



Clinical trial results:

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

Summary

EudraCT number	2012-000577-22
Trial protocol	NL
Global end of trial date	30 March 2016

Results information

Result version number	v1 (current)
This version publication date	19 November 2020
First version publication date	19 November 2020
Summary attachment (see zip file)	paper (BCP-83-2789.pdf)

Trial information

Trial identification

Sponsor protocol code	AKF-UMCN11.05
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands,
Public contact	David Burger, Radboud University Nijmegen Medical Centre, 31 243616405, d.bastiaans@akf.umcn.nl
Scientific contact	Diane Bastiaans, Radboud University Nijmegen Medical Centre, 31 243616405, david.burger@radboudumc.nl

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 March 2016
Global end of trial reached?	Yes
Global end of trial date	30 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine which of three newly developed formulations of valacyclovir is accepted best in children.

Protection of trial subjects:

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 total dose of the drug that will be administered to the subject during one taste assessment is 270 mg (4 ml of the 20 mg/ml solution, the 25 mg/ml suspension and the mixed formulation (22.5 mg/ml)) for children of 4-8 years and 540 mg for children of 8-12 years and the parent(s).

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.

DNA will be collected through obtaining a 2 ml saliva sample. This is a non-invasive and patient friendly way of obtaining DNA.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	33
Adolescents (12-17 years)	0
Adults (18-64 years)	31
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

30 children and their parent(s).

Inclusion criteria:

1. Subject is at least 4 years of age.
2. Subject weighs at least 15 kg.
3. Subject is capable of performing the taste assessment, according to the investigator's judgement.
4. The child and parent(s) are willing to participate in the taste assessment.
5. Signed informed consent

Pre-assignment

Screening details:

No tests have to be performed to decide whether the subject is allowed to participate in the taste assessment. The capability to perform the palatability testing is judged by the investigator. The investigator will also determine whether the in- and exclusion criteria are met.

Period 1

Period 1 title	treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The subject performing the taste assessment cannot be fully blinded for the different formulations, since the appearance of a solution and suspension is different. All formulations will be presented in similar plastic medication cups. The investigator is not blinded, because in case of spillage, solution can be replaced.

Arms

Are arms mutually exclusive?	No
Arm title	test

Arm description:

20 mg/ml valacyclovir solution

Arm type	Experimental
Investigational medicinal product name	valacyclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Children of 4-8 years will taste 4 ml of each solution and children of 8-12 years and the parent(s) will taste 8 ml of each solution.

Arm title	reference
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Arm description:

20 mg/ml valacyclovir solution from crushed tablets

Arm type	Active comparator
Investigational medicinal product name	valacyclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Crushed and suspended tablet. Children of 4-8 years will taste 4 ml of each solution and children of 8-12

years and the parent(s) will taste 8 ml of each solution.

Number of subjects in period 1	test	reference
Started	64	40
Completed	40	40
Not completed	24	0
Consent withdrawn by subject	24	-

Baseline characteristics

Reporting groups

Reporting group title	treatment
Reporting group description: -	

Reporting group values	treatment	Total	
Number of subjects	64	64	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	33	33	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	31	31	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	40	40	
Male	24	24	

Subject analysis sets

Subject analysis set title	evaluable
Subject analysis set type	Per protocol
Subject analysis set description: evaluable child parent pairs	

Reporting group values	evaluable		
Number of subjects	40		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	20		
Adolescents (12-17 years)	0		
Adults (18-64 years)	20		
From 65-84 years	0		
85 years and over	0		

Gender categorical			
Units: Subjects			
Female	17		
Male	23		

End points

End points reporting groups

Reporting group title	test
Reporting group description: 20 mg/ml valacyclovir solution	
Reporting group title	reference
Reporting group description: 20 mg/ml valacyclovir solution from crushed tablets	
Subject analysis set title	evaluable
Subject analysis set type	Per protocol
Subject analysis set description: evaluable child parent pairs	

Primary: VAS score

End point title	VAS score ^[1]
End point description:	
End point type	Primary
End point timeframe: entire study, 1 day	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: only descriptive difference was reported, no formal test was done

End point values	test	reference		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40 ^[2]	40 ^[3]		
Units: mm				
arithmetic mean (confidence interval 95%)	26 (18 to 34)	24 (16 to 32)		

Notes:

[2] - children only

[3] - results of children only

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

entire study

Assessment type	Non-systematic
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Dictionary used

Dictionary name	none
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Dictionary version	1
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Reporting groups

Reporting group title	ae group
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Reporting group description: -

Serious adverse events	ae group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 64 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	ae group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 64 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: only very limited exposure to medication, no adverse events were reported

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 March 2013	<ol style="list-style-type: none">1. Change from single centre to multicentre study.2. Include two additional investigators to the list.3. Adding description of a specific group of children that can be included.4. Further clarify the exclusion criteria.5. Minor changes
12 December 2014	<ol style="list-style-type: none">1. Restart of the trial2. Addition of second phase of the trial <p>In the first phase of the trial, children and one of their parents tested three newly developed, saccharose based, formulations. Twelve children and one of their parents were included into the first phase of this trial, of which 8 had evaluable data. In the second phase of the trial, two different valacyclovir liquids will be tested: one newly developed, glycerol based formulation (solution, concentration 20 mg/mL) and a reference formulation (suspension, concentration 25 mg/mL).</p> <ol style="list-style-type: none">3. Change of primary objective in the second phase of the trial4. Changes in trial set-up5. Addition of secondary objective

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 October 2014	problems with stability of oral formulation	08 May 2015

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Only the VAS results for the children were reported, this template does not allow for two different groups.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28800385>