Clinical trial results:
Randomized Multicenter Trial Comparing Valganciclovir CMV Prophylaxis Versus Pre-emptive Therapy after Renal Transplantation Using Proteomics for Monitoring of Graft Alteration

Summary

EudraCT number	2005-004695-20
Trial protocol	DE AT
Global end of trial date	26 October 2015

Results information

Result version number	v1 (current)
This version publication date	22 April 2017
First version publication date	22 April 2017

Trial information

Trial identification

Sponsor protocol code	ML19313

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00372229
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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	26 October 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 October 2015
Global end of trial reached?	Yes
Global end of trial date	26 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the incidence of cytomegalovirus (CMV) disease and corresponding renal graft alteration.

Protection of trial subjects:

All study subjects were required to read and sign an informed consent form.

Background therapy:

Subjects received immunosuppression with a calcineurin inhibitor (CNI; (cyclosporine A or tacrolimus), mycophenolate mofetil (MMF) and steroids, with dosing according to study center practice.

Evidence for comparator: -

Actual start date of recruitment	31 May 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	7 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 23
Country: Number of subjects enrolled	Germany: 276
Worldwide total number of subjects	299
EEA total number of subjects	299

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)	234
From 65 to 84 years	65

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

342 subjects were screened, and 43 subjects were not randomized. Central randomization stratified by study center and by induction immunosuppression with polyclonal antibodies, such as such as anti-thymocyte globuline (ATG), anti-lymphocyte globulin (ALG), or Muromonab-CD3 was performed.

Period 1

Period 1 title	Study Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Valganciclovir CMV Prophylaxis

Arm description:

900 mg valganciclovir, taken orally once daily, adjusted to renal function starting within 14 days of transplantation until Day 100 after transplantation.

Arm type	Experimental
Investigational medicinal product name	Valganciclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

900 mg valganciclovir, taken orally once daily, adjusted to renal function starting within 14 days of transplantation until Day 100 after transplantation.

Arm title	Pre-emptive CMV Therapy

Arm description:

If plasma polymerase chain reaction (PCR) ≥ 400 CMV copies/millilitre, then 1800 mg valganciclovir per day adjusted to renal function for at least 14 days until the second negative PCR (below 400 copies/ml) followed by secondary prophylaxis for 28 days with 900 mg valganciclovir adjusted to renal function. If CMV disease or no response to valganciclovir treatment after 14 days (not falling viral load), then intravenous (IV) ganciclovir or additional appropriate therapy could have been administered according to the local site’s standard, instead of valganciclovir.

Arm type	Experimental
Investigational medicinal product name	Valganciclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

If plasma polymerase chain reaction (PCR) ≥ 400 CMV copies/millilitre, then 1800 mg valganciclovir per day adjusted to renal function for at least 14 days until the second negative PCR (below 400 copies/ml) followed by secondary prophylaxis for 28 days with 900 mg valganciclovir adjusted to renal function.

Investigational medicinal product name	Ganciclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

If CMV disease or no response to valganciclovir treatment after 14 days (not falling viral load), then intravenous (IV) ganciclovir or additional appropriate therapy could have been administered according to the local site's standard, instead of valganciclovir.

Number of subjects in period 1	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy
Started	148	151
Completed	117	122
Not completed	31	29
Graft loss	-	3
Protocol voilation	3	4
Subject died	3	2
Refused treatment/did not cooperate	3	1
Lost to follow-up	3	3
Reason not specified	3	2
Consent withdrawn	16	14

Period 2

Period 2 title	Follow-Up Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Valganciclovir CMV Prophylaxis (Follow-Up)

Arm description:

900 mg valganciclovir, taken orally once daily, adjusted to renal function starting within 14 days of transplantation until Day 100 after transplantation.

Arm type	Experimental
Investigational medicinal product name	Valganciclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

900 mg valganciclovir, taken orally once daily, adjusted to renal function starting within 14 days of transplantation until Day 100 after transplantation.

Arm title	Pre-emptive CMV Therapy (Follow-Up)

Arm description:

If plasma polymerase chain reaction (PCR) ≥ 400 CMV copies/millilitre, then 1800 mg valganciclovir per day adjusted to renal function for at least 14 days until the second negative PCR (below 400 copies/ml) followed by secondary prophylaxis for 28 days with 900 mg valganciclovir adjusted to renal function. If CMV disease or no response to valganciclovir treatment after 14 days (not falling viral load), then intravenous (IV) ganciclovir or additional appropriate therapy could have been administered according to the local site's standard, instead of valganciclovir.

Arm type	Experimental
Investigational medicinal product name	Valganciclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

If plasma polymerase chain reaction (PCR) ≥ 400 CMV copies/millilitre, then 1800 mg valganciclovir per day adjusted to renal function for at least 14 days until the second negative PCR (below 400 copies/ml) followed by secondary prophylaxis for 28 days with 900 mg valganciclovir adjusted to renal function.

Investigational medicinal product name	Ganciclovir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

If CMV disease or no response to valganciclovir treatment after 14 days (not falling viral load), then intravenous (IV) ganciclovir or additional appropriate therapy could have been administered according to the local site's standard, instead of valganciclovir.

Number of subjects in period 2	Valganciclovir CMV Prophylaxis (Follow-Up)	Pre-emptive CMV Therapy (Follow-Up)
Started	117	122
Completed	71	70
Not completed	46	52
Administrative	1	-
Adverse event/intercurrent illness	1	-
Graft loss	8	7
Subject died	9	12
Refused treatment/did not cooperate	-	1
Reason not specified	2	3
Lost to follow-up	12	10
Consent withdrawn	13	19

Baseline characteristics

Reporting groups	
Reporting group title	Valganciclovir CMV Prophylaxis
Reporting group description:	
900 mg valganciclovir, taken orally once daily, adjusted to renal function starting within 14 days of transplantation until Day 100 after transplantation.	
Reporting group title	Pre-emptive CMV Therapy
Reporting group description:	
If plasma polymerase chain reaction (PCR) ≥ 400 CMV copies/millilitre, then 1800 mg valganciclovir per day adjusted to renal function for at least 14 days until the second negative PCR (below 400 copies/ml) followed by secondary prophylaxis for 28 days with 900 mg valganciclovir adjusted to renal function. If CMV disease or no response to valganciclovir treatment after 14 days (not falling viral load), then intravenous (IV) ganciclovir or additional appropriate therapy could have been administered according to the local site's standard, instead of valganciclovir.	

Reporting group values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy	Total
Number of subjects	148	151	299
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	51.18	54.24	
standard deviation	± 13.463	± 11.906	-
Gender categorical			
Units: Subjects			
Female	45	55	100
Male	103	96	199

End points

End points reporting groups

Reporting group title	Valganciclovir CMV Prophylaxis
Reporting group description:	
900 mg valganciclovir, taken orally once daily, adjusted to renal function starting within 14 days of transplantation until Day 100 after transplantation.	
Reporting group title	Pre-emptive CMV Therapy
Reporting group description:	
If plasma polymerase chain reaction (PCR) ≥ 400 CMV copies/millilitre, then 1800 mg valganciclovir per day adjusted to renal function for at least 14 days until the second negative PCR (below 400 copies/ml) followed by secondary prophylaxis for 28 days with 900 mg valganciclovir adjusted to renal function. If CMV disease or no response to valganciclovir treatment after 14 days (not falling viral load), then intravenous (IV) ganciclovir or additional appropriate therapy could have been administered according to the local site's standard, instead of valganciclovir.	
Reporting group title	Valganciclovir CMV Prophylaxis (Follow-Up)
Reporting group description:	
900 mg valganciclovir, taken orally once daily, adjusted to renal function starting within 14 days of transplantation until Day 100 after transplantation.	
Reporting group title	Pre-emptive CMV Therapy (Follow-Up)
Reporting group description:	
If plasma polymerase chain reaction (PCR) ≥ 400 CMV copies/millilitre, then 1800 mg valganciclovir per day adjusted to renal function for at least 14 days until the second negative PCR (below 400 copies/ml) followed by secondary prophylaxis for 28 days with 900 mg valganciclovir adjusted to renal function. If CMV disease or no response to valganciclovir treatment after 14 days (not falling viral load), then intravenous (IV) ganciclovir or additional appropriate therapy could have been administered according to the local site's standard, instead of valganciclovir.	

Primary: Percentage of Subjects with Active Cytomegalovirus (CMV) Infection Within 12 Months

End point title	Percentage of Subjects with Active Cytomegalovirus (CMV) Infection Within 12 Months
End point description:	
Active CMV infection was defined as plasma polymerase chain reaction (PCR) ≥ 400 copies/millilitre (ml). The intent-to-treat (ITT) population included all randomized subjects.	
End point type	Primary
End point timeframe:	
Up to 12 months	

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (confidence interval 96%)	14.1 (7 to 21.1)	42.6 (33.9 to 51.3)		

Statistical analyses

Statistical analysis title	Valganciclovir CMV Proph./Pre-emptive CMV Therapy
Comparison groups	Valganciclovir CMV Prophylaxis v Pre-emptive CMV Therapy
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference
Point estimate	-28.5
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	-39.7
upper limit	-17.3
Variability estimate	Standard error of the mean
Dispersion value	5.45

Primary: Percentage of Subjects with CMV Disease Within 12 months Including CMV Syndrome and Tissue Invasive Disease

End point title	Percentage of Subjects with CMV Disease Within 12 months Including CMV Syndrome and Tissue Invasive Disease

End point description:

CMV disease comprises the two components of CMV syndrome as well as CMV tissue invasive disease. CMV syndrome was defined as viremia according to plasma PCR ≥ 400 copies/ml and at least one of the following signs: fever of ≥38 °C; new or increased malaise (malaise defined as normal activity reduced >50%; cannot work or unable to care for self; leukopenia on 2 successive measurements separated by at least 24 hours thrombocytopenia; elevation of hepatic transaminases (alanine aminotransferase (ALT) or aspartate aminotransferase (AST) to at least 2 x upper limit of normal (ULN). CMV tissue invasive disease was defined as viremia according plasma PCR ≥ 400 copies/ml and clinical evidence of localized CMV infection (CMV inclusion cells or in situ detection of CMV antigen or deoxyribonucleic acid [DNA] by immunostaining or hybridization, respectively), cerebral spinal fluid [CSF]) and/or relevant symptoms or signs of organ dysfunction. Intent-to-treat (ITT) population.

End point type	Primary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (confidence interval 96%)	5.6 (1.4 to 9.8)	16.9 (10.3 to 23.6)		

Statistical analyses

Statistical analysis title	Valganciclovir CMV Proph./Pre-emptive CMV Therapy
Comparison groups	Valganciclovir CMV Prophylaxis v Pre-emptive CMV Therapy
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference
Point estimate	-11.3
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	-19.2
upper limit	-3.4
Variability estimate	Standard error of the mean
Dispersion value	3.83

Primary: Urine Proteomic Pattern at Month 12

End point title	Urine Proteomic Pattern at Month 12
End point description:	
Proteomics is the complete set of proteins expressed by an organism, tissue, or cell. Urine proteomic pattern was measured on a scale between -1, indicating no graft alteration, and +1, indicating graft alteration. The intent-to-treat (ITT) population included all randomized subjects.	
End point type	Primary
End point timeframe:	
Up to 12 months	

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: nephropathy index				
least squares mean (standard error)	-0.1057 (± 0.1538)	0.1452 (± 0.1006)		

Statistical analyses

Statistical analysis title	Valganciclovir CMV Proph./Pre-emptive CMV Therapy
Comparison groups	Valganciclovir CMV Prophylaxis v Pre-emptive CMV Therapy
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1739
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.2509

Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	-0.2271
upper limit	0.7289
Variability estimate	Standard error of the mean
Dispersion value	0.1838

Primary: Percentage of Subjects With Graft Loss at Month 84

End point title	Percentage of Subjects With Graft Loss at Month 84[1]

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Primary

End point timeframe:

Up to 84 months

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: Descriptive analysis only.

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (not applicable)	7.43	8.61		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with CMV Syndrome Within 12 Months

End point title	Percentage of Subjects with CMV Syndrome Within 12 Months

End point description:

CMV syndrome was defined as viremia according to plasma PCR ≥ 400 copies/ml and at least one of the following signs: fever of ≥38 °C; new or increased malaise (malaise defined as normal activity reduced >50%; cannot work or unable to care for self; leukopenia on 2 successive measurements separated by at least 24 hours thrombocytopenia; elevation of hepatic transaminases (alanine aminotransferase (ALT) or aspartate aminotransferase (AST) to at least 2 x upper limit of normal (ULN). The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (confidence interval 95%)	5.6 (1.6 to 9.7)	14.6 (8.7 to 20.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with CMV Tissue Invasive Disease Within 12 Months

End point title	Percentage of Subjects with CMV Tissue Invasive Disease Within 12 Months

End point description:

CMV tissue invasive disease was defined as viremia according plasma PCR ≥ 400 copies/ml and clinical evidence of localized CMV infection (CMV inclusion cells or in situ detection of CMV antigen or deoxyribonucleic acid [DNA] by immunostaining or hybridization, respectively), cerebral spinal fluid [CSF]) and/or relevant symptoms or signs of organ dysfunction. The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (confidence interval 95%)	3.3 (0.1 to 6.4)	3.6 (0.5 to 6.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Occurrence of First Viremia Within 12 Months

End point title	Time to Occurrence of First Viremia Within 12 Months

End point description:

Viremia was defined as plasma PCR ≥ 400 copies/ml. The intent-to-treat (ITT) population included all randomized subjects. Here, 99999 indicates not calculable.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148[2]	151[3]		
Units: days				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (160 to 99999)		

Notes:

[2] - Median and confidence limits were not reached.

[3] - Median and upper confidence limit were not reached.

Statistical analyses

No statistical analyses for this end point

Secondary: Viral Burden at Viremia

End point title	Viral Burden at Viremia

End point description:

Time-weighted area under the curve (AUC) of the polymerase chain reaction (PCR). Viremia was defined as plasma PCR ≥ 400 copies/ml. The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: copies/ml*days				
arithmetic mean (standard deviation)	5309.83 (± 14355.836)	3765.8 (± 8480.521)		

Statistical analyses

No statistical analyses for this end point

Secondary: Creatinine Clearance at Month 12

End point title	Creatinine Clearance at Month 12

End point description:

Creatinine clearance was estimated using the Cockcroft-Gault-formula. The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: millilitre(s)/minute				
arithmetic mean (standard deviation)	61.1 (± 23.3)	61.3 (± 22.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with at Least One Treated and Biopsy-Proven Acute Rejection Episode Within 12 Months

End point title	Percentage of Subjects with at Least One Treated and Biopsy-Proven Acute Rejection Episode Within 12 Months

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (not applicable)	18.2	13.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Days of Hospitalization

End point title	Days of Hospitalization

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: days				
median (full range (min-max))	26.5 (0 to 258)	32 (0 to 221)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship Between Proteomics Pattern and Graft Survival

End point title	Relationship Between Proteomics Pattern and Graft Survival

End point description:

Proteomics is the complete set of proteins expressed by an organism, tissue, or cell. The proteomics of CKD273, CMV, and nephropathy was measured on a scale between -1, indicating no graft alteration, and +1, indicating graft alteration. The intent-to-treat (ITT) population included all randomized subjects. Only subjects with data were included in the analysis. Here, 99999 indicates not calculable.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: score on a scale				
arithmetic mean (standard deviation)				
CKD273:Visit 6: With Graft Loss (n=1, 4)	0.4 (± 99999)	0.8 (± 0.2944)		
CKD273:Visit 6: Without Graft Loss (n=112, 110)	0.371 (± 0.3578)	0.379 (± 0.3499)		
CKD273:Visit 13: With Graft Loss (n=0, 1)	99999 (± 99999)	0.5 (± 99999)		
CKD273:Visit 13: Without Graft Loss (n=102, 109)	0.258 (± 0.3719)	0.293 (± 0.3648)		
CKD273:Visit 15: With Graft Loss (n=2, 0)	0.6 (± 0.5657)	99999 (± 99999)		
CKD273:Visit 15: Without Graft Loss (n=104, 102)	0.27 (± 0.3793)	0.326 (± 0.3618)		
CMV:Visit 6: With Graft Loss (n=1, 4)	-0.5 (± 99999)	-0.3 (± 0.7616)		

CMV:Visit 6: Without Graft Loss (n=112, 110)	0 (± 0.9535)	-0.007 (± 0.8984)		
CMV:Visit 13: With Graft Loss (n=0, 1)	99999 (± 99999)	-0.3 (± 99999)		
CMV:Visit 13: Without Graft Loss (n=102, 109)	0.036 (± 0.7976)	-0.048 (± 0.7614)		
CMV:Visit 15: With Graft Loss (n=2, 0)	0.1 (± 0.7071)	99999 (± 99999)		
CMV:Visit 15: Without Graft Loss (n=104, 102)	-0.076 (± 0.6922)	-0.068 (± 0.7081)		
Nephropathy:Visit 6: With Graft Loss (n=1, 4)	0.5 (± 99999)	1.1 (± 0.9933)		
Nephropathy:Visit 6:Without Graft Loss (n=112,110)	0.107 (± 1.1784)	0.086 (± 1.0489)		
Visit 13: With Graft Loss (n=0, 1)	99999 (± 99999)	-0.8 (± 99999)		
Nephropathy:Visit 13:Without Graft Loss(n=102,109)	-0.05 (± 1.0624)	0.008 (± 1.0848)		
Nephropathy:Visit 15: With Graft Loss (n=2, 0)	1.35 (± 2.8991)	99999 (± 99999)		
Nephropathy:Visit15: Without Graft Loss(n=104,102)	-0.007 (± 0.8535)	0.102 (± 1.1221)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship Between Proteomics Pattern and Subject Survival

End point title	Relationship Between Proteomics Pattern and Subject Survival

End point description:

The intent-to-treat (ITT) population included all randomized subjects. Only subjects with data were included in the analysis. Here, 99999 indicates not calculable.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: score on a scale				
arithmetic mean (standard deviation)				
CKD273:Visit 6: Did not Survive (n=2, 1)	0.4 (± 0.1414)	0.5 (± 99999)		
CKD273:Visit 6: Survived (n=111, 113)	0.371 (± 0.3591)	0.393 (± 0.357)		
CKD273:Visit 13: Did not Survive (n=1, 1)	0.7 (± 99999)	0.5 (± 99999)		
CKD273:Visit 13: Survived (n=101, 109)	0.253 (± 0.3711)	0.293 (± 0.3648)		

CKD273:Visit 15: Did not Survive (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
CKD273:Visit 15: Survived (n=106, 102)	0.276 (± 0.3824)	0.326 (± 0.3618)		
CMV:Visit 6: Did not Survive (n=2, 1)	1.15 (± 1.3435)	-0.9 (± 99999)		
CMV:Visit 6: Survived (n=111, 113)	-0.025 (± 0.9374)	-0.01 (± 0.8927)		
CMV:Visit 13: Did not Survive (n=1, 1)	0.4 (± 99999)	-0.3 (± 99999)		
CMV:Visit 13: Survived (n=101, 109)	0.033 (± 0.8008)	-0.048 (± 0.7614)		
CMV:Visit 15: Did not Survive (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
CMV:Visit 15: Survived (n=106, 102)	-0.073 (± 0.6894)	-0.068 (± 0.7081)		
Nephropathy:Visit 6: Did not Survive (n=2, 1)	0.15 (± 0.0707)	-0.1 (± 99999)		
Nephropathy:Visit 6: Survived (n=111, 113)	0.101 (± 1.1851)	0.124 (± 1.064)		
Nephropathy:Visit 13: Did not Survive (n=1, 1)	1.8 (± 99999)	-0.8 (± 99999)		
Nephropathy:Visit 13: Survived (n=101, 109)	-0.068 (± 1.0514)	0.008 (± 1.0848)		
Nephropathy:Visit 15: Did not Survive (n=0, 0)	99999 (± 99999)	99999 (± 99999)		
Nephropathy:Visit 15: Survived (n=106, 102)	0.019 (± 0.9105)	0.102 (± 1.1221)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proteomics Parameter: CKD273

End point title	Proteomics Parameter: CKD273

End point description:

The proteomics of CKD273 was measured on a scale between –1, indicating no graft alteration, and +1, indicating graft alteration. The intent-to-treat (ITT) population included all randomized subjects. Only subjects with data were included in the analysis.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: score on a scale				
arithmetic mean (standard deviation)				
Visit 6 (n=113, 114)	0.372 (± 0.3562)	0.394 (± 0.3556)		

Visit 13 (n=102, 110)	0.258 (± 0.3719)	0.295 (± 0.3637)		
Visit 15 (n=106, 102)	0.276 (± 0.3824)	0.326 (± 0.3618)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proteomics Parameter: CMV

End point title	Proteomics Parameter: CMV

End point description:

The proteomics of CMV was measured on a scale between –1, indicating no graft alteration, and +1, indicating graft alteration. The intent-to-treat (ITT) population included all randomized subjects. Only subjects with data were included in the analysis.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: score on a scale				
arithmetic mean (standard deviation)				
Visit 6 (n=113, 114)	-0.004 (± 0.9504)	-0.018 (± 0.8927)		
Visit 13 (n=102, 110)	0.036 (± 0.7976)	-0.05 (± 0.7583)		
Visit 15 (n=106, 102)	-0.073 (± 0.6894)	-0.068 (± 0.7081)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proteomics Parameter: Nephropathy

End point title	Proteomics Parameter: Nephropathy

End point description:

The proteomics of nephropathy was measured on a scale between –1, indicating no graft alteration, and +1, indicating graft alteration. The intent-to-treat (ITT) population included all randomized subjects. Only subjects with data were included in the analysis.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: score on a scale				
arithmetic mean (standard deviation)				
Visit 6 (n=113, 114)	0.102 (± 1.1745)	0.122 (± 1.0595)		
Visit 13 (n=102, 110)	-0.05 (± 1.0624)	0.001 (± 1.0826)		
Visit 15 (n=106, 102)	0.019 (± 0.9105)	0.102 (± 1.1221)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Surviving at Month 12

End point title	Percentage of Subjects Surviving at Month 12

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (not applicable)	98	98.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Graft Survival at Month 12

End point title	Percentage of Subjects with Graft Survival at Month 12

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (not applicable)	98.6	96		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Leukopenia and Neutropenia Within 12 Months

End point title	Percentage of Subjects with Leukopenia and Neutropenia Within 12 Months

End point description:

Leukopenia: white blood cell (WBC) of < 3,500/microlitre (µL) and < 1,000/µL. Neutropenia: absolute neutrophil count (ANC) < 750/µL within 12 months. The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (not applicable)				
Percentage of subjects with leukopenia	35.1	26.5		
Percentage of subjects with neutropenia	16.9	12.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Any Opportunistic Infection Within 12

Months	
End point title	Percentage of Subjects with Any Opportunistic Infection Within 12 Months
End point description:	
The intent-to-treat (ITT) population included all randomized subjects.	
End point type	Secondary
End point timeframe:	
Up to 12 months	

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (not applicable)	31.1	37.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Post-Transplant Diabetes Mellitus	
End point title	Percentage of Subjects with Post-Transplant Diabetes Mellitus
End point description:	
The intent-to-treat (ITT) population included all randomized subjects.	
End point type	Secondary
End point timeframe:	
Up to 12 months	

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (not applicable)				
Month 6	2.7	1.3		
Month 12	3.4	0.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Active CMV Infections not Responding to Valganciclovir or IV Ganciclovir Treatment

End point title	Percentage of Subjects with Active CMV Infections not Responding to Valganciclovir or IV Ganciclovir Treatment

End point description:

Active CMV infection was defined as plasma polymerase chain reaction (PCR) ≥ 400 copies/milliliter (ml). The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17[4]	82[5]		
Units: percentage of subjects				
number (not applicable)	11.8	18.3		

Notes:

[4] - Only subjects with data were included in the analysis.

[5] - Only subjects with data were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with CMV Viremia (Active CMV Infection) from Baseline to Month 24 and every 12 Months up to Month 84

End point title	Number of Subjects with CMV Viremia (Active CMV Infection) from Baseline to Month 24 and every 12 Months up to Month 84

End point description:

Viremia (active CMV Infection) was defined as PCR ≥ 400 copies/ml. The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: subjects				
24 months	16	59		
36 months	16	59		
48 months	16	59		

60 months	16	59		
72 months	17	60		
84 months	17	60		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with CMV Disease from Baseline to Month 24 and every 12 Months up to Month 84

End point title	Number of Subjects with CMV Disease from Baseline to Month 24 and every 12 Months up to Month 84

End point description:

CMV disease comprises the two components of CMV syndrome as well as CMV tissue invasive disease. CMV syndrome was defined as viremia according to plasma PCR ≥ 400 copies/ml and at least one of the following signs: fever of ≥38 °C; new or increased malaise (malaise defined as normal activity reduced >50%; cannot work or unable to care for self; leukopenia on 2 successive measurements separated by at least 24 hours thrombocytopenia; elevation of hepatic transaminases (alanine aminotransferase (ALT) or aspartate aminotransferase (AST) to at least 2 x upper limit of normal (ULN). CMV tissue invasive disease was defined as viremia according plasma PCR ≥ 400 copies/ml and clinical evidence of localized CMV infection (CMV inclusion cells or in situ detection of CMV antigen or deoxyribonucleic acid [DNA] by immunostaining or hybridization, respectively), cerebral spinal fluid [CSF]) and/or relevant symptoms or signs of organ dysfunction. Intent-to-treat (ITT) population.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: subjects				
24 months	7	23		
36 months	7	23		
48 months	7	23		
60 months	7	24		
72 months	7	24		
84 months	7	24		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with CMV Syndrome from Baseline to Month 24 and every 12 Months up to Month 84

End point title	Number of Subjects with CMV Syndrome from Baseline to Month 24 and every 12 Months up to Month 84

End point description:

CMV syndrome was defined as viremia according to plasma PCR ≥ 400 copies/ml and at least one of the following signs: fever of ≥38 °C; new or increased malaise (malaise defined as normal activity reduced >50%; cannot work or unable to care for self; leukopenia on 2 successive measurements separated by at least 24 hours thrombocytopenia; elevation of hepatic transaminases (alanine aminotransferase (ALT) or aspartate aminotransferase (AST) to at least 2 x upper limit of normal (ULN). The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: subjects				
24 months	7	20		
36 months	7	20		
48 months	7	20		
60 months	7	21		
72 months	7	21		
84 months	7	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with CMV Tissue Invasive Disease from Baseline to Month 24 and every 12 Months up to Month 84

End point title	Number of Subjects with CMV Tissue Invasive Disease from Baseline to Month 24 and every 12 Months up to Month 84

End point description:

CMV tissue invasive disease was defined as viremia according plasma PCR ≥ 400 copies/ml and clinical evidence of localized CMV infection (CMV inclusion cells or in situ detection of CMV antigen or deoxyribonucleic acid [DNA] by immunostaining or hybridization, respectively), cerebral spinal fluid [CSF]) and/or relevant symptoms or signs of organ dysfunction. The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: subjects				
24 months	4	5		
36 months	4	5		
48 months	4	5		
60 months	4	5		
72 months	4	5		
84 months	4	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Active CMV Infection after Month 24 and every 12 Months up to Month 84

End point title	Number of Subjects with Active CMV Infection after Month 24 and every 12 Months up to Month 84

End point description:

Active CMV infection was defined as plasma polymerase chain reaction (PCR) ≥ 400 copies/milliliter (ml). The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: subjects				
24 months	16	59		
36 months	16	59		
48 months	16	59		
60 months	16	59		
72 months	17	60		
84 months	17	60		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with CMV Disease after Month 24 and every 12

Months up to Month 84

End point title	Number of Subjects with CMV Disease after Month 24 and every 12 Months up to Month 84

End point description:

CMV disease comprises the two components of CMV syndrome as well as CMV tissue invasive disease. CMV syndrome was defined as viremia according to plasma PCR ≥ 400 copies/ml and at least one of the following signs: fever of ≥38 °C; new or increased malaise (malaise defined as normal activity reduced >50%; cannot work or unable to care for self; leukopenia on 2 successive measurements separated by at least 24 hours thrombocytopenia; elevation of hepatic transaminases (alanine aminotransferase (ALT) or aspartate aminotransferase (AST) to at least 2 x upper limit of normal (ULN). CMV tissue invasive disease was defined as viremia according plasma PCR ≥ 400 copies/ml and clinical evidence of localized CMV infection (CMV inclusion cells or in situ detection of CMV antigen or deoxyribonucleic acid [DNA] by immunostaining or hybridization, respectively), cerebral spinal fluid [CSF]) and/or relevant symptoms or signs of organ dysfunction. Intent-to-treat (ITT) population.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: subjects				
24 months	7	23		
36 months	7	23		
48 months	7	23		
60 months	7	24		
72 months	7	24		
84 months	7	24		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Surviving at Month 24 and every 12 Months up to Month 84

End point title	Percentage of Subjects Surviving at Month 24 and every 12 Months up to Month 84

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (not applicable)				
24 months	97.97	94.7		
36 months	95.95	94.04		
48 months	94.59	93.38		
60 months	92.57	92.05		
72 months	90.54	89.4		
84 months	90.54	88.74		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Died from Month 24 to Month 84

End point title	Number of Subjects who Died from Month 24 to Month 84

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: subjects				
24 months	3	8		
36 months	6	9		
48 months	8	10		
60 months	11	12		
72 months	14	16		
84 months	14	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Graft Survival at Month 24 and Every 12 Months up to Month 84

End point title	Percentage of Subjects with Graft Survival at Month 24 and Every 12 Months up to Month 84

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (not applicable)				
24 months	97.3	94.7		
36 months	97.3	93.38		
48 months	96.62	93.38		
60 months	95.95	92.05		
72 months	94.59	91.39		
84 months	92.57	91.39		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Had Lost Their Transplant from Months 24 to 84

End point title	Number of Subjects Who Had Lost Their Transplant from Months 24 to 84

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: subjects				
24 months	4	8		
36 months	4	10		
48 months	5	10		

60 months	6	12		
72 months	8	13		
84 months	11	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Graft Loss (with and without CMV Infection) at Month 84

End point title	Percentage of Subjects with Graft Loss (with and without CMV Infection) at Month 84

End point description:

Active CMV infection was defined as plasma polymerase chain reaction (PCR) ≥ 400 copies/millilitre (ml). The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

Up to 84 months

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (confidence interval 95%)				
Subjects with CMV infection (n = 77)	8.3 (0 to 24)	17.9 (7.2 to 28.6)		
Subjects without CMV infection (n = 222)	11.5 (4.7 to 18.4)	5.8 (0.1 to 11.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Had Lost Their Transplant or Died From Months 24 to 84

End point title	Number of Subjects Who Had Lost Their Transplant or Died From Months 24 to 84

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: subjects				
24 months	7	15		
36 months	9	18		
48 months	12	19		
60 months	16	23		
72 months	21	28		
84 months	24	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Graft Survival or Subject Survival at Month 24 and Every 12 Months up to Month 84

End point title	Percentage of Subjects with Graft Survival or Subject Survival at Month 24 and Every 12 Months up to Month 84
End point description:	
The intent-to-treat (ITT) population included all randomized subjects.	
End point type	Secondary
End point timeframe:	
From Month 24 to Month 84	

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: percentage of subjects				
number (not applicable)				
24 months	95.27	90.07		
36 months	93.92	88.08		
48 months	91.89	87.42		
60 months	89.19	84.77		
72 months	85.81	81.46		
84 months	83.78	80.79		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Graft Rejections from Months 24 to Month 84

End point title	Number of Graft Rejections from Months 24 to Month 84

End point description:

The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: graft rejections				
24 months	39	48		
36 months	42	51		
48 months	45	51		
60 months	46	52		
72 months	48	53		
84 months	48	53		

Statistical analyses

No statistical analyses for this end point

Secondary: Creatinine Clearance at Month 24 and every 12 Months up to Month 84

End point title	Creatinine Clearance at Month 24 and every 12 Months up to Month 84

End point description:

Creatinine Clearance estimated by Cockcroft-Gault formula. The intent-to-treat (ITT) population included all randomized subjects.

End point type	Secondary

End point timeframe:

From Month 24 to Month 84

End point values	Valganciclovir CMV Prophylaxis	Pre-emptive CMV Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	151		
Units: millimitres/minute				
arithmetic mean (standard deviation)				
24 months	63.2 (± 23.85)	62.9 (± 25.01)		
36 months	63.9 (± 24.14)	64.5 (± 25.33)		
48 months	63.1 (± 23.81)	62.6 (± 24.63)		
60 months	62.2 (± 22.58)	64.9 (± 27.85)		
72 months	63.3 (± 28.98)	64.7 (± 27.25)		
84 months	59.5 (± 26.76)	60.8 (± 25.39)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 7 years	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups	
Reporting group title	Pre-emptive CMV Therapy

Reporting group description:

If plasma polymerase chain reaction (PCR) ≥ 400 CMV copies/millilitre, then 1800 mg valganciclovir per day adjusted to renal function for at least 14 days until the second negative PCR (below 400 copies/ml) followed by secondary prophylaxis for 28 days with 900 mg valganciclovir adjusted to renal function. If CMV disease or no response to valganciclovir treatment after 14 days (not falling viral load), then intravenous (IV) ganciclovir or additional appropriate therapy could have been administered according to the local site's standard, instead of valganciclovir.

Reporting group title	Valganciclovir CMV Prophylaxis

Reporting group description:

900 mg valganciclovir, taken orally once daily, adjusted to renal function starting within 14 days of transplantation until Day 100 after transplantation.

Serious adverse events	Pre-emptive CMV Therapy	Valganciclovir CMV Prophylaxis	
Total subjects affected by serious adverse events			
subjects affected / exposed	96 / 151 (63.58%)	94 / 148 (63.51%)	
number of deaths (all causes)	17	14	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Angiosarcoma			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipoma			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			

subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsil cancer			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial stenosis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			

subjects affected / exposed	1 / 151 (0.66%)	4 / 148 (2.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 151 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	4 / 151 (2.65%)	6 / 148 (4.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 151 (0.66%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (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 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			

subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Arteriovenous fistula operation			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary arterial stent insertion			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatectomy			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Removal of ambulatory peritoneal catheter			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteral stent removal			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric operation			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (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			
Asthenia			
subjects affected / exposed	0 / 151 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chest pain			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Impaired healing			
subjects affected / exposed	3 / 151 (1.99%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 151 (1.32%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Kidney transplant rejection			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
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			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Epididymitis			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal oedema			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal prolapse			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (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			
Atelectasis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphonia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea at rest			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	3 / 151 (1.99%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory arrest			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood calcium increased			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine abnormal			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	17 / 151 (11.26%)	23 / 148 (15.54%)	
occurrences causally related to treatment / all	0 / 18	1 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood glucose abnormal			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood parathyroid hormone increased			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	0 / 151 (0.00%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Occult blood positive			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urine output decreased			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 151 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Abdominal wound dehiscence			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site complication			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complications of transplanted kidney			
subjects affected / exposed	1 / 151 (0.66%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft complication			
subjects affected / exposed	2 / 151 (1.32%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft dysfunction			
subjects affected / exposed	2 / 151 (1.32%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	2 / 151 (1.32%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			

subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirenal haematoma			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	2 / 151 (1.32%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt blood flow excessive			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant failure			
subjects affected / exposed	0 / 151 (0.00%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric anastomosis complication			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary anastomotic leak			

subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Congenital cystic kidney disease			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial fibrillation			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiopulmonary failure			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trifascicular block			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Benign intracranial hypertension			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			

subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			

subjects affected / exposed	0 / 151 (0.00%)	5 / 148 (3.38%)	
occurrences causally related to treatment / all	0 / 0	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrogenic anaemia			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Cupulolithiasis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness unilateral			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Charles Bonnet syndrome			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			

subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 151 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	5 / 151 (3.31%)	6 / 148 (4.05%)	
occurrences causally related to treatment / all	1 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			

subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flatulence			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 151 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 151 (0.66%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 151 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia, obstructive			

subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sclerosing encapsulating peritonitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Focal segmental glomerulosclerosis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			

subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	2 / 151 (1.32%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postrenal failure			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	0 / 151 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	1 / 151 (0.66%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	3 / 151 (1.99%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 151 (0.66%)	3 / 148 (2.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			

subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteral necrosis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric stenosis			
subjects affected / exposed	2 / 151 (1.32%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary fistula			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	3 / 151 (1.99%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bone pain			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Osteoarthritis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 151 (0.66%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess oral			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	0 / 151 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis staphylococcal			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	2 / 151 (1.32%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	2 / 151 (1.32%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 151 (0.66%)	5 / 148 (3.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected lymphocele			
subjects affected / exposed	0 / 151 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			

subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 151 (3.97%)	6 / 148 (4.05%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia escherichia			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia primary atypical			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 151 (1.32%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal abscess			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
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 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	1 / 151 (0.66%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Urinary tract infection			
subjects affected / exposed	13 / 151 (8.61%)	9 / 148 (6.08%)	
occurrences causally related to treatment / all	0 / 15	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	7 / 151 (4.64%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound abscess			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	2 / 151 (1.32%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes with hyperosmolarity			
subjects affected / exposed	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	0 / 151 (0.00%)	2 / 148 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 148 (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	0 / 151 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	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	Pre-emptive CMV Therapy	Valganciclovir CMV Prophylaxis	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	140 / 151 (92.72%)	139 / 148 (93.92%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	37 / 151 (24.50%)	30 / 148 (20.27%)	
occurrences (all)	41	33	
Hypotension			
subjects affected / exposed	9 / 151 (5.96%)	7 / 148 (4.73%)	
occurrences (all)	10	8	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	11 / 151 (7.28%)	5 / 148 (3.38%)	
occurrences (all)	11	5	
Oedema			
subjects affected / exposed	31 / 151 (20.53%)	27 / 148 (18.24%)	
occurrences (all)	37	30	
Oedema peripheral			
subjects affected / exposed	30 / 151 (19.87%)	34 / 148 (22.97%)	
occurrences (all)	40	42	
Pain			
subjects affected / exposed	11 / 151 (7.28%)	4 / 148 (2.70%)	
occurrences (all)	20	5	
Pyrexia			
subjects affected / exposed	9 / 151 (5.96%)	12 / 148 (8.11%)	
occurrences (all)	12	21	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 151 (7.95%)	23 / 148 (15.54%)	
occurrences (all)	17	27	
Dyspnoea			
subjects affected / exposed	12 / 151 (7.95%)	13 / 148 (8.78%)	
occurrences (all)	17	17	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	14 / 151 (9.27%)	17 / 148 (11.49%)	
occurrences (all)	15	24	
Sleep disorder			
subjects affected / exposed	13 / 151 (8.61%)	9 / 148 (6.08%)	
occurrences (all)	26	10	
Investigations			
Blood creatinine increased			
subjects affected / exposed	21 / 151 (13.91%)	23 / 148 (15.54%)	
occurrences (all)	25	28	
Blood uric acid increased			
subjects affected / exposed	7 / 151 (4.64%)	10 / 148 (6.76%)	
occurrences (all)	7	11	

C-reactive protein increased			
subjects affected / exposed	11 / 151 (7.28%)	13 / 148 (8.78%)	
occurrences (all)	19	19	
Gamma-glutamyltransferase increased			
subjects affected / exposed	12 / 151 (7.95%)	5 / 148 (3.38%)	
occurrences (all)	12	5	
Hepatic enzyme increased			
subjects affected / exposed	7 / 151 (4.64%)	14 / 148 (9.46%)	
occurrences (all)	8	17	
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 151 (9.27%)	12 / 148 (8.11%)	
occurrences (all)	18	19	
Tremor			
subjects affected / exposed	17 / 151 (11.26%)	16 / 148 (10.81%)	
occurrences (all)	19	16	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	38 / 151 (25.17%)	28 / 148 (18.92%)	
occurrences (all)	45	31	
Leukocytosis			
subjects affected / exposed	9 / 151 (5.96%)	7 / 148 (4.73%)	
occurrences (all)	12	9	
Leukopenia			
subjects affected / exposed	35 / 151 (23.18%)	37 / 148 (25.00%)	
occurrences (all)	42	47	
Thrombocytopenia			
subjects affected / exposed	9 / 151 (5.96%)	8 / 148 (5.41%)	
occurrences (all)	11	10	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	9 / 151 (5.96%)	3 / 148 (2.03%)	
occurrences (all)	10	6	
Constipation			
subjects affected / exposed	15 / 151 (9.93%)	13 / 148 (8.78%)	
occurrences (all)	28	14	

Diarrhoea			
subjects affected / exposed	42 / 151 (27.81%)	41 / 148 (27.70%)	
occurrences (all)	64	66	
Dyspepsia			
subjects affected / exposed	8 / 151 (5.30%)	5 / 148 (3.38%)	
occurrences (all)	9	9	
Nausea			
subjects affected / exposed	16 / 151 (10.60%)	16 / 148 (10.81%)	
occurrences (all)	26	20	
Vomiting			
subjects affected / exposed	9 / 151 (5.96%)	11 / 148 (7.43%)	
occurrences (all)	13	12	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	8 / 151 (5.30%)	5 / 148 (3.38%)	
occurrences (all)	8	5	
Pruritus			
subjects affected / exposed	10 / 151 (6.62%)	2 / 148 (1.35%)	
occurrences (all)	10	2	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	8 / 151 (5.30%)	8 / 148 (5.41%)	
occurrences (all)	8	9	
Leukocyturia			
subjects affected / exposed	15 / 151 (9.93%)	5 / 148 (3.38%)	
occurrences (all)	18	6	
Proteinuria			
subjects affected / exposed	23 / 151 (15.23%)	18 / 148 (12.16%)	
occurrences (all)	26	22	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 151 (5.96%)	8 / 148 (5.41%)	
occurrences (all)	9	8	
Back pain			
subjects affected / exposed	7 / 151 (4.64%)	9 / 148 (6.08%)	
occurrences (all)	7	10	

Muscle spasms			
subjects affected / exposed	5 / 151 (3.31%)	13 / 148 (8.78%)	
occurrences (all)	5	13	
Pain in extremity			
subjects affected / exposed	16 / 151 (10.60%)	8 / 148 (5.41%)	
occurrences (all)	28	12	
Infections and infestations			
Bronchitis			
subjects affected / exposed	8 / 151 (5.30%)	6 / 148 (4.05%)	
occurrences (all)	10	6	
Nasopharyngitis			
subjects affected / exposed	34 / 151 (22.52%)	36 / 148 (24.32%)	
occurrences (all)	49	46	
Urinary tract infection			
subjects affected / exposed	49 / 151 (32.45%)	53 / 148 (35.81%)	
occurrences (all)	81	98	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	11 / 151 (7.28%)	4 / 148 (2.70%)	
occurrences (all)	12	4	
Diabetes mellitus			
subjects affected / exposed	25 / 151 (16.56%)	19 / 148 (12.84%)	
occurrences (all)	26	19	
Glucose tolerance impaired			
subjects affected / exposed	8 / 151 (5.30%)	3 / 148 (2.03%)	
occurrences (all)	8	3	
Hypercalcaemia			
subjects affected / exposed	17 / 151 (11.26%)	7 / 148 (4.73%)	
occurrences (all)	18	9	
Hypercholesterolaemia			
subjects affected / exposed	16 / 151 (10.60%)	17 / 148 (11.49%)	
occurrences (all)	17	17	
Hyperkalaemia			
subjects affected / exposed	20 / 151 (13.25%)	15 / 148 (10.14%)	
occurrences (all)	28	17	
Hyperlipidaemia			

subjects affected / exposed	23 / 151 (15.23%)	14 / 148 (9.46%)	
occurrences (all)	24	14	
Hyperuricaemia			
subjects affected / exposed	25 / 151 (16.56%)	23 / 148 (15.54%)	
occurrences (all)	25	24	
Hypocalcaemia			
subjects affected / exposed	6 / 151 (3.97%)	13 / 148 (8.78%)	
occurrences (all)	6	14	
Hypokalaemia			
subjects affected / exposed	18 / 151 (11.92%)	18 / 148 (12.16%)	
occurrences (all)	25	20	
Hypophosphataemia			
subjects affected / exposed	9 / 151 (5.96%)	12 / 148 (8.11%)	
occurrences (all)	12	13	
Metabolic acidosis			
subjects affected / exposed	21 / 151 (13.91%)	17 / 148 (11.49%)	
occurrences (all)	21	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 May 2006	Protocol Amendment 1 included revised study timelines; increased number of centers from 15 to 20; changes in laboratory parameters to be measured; changes in the clinical examination at Visit 1; viral load measured at central laboratory for all centers; and an increase in the adverse event reporting period from 12 to 14 months.
11 April 2008	Protocol Amendment 2 included changes in the study timelines, recruitment period, last subject at 12 months, last subject out and total study duration; increase in the number of centers to approximately 25; changes in exclusion criteria; changes in documentation of concomitant medication; changes in CMV measurements in follow-up phase; changes in packaging and labeling; safety precautions for handling of study drug; guidance for documentation of CMV infections, rejections, opportunistic infections, and adverse events in the electronic case report form; changes in serious adverse event reporting; and inclusion of two secondary basic research projects.
09 August 2010	Protocol Amendment 3 included the following changes: for withdrawn subjects, survival of the transplant and the subject could be followed up by telephone contact, if subject gave consent, according to the German data protection law; sample for proteomics was taken only until Month 24; and removal of one of the secondary basic research projects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported