Clinical trial results:
Pharmacokinetics of a new paediatric formulation of valacyclovir used for prophylaxis and treatment of VZV and HSV infections in children, phase II (VALID II)

Summary

EudraCT number	2017-001451-30
Trial protocol	NL
Global end of trial date	12 May 2021

Results information

Result version number	v1 (current)
This version publication date	24 August 2024
First version publication date	24 August 2024

Trial information

Trial identification

Sponsor protocol code	UMCN-AKF12.07

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Radboud university medical center
Sponsor organisation address	Geert grooteplein Zuid 10, Nijmegen, Netherlands, 6525GA
Public contact	David Burger, Radboud university medical center, 31 243616405, david.burger@radboudumc.nl
Scientific contact	David Burger, Radboud university medical center, 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	06 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 May 2021
Global end of trial reached?	Yes
Global end of trial date	12 May 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the pharmacokinetics of valacyclovir oral so-lution in children who have received stem cell transplanta-tion (plasma) by determining the AUC0-12, time above Ccrit, Cmax and Tmax of acyclovir and comparing them with Ccrit (0.18 mg/L)and AUCcrit24 (4.3 mg*h/L).

Protection of trial subjects:

Subject’s parents have signed the Informed Consent Form prior to screening evaluations.
Subject is willing to participate after study procedures are explained in comprehensible language for the child.
A subject may decide to withdraw from the trial at any time. If so, the investigator must be informed immediately. The investigator may decide to terminate participation of a sub-ject if it is difficult to obtain blood samples, if there has been a violation of the protocol, if a serious adverse event occurs, or if it is in the best interest of the subject that he/she is withdrawn. If there is a medical reason for withdrawal, the subject will remain under the care of the investigator until the problem prompting withdrawal has been resolved or until referral to his general practitioner. On the basis of the occurrence of adverse events, the investigator may decide to discontinue the trial.
Data are collected pseudonymised.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 September 2019
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: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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	0

months)	
Children (2-11 years)	7
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Seven patients (4 boys, 3 girls) were included in the Princes Maxima Centre in Utrecht, The Netherlands. Five patients in the range of 1-6 years old and two patients in the range of 7-12 years old. All seven patients received a stemcell transplantation and therefore used prophylactic valacyclovir.

Pre-assignment

Screening details:

Subjects must meet the following criteria to be eligible for participation in this trial:
1. Subject is in the age of 1-12 years.
2. Subject has an indication for (val)acyclovir prophylaxis and are planned to receive valacyclovir oral solution.
3. Subject is managed with a central venous catheter (CVC/Port-a-Cath).

Period 1

Period 1 title	screening (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Arm title	valacyclovir

Arm description:

Subjects will receive the following medication (according to standard of care):
- Valacyclovir oral solution 20 mg/mL FNA (national standard formulation)

Patients < 40 kg will receive 10 mg/kg and patients > 40 kg will receive 500 mg (25 mL) valacylcovir as oral solution at approximately 8 AM.

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

Dosage and administration details:

Valacyclovir oral solution 20 mg/mL FNA (national standard formulation)

Patients < 40 kg will receive 10 mg/kg and patients > 40 kg will receive 500 mg (25 mL) valacylcovir as oral solution at approximately 8 AM.

Number of subjects in period 1	valacyclovir
Started	7
Completed	7

Baseline characteristics

Reporting groups	
Reporting group title	screening

Reporting group description: -

Reporting group values	screening	Total	
Number of subjects	7	7	
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)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	5		
full range (min-max)	2 to 8	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	4	4	

End points

End points reporting groups

Reporting group title	valacyclovir

Reporting group description:

Subjects will receive the following medication (according to standard of care):
- Valacyclovir oral solution 20 mg/mL FNA (national standard formulation)

Patients < 40 kg will receive 10 mg/kg and patients > 40 kg will receive 500 mg (25 mL) valacylcovir as oral solution at approximately 8 AM.

Primary: AUC

End point title	AUC[1]

End point description:

End point type	Primary

End point timeframe:

over 12 hours

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 descirptive satistics were done

End point values	valacyclovir			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: mg*h/L				
median (inter-quartile range (Q1-Q3))	11.9 (10 to 12)			

Statistical analyses

No statistical analyses for this end point

Secondary: % above Crit AUC (4.3)

End point title	% above Crit AUC (4.3)

End point description:

End point type	Secondary

End point timeframe:

24 hours

End point values	valacyclovir			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: %	100			

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

Dictionary used	
Dictionary name	none
Dictionary version	0

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

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: No adverse events were reported

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2015	1 Including children with a Hb between 5 and 6 mmol/L The children who already use valacyclovir oral solution appeared to have in some cases a Hb below 6 mmol/L. Since these children belong to the population who will use this oral solu-tion, inclusion of these children will be valuable. The amount of blood that will be taken is al-ready low, maximum om 25 ml in total. The percentage blood taken, will never be more than 5%. According to the WHO Bulletin on blood sample volume in child health research, the effect on Hb is minimal if the total amount of blood loss is below 5%. 2 Including children between one and two years old The oral solution of valacyclovir is already used in children between one and two years old. When considering the pharmacokinetics of valacyclovir in children in between this age, there is barely any difference between children between one and two years old and children be-tween two and five years old. Therefore it will be valuable to include these children in this study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

this study did not fully recruit

Notes: