



## 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:

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**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:

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**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:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |           |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Japan: 40 |
| Worldwide total number of subjects   | 40        |
| EEA total number of subjects         | 0         |

Notes:

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**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                                                          |
| <b>Arm title</b>             | 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.

|                  |                                                      |
|------------------|------------------------------------------------------|
| <b>Arm title</b> | 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                                        |

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**Dosage and administration details:**

Given orally at a dose of 25 mg/kg body weight twice daily

| <b>Number of subjects in period 1</b> | Adult participants:<br>Valaciclovir<br>hydrochloride 500<br>mg tablet | Pediatric<br>participants: VACV<br>500 mg<br>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:<br>Valaciclovir<br>hydrochloride 500<br>mg tablet | Pediatric<br>participants: VACV<br>500 mg<br>granules/tablets | Total |
|-----------------------------------------------|-----------------------------------------------------------------------|---------------------------------------------------------------|-------|
| Number of subjects                            | 21                                                                    | 19                                                            | 40    |
| Age categorical<br>Units: Subjects            |                                                                       |                                                               |       |
| Age continuous                                |                                                                       |                                                               |       |
| Age continuous description                    |                                                                       |                                                               |       |
| Units: years                                  |                                                                       |                                                               |       |
| arithmetic mean                               | 48.6                                                                  | 7.5                                                           |       |
| standard deviation                            | ± 14.32                                                               | ± 4.69                                                        | -     |
| Gender categorical                            |                                                                       |                                                               |       |
| Gender categorical description                |                                                                       |                                                               |       |
| Units: Subjects                               |                                                                       |                                                               |       |
| Female                                        | 9                                                                     | 7                                                             | 16    |
| Male                                          | 12                                                                    | 12                                                            | 24    |
| Race/Ethnicity, Customized<br>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 <sup>[1]</sup> |
| 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 <sup>[2]</sup>                                            | 19 <sup>[3]</sup>                                    |  |  |
| Units: Participants         | 0                                                            | 0                                                    |  |  |

Notes:

[2] - Full Analysis Set

[3] - Full Analysis Set

### Statistical analyses

**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:<br>Valaciclovir hydrochloride 500 mg tablets | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|-----------------------------|------------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type          | Reporting group                                                  | Reporting group                                         |  |  |
| Number of subjects analysed | 21 <sup>[4]</sup>                                                | 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:<br>Valaciclovir hydrochloride<br>500 mg tablet | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|---------------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type                          | Reporting group                                                    | Reporting group                                         |  |  |
| Number of subjects analysed                 | 21 <sup>[5]</sup>                                                  | 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:<br>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:<br>Valaciclovir hydrochloride<br>500 mg tablet | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|--------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type                   | Reporting group                                                    | Reporting group                                         |  |  |
| Number of subjects analysed          | 21 <sup>[6]</sup>                                                  | 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

| <b>End point values</b>              | Adult participants:<br>Valaciclovir hydrochloride<br>500 mg tablet | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|--------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type                   | Reporting group                                                    | Reporting group                                         |  |  |
| Number of subjects analysed          | 21 <sup>[7]</sup>                                                  | 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:<br>Valaciclovir hydrochloride 500 mg tablet | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|--------------------------------------|-----------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type                   | Reporting group                                                 | Reporting group                                         |  |  |
| Number of subjects analysed          | 21 <sup>[8]</sup>                                               | 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:<br>Valaciclovir hydrochloride 500 mg tablet | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|--------------------------------------|-----------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type                   | Reporting group                                                 | Reporting group                                         |  |  |
| Number of subjects analysed          | 21 <sup>[9]</sup>                                               | 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 tablets | Pediatric participants: VACV 500 mg granules/tablets |  |  |
|-------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------|--|--|
| Subject group type                              | Reporting group                                               | Reporting group                                      |  |  |
| Number of subjects analysed                     | 21 <sup>[10]</sup>                                            | 19                                                   |  |  |
| Units: giga (10 <sup>9</sup> ) 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:<br>Valaciclovir hydrochloride<br>500 mg tablet | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|--------------------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type                               | Reporting group                                                    | Reporting group                                         |  |  |
| Number of subjects analysed                      | 21 <sup>[11]</sup>                                                 | 19                                                      |  |  |
| Units: tera (10 <sup>12</sup> ) 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:<br>Valaciclovir hydrochloride<br>500 mg tablet | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|--------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type                   | Reporting group                                                    | Reporting group                                         |  |  |
| Number of subjects analysed          | 21 <sup>[12]</sup>                                                 | 19 <sup>[13]</sup>                                      |  |  |
| 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:<br>Valaciclovir hydrochloride<br>500 mg tablet | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|-----------------------------|--------------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type          | Reporting group                                                    | Reporting group                                         |  |  |
| Number of subjects analysed | 21 <sup>[14]</sup>                                                 | 19 <sup>[15]</sup>                                      |  |  |
| 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

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

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|                 |                                                                     |
|-----------------|---------------------------------------------------------------------|
| 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 tablets | Pediatric participants: VACV 500 mg granules/tablets |  |  |
|--------------------------------------|---------------------------------------------------------------|------------------------------------------------------|--|--|
| Subject group type                   | Reporting group                                               | Reporting group                                      |  |  |
| Number of subjects analysed          | 21 <sup>[16]</sup>                                            | 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

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**Statistical analyses**

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No statistical analyses for this end point

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

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|                 |                                                                                                           |
|-----------------|-----------------------------------------------------------------------------------------------------------|
| 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:<br>Valaciclovir hydrochloride 500 mg tablet | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|--------------------------------------|-----------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type                   | Reporting group                                                 | Reporting group                                         |  |  |
| Number of subjects analysed          | 21 <sup>[17]</sup>                                              | 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:<br>Valaciclovir hydrochloride 500 mg tablet | Pediatric participants:<br>VACV 500 mg granules/tablets |  |  |
|--------------------------------------|-----------------------------------------------------------------|---------------------------------------------------------|--|--|
| Subject group type                   | Reporting group                                                 | Reporting group                                         |  |  |
| Number of subjects analysed          | 21 <sup>[18]</sup>                                              | 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 <sup>[19]</sup>                                           | 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:<br>VACV 500 mg tablet | Pediatric<br>participants: VACV<br>500 mg<br>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 %

| <b>Non-serious adverse events</b>                     | Adult participants:<br>VACV 500 mg tablet | Pediatric<br>participants: VACV<br>500 mg<br>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<br>occurrences (all)                                                                       | 0 / 21 (0.00%)<br>0  | 2 / 19 (10.53%)<br>2 |  |
| Hepatic enzyme increased<br>subjects affected / exposed<br>occurrences (all)                                           | 2 / 21 (9.52%)<br>2  | 0 / 19 (0.00%)<br>0  |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                               | 2 / 21 (9.52%)<br>2  | 2 / 19 (10.53%)<br>3 |  |
| Blood and lymphatic system disorders<br>Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)           | 3 / 21 (14.29%)<br>3 | 4 / 19 (21.05%)<br>4 |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                                                            | 2 / 21 (9.52%)<br>3  | 3 / 19 (15.79%)<br>3 |  |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all)                                                | 6 / 21 (28.57%)<br>6 | 0 / 19 (0.00%)<br>0  |  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)                                                         | 0 / 21 (0.00%)<br>0  | 4 / 19 (21.05%)<br>4 |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)                                                        | 0 / 21 (0.00%)<br>0  | 3 / 19 (15.79%)<br>3 |  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)                                                        | 0 / 21 (0.00%)<br>0  | 2 / 19 (10.53%)<br>2 |  |
| General disorders and administration<br>site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all) | 5 / 21 (23.81%)<br>5 | 2 / 19 (10.53%)<br>2 |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                                                            | 2 / 21 (9.52%)<br>2  | 3 / 19 (15.79%)<br>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<br>occurrences (all) | 0 / 21 (0.00%)<br>0 | 2 / 19 (10.53%)<br>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<br>occurrences (all) | 1 / 21 (4.76%)<br>1 | 1 / 19 (5.26%)<br>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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported