Clinical trial results:
A Phase 3, Multicenter, Randomized, Double blind, Double-dummy, Active-controlled Study to Assess the Efficacy and Safety of Maribavir Compared to Valganciclovir for the Treatment of Cytomegalovirus (CMV) Infection in Hematopoietic Stem Cell Transplant Recipients

Summary

EudraCT number	2015-004726-34
Trial protocol	HU DE GB ES BE CZ PL FR HR IT GR AT Outside EU/EEA
Global end of trial date	01 July 2022

Results information

Result version number	v1 (current)
This version publication date	04 January 2023
First version publication date	04 January 2023

Trial information

Trial identification

Sponsor protocol code	SHP620-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02927067
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	300 Shire Way, Lexington, MA, United States, 02421
Public contact	Study Director, Shire, ClinicalTransparency@shire.com
Scientific contact	Study Director, Shire, ClinicalTransparency@shire.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000353-PIP02-16
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study is to compare the efficacy of maribavir to valganciclovir in CMV viremia clearance at the end of Study Week 8 in asymptomatic CMV infection in Hematopoietic Stem Cell Transplant (HSCT) recipients.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 April 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 32
Country: Number of subjects enrolled	China: 18
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	New Zealand: 17
Country: Number of subjects enrolled	Singapore: 18
Country: Number of subjects enrolled	Belgium: 61
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Spain: 130
Country: Number of subjects enrolled	France: 48
Country: Number of subjects enrolled	United Kingdom: 28
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Croatia: 8
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Turkey: 11
Country: Number of subjects enrolled	Canada: 15

Country: Number of subjects enrolled	United States: 111
Worldwide total number of subjects	553
EEA total number of subjects	287

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	4
Adults (18-64 years)	421
From 65 to 84 years	128
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were randomized at 97 sites in United States,Spain,France,Germany,United Kingdom,Belgium,China,Italy,Israel,Australia,Canada,Singapore,Croatia, Czech Republic,Greece,Hungary,Korea,New Zealand,Poland,Russia,Switzerland, and Turkey from 14 April 2017(first participant first visit) to 01 July 2022(last participant last visit).

Pre-assignment

Screening details:

Participants who were hematopoietic stem cell transplant (HSCT) recipients with a diagnosis of asymptomatic cytomegalovirus (CMV) infection were enrolled then randomized in a 1:1 ratio to receive either maribavir or valganciclovir (along with placebo matched to comparator) in each arm in a double-blind, double-dummy fashion.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Valganciclovir 900 mg BID

Arm description:

Participants received 900 milligrams (mg) of valganciclovir along with a placebo matched to maribavir, twice daily (BID) orally for 8 weeks. Valganciclovir dose was allowed to be adjusted to 450 mg BID or 450 mg QD based on renal function impairment assessed at baseline or development of neutropenia during the study.

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

Dosage and administration details:

Placebo tablets matched to maribavir.

Investigational medicinal product name	Valganciclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Valganciclovir 900 mg, BID. Dose was adjusted to 450 mg BID or 450 mg QD during the study for renal function impairment or neutropenia.

Arm title	Maribavir 400 mg BID

Arm description:

Participants received 400 mg of maribavir along with a placebo matched to valganciclovir, BID orally for 8 weeks.

Arm type	Experimental

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets matched to valganciclovir.

Investigational medicinal product name	Maribavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Maribavir 400 mg BID.

Number of subjects in period 1	Valganciclovir 900 mg BID	Maribavir 400 mg BID
Started	277	276
Treated Participants	274	273
Participants Received 8 Weeks Treatment	140 [1]	179 [2]
Completed	217	215
Not completed	60	61
Adverse event, serious fatal	18	31
Adverse event, non-fatal	13	10
Withdrawn Consent	20	12
Reason not Specified	4	6
Noncompliance	5	2

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants who received 8 weeks of treatment include the participants who completed study drug treatment.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Treated participants (full analysis set) included the participants from the randomized set who took at least one dose of assigned study drug and were analyzed for efficacy and safety evaluations.

Baseline characteristics

Reporting groups	
Reporting group title	Valganciclovir 900 mg BID
Reporting group description:	
Participants received 900 milligrams (mg) of valganciclovir along with a placebo matched to maribavir, twice daily (BID) orally for 8 weeks. Valganciclovir dose was allowed to be adjusted to 450 mg BID or 450 mg QD based on renal function impairment assessed at baseline or development of neutropenia during the study.	
Reporting group title	Maribavir 400 mg BID
Reporting group description:	
Participants received 400 mg of maribavir along with a placebo matched to valganciclovir, BID orally for 8 weeks.	

Reporting group values	Valganciclovir 900 mg BID	Maribavir 400 mg BID	Total
Number of subjects	277	276	553
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	51.8	53.1	
standard deviation	± 15.22	± 13.96	-
Gender categorical Units: Subjects			
Female	110	126	236
Male	167	150	317
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	39	36	75
Native Hawaiian or Other Pacific Islander	3	0	3
Black or African American	9	10	19
White	200	221	421
More than one race	0	0	0
Unknown or Not Reported	25	9	34
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	37	35	72
Not Hispanic or Latino	193	216	409
Unknown or Not Reported	47	25	72
Region of Enrollment Units: Subjects			
Australia Australia	13	19	32
China China	9	9	18
Korea, South Korea, Republic of	3	2	5
New Zealand New Zealand	10	7	17
Belgium Belgium	31	30	61
Switzerland Switzerland	4	2	6

Czech Republic Czechia	0	2	2
Germany Germany	9	11	20
Spain Spain	61	69	130
France France	34	14	48
United Kingdom United Kingdom	14	14	28
Greece Greece	1	0	1
Croatia Croatia	4	4	8
Hungary Hungary	2	1	3
Israel Israel	2	2	4
Italy Italy	7	4	11
Poland Poland	1	2	3
Russia Russia	1	0	1
Turkey Turkey	6	5	11
Canada Canada	8	7	15
United States United States	50	61	111
Singapore Singapore	7	11	18
Height			
Units: cm			
arithmetic mean	169.58	168.75	
standard deviation	± 9.391	± 9.579	-
Weight			
Units: kg			
arithmetic mean	70.31	70.98	
standard deviation	± 15.247	± 16.779	-
Body Mass Index (BMI)			
BMI = Body Mass Index. It is computed by [weight (kg) / height (cm)^2] x 10,000.			
Units: kg/m^2			
arithmetic mean	24.38	24.90	
standard deviation	± 4.628	± 5.007	-

End points

End points reporting groups

Reporting group title	Valganciclovir 900 mg BID
Reporting group description:	
Participants received 900 milligrams (mg) of valganciclovir along with a placebo matched to maribavir, twice daily (BID) orally for 8 weeks. Valganciclovir dose was allowed to be adjusted to 450 mg BID or 450 mg QD based on renal function impairment assessed at baseline or development of neutropenia during the study.	
Reporting group title	Maribavir 400 mg BID
Reporting group description:	
Participants received 400 mg of maribavir along with a placebo matched to valganciclovir, BID orally for 8 weeks.	

Primary: Number of Participants Who Achieved Confirmed Clearance of Plasma Cytomegalovirus (CMV) Deoxyribose Nucleic Acid (DNA) at the end of Study Week 8

End point title	Number of Participants Who Achieved Confirmed Clearance of Plasma Cytomegalovirus (CMV) Deoxyribose Nucleic Acid (DNA) at the end of Study Week 8
End point description:	
Confirmed CMV viremia clearance is defined as plasma CMV DNA concentrations less than lower limit of quantification (LLOQ; i.e. <137 International units per milliliter [IU/mL]), when assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV Test in 2 consecutive post baseline samples separated by at least 5 days. To be considered a responder for the primary endpoint, the participant must have received exclusively study-assigned treatment (regardless of whether study-assigned treatment was completed).	
End point type	Primary
End point timeframe:	
Week 8	

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	273		
Units: participants	212	190		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Maribavir 400 mg BID v Valganciclovir 900 mg BID
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in Percentage of Responders
Point estimate	-7.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.98
upper limit	-0.36

Notes:

[1] - The non-inferiority (NI) margin of the primary efficacy endpoint was 7%. If the lower limit of the 95% confidence interval (CI) was greater than -7%, then NI was assumed. Assuming 68% (maribavir) and 60% (valganciclovir) subjects achieve confirmed viremia clearance, 494 subjects (247 per group) will yield >90% power to declare NI based on 2-group test of equivalence in proportions (nQuery Advisor 7.0). Considering 10% dropout, 550 subjects (275 subjects per group) were enrolled and randomized.

Secondary: Number of Participants who Achieved Confirmed CMV Viremia Clearance and CMV Infection Symptom Control at the end of Week 8, Followed by Maintenance of Treatment Effect at Week 16

End point title	Number of Participants who Achieved Confirmed CMV Viremia Clearance and CMV Infection Symptom Control at the end of Week 8, Followed by Maintenance of Treatment Effect at Week 16

End point description:

Confirmed CMV viremia clearance is defined as plasma CMV DNA concentrations less than lower limit of quantification (LLOQ; i.e. <137 International units per milliliter [IU/mL]), when assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV Test in 2 consecutive post baseline samples separated by at least 5 days. To be considered a responder for this key secondary endpoint, the participant must have received exclusively study-assigned treatment (regardless of whether study-assigned treatment was completed).

End point type	Secondary

End point timeframe:

Week 8 up to Week 16

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	273		
Units: participants	133	144		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Valganciclovir 900 mg BID v Maribavir 400 mg BID
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in Percentage of Responders
Point estimate	4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.91
upper limit	12.76

Notes:

[2] - The non-inferiority margin of the key secondary efficacy endpoint was 7%. If the lower limit of the 95% CI was greater than -7%, then noninferiority (NI) was assumed. Because the NI of the primary efficacy endpoint was not established, the NI hypothesis of the key secondary endpoint was not tested formally.

Secondary: Number of Participants who Achieved Confirmed Clearance of Plasma CMV DNA (CMV Viremia Clearance) at Week 8 After Receiving 8 Weeks of Study Assigned Treatment

End point title	Number of Participants who Achieved Confirmed Clearance of Plasma CMV DNA (CMV Viremia Clearance) at Week 8 After Receiving 8 Weeks of Study Assigned Treatment

End point description:

Confirmed CMV viremia clearance is defined as plasma CMV DNA concentrations less than lower limit of quantification (LLOQ; i.e. <137 International units per milliliter [IU/mL]), when assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV Test in 2 consecutive post baseline samples separated by at least 5 days. To be considered a responder for this secondary endpoint, the participant must have received exclusively study-assigned treatment for 8 weeks. Participants who discontinued treatment early were non-responders for this endpoint.

End point type	Secondary

End point timeframe:

Week 8

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	273		
Units: participants	137	158		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Valganciclovir 900 mg BID v Maribavir 400 mg BID
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.061 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Responders
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	16.3

Notes:

[3] - The CMH weighted average approach (stratified for baseline plasma CMV DNA concentration and acute GVHD status) was used for the adjusted difference in percentage of responders (Maribavir−Valganciclovir), the corresponding 95% CI, and the p−value.

Secondary: Number of Participants who Achieved Confirmed CMV Viremia Clearance

After Receiving 8 Weeks of Study-assigned Treatment Through Weeks 12, 16 and 20	
End point title	Number of Participants who Achieved Confirmed CMV Viremia Clearance After Receiving 8 Weeks of Study-assigned Treatment Through Weeks 12, 16 and 20

End point description:

Confirmed CMV viremia clearance is defined as plasma CMV DNA concentrations less than lower limit of quantification (LLOQ; i.e. <137 International units per milliliter [IU/mL]), when assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV Test in 2 consecutive post baseline samples separated by at least 5 days. To be considered a responder for this secondary endpoint, the participant must have received exclusively study-assigned treatment for 8 weeks.

End point type	Secondary

End point timeframe:

Week 8 through Weeks 12, 16 and 20

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	273		
Units: participants				
Week 8	137	158		
Week 12	98	134		
Week 16	82	119		
Week 20	72	98		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 8

Comparison groups	Valganciclovir 900 mg BID v Maribavir 400 mg BID
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.061 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Responders
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	16.3

Notes:

[4] - The CMH weighted average approach (stratified for baseline plasma CMV DNA concentration and acute GVHD status) was used for the adjusted difference in percentage of responders (Maribavir−Valganciclovir), the corresponding 95% CI, and the p−value.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:	
Week 12	
Comparison groups	Valganciclovir 900 mg BID v Maribavir 400 mg BID
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Responders
Point estimate	13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.23
upper limit	21.62

Notes:

[5] - The CMH weighted average approach (stratified for baseline plasma CMV DNA concentration and acute GVHD status) was used for the adjusted difference in percentage of responders (Maribavir−Valganciclovir), the corresponding 95% CI, and the p−value.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Week 16	
Comparison groups	Valganciclovir 900 mg BID v Maribavir 400 mg BID
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Responders
Point estimate	13.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.8
upper limit	21.87

Notes:

[6] - The CMH weighted average approach (stratified for baseline plasma CMV DNA concentration and acute GVHD status) was used for the adjusted difference in percentage of responders (Maribavir−Valganciclovir), the corresponding 95% CI, and the p−value.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Week 20	
Comparison groups	Valganciclovir 900 mg BID v Maribavir 400 mg BID
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Responders
Point estimate	9.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.98
upper limit	17.5

Notes:

[7] - The CMH weighted average approach (stratified for baseline plasma CMV DNA concentration and acute GVHD status) was used for the adjusted difference in percentage of responders (Maribavir−Valganciclovir), the corresponding 95% CI, and the p−value.

Secondary: Number of Participants who Achieved Confirmed CMV Viremia Clearance and CMV Infection Symptom Control at Study Week 8 With Maintenance Through Weeks 12 and 20

End point title	Number of Participants who Achieved Confirmed CMV Viremia Clearance and CMV Infection Symptom Control at Study Week 8 With Maintenance Through Weeks 12 and 20

End point description:

Confirmed CMV viremia clearance is defined as plasma CMV DNA concentrations less than lower limit of quantification (LLOQ; i.e. <137 International units per milliliter [IU/mL]), when assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV Test in 2 consecutive post baseline samples separated by at least 5 days. To be considered a responder for this secondary endpoint, the participant must have received exclusively study-assigned treatment (regardless of whether study-assigned treatment was completed) and had no symptoms of tissue invasive CMV disease at Week 8, Week 8 through Week 12, and Week 8 through Week 20, respectively.

End point type	Secondary

End point timeframe:

Week 8 through Weeks 12 and 20

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	273		
Units: participants				
Week 8	211	190		
Week 12	157	162		
Week 20	116	118		

Statistical analyses

Statistical analysis title	Statisctical Analysis 1

Statistical analysis description:

Week 8

Comparison groups	Valganciclovir 900 mg BID v Maribavir 400 mg BID
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Responders
Point estimate	-7.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.64
upper limit	0.02

Notes:

[8] - The CMH weighted average approach (stratified for baseline plasma CMV DNA concentration and acute GVHD status) was used for the adjusted difference in percentage of responders (Maribavir−Valganciclovir), the corresponding 95% CI, and the p−value.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Week 20

Comparison groups	Valganciclovir 900 mg BID v Maribavir 400 mg BID
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.809 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Responders
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.27
upper limit	9.31

Notes:

[9] - The CMH weighted average approach (stratified for baseline plasma CMV DNA concentration and acute GVHD status) was used for the adjusted difference in percentage of responders (Maribavir−Valganciclovir), the corresponding 95% CI, and the p−value.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Week 12

Comparison groups	Valganciclovir 900 mg BID v Maribavir 400 mg BID
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.606 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Percentage of Responders
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.05
upper limit	10.37

Notes:

[10] - The CMH weighted average approach (stratified for baseline plasma CMV DNA concentration and acute GVHD status) was used for the adjusted difference in percentage of responders (Maribavir−Valganciclovir), the corresponding 95% CI, and the p−value.

Secondary: Number of Participants With Confirmed Recurrence of Viremia During First 8 Weeks of the Study

End point title	Number of Participants With Confirmed Recurrence of Viremia During First 8 Weeks of the Study

End point description:

Recurrence of CMV viremia is defined as plasma CMV DNA concentration greater than or equal to (>=) LLOQ when assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV Test in 2 consecutive plasma samples at least 5 days apart, after being unquantifiable (<LLOQ) for at least 5 days in 2 consecutive samples during the first 8 weeks of the study, during the 12 weeks of the follow up study phase, and at any time during the study.

End point type	Secondary

End point timeframe:

Up to Week 8

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	236	226		
Units: participants	6	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Confirmed Recurrence of Viremia During the Follow-up Period

End point title	Number of Participants With Confirmed Recurrence of Viremia During the Follow-up Period

End point description:

Recurrence of CMV viremia is defined as plasma CMV DNA concentration greater than or equal to (>=) LLOQ when assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV Test in 2 consecutive plasma samples at least 5 days apart, after being unquantifiable (<LLOQ) for at least 5 days in 2 consecutive samples during the first 8 weeks of the study, during the 12 weeks of the follow up study phase, and at any time during the study.

End point type	Secondary

End point timeframe:

From Week 9 up to Week 20

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	236	226		
Units: participants	47	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Confirmed Recurrence of Viremia While on Study Treatment and Off Treatment

End point title	Number of Participants With Confirmed Recurrence of Viremia While on Study Treatment and Off Treatment

End point description:

Recurrence of CMV viremia is defined as plasma CMV DNA concentration greater than or equal to (>=) LLOQ when assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV Test in 2 consecutive plasma samples at least 5 days apart, after being unquantifiable (<LLOQ) for at least 5 days in 2 consecutive samples during the first 8 weeks of the study, during the 12 weeks of the follow up study phase, and at any time during the study.

End point type	Secondary

End point timeframe:

Baseline up to Week 20

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	236	226		
Units: participants				
On Study	0	14		
Off Study	53	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Confirmed Recurrence of Viremia at any Time During the Study

End point title	Number of Participants With Confirmed Recurrence of Viremia at any Time During the Study

End point description:

Recurrence of CMV viremia is defined as plasma CMV DNA concentration greater than or equal to (>=) LLOQ when assessed by COBAS® AmpliPrep/COBAS® TaqMan® CMV Test in 2 consecutive plasma samples at least 5 days apart, after being unquantifiable (<LLOQ) for at least 5 days in 2 consecutive samples during the first 8 weeks of the study, during the 12 weeks of the follow up study phase, and at any time during the study.

End point type	Secondary

End point timeframe:

Up to Week 20

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	236	226		
Units: participants	53	43		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Grade 3 or 4 (Shift from Baseline Grade <3) and Grade 4 Neutropenia (Shift from Baseline Grade <4) While on Study Treatment

End point title	Incidence of Grade 3 or 4 (Shift from Baseline Grade <3) and Grade 4 Neutropenia (Shift from Baseline Grade <4) While on Study Treatment

End point description:

Grade 3 and grade 4 neutropenia are defined as absolute neutrophil count (ANC) <1000 per cubic millimeter (/mm^3) and ANC <500/mm^3 respectively. Incidence of Grade 3 or 4 neutropenia represents the percentage of participants with Grade <3 (or missing) neutropenia at baseline, but Grade 3 or 4 while on study treatment. Incidence of Grade 4 neutropenia represents the number of participants with Grade <4 (or missing) neutropenia at baseline, but Grade 4 while on study treatment.

End point type	Secondary

End point timeframe:

From start of study drug to end of study drug + 1 day (up to approximately Week 8)

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	273		
Units: participants				
Grade 3 or Grade 4 Neutropenia	137	44		
Grade 4 Neutropenia	61	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events During the on-Treatment Period

End point title	Number of Participants With Treatment-Emergent Adverse Events During the on-Treatment Period

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical investigation participants administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE that has a start date on or after the first dose of study treatment, or that has a start date before the date of first dose of study treatment but increases in severity after the first dose of study treatment, will be considered a treatment-emergent AE (TEAE).

End point type	Secondary

End point timeframe:

From the start of the study treatment to 7 days after the last dose of study treatment (up to approximately Week 9)

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	273		
Units: participants	269	268		

Statistical analyses

No statistical analyses for this end point

Secondary: Predose Concentration (Cmin) of Maribavir

End point title	Predose Concentration (Cmin) of Maribavir [11]

End point description:

The primary plasma maribavir concentration dataset (primary concentration dataset) includes all plasma maribavir concentrations. Missing PK sampling times are imputed according to the sparse sampling schedule in primary concentration dataset.

End point type	Secondary

End point timeframe:

Weeks 1, 4, and 8: pre-morning dose

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint.

End point values	Maribavir 400 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	225			
Units: micrograms per milliliter (µg/mL)				
arithmetic mean (standard deviation)				
Week 8 (n=225)	9.17 (± 7.69)			
Week 4 (n=190)	8.71 (± 9.20)			
Week 8 (n=164)	7.02 (± 6.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve Over the 12-Hour Dosing Interval at Steady State AUC(0-tau) of Maribavir for Adolescent Participants Only

End point title	Area Under the Concentration-Time Curve Over the 12-Hour

	Dosing Interval at Steady State AUC(0-tau) of Maribavir for Adolescent Participants Only[12]

End point description:

End point type	Secondary

End point timeframe:

Pre-morning dose, 1, 2, 3, 4, 6, 8, and 12 hours post-morning dose of Week 1

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint.

End point values	Maribavir 400 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: hours (h)*µg/mL				
arithmetic mean (full range (min-max))	161 (161 to 161)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Maribavir for Adolescent Participants Only

End point title	Maximum Observed Plasma Concentration (Cmax) of Maribavir for Adolescent Participants Only[13]

End point description:

End point type	Secondary

End point timeframe:

Pre-morning dose, 1, 2, 3, 4, 6, 8, and 12 hours post-morning dose of Week 1

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint.

End point values	Maribavir 400 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: µg/mL				
arithmetic mean (full range (min-max))	22.0 (22.0 to 22.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time When Maximum Concentration is Observed (Tmax) of Maribavir for Adolescent Participants Only

End point title	Time When Maximum Concentration is Observed (Tmax) of Maribavir for Adolescent Participants Only [14]

End point description:

End point type	Secondary

End point timeframe:

Pre-morning dose, 1, 2, 3, 4, 6, 8, and 12 hours post-morning dose of Week 1

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint.

End point values	Maribavir 400 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: hours (h)				
median (full range (min-max))	0.92 (0.92 to 0.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Oral Clearance (CL/F) of Maribavir for Adolescent Participants Only

End point title	Apparent Oral Clearance (CL/F) of Maribavir for Adolescent Participants Only[15]

End point description:

End point type	Secondary

End point timeframe:

Pre-morning dose, 1, 2, 3, 4, 6, 8, and 12 hours post-morning dose of Week 1

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint.

End point values	Maribavir 400 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: liters per hour (L/h)				
arithmetic mean (full range (min-max))	2.49 (2.49 to 2.49)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution (Vz/F) of Maribavir for Adolescent Participants Only

End point title	Apparent Volume of Distribution (Vz/F) of Maribavir for Adolescent Participants Only[16]

End point description:

End point type	Secondary

End point timeframe:

Pre-morning dose, 1, 2, 3, 4, 6, 8, and 12 hours post-morning dose of Week 1

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was planned for this endpoint.

End point values	Maribavir 400 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: liters (L)				
arithmetic mean (full range (min-max))	18.3 (18.3 to 18.3)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants Developing Resistance

End point title	Percentage of Participants Developing Resistance

End point description:

Resistance development was low in the two treatment arms and numerically higher in the maribavir arm. Percentages are rounded to one decimal place.

End point type	Other pre-specified

End point timeframe:

From start of study drug up to end of the study (up to Week 20)

End point values	Valganciclovir 900 mg BID	Maribavir 400 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	273		
Units: percentage of participants				
number (not applicable)	2.9	8.8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: From start of study drug up to end of the study (up to Week 20); Serious and Other Adverse Events: From the start of the study drug to 7 days after the last dose of study treatment (up to approximately Week 9)

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Maribavir 400 mg BID

Reporting group description:

Participants received 400 mg of maribavir along with a placebo matched to valganciclovir, BID orally for 8 weeks.

Reporting group title	Valganciclovir 900 mg BID

Reporting group description:

Participants received 900 mg of valganciclovir along with a placebo matched to maribavir, twice daily (BID) orally for 8 weeks. Valganciclovir dose was allowed to be adjusted to 450 mg BID or 450 mg QD based on renal function impairment assessed at baseline or development of neutropenia during the study.

Serious adverse events	Maribavir 400 mg BID	Valganciclovir 900 mg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	88 / 273 (32.23%)	95 / 274 (34.67%)	
number of deaths (all causes)	37	29	
number of deaths resulting from adverse events	18	12	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia recurrent			
subjects affected / exposed	0 / 273 (0.00%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute myeloid leukaemia recurrent			

subjects affected / exposed	2 / 273 (0.73%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
B precursor type acute leukaemia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Leukaemic infiltration			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 273 (0.37%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lymphoma			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-Hodgkin's lymphoma recurrent			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transformation to acute myeloid leukaemia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			

subjects affected / exposed	2 / 273 (0.73%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 273 (0.37%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 273 (0.37%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	8 / 273 (2.93%)	13 / 274 (4.74%)	
occurrences causally related to treatment / all	0 / 9	1 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Acute graft versus host disease in skin			
subjects affected / exposed	4 / 273 (1.47%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute graft versus host disease in intestine			
subjects affected / exposed	10 / 273 (3.66%)	4 / 274 (1.46%)	
occurrences causally related to treatment / all	0 / 11	0 / 4	
deaths causally related to treatment / all	0 / 6	0 / 0	
Chronic graft versus host disease			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute graft versus host disease oral			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease in eye			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic graft versus host disease in intestine			
subjects affected / exposed	2 / 273 (0.73%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant rejection			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vulvovaginal pruritus			

subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cough			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 273 (1.10%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Platelet count decreased			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatic enzyme increased			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product use issue			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arrhythmia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Acute polyneuropathy			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system lesion			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cerebral haemorrhage			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dizziness			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limbic encephalitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 273 (0.00%)	3 / 274 (1.09%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	2 / 273 (0.73%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nystagmus			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	3 / 273 (1.10%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Autoimmune haemolytic anaemia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 273 (0.37%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone marrow failure			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 273 (0.37%)	8 / 274 (2.92%)	
occurrences causally related to treatment / all	1 / 1	4 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 273 (0.00%)	3 / 274 (1.09%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolysis			

subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	2 / 273 (0.73%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 273 (0.00%)	3 / 274 (1.09%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	4 / 273 (1.47%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Warm type haemolytic anaemia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Neurosensory hypoacusis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	4 / 273 (1.47%)	6 / 274 (2.19%)	
occurrences causally related to treatment / all	0 / 4	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysbiosis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	2 / 273 (0.73%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	2 / 273 (0.73%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 273 (0.73%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis haemorrhagic			
subjects affected / exposed	2 / 273 (0.73%)	5 / 274 (1.82%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysuria			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis viral			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus colitis			
subjects affected / exposed	2 / 273 (0.73%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cytomegalovirus enterocolitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus gastritis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus gastroenteritis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus gastrointestinal infection			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cytomegalovirus infection			
subjects affected / exposed	3 / 273 (1.10%)	3 / 274 (1.09%)	
occurrences causally related to treatment / all	0 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection reactivation			
subjects affected / exposed	2 / 273 (0.73%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus oesophagitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 273 (0.37%)	4 / 274 (1.46%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 273 (0.37%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated toxoplasmosis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Epstein-Barr viraemia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			

subjects affected / exposed	2 / 273 (0.73%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Eye infection toxoplasmal			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fournier's gangrene			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fungal infection			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal sepsis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastroenteritis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis astroviral			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			

subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster disseminated			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster meningoencephalitis			
subjects affected / exposed	2 / 273 (0.73%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster reactivation			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection fungal			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nasopharyngitis			

subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	1 / 273 (0.37%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 273 (1.10%)	3 / 274 (1.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 273 (0.37%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia parainfluenzae viral			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 273 (0.37%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal sepsis			
subjects affected / exposed	0 / 273 (0.00%)	2 / 274 (0.73%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal infection			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	3 / 273 (1.10%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 273 (0.00%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxoplasmosis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella zoster virus infection			

subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	2 / 273 (0.73%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food intolerance			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 274 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 273 (0.37%)	1 / 274 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Maribavir 400 mg BID	Valganciclovir 900 mg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	245 / 273 (89.74%)	256 / 274 (93.43%)	
Investigations			
Blood creatinine increased			
subjects affected / exposed	18 / 273 (6.59%)	12 / 274 (4.38%)	
occurrences (all)	18	13	
Neutrophil count decreased			
subjects affected / exposed	13 / 273 (4.76%)	29 / 274 (10.58%)	
occurrences (all)	28	52	
White blood cell count decreased			
subjects affected / exposed	3 / 273 (1.10%)	14 / 274 (5.11%)	
occurrences (all)	4	15	
Platelet count decreased			
subjects affected / exposed	17 / 273 (6.23%)	16 / 274 (5.84%)	
occurrences (all)	21	19	
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 273 (5.13%)	17 / 274 (6.20%)	
occurrences (all)	15	19	
Nervous system disorders			
Headache			
subjects affected / exposed	30 / 273 (10.99%)	14 / 274 (5.11%)	
occurrences (all)	31	16	
Dysgeusia			
subjects affected / exposed	47 / 273 (17.22%)	16 / 274 (5.84%)	
occurrences (all)	51	17	
Taste disorder			
subjects affected / exposed	23 / 273 (8.42%)	6 / 274 (2.19%)	
occurrences (all)	24	6	
Tremor			
subjects affected / exposed	10 / 273 (3.66%)	15 / 274 (5.47%)	
occurrences (all)	13	16	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	7 / 273 (2.56%)	27 / 274 (9.85%)	
occurrences (all)	10	37	

Anaemia			
subjects affected / exposed	62 / 273 (22.71%)	49 / 274 (17.88%)	
occurrences (all)	89	57	
Thrombocytopenia			
subjects affected / exposed	31 / 273 (11.36%)	62 / 274 (22.63%)	
occurrences (all)	32	79	
Neutropenia			
subjects affected / exposed	44 / 273 (16.12%)	144 / 274 (52.55%)	
occurrences (all)	60	247	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	13 / 273 (4.76%)	19 / 274 (6.93%)	
occurrences (all)	14	22	
Fatigue			
subjects affected / exposed	13 / 273 (4.76%)	19 / 274 (6.93%)	
occurrences (all)	13	20	
Oedema peripheral			
subjects affected / exposed	27 / 273 (9.89%)	26 / 274 (9.49%)	
occurrences (all)	29	27	
Pyrexia			
subjects affected / exposed	24 / 273 (8.79%)	25 / 274 (9.12%)	
occurrences (all)	29	29	
Immune system disorders			
Acute graft versus host disease in skin			
subjects affected / exposed	46 / 273 (16.85%)	32 / 274 (11.68%)	
occurrences (all)	55	35	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	14 / 273 (5.13%)	19 / 274 (6.93%)	
occurrences (all)	16	22	
Constipation			
subjects affected / exposed	16 / 273 (5.86%)	10 / 274 (3.65%)	
occurrences (all)	17	11	
Diarrhoea			
subjects affected / exposed	50 / 273 (18.32%)	44 / 274 (16.06%)	
occurrences (all)	67	55	

Nausea			
subjects affected / exposed	74 / 273 (27.11%)	64 / 274 (23.36%)	
occurrences (all)	89	79	
Vomiting			
subjects affected / exposed	55 / 273 (20.15%)	47 / 274 (17.15%)	
occurrences (all)	70	59	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	20 / 273 (7.33%)	26 / 274 (9.49%)	
occurrences (all)	20	28	
Dyspnoea			
subjects affected / exposed	2 / 273 (0.73%)	14 / 274 (5.11%)	
occurrences (all)	2	16	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	10 / 273 (3.66%)	17 / 274 (6.20%)	
occurrences (all)	10	19	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	24 / 273 (8.79%)	15 / 274 (5.47%)	
occurrences (all)	27	19	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	18 / 273 (6.59%)	16 / 274 (5.84%)	
occurrences (all)	19	16	
Hypokalaemia			
subjects affected / exposed	23 / 273 (8.42%)	22 / 274 (8.03%)	
occurrences (all)	28	23	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2017	-Modification of primary, key secondary, and secondary objectives to include participants who discontinue study treatment early and meet the criteria of confirmed CMV viremia clearance as responders in the primary efficacy analysis. -Modified Inclusion Criterion 5 to indicate that the current CMV infection must be the first episode of CMV viremia after HSCT, either primary or reactivation. -Clarified Inclusion Criterion 8 to indicate that urine pregnancy tests may be done per institutional requirements in addition to serum; however, they are not sufficient for eligibility determination. -Added a new Exclusion Criterion 3 to exclude participants with recurrent CMV infection. -Amended Exclusion Criterion 6 to indicate that participants must not be on treatment with anti-CMV agents (ganciclovir, valganciclovir, foscarnet or cidofovir) for the current CMV infection for longer than 72 hours. -Clarified in Exclusion Criterion 13 that subjects who have received an unapproved agent or device within 30 days before initiation of study treatment were not eligible. -Clarified Exclusion Criterion 16 indicating that known (previously documented) HIV historical results were accepted and no additional study testing was required. -Added an intensive PK sampling schedule for adolescents. -An additional pregnancy test at 4 weeks (Visit 6/Week 4) to obtain a monthly testing interval. -Addition of highly effective method of female and male contraception per the recommendations related to contraception and pregnancy testing in clinical trials by clinical trial facilitation group. -Addition recommendation for careful monitoring of concentration levels of concomitant medications that are substrates of CYP2C19 and P-gp both after initiation of maribavir (when substrate levels may increase) and after discontinuation of maribavir (when substrate levels may decrease), in alignment with the guidance to the investigators provided in the maribavir investigator's brochure.
01 June 2017	- Added "CMV CNS infection" as one of the reasons for discontinuation and/or withdrawal. -Added basic descriptive statistics generally for all endpoints. -Added sensitivity analysis for investigation of homogeneity of treatment effect across centers/regions. -Added rules for conducting the interim population PK analysis.
01 September 2017	-Revised storage conditions of investigational product.
04 February 2019	-Expanded eligibility criteria for viral load and creatinine clearance (CrCl). -Added a third viral-load stratum for participants with very low viral load and high-risk infection, in addition to the existing low viral-load and high viral-load strata. -Added a study visit at Study Day 4 (±1) for participants taking a narrow therapeutic index immunosuppressive agent at baseline. -Added a visit 4 days after starting new therapy with a narrow therapeutic index immunosuppressive agent for participants who begin new therapy during the course of the treatment period to align the protocol with a recent recommendation from the DMC for Study SHP620-303. -Updated contact list, including removal of contacts for sites in Latin America. -Updated safety reporting contacts to a single Global Safety e-mail and fax contact per revised safety reporting procedures. -Added exclusion for concomitant letermovir and specified required washout period. -Clarified end of period for collecting nonserious AEs as up to 30 days after the last dose of study medication. -Modified the definition of overall study AEs to include events during the overall study period through the end of study, regardless of initiation of alternative anti-CMV treatment. -Modified criteria for reporting of CMV as an AE or SAE to harmonize with the reporting format used in Study SHP620-303. -Updated Table 12 Assessments of Responders for Key Secondary Endpoint (confirmed CMV viremia clearance at the end of Study Week 8 through Week 16) to ensure assessment of responder rates consistent with assessment specified in Study SHP620-303. -Eliminated the Hematopoietic Cell Transplant Comorbidity Index (HCT-CI) assessment and deleted Appendix 5 containing the index. -Clarified language regarding starting dosage regimens, as updated entry criteria require expansion of starting doses. -Added Graft Versus Host Disease (GVHD) assessment criteria forms and added tables for GVHD diagnosis criteria.

11 February 2020	-Added Modified Randomized Set, consisting of all participants in Randomized Set who take at least 1 dose of assigned study treatment. -Revised the exploratory efficacy endpoint of duration between the first confirmed CMV viremia clearance to viremia recurrence in all participants within 8 weeks of the study and through the end of study to time from the CMV viremia clearance at Week 8 to CMV viremia recurrence requiring alternative treatment. -Updated comorbidity status evaluation. -To align with the investigator's brochure, updated the Cmax and AUC values for the increased tacrolimus when concomitantly administered with maribavir and changed 2D6 substrate to CYP2C19 substrate. -Updated number of completed for Phase 1 studies. -Removed references to an electronic diary (e-diary) due to the introduction of paper back-up diaries. -Updated the versions of the Valcyte Prescribing Information and Summary of Product Characteristics (SmPC) to specify the current version as documented in the Study Pharmacy Manual. -Corrected the unit of measure for hemoglobin. -Clarified that timing of comorbidity status evaluation is at Visit 6/Week 4 and Visit 10/Week 8. -Clarified follow-up to closure of unresolved SAEs rather than AEs at end of study. -Corrected pregnancy reporting information to indicate that it is the investigator's responsibility to obtain pregnancy outcome/infant condition information within approximately 30 calendar days and 1 year postpartum. Removed requirement for a copy of the Investigational and Marketed Products Pregnancy Report Form being sent to the CRO/ sponsor medical monitor using details specified in the emergency contact information section of protocol. -Corrected information regarding reporting of SAEs. -Removed CIs from 3 secondary efficacy endpoints as they are not clinically meaningful for these analyses.
06 December 2020	-The protocol was amended to maintain participants safety, confidentiality, and study integrity in the context of healthcare delivery challenges presented by the COVID-19 pandemic. Amendment 6 provided flexibility to subjects to opt for home healthcare solutions as permitted by local regulations. This "hybrid study design" would offer subjects the option of in clinic or home healthcare for all study visits in the treatment phase. -Guidance was provided regarding changes to the study procedures that could be implemented for subjects or study sites affected by the COVID 19 Public Health Emergency. The guidance took references from the Food and Drug Administration Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency - Guidance for Industry, Investigators, and Institutional Review Boards, March 2020, updated 03 June 2020, and the European Medicines Agency (EMA) Guidance on the Management of Clinical Trials During the COVID 19 (Coronavirus) Pandemic, Version 3 (28 Apr 2020).
24 March 2021	-Removed language extending measures to other situations beyond the COVID-19 pandemic ("or other future similar unexpected public health concerns" as this section applies only to the current COVID 19 pandemic. -Updated the guidance on management of clinical trials during the COVID 19 pandemic. Clarified that the site must contact the sponsor for approval of the alternative method for obtaining informed consent prior to implementation. -Clarified the recording of abuse, misuse, overdose, and medication errors on the AE CRF.
02 July 2021	The main purpose of Amendment 8 was to update the sponsor name and address from Shire ViroPharma, Inc (Shire) to Takeda Development Center Americas, Inc (TDC Americas; Takeda) and to clarify the secondary endpoints.
15 September 2021	The main purpose of Amendment 9 was to update description of drug interactions consistent with the latest Investigator's Brochure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported