Clinical trial results:
A multicenter, open-label study to evaluate preventive efficacy for herpes simplex virus infection and safety of 256U87 (valaciclovir hydrochloride) in adult and pediatric hematopoietic stem cell transplantation patients

Summary

EudraCT number	2015-004869-88
Trial protocol	Outside EU/EEA
Global end of trial date	24 May 2013

Results information

Result version number	v1 (current)
This version publication date	21 January 2017
First version publication date	21 January 2017

Trial information

Trial identification

Sponsor protocol code	116100

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 July 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 May 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To be decided

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 May 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	Japan: 40
Worldwide total number of subjects	40
EEA total number of subjects	0

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)	2
Children (2-11 years)	13
Adolescents (12-17 years)	5
Adults (18-64 years)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 40 subjects (21 adults, 19 pediatrics) who gave consent to participate in the study and were confirmed to be eligible for the study during the screening period were enrolled in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Adult participants: Valaciclovir hydrochloride 500 mg tablet

Arm description:

Adult participants (between 16 and 65 years of age) received a valaciclovir hydrochloride (VACV) tablet containing 500 milligrams (mg) of valaciclovir orally twice daily for 43 days, from 7 days before hematopoietic stem cell transplantation (HSCT) to 35 days after HSCT. A VACV tablet was administered once daily on Day -7 (7 days before HSCT) and on Day 35 (35 days after the final administration of HSCT).

Arm type	Experimental
Investigational medicinal product name	256U87 (VACV) tablets (containing 500 mg of valaciclovir)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Given orally twice daily.

Arm title	Pediatric participants: VACV 500 mg granules/tablets

Arm description:

Pediatric participants (between 1 and <16 years of age) received VACV granules orally at a dose of 25 mg/kilogram (kg) body weight twice daily for 43 days, from 7 days before HSCT to 35 days after HSCT. The maximum dose per treatment was limited to 500 mg. Participants weighing 40 kg or more could have been given a VACV tablet (containing 500 mg of valaciclovir) orally twice daily. VACV granules were administered once daily on Day -7 (7 days before HSCT) and on Day 35 (35 days after the final administration of HSCT).

Arm type	Experimental
Investigational medicinal product name	256U87 (VACV) tablets (containing 500 mg of valaciclovir)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Given orally twice daily.

Investigational medicinal product name	256U87 (VACV) granules (500 mg of valaciclovir)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:
Given orally at a dose of 25 mg/kg body weight twice daily

Number of subjects in period 1	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets
Started	21	19
Completed	16	16
Not completed	5	3
Consent withdrawn by subject	1	1
Physician decision	1	1
Adverse event, non-fatal	3	1

Baseline characteristics

Reporting groups

Reporting group title	Adult participants: Valaciclovir hydrochloride 500 mg tablet

Reporting group description:

Adult participants (between 16 and 65 years of age) received a valaciclovir hydrochloride (VACV) tablet containing 500 milligrams (mg) of valaciclovir orally twice daily for 43 days, from 7 days before hematopoietic stem cell transplantation (HSCT) to 35 days after HSCT. A VACV tablet was administered once daily on Day -7 (7 days before HSCT) and on Day 35 (35 days after the final administration of HSCT).

Reporting group title	Pediatric participants: VACV 500 mg granules/tablets

Reporting group description:

Pediatric participants (between 1 and <16 years of age) received VACV granules orally at a dose of 25 mg/kilogram (kg) body weight twice daily for 43 days, from 7 days before HSCT to 35 days after HSCT. The maximum dose per treatment was limited to 500 mg. Participants weighing 40 kg or more could have been given a VACV tablet (containing 500 mg of valaciclovir) orally twice daily. VACV granules were administered once daily on Day -7 (7 days before HSCT) and on Day 35 (35 days after the final administration of HSCT).

Reporting group values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets	Total
Number of subjects	21	19	40
Age categorical Units: Subjects			
Age continuous			
Age continuous description			
Units: years arithmetic mean standard deviation	 48.6 ± 14.32	 7.5 ± 4.69	 -
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	9	7	16
Male	12	12	24
Race/Ethnicity, Customized Units: Subjects			
Asian - Japanese Heritage	21	19	40

End points

End points reporting groups

Reporting group title	Adult participants: Valaciclovir hydrochloride 500 mg tablet

Reporting group description:

Adult participants (between 16 and 65 years of age) received a valaciclovir hydrochloride (VACV) tablet containing 500 milligrams (mg) of valaciclovir orally twice daily for 43 days, from 7 days before hematopoietic stem cell transplantation (HSCT) to 35 days after HSCT. A VACV tablet was administered once daily on Day -7 (7 days before HSCT) and on Day 35 (35 days after the final administration of HSCT).

Reporting group title	Pediatric participants: VACV 500 mg granules/tablets

Reporting group description:

Pediatric participants (between 1 and <16 years of age) received VACV granules orally at a dose of 25 mg/kilogram (kg) body weight twice daily for 43 days, from 7 days before HSCT to 35 days after HSCT. The maximum dose per treatment was limited to 500 mg. Participants weighing 40 kg or more could have been given a VACV tablet (containing 500 mg of valaciclovir) orally twice daily. VACV granules were administered once daily on Day -7 (7 days before HSCT) and on Day 35 (35 days after the final administration of HSCT).

Primary: Number of participants with a herpes simplex virus (HSV) infection

End point title	Number of participants with a herpes simplex virus (HSV) infection[1]

End point description:

Viral isolation/identification was conducted if the investigator (or subinvestigator) suspected HSV infection according to the relevant clinical symptoms (oral mucositis, skin infection, genital herpes, and pneumonia). If the result of viral isolation/identification was positive, the participant concerned was defined as a case of HSV infection. For reference, a virus deoxyribonucleic acid (DNA) identification (PCR) was simultaneously performed. Full Analysis Set (FAS): All participants who were given VACV more than once and who could provide data evaluable with respect to the occurrence of HSV infection. Percentage of participants with a herpes simplex virus infection were zero in the adult participant group and pediatric participant group, with 2-sided 95% confidence interval 0.00-16.11 and 0.00-17.65 respectively.

End point type	Primary

End point timeframe:

From Day -7 (7 days before HSCT) to Day 35 (35 days after HSCT)

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: There are no statistical data to report

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[2]	19[3]		
Units: Participants	0	0		

Notes:

[2] - Full Analysis Set

[3] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) or any serious adverse event (SAE)

End point title	Number of participants with any adverse event (AE) or any serious adverse event (SAE)

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in this definition, or is an event of possible drug-induced liver injury. Refer to the general AE/SAE module for a list of AEs and SAEs.

End point type	Secondary

End point timeframe:

From Day -7 (7 days before HSCT) to Day 35 (35 days after HSCT)

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[4]	19		
Units: Participants				
Any AE	13	11		
Any SAE	2	1		

Notes:

[4] - Safety Population: All participants who received VACV more than once .

Statistical analyses

No statistical analyses for this end point

Secondary: Mean alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine phosphokinase (CPK), gamma glutamyl transferase (GGT), and lactate dehydrogenase (LD) values at Screening, Day 14, and Day 35

End point title	Mean alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine phosphokinase (CPK), gamma glutamyl transferase (GGT), and lactate dehydrogenase (LD) values at Screening, Day 14, and Day 35

End point description:

Blood samples were collected for the measurement of ALP, ALT, AST, CPK, GGT, and LD at Screening, Day 14, and Day 35. Safety Population. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles). Different participants may have been analyzed for different parameters/a t different time points, so the overall number of participants analyzed reflects everyone in the Safety Population.

End point type	Secondary

End point timeframe:

Screening (SCR), Day 14, and Day 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[5]	19		
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
ALP, SCR, n=21, 19	247.1 (± 105.09)	598.8 (± 132.37)		
ALP, Day 14, n=18, 17	358.7 (± 206.04)	456.7 (± 206.98)		
ALP, Day 35, n=16, 16	314.9 (± 111.65)	519.9 (± 183.83)		
ALT, SCR, n=21, 19	23.7 (± 10.98)	20.7 (± 12.55)		
ALT, Day 14, n=18, 17	53.2 (± 63.38)	62.1 (± 84.64)		
ALT, Day 35, n=16, 16	58.9 (± 36.92)	62 (± 76.59)		
AST, SCR, n=21, 19	23.2 (± 9.01)	27.1 (± 9.62)		
AST, Day 14, n=18, 17	39.8 (± 39.82)	35 (± 34.88)		
AST, Day 35, n=16, 16	45.1 (± 19.12)	54 (± 48.96)		
CPK, SCR, n=21, 19	65.1 (± 70.37)	72 (± 40.63)		
CPK, Day 14, n=18, 17	20.5 (± 9.88)	27.4 (± 28.85)		
CPK, Day 35, n=16, 16	42.1 (± 26.74)	38.4 (± 26.48)		
GGT, SCR, n=21, 19	47.2 (± 34.94)	24.8 (± 24.74)		
GGT, Day 14, n=18, 17	118.4 (± 113.63)	27.5 (± 10.61)		
GGT, Day 35, n=16, 16	90.3 (± 70.96)	50.7 (± 43.34)		
LD, SCR, n=21, 19	251.8 (± 179.06)	213.3 (± 77.51)		
LD, Day 14, n=18, 17	215.4 (± 68.15)	210.6 (± 103.09)		
LD, Day 35, n=16, 16	256.7 (± 65.92)	255.9 (± 92.84)		

Notes:

[5] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean direct bilirubin, total bilirubin, creatinine, and uric acid values at Screening, Day 14, and Day 35

End point title	Mean direct bilirubin, total bilirubin, creatinine, and uric acid values at Screening, Day 14, and Day 35

End point description:

Blood samples were collected for the measurement of direct bilirubin, total bilirubin, creatinine, and uric acid at Screening, Day 14, and Day 35.

End point type	Secondary

End point timeframe:

Screening (SCR), Day 14, and Day 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[6]	19		
Units: Micromoles per liter (µmol/L)				
arithmetic mean (standard deviation)				
Direct bilirubin, SCR, n=21, 19	2.931 (± 1.8843)	2.97 (± 1.8769)		
Direct bilirubin, Day 14, n=18, 17	7.41 (± 11.5234)	3.923 (± 3.0688)		
Direct bilirubin, Day 35, n=16, 16	2.351 (± 0.855)	2.565 (± 1.2488)		
Total bilirubin, SCR, n=21, 19	8.224 (± 5.4242)	8.19 (± 3.9728)		
Total bilirubin, Day 14, n=18, 17	12.54 (± 14.8264)	9.858 (± 8.6251)		
Total bilirubin, Day 35, n=16, 16	6.306 (± 1.9466)	6.733 (± 3.1512)		
Creatinine, SCR, n=21, 19	62.6798 (± 19.71123)	30.1025 (± 10.12416)		
Creatinine, Day 14, n=18, 17	46.7047 (± 16.31214)	25.532 (± 12.84039)		
Creatinine, Day 35, n=16, 16	58.786 (± 18.8301)	33.371 (± 19.49749)		
Uric acid, SCR, n=21, 19	276.1571 (± 80.38764)	259.5206 (± 63.88405)		
Uric acid, Day 14, n=18, 17	133.1691 (± 62.35442)	137.5038 (± 56.34464)		
Uric acid, Day 35, n=16, 16	255.0205 (± 96.37167)	238.6635 (± 101.474)		

Notes:

[6] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean cholesterol, chloride, glucose, potassium, sodium, triglyceride, and urea/blood urea nitrogen (BUN) values at Screening, Day 14, and Day 35

End point title	Mean cholesterol, chloride, glucose, potassium, sodium, triglyceride, and urea/blood urea nitrogen (BUN) values at Screening, Day 14, and Day 35

End point description:

Blood samples were collected for the measurement of cholesterol, chloride, glucose, potassium, sodium, triglycerides, and urea/BUN at Screening, Day 14, and Day 35.

End point type	Secondary

End point timeframe:

Screening (SCR), Day 14, and Day 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[7]	19		
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Cholesterol, SCR, n=21, 19	4.8149 (± 1.33518)	4.1703 (± 0.70625)		
Cholesterol, Day 14, n=18, 17	4.0255 (± 1.06483)	3.5504 (± 1.2561)		
Cholesterol, Day 35, n=16, 16	5.5324 (± 1.45536)	4.1279 (± 1.01828)		
Chloride, SCR, n=21, 19	105.2 (± 2.83)	103.3 (± 2.21)		
Chloride, Day 14, n=18, 17	104.4 (± 4.06)	105 (± 2.06)		
Chloride, Day 35, n=16, 16	106 (± 2.99)	104 (± 2.31)		
Glucose, SCR, n=21, 19	5.8127 (± 1.38621)	6.0214 (± 1.83355)		
Glucose, Day 14, n=18, 17	7.2656 (± 2.31056)	6.0996 (± 2.13721)		
Glucose, Day 35, n=16, 16	6.4808 (± 1.3516)	5.78 (± 1.41869)		
Potassium, SCR, n=21, 19	4.08 (± 0.402)	4.01 (± 0.283)		
Potassium, Day 14, n=18, 17	3.93 (± 0.457)	4.34 (± 0.449)		
Potassium, Day 35, n=16, 16	4.31 (± 0.521)	4.09 (± 0.359)		
Sodium, SCR, n=21, 19	142 (± 1.92)	140.2 (± 1.92)		
Sodium, Day 14, n=18, 17	140.3 (± 4.16)	139.2 (± 1.55)		
Sodium, Day 35, n=16, 16	141.8 (± 2.29)	139.3 (± 1.39)		
Triglycerides, SCR, n=21, 19	2.076 (± 1.30955)	1.3489 (± 0.75044)		
Triglycerides, Day 14, n=18, 17	1.8789 (± 0.95581)	1.4185 (± 1.02762)		
Triglycerides, Day 35, n=16, 16	2.9486 (± 1.49324)	1.6646 (± 1.04585)		
Urea/BUN, SCR, n=21, 19	4.2721 (± 1.61486)	3.6903 (± 0.93331)		
Urea/BUN, Day 14, n=18, 17	4.8274 (± 3.76473)	3.1332 (± 1.35997)		
Urea/BUN, Day 35, n=16, 16	3.7619 (± 1.72437)	4.1657 (± 1.99412)		

Notes:

[7] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean albumin and total protein values at Screening, Day 14, and Day 35

End point title	Mean albumin and total protein values at Screening, Day 14, and Day 35

End point description:

Blood samples were collected for the measurement of albumin and total protein at Screening, Day 14, and Day 35.

End point type	Secondary

End point timeframe:

Screening (SCR), Day 14, and Day 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[8]	19		
Units: Grams per liter (G/L)				
arithmetic mean (standard deviation)				
Albumin, SCR, n=21, 19	41 (± 3.07)	41.5 (± 2.04)		
Albumin, Day 14, n=18, 17	34.6 (± 3.87)	39.1 (± 3.04)		
Albumin, Day 35, n=16, 16	40.8 (± 3.34)	40.9 (± 3.02)		
Total protein, SCR, n=21, 19	64.2 (± 5.83)	66.2 (± 5.34)		
Total protein, Day 14, n=18, 17	57.6 (± 5.76)	62.7 (± 5.08)		
Total protein, Day 35, n=16, 16	62.9 (± 4.75)	65.3 (± 5.84)		

Notes:

[8] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean basophil, eosinophil, lymphocyte, monocyte, and total neutrophil values at Screening, Day 14, and Day 35

End point title	Mean basophil, eosinophil, lymphocyte, monocyte, and total neutrophil values at Screening, Day 14, and Day 35

End point description:

Blood samples were collected for the measurement of basophils, eosinophils, lymphocytes, monocytes, and total neutrophils at Screening, Day 14, and Day 35.

End point type	Secondary

End point timeframe:

Screening (SCR), Day 14, and Day 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[9]	19		
Units: Percentage of cells in blood				
arithmetic mean (standard deviation)				

Basophils, SCR, n=21,19	1.05 (± 1.473)	0.49 (± 0.47)		
Basophils, Day 14, n=16, 16	0.69 (± 1.661)	0.14 (± 0.352)		
Basophils, Day 35, n=16, 15	1.09 (± 0.903)	0.59 (± 0.38)		
Eosinophils, SCR, n=21, 19	3.67 (± 4.754)	2.06 (± 1.974)		
Eosinophils, Day 14, n=16, 16	0.79 (± 2.77)	0.59 (± 1.517)		
Eosinophils, Day 35, n=16, 15	4.1 (± 2.672)	7.51 (± 10.357)		
Lymphocytes, SCR, n=21,19	32.72 (± 16.104)	38.94 (± 21.616)		
Lymphocytes, Day 14, n=16, 16	13.61 (± 8.897)	16.73 (± 17.909)		
Lymphocytes, Day 35, n=16, 15	37.08 (± 15.496)	30.85 (± 20.338)		
Monocytes, SCR, n=21,19	7.9 (± 3.337)	10.99 (± 7.565)		
Monocytes, Day 14, n=16, 16	15.32 (± 7.263)	17.33 (± 12.061)		
Monocytes, Day 35, n=16, 15	14.54 (± 6.609)	13.33 (± 7.021)		
Total neutrophils, SCR, n=21,19	54.46 (± 15.003)	47.52 (± 22.667)		
Total neutrophils, Day 14, n=16, 16	63.53 (± 18.117)	62.21 (± 23.273)		
Total neutrophils, Day 35, n=16, 15	42.76 (± 13.336)	47.63 (± 20.745)		

Notes:

[9] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean platelet count and white blood cell (WBC) count at Screening, Day 14, and Day 35

End point title	Mean platelet count and white blood cell (WBC) count at Screening, Day 14, and Day 35

End point description:

Blood samples were collected for the measurement of platelet count and WBC count at Screening, Day 14, and Day 35.

End point type	Secondary

End point timeframe:

Screening (SCR), Day 14, and Day 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[10]	19		
Units: giga (10^9) per liter (GI/L)				
arithmetic mean (standard deviation)				
Platelet count, SCR, n=21,19	190.2 (± 126.32)	167.7 (± 98.15)		

Platelet count, Day 14, n=18, 17	40.3 (± 20.73)	58.2 (± 37.41)		
Platelet count, Day 35, n=16, 16	139.4 (± 79.29)	119 (± 89.31)		
WBC count, SCR, n=21,19	4.01 (± 1.842)	3.03 (± 1.873)		
WBC count, Day 14, n=16, 12	3.46 (± 2.955)	2.23 (± 2.403)		
WBC count, Day 35, n=16, 14	5 (± 3.524)	3.71 (± 2.189)		

Notes:

[10] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean red blood cell count at Screening, Day 14, and Day 35

End point title	Mean red blood cell count at Screening, Day 14, and Day 35

End point description:

Blood samples were collected for the measurement of the red blood cell count at Screening, Day 14, and Day 35.

End point type	Secondary

End point timeframe:

Screening (SCR), Day 14, and Day 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[11]	19		
Units: tera (10^12) per liter (TI/L)				
arithmetic mean (standard deviation)				
SCR, n=21,19	3.165 (± 0.7583)	3.293 (± 0.6529)		
Day 14, n=18, 17	2.932 (± 0.3479)	2.908 (± 0.3854)		
Day 35, n=16, 16	3.297 (± 0.5021)	3.073 (± 0.4797)		

Notes:

[11] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean hemoglobin values at Screening, Day 14, and Day 35

End point title	Mean hemoglobin values at Screening, Day 14, and Day 35

End point description:

Blood samples were collected for the measurement of hemoglobin at Screening, Day 14, and Day 35.

End point type	Secondary

End point timeframe:

Screening (SCR), Day 14, and Day 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[12]	19[13]		
Units: Grams per liter (G/L)				
arithmetic mean (standard deviation)				
SCR, n=21,19	101.6 (± 24.84)	99.3 (± 17.94)		
Day 14, n=18, 17	91.6 (± 10.02)	85.1 (± 12.1)		
Day 35, n=16, 16	106.5 (± 16.36)	94.4 (± 15.23)		

Notes:

[12] - Safety Population.

[13] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated result for the indicated urinalysis parameters tested by dipstick at Screening, Day 14, and Day 35

End point title	Number of participants with the indicated result for the indicated urinalysis parameters tested by dipstick at Screening, Day 14, and Day 35

End point description:

Urinalysis parameters included: urine bilirubin (UB), urine occult blood (UOB), urine glucose (UG), urine ketones (UK), urine protein (UP), and urine urobilinogen (UUG). The dipstick is a strip used to detect the presence or absence of these parameters in the urine sample. The dipstick test gives results in a semi-quantitative manner, and results for urinalysis parameters can be read as negative (Neg), Trace, 1+, 2+, and 3+ (in order of increasing levels). Data are reported as the number of participants who had Neg, Trace, 1+, 2+, and 3+ levels at Screening, Day 14, and Day 35. If a category has not been reported for a specific parameter, then no participants were measured in that category.

End point type	Secondary

End point timeframe:

Screening (SCR), Day 14, and 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[14]	19[15]		
Units: Participants				
UB, Neg, SCR, n=21, 19	21	19		
UB, Neg, Day 14, n=18, 17	18	17		

UB, Neg, Day 35, n=16, 16	16	16		
UOB, Neg, SCR, n=21, 19	19	19		
UOB, 2+, SCR, n=21, 19	2	0		
UOB, Neg, Day 14, n=18, 17	14	14		
UOB, Trace, Day 14, n=18, 17	2	2		
UOB, 1+, Day 14, n=18, 17	2	0		
UOB, 3+, Day 14, n=18, 17	0	1		
UOB, Neg, Day 35, n=16, 16	12	16		
UOB, Trace, Day 35, n=16, 16	1	0		
UOB, 1+, Day 35, n=16, 16	2	0		
UOB, 3+, Day 35, n=16, 16	1	0		
UG, Neg, SCR, n=21, 19	19	19		
UG, Trace, SCR, n=21, 19	2	0		
UG, Neg, Day 14, n=18, 17	14	17		
UG, Trace, Day 14, n=18, 17	1	0		
UG, 1+, Day 14, n=18, 17	1	0		
UG, 2+, Day 14, n=18, 17	1	0		
UG, 3+, Day 14, n=18, 17	1	0		
UG, Neg, Day 35, n=16, 16	15	16		
UG, Trace, Day 35, n=16, 16	1	0		
UK, Neg, SCR, n=21, 19	21	19		
UK, Neg, Day 14, n=18, 17	17	17		
UK, 1+, Day 14, n=18, 17	1	0		
UK, Neg, Day 35, n=16, 16	16	15		
UK, 1+, Day 35, n=16, 16	0	1		
UP, Neg, SCR, n=21, 19	19	14		
UP, Trace, SCR, n=21, 19	0	4		
UP, 1+, SCR, n=21, 19	0	1		
UP, 2+, SCR, n=21, 19	2	0		
UP, Neg, Day 14, n=18, 17	9	12		
UP, Trace, Day 14, n=18, 17	5	4		
UP, 1+, Day 14, n=18, 17	2	0		
UP, 2+, Day 14, n=18, 17	2	1		
UP, Neg, Day 35, n=16, 16	13	13		
UP, Trace, Day 35, n=16, 16	2	1		
UP, 1+, Day 35, n=16, 16	1	2		
UUG, Trace, SCR, n=21, 19	19	19		
UUG, 2+, SCR, n=21, 19	2	0		
UUG, Trace, Day 14, n=18, 17	17	15		
UUG, 1+, Day 14, n=18, 17	1	0		
UUG, 2+, Day 14, n=18, 17	0	1		
UUG, 3+, Day 14, n=18, 17	0	1		
UUG, Trace, Day 35, n=16, 16	16	15		
UUG, 3+, Day 35, n=16, 16	0	1		

Notes:

[14] - Safety Population

[15] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean urine specific gravity values at Screening, Day 14, and Day 35

End point title	Mean urine specific gravity values at Screening, Day 14, and Day 35

End point description:

Safety Population. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the Safety Population.

End point type	Secondary

End point timeframe:

Screening (SCR), Day 14, and Day 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[16]	19		
Units: ratio				
arithmetic mean (standard deviation)				
SCR, n=21, 19	1.0146 (± 0.00705)	1.0188 (± 0.00912)		
Day 14, n=18, 17	1.0158 (± 0.00628)	1.0155 (± 0.00685)		
Day 35, n=16, 16	1.0137 (± 0.00572)	1.0153 (± 0.00642)		

Notes:

[16] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in systolic blood pressure and diastolic blood pressure at Days 0, 7, 14, 21, and 35

End point title	Change from Baseline in systolic blood pressure and diastolic blood pressure at Days 0, 7, 14, 21, and 35

End point description:

Blood pressure measurement included systolic blood pressure (SBP) and diastolic blood pressure (DBP). Change from Baseline was calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline; Days 0, 7, 14, 21, and 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[17]	19		
Units: Millimeters of mercury				
arithmetic mean (standard deviation)				
SBP, Day 0, n=21, 19	-1.8 (± 18.23)	-4.7 (± 16.85)		
SBP, Day 7, n=19, 17	0.9 (± 18.88)	-6.1 (± 16.34)		
SBP, Day 14, n=18, 17	4.3 (± 20.68)	-7.6 (± 18.61)		
SBP, Day 21, n=17, 17	-1.4 (± 14.98)	-7 (± 13.88)		
SBP, Day 35, n=16, 16	2.8 (± 20.14)	-4.5 (± 15.08)		
DBP, Day 0, n=21, 19	-2.7 (± 16.04)	-1.8 (± 13.63)		
DBP, Day 7, n=19, 17	1.6 (± 16.37)	0.3 (± 13.87)		
DBP, Day 14, n=18, 17	3.4 (± 18.29)	-5.9 (± 14.69)		
DBP, Day 21, n=17, 17	1.5 (± 11.41)	-1.2 (± 11.91)		
DBP, Day 35, n=16, 16	4.7 (± 14.74)	-1.1 (± 11.2)		

Notes:

[17] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in heart rate at Days 0, 7, 14, 21, and 35

End point title	Change from Baseline in heart rate at Days 0, 7, 14, 21, and 35

End point description:

Heart rate is defined as the number of heartbeats per unit of time. Change from Baseline was calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline; Days 0, 7, 14, 21, and 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[18]	19		
Units: Beats per minute				
arithmetic mean (standard deviation)				
Day 0, n=21, 19	1.1 (± 13.66)	-1 (± 17.15)		
Day 7, n=19, 17	13.3 (± 14.41)	3.8 (± 20.42)		
Day 14, n=18, 17	12.5 (± 14.7)	3.6 (± 25.47)		
Day 21, n=17, 17	16.4 (± 14.54)	1.8 (± 21.14)		
Day 35, n=16, 16	19.2 (± 18.99)	3.6 (± 23.6)		

Notes:

[18] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated electrocardiogram (ECG) findings at Screening and Day 35

End point title	Number of participants with the indicated electrocardiogram (ECG) findings at Screening and Day 35

End point description:

The number of participants with normal, abnormal - clinically significant (CS), and abnormal - not clinically significant (NCS) ECG findings, as well as the number of participants with no results (NR), at Screening and Day 35 are presented. Findings were determined to be normal, abnormal CS, and NCS by the investigator.

End point type	Secondary

End point timeframe:

Screening (SCR) and Day 35

End point values	Adult participants: Valaciclovir hydrochloride 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[19]	19		
Units: Participants				
SCR, Normal, n=21, 19	16	19		
SCR, NCS, n=21, 19	5	0		
SCR, CS, n=21, 19	0	0		
SCR, NR, n=21, 19	0	0		
Day 35, Normal, n=16, 16	15	13		
Day 35, NCS, n=16, 16	1	2		
Day 35, CS, n=16, 16	0	0		
Day 35, NR, n=16, 16	0	1		

Notes:

[19] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study medication until the end of the treatment (up to Day 43).

Adverse event reporting additional description:

SAEs and non-serious AEs are reported for members of the Safety Population, comprised of all participants who received VACV more than once.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Adult participants: VACV 500 mg tablet

Reporting group description:

Adult participants (between 16 and 65 years of age) received a VACV tablet containing 500 mg of valaciclovir orally twice daily for 43 days, from 7 days before HSCT to 35 days after HSCT. A VACV tablet was administered once daily on Day -7 (7 days before HSCT) and on Day 35 (35 days after the final administration of HSCT).

Reporting group title	Pediatric participants: VACV 500 mg granules/tablets

Reporting group description:

Pediatric participants (between 1 and <16 years of age) received VACV granules orally at a dose of 25 mg/kg body weight twice daily for 43 days, from 7 days before HSCT to 35 days after HSCT. The maximum dose per treatment was limited to 500 mg. Participants weighing 40 kg or more could have been given a VACV tablet (containing 500 mg of valaciclovir) orally twice daily. VACV granules were administered once daily on Day -7 (7 days before HSCT) and on Day 35 (35 days after the final administration of HSCT).

Serious adverse events	Adult participants: VACV 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Hepatobiliary disorders			
Liver Injury			
subjects affected / exposed	0 / 21 (0.00%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Lung disorder			

subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Toxic skin eruption			
subjects affected / exposed	1 / 21 (4.76%)	0 / 19 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Adult participants: VACV 500 mg tablet	Pediatric participants: VACV 500 mg granules/tablets	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 21 (47.62%)	8 / 19 (42.11%)	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 21 (4.76%)	4 / 19 (21.05%)	
occurrences (all)	1	6	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 21 (4.76%)	4 / 19 (21.05%)	
occurrences (all)	1	5	
Amylase increased			
subjects affected / exposed	0 / 21 (0.00%)	3 / 19 (15.79%)	
occurrences (all)	0	4	
C-reactive protein increased			
subjects affected / exposed	0 / 21 (0.00%)	3 / 19 (15.79%)	
occurrences (all)	0	3	
Blood bilirubin increased			
subjects affected / exposed	2 / 21 (9.52%)	1 / 19 (5.26%)	
occurrences (all)	2	1	
Blood urine present			
subjects affected / exposed	0 / 21 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Occult blood			

subjects affected / exposed	0 / 21 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Hepatic enzyme increased			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 21 (9.52%)	2 / 19 (10.53%)	
occurrences (all)	2	3	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	3 / 21 (14.29%)	4 / 19 (21.05%)	
occurrences (all)	3	4	
Anaemia			
subjects affected / exposed	2 / 21 (9.52%)	3 / 19 (15.79%)	
occurrences (all)	3	3	
Febrile neutropenia			
subjects affected / exposed	6 / 21 (28.57%)	0 / 19 (0.00%)	
occurrences (all)	6	0	
Leukopenia			
subjects affected / exposed	0 / 21 (0.00%)	4 / 19 (21.05%)	
occurrences (all)	0	4	
Neutropenia			
subjects affected / exposed	0 / 21 (0.00%)	3 / 19 (15.79%)	
occurrences (all)	0	3	
Lymphopenia			
subjects affected / exposed	0 / 21 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 21 (23.81%)	2 / 19 (10.53%)	
occurrences (all)	5	2	
Pyrexia			
subjects affected / exposed	2 / 21 (9.52%)	3 / 19 (15.79%)	
occurrences (all)	2	4	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	8 / 21 (38.10%)	4 / 19 (21.05%)	
occurrences (all)	9	6	
Vomiting			
subjects affected / exposed	3 / 21 (14.29%)	5 / 19 (26.32%)	
occurrences (all)	3	6	
Stomatitis			
subjects affected / exposed	4 / 21 (19.05%)	2 / 19 (10.53%)	
occurrences (all)	4	2	
Nausea			
subjects affected / exposed	5 / 21 (23.81%)	3 / 19 (15.79%)	
occurrences (all)	5	3	
Abdominal pain			
subjects affected / exposed	2 / 21 (9.52%)	3 / 19 (15.79%)	
occurrences (all)	2	3	
Constipation			
subjects affected / exposed	2 / 21 (9.52%)	3 / 19 (15.79%)	
occurrences (all)	2	3	
Abdominal pain upper			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Proctalgia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Tongue coated			
subjects affected / exposed	0 / 21 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 21 (9.52%)	2 / 19 (10.53%)	
occurrences (all)	3	2	
Oropharyngeal pain			
subjects affected / exposed	4 / 21 (19.05%)	1 / 19 (5.26%)	
occurrences (all)	4	1	
Cough			

subjects affected / exposed	0 / 21 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 21 (14.29%)	1 / 19 (5.26%)	
occurrences (all)	3	1	
Alopecia			
subjects affected / exposed	0 / 21 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Urticaria			
subjects affected / exposed	1 / 21 (4.76%)	2 / 19 (10.53%)	
occurrences (all)	1	2	
Pruritus			
subjects affected / exposed	0 / 21 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 21 (19.05%)	0 / 19 (0.00%)	
occurrences (all)	4	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 21 (14.29%)	0 / 19 (0.00%)	
occurrences (all)	4	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 21 (4.76%)	2 / 19 (10.53%)	
occurrences (all)	1	2	
Bacteraemia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Sepsis			

subjects affected / exposed	1 / 21 (4.76%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	7 / 21 (33.33%)	2 / 19 (10.53%)	
occurrences (all)	7	2	
Fluid retention			
subjects affected / exposed	3 / 21 (14.29%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
Hyponatraemia			
subjects affected / exposed	0 / 21 (0.00%)	3 / 19 (15.79%)	
occurrences (all)	0	3	
Hyperglycaemia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Hypomagnesaemia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 19 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported