Clinical trial results:
A Phase 3, Open-Label, Single-Arm Study to Assess the Efficacy, Safety, and Pharmacokinetics of Maribavir for the Treatment of Cytomegalovirus (CMV) Infection in Japanese Recipients of a Hematopoietic Stem Cell Transplant (HSCT) or Solid Organ Transplant (SOT)

Summary

EudraCT number	2022-002374-82
Trial protocol	Outside EU/EEA
Global end of trial date	27 June 2023

Results information

Result version number	v1 (current)
This version publication date	23 June 2024
First version publication date	23 June 2024

Trial information

Trial identification

Sponsor protocol code	TAK-620-3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05137717
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Avenue, Lexington, United States, MA 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 June 2023
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 evaluate the efficacy of maribavir in CMV viremia clearance at the end of Study Week 8 (8 weeks after start of administration) in Japanese HSCT or SOT recipients with CMV infection. Also, to assess the safety and tolerability of maribavir in Japanese transplant recipients with CMV infection.

Protection of trial subjects:

This study was conducted in accordance with the protocol, the International Council for Harmonisation Guideline for GCP E6 (ICH GCP, 1996; ICH E6 R2, 2016), Title 21 of the US Code of Federal Regulations (US CFR), the European Union Directives (2001/20/EC; 2005/28/EC), and applicable national and local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 January 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 41
Worldwide total number of subjects	41
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	34
From 65 to 84 years	7

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 23 sites in Japan from 18 January 2022 to 27 June 2023.

Pre-assignment

Screening details:

A total of 61 Japanese participants with cytomegalovirus (CMV) infection were screened and enrolled, of which 41 participants received maribavir treatment in this 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

Arm title	Maribavir

Arm description:

Participants received maribavir 400 milligrams (mg), oral tablet, twice a day (BID) for up to 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Maribavir
Investigational medicinal product code	
Other name	SHP620, TAK-620
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Maribavir 400 mg, tablets, orally, BID for up to 8 weeks.

Number of subjects in period 1	Maribavir
Started	41
Completed	33
Not completed	8
Adverse event, serious fatal	2
Consent withdrawn by subject	6

Baseline characteristics

Reporting groups	
Reporting group title	Maribavir
Reporting group description:	
Participants received maribavir 400 milligrams (mg), oral tablet, twice a day (BID) for up to 8 weeks.	

Reporting group values	Maribavir	Total	
Number of subjects	41	41	
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	53.9		
standard deviation	± 11.16	-	
Gender categorical Units: Subjects			
Female	21	21	
Male	20	20	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	41	41	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	0	0	
More than one race	0	0	
Unknown or Not Reported	0	0	
Region of Enrollment Units: Subjects			
Japan	41	41	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	41	41	
Unknown or Not Reported	0	0	
Height Units: centimetres (cm)			
arithmetic mean	164.46		
standard deviation	± 8.702	-	
Body Mass Index (BMI)			
BMI was calculated as weight (kg)/ (height [meter]) ^2.			
Units: kilograms per meter square (kg/m^2)			
arithmetic mean	21.26		
standard deviation	± 3.538	-	
Weight			

Units: kilograms (kg)			
arithmetic mean	57.47		
standard deviation	± 10.707	-	

End points

End points reporting groups

Reporting group title	Maribavir

Reporting group description:

Participants received maribavir 400 milligrams (mg), oral tablet, twice a day (BID) for up to 8 weeks.

Primary: Percentage of Participants Who Achieved Confirmed Clearance of Plasma CMV Deoxyribose Nucleic Acid (DNA) at Week 8

End point title	Percentage of Participants Who Achieved Confirmed Clearance of Plasma CMV Deoxyribose Nucleic Acid (DNA) at Week 8[1]

End point description:

The confirmed viremia clearance was defined as a plasma CMV DNA concentration below the lower limit of quantification (LLOQ) (that is [i.e.], less than [<] 34.5 international units per milliliter [IU/mL]) when assessed by the COBAS® 8800/COBAS® CMV Test, in two 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). FAS included of all participants who had taken at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

At Week 8

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: No statistical analysis was planned for this endpoint.

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: percentage of participants				
number (confidence interval 95%)	68.3 (51.9 to 81.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs[2]

End point description:

A TEAEs was defined as any event emerging or manifesting at or after the initiation of treatment with an investigational product or medicinal product or any existing event that worsened in either intensity or frequency following exposure to the investigational product or medicinal product. An SAE was any untoward medical occurrence or effect that at any dose resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability / incapacity, was a congenital anomaly / birth defect or was medically important due to other reasons than the above mentioned criteria. Safety set included of all participants who had taken at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

From first dose of study drug up to Week 20

Notes:

[2] - 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: No statistical analysis was planned for this endpoint.

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: participants				
Participants with TEAEs	39			
Participants with Serious TEAEs	13			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With TEAEs Leading to Treatment Discontinuation with Maribavir

End point title	Number of Participants With TEAEs Leading to Treatment Discontinuation with Maribavir[3]

End point description:

The number of participants with TEAEs leading to maribavir study treatment discontinuation (including treatment interruption or withdrawal) were reported. Safety set included of all participants who had taken at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

From first dose of study drug up to Week 20

Notes:

[3] - 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: No statistical analysis was planned for this endpoint.

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: participants	9			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Meaningful Changes in Vital Signs

End point title	Number of Participants With Clinically Meaningful Changes in Vital Signs[4]

End point description:

Vital sign assessments included blood pressure, pulse, respiratory rate and body temperature. Any clinically meaningful change in vital signs which were deemed clinically significant by the investigator were reported. Safety set included of all participants who had taken at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

From first dose of study drug up to Week 20

Notes:

[4] - 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: No statistical analysis was planned for this endpoint.

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Meaningful Abnormalities in Physical Examination Findings

End point title	Number of Participants With Clinically Meaningful Abnormalities in Physical Examination Findings[5]

End point description:

Physical examination included assessments of the head, eyes, ears, nose, throat, neck, lymph nodes, and the cardiovascular, dermatological, musculoskeletal, respiratory, gastrointestinal, genitourinary, and neurological systems. Any clinically meaningful change in physical examination which were deemed clinically significant by the investigator were reported. Safety set included of all participants who had taken at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

From first dose of study drug up to Week 20

Notes:

[5] - 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: No statistical analysis was planned for this endpoint.

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Meaningful Abnormalities in Clinical

Laboratory Parameters

End point title	Number of Participants With Clinically Meaningful Abnormalities in Clinical Laboratory Parameters[6]

End point description:

Clinical laboratory parameters included evaluations of hematology, chemistry, urinalysis. Any clinically meaningful change in clinical laboratory parameters which were deemed clinically significant by the investigator were reported. Safety set included of all participants who had taken at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

From first dose of study drug up to Week 20

Notes:

[6] - 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: No statistical analysis was planned for this endpoint.

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Meaningful Changes in Electrocardiograms (ECGs)

End point title	Number of Participants With Clinically Meaningful Changes in Electrocardiograms (ECGs)[7]

End point description:

12-lead ECG were evaluated. Any change in ECG assessments which are deemed clinically meaningful by the investigator were reported. Safety set included of all participants who had taken at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

From first dose of study drug up to Week 20

Notes:

[7] - 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: No statistical analysis was planned for this endpoint.

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Events of Immunosuppressant Drug Level Increased in Blood

End point title	Number of Participants With Events of Immunosuppressant Drug Level Increased in Blood[8]

End point description:

Immunosuppressant drug concentration testing was solely for participants who received immunosuppressive therapy with tacrolimus, cyclosporine, or everolimus. The number of participants with an increased level of at least one immunosuppressant drug was reported. Safety set included of all participants who had taken at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

From first dose of study drug up to Week 8

Notes:

[8] - 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: No statistical analysis was planned for this endpoint.

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with TEAEs of New Onset of Acute or Chronic Graft-versus-host Disease (GVHD), Graft Rejection, or Graft Loss

End point title	Number of Participants with TEAEs of New Onset of Acute or Chronic Graft-versus-host Disease (GVHD), Graft Rejection, or Graft Loss[9]

End point description:

New onset of acute or chronic GVHD assessed as TEAEs, and graft rejection, or graft loss assessed were reported. Safety set included of all participants who had taken at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

From first dose of study drug up to Week 20

Notes:

[9] - 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: No statistical analysis was planned for this endpoint.

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: participants				
TEAEs of Acute or Chronic GVHD	2			
TEAEs of Graft Rejection, or Graft Loss	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Confirmed CMV Viremia Clearance

End point title	Time to First Confirmed CMV Viremia Clearance

End point description:

Time to first confirmed viremia clearance was defined as time from the start date of first dose of study treatment to the date of confirmed viremia clearance (event), or the date of last CMV DNA assessment on study before the initiation of alternative anti-CMV treatment (censored). The time to first confirmed CMV viremia clearance was calculated as date of first confirmed CMV viremia clearance – randomization date + 1). The date of first confirmed CMV viremia clearance was the date of first of two consecutive samples with plasma CMV DNA <LLOQ that meet the criteria of confirmed CMV viremia clearance. FAS included of all participants who had taken at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

From first dose of study drug up to Week 20

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: days				
median (confidence interval 95%)	22.0 (15.0 to 23.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Maintained CMV Viremia Clearance and CMV Infection Symptom Control at Week 8 Through Weeks 12, 16 and 20

End point title	Percentage of Participants Who Maintained CMV Viremia Clearance and CMV Infection Symptom Control at Week 8 Through Weeks 12, 16 and 20

End point description:

The confirmed viremia clearance was defined as a plasma CMV DNA concentration below the LLOQ (i.e., <34.5 IU/mL) when assessed by the COBAS® 8800/COBAS® CMV Test, in two consecutive post-baseline samples, separated by at least 5 days. Percentage of participants who maintained combined CMV viremia clearance and CMV infection symptom control at Week 8 Through Weeks 12, 16 and 20 were reported. FAS included of all participants who had taken at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

At Week 8 through Weeks 12, 16 and 20

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: percentage of participants				
number (confidence interval 95%)				
At Week 8	68.3 (51.9 to 81.9)			
At Week 12	34.1 (20.1 to 50.6)			
At Week 16	29.3 (16.1 to 45.5)			
At Week 20	26.8 (14.2 to 42.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Recurrence of Confirmed CMV Viremia During Follow-up Period in Participants With Confirmed Viremia Clearance at Week 8 who Required Additional Anti-CMV Treatment

End point title	Percentage of Participants With Recurrence of Confirmed CMV Viremia During Follow-up Period in Participants With Confirmed Viremia Clearance at Week 8 who Required Additional Anti-CMV Treatment

End point description:

Recurrence of confirmed CMV viremia was defined as plasma CMV DNA concentration greater than or equal to (>= 34.5 IU/mL) LLOQ when assessed by the COBAS® 8800/COBAS®CMV Test in 2 consecutive plasma samples at least 5 days apart, after achieving confirmed viremia clearance. FAS included of all participants who had taken at least 1 dose of study treatment. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Week 9 up to Week 20

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: percentage of participants				
number (not applicable)	42.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma CMV Viremia Load

End point title	Change From Baseline in Plasma CMV Viremia Load

End point description:

The change from baseline in plasma CMV viral load, i.e., plasma CMV DNA concentration was assessed and reported. FAS included of all participants who had taken at least 1 dose of study treatment. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies those participants who were evaluable for the specified timepoints.

End point type	Secondary

End point timeframe:

Baseline, Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11,12, 14, 16, 18 and 20

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: IU/mL				
arithmetic mean (standard deviation)				
Change at Week 1 (n=36)	-0.7821 (± 0.62350)			
Change at Week 2 (n=35)	-1.4813 (± 0.71540)			
Change at Week 3 (n=36)	-1.7935 (± 0.86625)			
Change at Week 4 (n=37)	-1.9555 (± 0.90538)			
Change at Week 5 (n=38)	-2.0383 (± 0.97092)			
Change at Week 6 (n=36)	-1.9922 (± 1.02593)			
Change at Week 7 (n=33)	-1.9718 (± 1.10335)			
Change at Week 8 (n=35)	-1.7971 (± 1.28349)			
Change at Week 9 (n=31)	-1.7771 (± 0.92825)			
Change at Week 10 (n=30)	-1.6819 (± 0.93517)			
Change at Week 11 (n=27)	-1.5275 (± 0.94430)			
Change at Week 12 (n=25)	-1.5383 (± 1.07532)			
Change at Week 14 (n=20)	-1.7712 (± 1.08735)			
Change at Week 16 (n=19)	-1.7042 (± 1.05775)			
Change at Week 18 (n=18)	-1.9569 (± 0.83577)			
Change at Week 20 (n=18)	-1.9734 (± 0.91902)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Recurrence of CMV Viremia During Study Treatment and in the Follow-Up Period After the Participants are Discontinued from Study Treatment and While On/Off Study Assigned Treatment

End point title	Percentage of Participants With Recurrence of CMV Viremia During Study Treatment and in the Follow-Up Period After the Participants are Discontinued from Study Treatment and While On/Off Study Assigned Treatment

End point description:

Recurrence of CMV viremia was defined as plasma CMV DNA concentration >= lower limit of quantification (LLOQ, i.e. >=34.5 IU/mL) when assessed by COBAS® 8800/COBAS® CMV Test in 2 consecutive plasma samples at least 5 days apart, after being unquantifiable (<LLOQ, i.e. <34.5 IU/mL) for at least 5 days in 2 consecutive samples during the first 8 weeks of the study. Study Treatment: The first stipulated 8 weeks treatment. Follow up period: period started after completion of stipulated 8 weeks treatment to Week 20. While on study assigned treatment: period over which participants received actual dosing regardless of stipulated 8 weeks completion (Week 8 or earlier). While off study assigned treatment: period after study treatment, regardless of stipulated 8 weeks completion (Week 8 or earlier up to Week 20). FAS included of all participants who had taken at least 1 dose of study treatment. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Study treatment: Week 0 to Week 8; Follow-up Period:Week 9 to Week 20; At Any time during study:Week 0 to Week 20; While on study assigned treatment: Week 0 to EOT(Week 8 or earlier); While off study assigned treatment: EOT (Week 8 or earlier) to Week 20

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: percentage of participants				
number (not applicable)				
Study Treatment: (Week 0 to Week 8)	13.9			
Follow-up Period: (Weeks 9-20)	44.4			
At Any Time During the Study (Weeks 0-20)	58.3			
While On Study Assigned Treatment	8.3			
While Off Study Assigned Treatment	50.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Any Mutations in the CMV Genes Conferring Resistance to Maribavir

End point title	Percentage of Participants With Any Mutations in the CMV Genes Conferring Resistance to Maribavir

End point description:

Plasma samples were obtained and tested to identify mutations in the viral UL97 and UL54 genes confer resistance to maribavir. Percentage of participants with any mutations in the CMV genes conferring

resistance to maribavir was reported. FAS included of all participants who had taken at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

From first dose of study drug up to Week 20

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: percentage of participants				
number (not applicable)	12.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved Confirmed CMV Viremia Clearance at Week 8 to be less than (<) 137 IU/mL

End point title	Percentage of Participants Who Achieved Confirmed CMV Viremia Clearance at Week 8 to be less than (<) 137 IU/mL

End point description:

The confirmed CMV viremia clearance at Week 8 was defined as plasma CMV DNA concentrations <137 IU/mL, in 2 consecutive post-baseline samples separated by at least 5 days, regardless of whether study treatment was discontinued before the end of the stipulated 8 weeks of therapy. FAS included of all participants who had taken at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

At Week 8

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: percentage of participants				
number (confidence interval 95%)	73.2 (57.1 to 85.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Plasma Concentration (Cmin) of Maribavir

End point title	Minimum Observed Plasma Concentration (Cmin) of Maribavir

End point description:

Cmin (pre-dose) of maribavir was assessed. Pharmacokinetic set included of all participants in the safety set who had plasma sample drawn and tested for maribavir concentrations. Here, "number of participants analyzed" signifies participants who were evaluable for this endpoint and "n" signifies those participants who were evaluable for the specified timepoints.

End point type	Secondary

End point timeframe:

At Weeks 1, 4, and 8: Pre-dose

End point values	Maribavir			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: micrograms per milliliter (mcg/mL)				
geometric mean (geometric coefficient of variation)				
Week 1: Pre-dose (n=36)	10.08 (± 105.73)			
Week 4: Pre-dose (n=31)	12.31 (± 108.05)			
Week 8: Pre-dose (n=29)	12.37 (± 95.26)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the first dose of study drug up to Week 20	
Adverse event reporting additional description:	
Safety set included of all participants who had taken at least 1 dose of study treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26

Reporting groups	
Reporting group title	Maribavir
Reporting group description:	
Participants received maribavir 400 mg, oral tablet, BID for up to 8 weeks.	

Serious adverse events	Maribavir		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 41 (31.71%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic myeloid leukaemia recurrent			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Transplantation complication			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			

Neutropenia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Graft versus host disease			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Melaena			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Laryngeal pain			

subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis chronic				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hyperbilirubinaemia				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Cytomegalovirus chorioretinitis				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus enterocolitis				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia legionella				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COVID-19				

subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Maribavir		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 41 (63.41%)		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	5		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	6		
Taste disorder			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		

Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 7 / 41 (17.07%) 9		
General disorders and administration site conditions Generalised oedema subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 4 / 41 (9.76%) 4 3 / 41 (7.32%) 3 6 / 41 (14.63%) 6		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	 10 / 41 (24.39%) 10		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 4 / 41 (9.76%) 4		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 4 / 41 (9.76%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2021	-Standardized the deadline for reporting SAE to the sponsor/emergency reception center for safety information (ERCSI) to "within 24 hours of first awareness of the event."- Added cidofovir as currently available systemic anti-CMV agents outside Japan.- Deleted a sentence regarding dose proportionality.- Changed the description of concurrent administration with Cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) inducers, focusing on rifampin and maribavir interaction.- Modified the wording of efficacy endpoints and inclusion criteria for clarity and specificity.- Unified the terminology from "beta-human chorionic gonadotropin (β-hCG)" to "human chorionic gonadotropin (hCG)."- Adjusted secondary objectives and endpoints related to CMV infections and resistance.- Modified HIV testing to be available at both local and central laboratories.- Specified the dose of maribavir per dose.- Updated Table 6 "Common Excluded Treatments and Associated Washout Period" and its footnotes.- Revised descriptions of prohibited concomitant medications and treatments to align with changes in Table 6.- Added "CMV history" as an item to be collected at the Screening Visit.- Revised the description of screen failure and eligibility criteria. - Modified CMV genotyping procedures and frequency.- Clarified the terminology related to CMV recurrence and rebound.- Aligned efficacy endpoints with the protocol of Study SHP620-302.- Changed "exploratory" to "secondary" in describing certain analyses.- Added Baseline safety analyses definition.- Included a list of CMV mutations known to confer resistance to valganciclovir and other anti-CMV agents as Appendix 6.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported