sensitivity/idiosyncrasy to medicinal products or excipients (as used in the study formulation). An exception is a sensitivity reaction on asparaginase, since this is a common reaction in children, and no cross sensitivity with other medicinal products has been demonstrated.
2. Presence of any condition that influences taste sensation (such as upper respiratory infection, febrile illness within 3 days before the first dose, mucositis or use of medication (not included in standard protocol for treatment of underlying disease) that influences taste perception, as described in the label information).

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-11-2015
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	valacyclovir
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	20-04-2012
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-07-2012
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-03-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-07-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	04-07-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-11-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-01-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-04-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-02-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2012-000577-22-NL
ClinicalTrials.gov	NCT01682109
CCMO	NL39424.000.12