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Protocol Registration and Results System

ID: 1263-301 Maribavir Versus Oral Ganciclovir For The Prevention of Cytomegalovirus (CMV) Disease in Liver Transplant Recipients NCT00497796

Results Preview

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Participant Flow

Recruitment Details	
Pre-Assignment Details	

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID	Total (Not public)
Arm/Group Description	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.	
Period Title: **Overall Study**			
Started	147	160	307
Completed	62	101	163
Not Completed	85	59	144
Reason Not Completed			
Adverse event (not related)	9	9	18
Adverse event (related)	5	4	9
CMV infection or disease treatment	30	4	34
Consent withdrawn	10	3	13
Investigator/sponsor discretion	31	34	65
Lost to Follow-up	0	1	1
Not applicable (randomized not treated)	0	4	4
(Not Public)	Not Completed = 85 Total from all reasons = 85	Not Completed = 59 Total from all reasons = 59	

Baseline Characteristics

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID	Total
Arm/Group Description	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.	
Overall Number of Baseline	147	156	**303**

Participants			
▼ Baseline Analysis Population Description	The Intent-to-Treat Safety (ITT-S) population, defined as all randomized subjects who received at least one dose of study drug, regardless of whether they had any post-baseline evaluations.		
Age, Continuous Mean (Standard Deviation) Units: years	55 (9.0)	53 (8.9)	54 (9.0)
Gender, Male/Female Measure Type: Number Units: participants			
Female	27	37	64
Male	120	119	239
Distribution of age Measure Type: Number Units: participants			
18 to 44 years	19	22	41
45 to 64 years	109	123	232
65 to 75 years	19	11	30

Outcome Measures

1. Primary Outcome

Title:	Number of Participants With Endpoint Committee (EC)-Confirmed Cytomegalovirus (CMV) Disease Within 6 Months Post-Transplantation
▼ Description:	All investigator-determined (protocol-defined) cases of CMV disease (i.e., symptomatic CMV infection or CMV organ disease), were adjudicated by an independent, blinded EC. Symptomatic CMV infection was defined as: CMV infection detected by a positive result from a CMV laboratory assay from at least one central laboratory assay (pp65 antigenemia or CMV DNA polymerase chain reaction [PCR] assay in plasma) and fever >/=38 °C on >/=2 occasions >/=24 hours apart within a 7-day period and at least one of the following: new or increased malaise, two successive measurements of leucopenia (white blood cell [WBC] count <3500/mm3 or a WBC count decrease of 20% if the cell count prior to onset of clinical symptoms was >4000/mm3) >/=24 hours apart, atypical lymphocytosis >/=5%, and thrombocytopenia. CMV organ disease was defined as described by Ljungman et al., 2002.
Time Frame:	6 months post-transplant
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

The modified Intent-to-Treat (ITT-M) population, defined as all randomized subjects who received at least one dose of study drug and had participated in the study for at least 14 weeks or had the potential to receive 14 weeks of therapy by 12-Feb-2009.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants Analyzed	113	120
Measure Type: Number Units: number of participants with event	14	10

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Based on the ICH guidance, the hypothesis of non-inferiority can be tested using a one-sided 97.5% confidence interval's (CI) upper bound comparing with the non-

		inferiority margin of 5% (0.05).
Method of Estimation	Estimation Parameter	Other[Rate difference]
	Estimated Value	0.041
	Confidence Interval	(2-Sided) 95% -0.038 to 0.119
	Estimation Comments	Rate difference is the rate of maribavir minus the rate of ganciclovir

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2754
	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.586
	Confidence Interval	(2-Sided) 95% 0.682 to 3.690
	Estimation Comments	[Not specified]

2. Secondary Outcome

Title:	Number of Participants With CMV Infection or EC-confirmed CMV Disease Within 6 Months Post-Transplantation
▼ Description:	Incidence of CMV infection or EC-confirmed CMV disease within the 6-month post-transplant period included in this section were defined (1) with infection assessed by pp65 antigenemia assay; (2) with infection assessed by CMV DNA PCR; (3) with infection assessed by either assay (pp65 antigenemia or CMV

	DNA PCR); and (4) with infection assessed by initiation of anti-CMV therapy.
Time Frame:	6 months post-transplant
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

The ITT-M population, defined as all randomized subjects who received at least one dose of study drug and had participated in the study for at least 14 weeks or had the potential to receive 14 weeks of therapy by 12-Feb-2009.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants Analyzed	113	120
Measure Type: Number Units: participants		
pp65 antigenemia assay	63	49
CMV DNA PCR assay	72	52
pp65 antigenemia or CMV DNA PCR assay	81	64
Initiation of anti-CMV therapy	46	39

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	Analysis of the pp65 antigenemia assay
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	0.0283
	Comments	The p-value is from the Cochran-

Hypothesis		Mantel-Haenszel test, adjusting for receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.793
	Confidence Interval	(2-Sided) 95% 1.065 to 3.020
	Estimation Comments	Mantel-Haenszel odds ratio for maribavir versus ganciclovir

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	Analysis of CMV DNA PCR assay
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0024
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for receipt of induction ALA and geographic region (US or Europe).
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	2.284
	Confidence Interval	(2-Sided) 95% 1.338 to 3.900
	Estimation Comments	Mantel-Haenszel odds ratio for maribavir versus ganciclovir

▼ Statistical Analysis 3 ✔

Statistical	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000

Analysis Overview		mg TID
	Comments	Analysis of pp65 antigenemia or CMV DNA PCR assay
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0053
	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	2.177
	Confidence Interval	(2-Sided) 95% 1.259 to 3.767
	Estimation Comments	Mantel-Haenszel odds ratio for maribavir versus ganciclovir

▼ Statistical Analysis 4 ✓

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	Analysis of initiation of anti-CMV therapy
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.2339
	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.388
	Confidence Interval	(2-Sided) 95% 0.811 to 2.377
	Estimation Comments	Mantel-Haenszel odds ratio for maribavir versus ganciclovir

3. Secondary Outcome

Title:	Time to Onset of CMV Infection or EC-confirmed CMV Disease Within 6 Months Post-Transplantation
▼ Description:	All investigator-determined (protocol-defined) cases of CMV disease (i.e., symptomatic CMV infection or CMV organ disease) were adjudicated by an independent, blinded EC. CMV infection was assessed by pp65 Antigenemia or CMV DNA PCR from a central or local lab. CMV organ disease was defined as described by Ljungman et al., 2002.
Time Frame:	6 months post-transplant
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description

The ITT-M population, defined as all randomized subjects who received at least one dose of study drug and had participated in the study for at least 14 weeks or had the potential to receive 14 weeks of therapy by 12-Feb-2009.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants Analyzed	113	120
Median (Inter-Quartile Range) Units: days	45 (41 to 68)	127 (125 to 161)

▼ Statistical Analysis 1 

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	Analysis of time to onset
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other[Adjusted Hazard Ratio]
	Estimated Value	2.25
	Confidence Interval	(2-Sided) 95% 1.62 to 3.14
	Estimation Comments	Maribavir versus ganciclovir; Cox's proportional hazards regression model: time = receipt of induction ALA and geographic region (US or Europe) + treatment.

4. Secondary Outcome

Title:	Number of Participants With Investigator-determined CMV Disease
▼ Description:	Symptomatic CMV infection was defined as: CMV infection detected by a positive result from a CMV laboratory assay from at least one central laboratory assay (pp65 antigenemia or CMV DNA polymerase chain reaction [PCR] assay in plasma) and fever >/=38 °C on >/=2 occasions >/=24 hours apart within a 7-day period and at least one of the following: new or increased malaise, two successive measurements of leucopenia (white blood cell [WBC] count <3500/mm3 or a WBC count decrease of 20% if the cell count prior to onset of clinical symptoms was >4000/mm3) >/=24 hours apart, atypical lymphocytosis >/=5%, and thrombocytopenia. CMV organ disease was defined as described by Ljungman et al., 2002.
Time Frame:	Through 6 months post-transplant (Day 1 to 100 days and 6 months post-transplant)
Safety Issue?	No

▼ Outcome Measure Data

▼ Analysis Population Description

The ITT-M population, defined as all randomized subjects who received at least one dose of study drug and had participated in the study for at least 14 weeks or had the potential to receive 14 weeks of therapy by 12-Feb-2009.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants	113	120

Analyzed		
Measure Type: Number Units: participants		
100 days post-transplant	17	3
6 months post-transplant	22	18

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	Analysis of 100 days post-transplant
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of	P-Value	0.0008

Hypothesis	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	Analysis of 6 months post-transplant
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.3742
	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

5. Secondary Outcome

Title:	Number of Participants With EC-confirmed CMV Disease Within 100 Days Post-Transplantation
▼ Description:	All investigator-determined (protocol-defined) cases of CMV disease (i.e., symptomatic CMV infection or CMV organ disease), were adjudicated by an independent, blinded EC. Symptomatic CMV infection was defined as: CMV infection detected by a positive result from a CMV laboratory assay from at least one central laboratory assay (pp65 antigenemia or CMV DNA polymerase chain reaction [PCR] assay in plasma) and fever >/=38 °C on >/=2 occasions >/=24 hours apart within a 7-day period and at least one of the following: new or increased malaise, two successive measurements of leucopenia (white blood cell [WBC] count <3500/mm3 or a WBC count decrease of 20% if the cell count prior to onset of clinical symptoms was >4000/mm3) >/=24 hours apart, atypical lymphocytosis >/=5%, and thrombocytopenia. CMV organ disease was defined as described by Ljungman et al., 2002.
Time Frame:	100 days post-transplant
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

The ITT-M population, defined as all randomized subjects who received at least one dose of study drug and had participated in the study for at least 14 weeks or had the potential to receive 14 weeks of therapy by 12-Feb-2009.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants Analyzed	113	120
Measure Type: Number Units: participants	10	0

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0007
	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for

		receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

6. Secondary Outcome

Title:	Number of Participants With CMV Infection or EC-confirmed CMV Disease Within 100 Days Post-Transplantation
▼ Description:	Incidence of CMV infection or EC-confirmed CMV disease within the 6-month post-transplant period included in this section were defined (1) with infection assessed by pp65 antigenemia assay; (2) with infection assessed by CMV DNA PCR; (3) with infection assessed by either assay (pp65 antigenemia or CMV DNA PCR); and (4) with infection assessed by initiation of anti-CMV therapy.
Time Frame:	100 days post-transplant
Safety Issue?	No

▼ Outcome Measure Data 

▼ Analysis Population Description

The ITT-M population, defined as all randomized subjects who received at least one dose of study drug and had participated in the study for at least 14 weeks or had the potential to receive 14 weeks of therapy by 12-Feb-2009.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants Analyzed	113	120
Measure Type: Number Units: participants		
pp65 antigenemia assay	49	19
CMV DNA PCR assay	59	18
pp65 antigenemia or CMV DNA PCR assay	68	24
Initiation of anti-CMV therapy	37	5

▼ Statistical Analysis 1 

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	Analysis of pp65 antigenemia assay

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	4.041
	Confidence Interval	(2-Sided) 95% 2.179 to 7.494
	Estimation Comments	Mantel-Haenszel odds ratio for maribavir versus ganciclovir

▼ Statistical Analysis 2

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	Analysis of CMV DNA PCR assay
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	6.448
	Confidence Interval	(2-Sided) 95% 3.404 to 12.213

	Estimation Comments	Mantel-Haenszel odds ratio for maribavir versus ganciclovir

▼ Statistical Analysis 3 ✓

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	Analysis of pp65 antigenemia or CMV DNA PCR assay
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	6.020
	Confidence Interval	(2-Sided) 95% 3.342 to 10.843
	Estimation Comments	Mantel-Haenszel odds ratio for maribavir versus ganciclovir

▼ Statistical Analysis 4 ✓

Statistical Analysis Overview	Comparison Groups	Maribavir 100 mg BID, Ganciclovir 1000 mg TID
	Comments	Analysis of initiation of anti-CMV therapy
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	The p-value is from the Cochran-Mantel-Haenszel test, adjusting for

		receipt of induction ALA and geographic region (US or Europe).
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	11.165
	Confidence Interval	(2-Sided) 95% 4.146 to 30.069
	Estimation Comments	Mantel-Haenszel odds ratio for maribavir versus ganciclovir

7. Secondary Outcome

Title:	Number of Participants With Retransplantation
▼ Description:	[Not specified]
Time Frame:	Through 6 months post-transplant (From Day 1 to 100 days and 6 months post-transplant)
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

The ITT-Safety (ITT-S) population, defined as all participants who received at least one dose of study drug.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants Analyzed	147	156
Measure Type: Number Units: participants		
At 100 days post-transplant	1	2
At 6 months post-transplant	2	2

8. Secondary Outcome

Title:	Number of Participants With Graft Failure Related Death
▼	[Not specified]

Description:	
Time Frame:	Through 6 months post-transplant (From Day 1 to 100 days and 6 months post-transplant)
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

The ITT-S population, defined as all participants who received at least one dose of study drug.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants Analyzed	147	156
Measure Type: Number Units: participants		
100 days post-transplant	0	2
6 months post-transplant	1	2

9. Secondary Outcome

Title:	Number of Participants With Acute Graft Rejection
▼ Description:	Rejection was assessed by examining a liver biopsy sample. Diagnosis of graft rejection included a global assessment grade and a rejection activity index score.
Time Frame:	26 weeks post-transplant
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

The ITT-S population, defined as all participants who received at least one dose of study drug.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants Analyzed	147	156
Measure Type: Number Units: participants		

100 days post-transplant	16	19
6 months post-transplant	20	23

10. Secondary Outcome

Title:	Number of Participants Who Died Within 6 Months Post-Transplantation
▼ Description:	[Not specified]
Time Frame:	6 months post-transplant
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

The ITT-S population, defined as all participants who received at least one dose of study drug.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants Analyzed	147	156
Measure Type: Number Units: participants	9	6

11. Secondary Outcome

Title:	Percent of Participants With Signs of Bone Marrow Suppression
▼ Description:	Bone marrow suppression was assessed by the occurrence of adverse events (AEs) of investigator-reported leukopenia, neutropenia, thrombocytopenia, and pancytopenia; absolute neutrophil count (ANC) <1000/mm3; white blood cell (WBC) count toxicity grade shifts from 0-2 at baseline to a maximum of 3-4 post-baseline; and use of hematopoietic growth factors during the 6 month post-transplant period.
Time Frame:	15 weeks
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

The ITT-S population, defined as all participants who received at least one dose of study drug.

Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.
Number of Participants Analyzed	147	156
Measure Type: Number Units: percent of participants		
Hematology AEs	14	21
ANC <1000/mm3	9	16
WBC count toxicity grade shifts	16	21
Use of hematopoietic growth factors	15	20

12. Secondary Outcome

Title:	Plasma Concentration of Maribavir During Treatment
▼ Description:	For the first 16 subjects to have PK profiling performed, PK sampling was collected at Weeks 2, 6 and 10. For subsequent subjects that have PK profiling performed, PK sampling was collected at Weeks 2 and 6. Samples were collected 12 hours after the morning dose of maribavir. Permissible assessment windows for pharmacokinetic profile sampling purposes were +/- 5 days for each sampling day. Samples for determination of maribavir concentration were analyzed by a validated liquid chromatography tandem mass spectrometry (LC/MS/MS) method. For plasma, the minimum detectable concentration for maribavir was 0.2 µg/mL.
Time Frame:	12 hours post-dose after 2, 6, and 10 weeks of treatment
Safety Issue?	No

▼ Outcome Measure Data ✔

▼ Analysis Population Description

The Pharmacokinetic (PK) population, defined as those participants in the ITT-S population from whom plasma samples were drawn, tested for maribavir concentrations, and complete, evaluable PK data were available.

Arm/Group Title	Maribavir 100 mg BID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.
Number of Participants Analyzed	11
Mean (Standard Deviation) Units: µg/mL	
2 weeks, n=10	1.65 (2.01)
6 weeks, n=7	1.36 (1.25)
10 weeks, n=8	1.55 (1.17)

13. Secondary Outcome

Title:	Plasma Concentration of Maribavir Metabolite VP 44469 During Treatment
▼ Description:	For the first 16 subjects to have PK profiling performed, PK sampling was collected at Weeks 2, 6 and 10. For subsequent subjects that have PK profiling performed, PK sampling was collected at Weeks 2 and 6. Samples were collected 12 hours after the morning dose of maribavir. Permissible assessment windows for pharmacokinetic profile sampling purposes were +/- 5 days for each sampling day. Samples for determination of VP 44469 (a metabolite of maribavir) concentration were analyzed by a validated liquid chromatography tandem mass spectrometry (LC/MS/MS) method. For plasma, the minimum detectable concentration for VP 44469 was 0.2 µg/mL.
Time Frame:	12 hours post-dose after 2, 6, and 10 weeks of treatment
Safety Issue?	No

▼ Outcome Measure Data ✓

▼ Analysis Population Description

The PK population, defined as those participants in the ITT-S population from whom plasma samples were drawn, tested for maribavir concentrations, and complete, evaluable PK data were available.

Arm/Group Title	Maribavir 100 mg BID
▼ Arm/Group Description:	Maribavir: 100mg twice a day (BID) for 14 weeks.
Number of Participants Analyzed	11
Mean (Standard Deviation) Units: µg/mL	
2 weeks, n=10	0.609 (0.648)
6 weeks, n=7	0.506 (0.224)
10 weeks, n=8	0.666 (0.656)

Adverse Events

Time Frame		
Additional Description		
Source Vocabulary Name	MedDRA Version 10.0	
Assessment Type	Systematic Assessment	
Arm/Group Title	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
▼ Arm/Group Description	Maribavir: 100mg twice a day (BID) for 14 weeks.	Ganciclovir: 1000mg three times per (TID) day for 14 weeks.

Serious Adverse Events

	Maribavir 100 mg BID	Ganciclovir 1000 mg TID
	Affected / at Risk (%)	Affected / at Risk (%)
Total	71/147 (48.3%)	76/156 (48.72%)
Blood and lymphatic system disorders		
Anaemia † A	1/147 (0.68%)	4/156 (2.56%)
Haemolytic Anaemia † A	1/147 (0.68%)	1/156 (0.64%)
Leukocytosis † A	1/147 (0.68%)	0/156 (0%)
Leukopenia † A	0/147 (0%)	1/156 (0.64%)
Neutropenia † A	0/147 (0%)	1/156 (0.64%)
Splenomegaly † A	0/147 (0%)	1/156 (0.64%)
Thrombocytopenia † A	0/147 (0%)	1/156 (0.64%)
Cardiac disorders		
Atrial Fibrillation † A	0/147 (0%)	1/156 (0.64%)
Bradycardia † A	0/147 (0%)	1/156 (0.64%)
Cardiac Failure † A	1/147 (0.68%)	0/156 (0%)
Myocardial Infarction † A	1/147 (0.68%)	2/156 (1.28%)
Supraventricular Extrasystoles † A	1/147 (0.68%)	0/156 (0%)
Endocrine disorders		
Diabetes Mellitus † A	2/147 (1.36%)	0/156 (0%)
Eye disorders		
Cataract † A	1/147 (0.68%)	0/156 (0%)
Ulcerative Keratitis † A	1/147 (0.68%)	0/156 (0%)
Gastrointestinal disorders		
Abdominal Abscess † A	1/147 (0.68%)	1/156 (0.64%)
Abdominal Pain † A	1/147 (0.68%)	2/156 (1.28%)
Abdominal Pain Upper † A	0/147 (0%)	1/156 (0.64%)
Abdominal Strangulated Hernia † A	0/147 (0%)	1/156 (0.64%)
Clostridium Difficile Colitis † A	3/147 (2.04%)	3/156 (1.92%)
Colitis Ulcerative † A	0/147 (0%)	1/156 (0.64%)
Constipation † A	1/147 (0.68%)	0/156 (0%)
Diarrhoea † A	2/147 (1.36%)	4/156 (2.56%)
Diverticulitis † A	1/147 (0.68%)	0/156 (0%)
Fungal Peritonitis † A	0/147 (0%)	1/156 (0.64%)
Gastroenteritis † A	0/147 (0%)	2/156 (1.28%)
Ileus † A	1/147 (0.68%)	0/156 (0%)
Inguinal Hernia † A	0/147 (0%)	3/156 (1.92%)
Intra-Abdominal Haemorrhage † A	1/147 (0.68%)	0/156 (0%)
† A		

Nausea	1/147 (0.68%)	2/156 (1.28%)
Obstruction Gastric † A	1/147 (0.68%)	0/156 (0%)
Oesophageal Candidiasis † A	1/147 (0.68%)	0/156 (0%)
Oesophagitis † A	0/147 (0%)	1/156 (0.64%)
Pancreatitis † A	0/147 (0%)	2/156 (1.28%)
Peritonitis † A	1/147 (0.68%)	2/156 (1.28%)
Umbilical Hernia † A	2/147 (1.36%)	1/156 (0.64%)
Vomiting † A	1/147 (0.68%)	3/156 (1.92%)
General disorders		
Asthenia † A	0/147 (0%)	1/156 (0.64%)
Non-Cardiac Chest Pain † A	1/147 (0.68%)	0/156 (0%)
Oedema † A	1/147 (0.68%)	0/156 (0%)
Oedema Peripheral † A	2/147 (1.36%)	0/156 (0%)
Pyrexia † A	4/147 (2.72%)	7/156 (4.49%)
Hepatobiliary disorders		
Alcoholic Liver Disease † A	1/147 (0.68%)	0/156 (0%)
Ascites † A	3/147 (2.04%)	4/156 (2.56%)
Bile Duct Obstruction † A	0/147 (0%)	1/156 (0.64%)
Bile Duct Stenosis † A	4/147 (2.72%)	2/156 (1.28%)
Cholangitis † A	3/147 (2.04%)	2/156 (1.28%)
Cholestasis † A	3/147 (2.04%)	0/156 (0%)
Cytolytic Hepatitis † A	0/147 (0%)	1/156 (0.64%)
Hepatic Artery Aneurysm † A	0/147 (0%)	2/156 (1.28%)
Hepatic Artery Occlusion † A	0/147 (0%)	2/156 (1.28%)
Hepatic Artery Stenosis † A	1/147 (0.68%)	0/156 (0%)
Hepatic Artery Thrombosis † A	1/147 (0.68%)	3/156 (1.92%)
Hepatic Haematoma † A	1/147 (0.68%)	0/156 (0%)
Hepatic Necrosis † A	0/147 (0%)	1/156 (0.64%)
Hepatic Steatosis † A	0/147 (0%)	1/156 (0.64%)
Hepatitis C † A	2/147 (1.36%)	3/156 (1.92%)
Liver Abscess † A	1/147 (0.68%)	1/156 (0.64%)
Portal Hypertension † A	0/147 (0%)	1/156 (0.64%)
Post Procedural Bile Leak † A	4/147 (2.72%)	2/156 (1.28%)
Immune system disorders		
Acute Graft Versus Host Disease † A	1/147 (0.68%)	1/156 (0.64%)
Hypersensitivity † A	1/147 (0.68%)	0/156 (0%)
Liver Transplant Rejection † A	4/147 (2.72%)	12/156 (7.69%)
Infections and infestations		
Abdominal Sepsis † A	0/147 (0%)	1/156 (0.64%)
Bacterial Sepsis † A	0/147 (0%)	1/156 (0.64%)
Cytomegalovirus	2/147 (1.36%)	1/156 (0.64%)

Gastroenteritis † A		
Cytomegalovirus Hepatitis † A	2/147 (1.36%)	0/156 (0%)
Cytomegalovirus Infection † A	12/147 (8.16%)	2/156 (1.28%)
Pneumonia Cytomegaloviral † A	2/147 (1.36%)	0/156 (0%)
Sepsis † A	1/147 (0.68%)	2/156 (1.28%)
Injury, poisoning and procedural complications		
Complications Of Transplanted Liver † A	1/147 (0.68%)	0/156 (0%)
Fall † A	0/147 (0%)	1/156 (0.64%)
Incision Site Cellulitis † A	0/147 (0%)	1/156 (0.64%)
Incision Site Pain † A	0/147 (0%)	1/156 (0.64%)
Incisional Hernia † A	1/147 (0.68%)	0/156 (0%)
Post Procedural Haemorrhage † A	1/147 (0.68%)	0/156 (0%)
Postoperative Wound Infection † A	0/147 (0%)	1/156 (0.64%)
Therapeutic Agent Toxicity † A	0/147 (0%)	1/156 (0.64%)
Wound Dehiscence † A	0/147 (0%)	1/156 (0.64%)
Wound Infection † A	3/147 (2.04%)	3/156 (1.92%)
Wound Secretion † A	1/147 (0.68%)	1/156 (0.64%)
Investigations		
Band Neutrophil Count Increased † A	0/147 (0%)	1/156 (0.64%)
Biopsy Liver Abnormal † A	1/147 (0.68%)	0/156 (0%)
Blood Bilirubin Increased † A	1/147 (0.68%)	1/156 (0.64%)
Blood Creatinine Increased † A	0/147 (0%)	1/156 (0.64%)
Hepatic Enzyme Increased † A	8/147 (5.44%)	4/156 (2.56%)
International Normalised Ratio Increased † A	0/147 (0%)	1/156 (0.64%)
Metabolism and nutrition disorders		
Dehydration † A	2/147 (1.36%)	1/156 (0.64%)
Hyperglycaemia † A	1/147 (0.68%)	0/156 (0%)
Hyperkalaemia † A	1/147 (0.68%)	3/156 (1.92%)
Hypocalcaemia † A	0/147 (0%)	1/156 (0.64%)
Hypoglycaemia † A	0/147 (0%)	1/156 (0.64%)
Hypomagnesaemia † A	1/147 (0.68%)	0/156 (0%)
Hyponatraemia † A	0/147 (0%)	1/156 (0.64%)
Hypovolaemia † A	0/147 (0%)	1/156 (0.64%)
Musculoskeletal and connective tissue disorders		
Arthritis Fungal † A	0/147 (0%)	1/156 (0.64%)

Femoral Neck Fracture † A	1/147 (0.68%)	0/156 (0%)
Musculoskeletal Chest Pain † A	0/147 (0%)	1/156 (0.64%)
Nervous system disorders		
Cerebral Haemorrhage † A	1/147 (0.68%)	0/156 (0%)
Convulsion † A	1/147 (0.68%)	1/156 (0.64%)
Dizziness † A	0/147 (0%)	1/156 (0.64%)
Haemorrhage Intracranial † A	1/147 (0.68%)	0/156 (0%)
Hypoglycaemic Seizure † A	0/147 (0%)	1/156 (0.64%)
Psychiatric disorders		
Adjustment Disorder † A	1/147 (0.68%)	0/156 (0%)
Bipolar Disorder † A	1/147 (0.68%)	0/156 (0%)
Confusional State † A	0/147 (0%)	1/156 (0.64%)
Delirium † A	0/147 (0%)	2/156 (1.28%)
Mental Status Changes † A	1/147 (0.68%)	0/156 (0%)
Psychotic Disorder † A	1/147 (0.68%)	1/156 (0.64%)
Renal and urinary disorders		
Mesangioproliferative Glomerulonephritis † A	1/147 (0.68%)	0/156 (0%)
Nephritis Interstitial † A	0/147 (0%)	1/156 (0.64%)
Nephrolithiasis † A	1/147 (0.68%)	0/156 (0%)
Renal Failure † A	4/147 (2.72%)	3/156 (1.92%)
Urinary Tract Infection † A	1/147 (0.68%)	1/156 (0.64%)
Respiratory, thoracic and mediastinal disorders		
Dyspnoea † A	0/147 (0%)	1/156 (0.64%)
Lung Neoplasm Malignant † A	0/147 (0%)	1/156 (0.64%)
Pleural Effusion † A	2/147 (1.36%)	3/156 (1.92%)
Pleural Infection † A	1/147 (0.68%)	0/156 (0%)
Pleuritic Pain † A	0/147 (0%)	1/156 (0.64%)
Pneumonia † A	2/147 (1.36%)	1/156 (0.64%)
Pneumonia Staphylococcal † A	1/147 (0.68%)	0/156 (0%)
Pulmonary Oedema † A	0/147 (0%)	1/156 (0.64%)
Respiratory Arrest † A	1/147 (0.68%)	0/156 (0%)
Respiratory Distress † A	2/147 (1.36%)	0/156 (0%)
Respiratory Failure † A	1/147 (0.68%)	0/156 (0%)
Respiratory Syncytial Virus Infection † A	0/147 (0%)	1/156 (0.64%)
Upper Respiratory Tract Infection † A	1/147 (0.68%)	0/156 (0%)
Skin and subcutaneous tissue disorders		
Cellulitis † A	1/147 (0.68%)	2/156 (1.28%)

Rash † A	1/147 (0.68%)	0/156 (0%)
Vascular disorders		
Arterial Haemorrhage † A	0/147 (0%)	1/156 (0.64%)
Deep Vein Thrombosis † A	1/147 (0.68%)	0/156 (0%)
Hypotension † A	1/147 (0.68%)	0/156 (0%)
Syncope † A	0/147 (0%)	1/156 (0.64%)
Thrombophlebitis † A	1/147 (0.68%)	0/156 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA Version 10.0

▼ Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%	
	Maribavir 100 mg BID	**Ganciclovir 1000 mg TID**
	Affected / at Risk (%)	Affected / at Risk (%)
Total	127/147 (86.39%)	140/156 (89.74%)
Blood and lymphatic system disorders		
Anaemia † A	9/147 (6.12%)	13/156 (8.33%)
Leukocytosis † A	8/147 (5.44%)	5/156 (3.21%)
Leukopenia † A	12/147 (8.16%)	19/156 (12.18%)
Neutropenia † A	8/147 (5.44%)	10/156 (6.41%)
Gastrointestinal disorders		
Abdominal Distension † A	0/147 (0%)	8/156 (5.13%)
Abdominal Pain † A	12/147 (8.16%)	15/156 (9.62%)
Abdominal Pain Upper † A	7/147 (4.76%)	8/156 (5.13%)
Constipation † A	9/147 (6.12%)	11/156 (7.05%)
Diarrhoea † A	41/147 (27.89%)	36/156 (23.08%)
Dysgeusia † A	22/147 (14.97%)	20/156 (12.82%)
Nausea † A	14/147 (9.52%)	28/156 (17.95%)
Vomiting † A	14/147 (9.52%)	15/156 (9.62%)
General disorders		
Asthenia † A	1/147 (0.68%)	8/156 (5.13%)
Fatigue † A	10/147 (6.8%)	18/156 (11.54%)
Oedema Peripheral † A	19/147 (12.93%)	15/156 (9.62%)
Pyrexia † A	15/147 (10.2%)	13/156 (8.33%)
Hepatobiliary disorders		
Ascites † A	9/147 (6.12%)	7/156 (4.49%)
Bile Duct Stenosis † A	9/147 (6.12%)	9/156 (5.77%)
Hepatitis C † A	14/147 (9.52%)	7/156 (4.49%)
Immune system disorders		

Liver Transplant Rejection † A	11/147 (7.48%)	8/156 (5.13%)
Investigations		
Hepatic Enzyme Increased † A	16/147 (10.88%)	13/156 (8.33%)
Metabolism and nutrition disorders		
Decreased Appetite † A	14/147 (9.52%)	6/156 (3.85%)
Hyperkalaemia † A	19/147 (12.93%)	21/156 (13.46%)
Hypokalaemia † A	8/147 (5.44%)	4/156 (2.56%)
Hypomagnesaemia † A	14/147 (9.52%)	12/156 (7.69%)
Musculoskeletal and connective tissue disorders		
Arthralgia † A	4/147 (2.72%)	8/156 (5.13%)
Back Pain † A	13/147 (8.84%)	11/156 (7.05%)
Muscle Spasms † A	3/147 (2.04%)	8/156 (5.13%)
Nervous system disorders		
Dizziness † A	3/147 (2.04%)	12/156 (7.69%)
Headache † A	20/147 (13.61%)	29/156 (18.59%)
Insomnia † A	13/147 (8.84%)	17/156 (10.9%)
Tremor † A	25/147 (17.01%)	20/156 (12.82%)
Psychiatric disorders		
Anxiety † A	11/147 (7.48%)	4/156 (2.56%)
Renal and urinary disorders		
Renal Failure † A	12/147 (8.16%)	11/156 (7.05%)
Urinary Tract Infection † A	22/147 (14.97%)	11/156 (7.05%)
Respiratory, thoracic and mediastinal disorders		
Dyspnoea † A	5/147 (3.4%)	9/156 (5.77%)
Pleural Effusion † A	9/147 (6.12%)	7/156 (4.49%)
Skin and subcutaneous tissue disorders		
Pruritus † A	9/147 (6.12%)	12/156 (7.69%)
Rash † A	8/147 (5.44%)	7/156 (4.49%)
Vascular disorders		
Hypertension † A	18/147 (12.24%)	21/156 (13.46%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA Version 10.0

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

If a multicenter publication is not submitted within twelve (12) months after conclusion, abandonment or termination of the Study at all sites, or after Sponsor confirms there shall be no multicenter Study publication, the Institution and/or such Principal Investigator may publish the results from the Institution site individually.

Results Point of Contact

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