



Clinical trial results:

Tolerability of up to 200 Days of Valganciclovir Oral Solution or Tablets in Pediatric Kidney Transplant Recipients

Summary

EudraCT number	2010-022514-47
Trial protocol	GB DE SE FR ES
Global end of trial date	23 May 2013

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	08 August 2015

Trial information

Trial identification

Sponsor protocol code	NV25409
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01376804
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	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, 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)	Yes
EMA paediatric investigation plan number(s)	EMA-000726-PIP01-09
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	01 August 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	23 May 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was a multi-center, open-label, non-comparative study for a total duration of 52 weeks and was designed to describe the tolerability profile of up to 200 days prophylaxis of valganciclovir powder for oral solution and film-coated tablets in pediatric kidney transplant recipients.

Protection of trial subjects:

The protection of trial participants was ensured by obtaining a written signed informed consent from the participants. Participants who were not qualified or incapable of giving legal consent, written consent was obtained from the participant's legally acceptable representative and the participant's assent. Participants were informed to participate in the study after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 July 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Brazil: 6
Country: Number of subjects enrolled	United States: 22
Country: Number of subjects enrolled	Mexico: 15
Worldwide total number of subjects	57
EEA total number of subjects	9

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)	3
Children (2-11 years)	21
Adolescents (12-17 years)	33
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A screening examination was performed before the participant was enrolled but no later than 10 days post-transplant. An eligibility screening form documenting the investigator's assessment of each screened participant with regards to the protocol's inclusion and exclusion criteria was completed by the investigator.

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Valganciclovir
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Arm description:

Participants received a once daily oral dose (solution or tablets) of valganciclovir starting within 10 days of kidney transplant for up to 200 days post-transplant. Dose (in milligrams [mg]) was calculated using the algorithm ($7 \times \text{Body Surface Area} \times \text{Creatinine Clearance}$).

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

Dosage and administration details:

Treatment with valganciclovir was commenced as soon after transplant as the participant could tolerate oral medication (but not later than 10 days post-transplant) and continued for up to a maximum of 200 days post-transplant.

Number of subjects in period 1	Valganciclovir
Started	57
Received At least 1 Dose of Study Drug	56
Completed	49
Not completed	8
Consent withdrawn by subject	1
Adverse event, non-fatal	6
Did not receive study drug	1

Period 2

Period 2 title	Off-Treatment Follow-up Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Off-Treatment Follow-Up Period
Arm description: -	
Arm type	Follow-up Period
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Off-Treatment Follow-Up Period
Started	49
Completed	55

Joined	6
Withdrew treatment; continued follow-up period	6

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period
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Reporting group description:

Participants received a once daily oral dose (solution or tablets) of valganciclovir starting within 10 days of kidney transplant for up to 200 days post-transplant. Dose (in mg) was calculated using the algorithm [7 * Body Surface Area * Creatinine Clearance].

Reporting group values	Treatment Period	Total	
Number of subjects	57	57	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	10.6 ± 4.6	-	
Gender categorical Units: Subjects			
Female	26	26	
Male	31	31	

End points

End points reporting groups

Reporting group title	Valganciclovir
Reporting group description:	
Participants received a once daily oral dose (solution or tablets) of valganciclovir starting within 10 days of kidney transplant for up to 200 days post-transplant. Dose (in milligrams [mg]) was calculated using the algorithm (7 * Body Surface Area * Creatinine Clearance).	
Reporting group title	Off-Treatment Follow-Up Period
Reporting group description: -	
Subject analysis set title	Intent-to-Treat Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Baseline measures were based on the Intent-to-treat population that included all enrolled participants who had taken at least one dose of study drug.	

Primary: Number of Participants With Adverse Events (AEs), Serious Adverse Events (SAEs) or Withdrawal Due to AEs

End point title	Number of Participants With Adverse Events (AEs), Serious Adverse Events (SAEs) or Withdrawal Due to AEs ^[1]
End point description:	
An AE was any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product. Pre-existing conditions which worsen during a study were reported as AEs. A SAE was any experience that: resulted in death, was life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect or was medically significant. Safety Population included all enrolled participants who received at least one dose of study medication and had at least one post-baseline assessment of safety.	
End point type	Primary
End point timeframe:	
52 weeks	

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: Safety analysis was purely descriptive as the study was not powered for statistical comparison.

End point values	Valganciclovir			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: participants				
number (not applicable)				
AEs	56			
SAEs	41			
Withdrawals Due to AE	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Cytomegalovirus (CMV) Infection in the First 52 Weeks Post-Transplant as Assessed by the Investigator

End point title	Number of Participants With Cytomegalovirus (CMV) Infection in the First 52 Weeks Post-Transplant as Assessed by the Investigator
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End point description:

A polymerase chain reaction (PCR) based assay or antigenaemia assay was used for the qualitative assessment of CMV viremia (presence of CMV in the blood) by each study center as part of the clinical assessment required for diagnosis of CMV infection

Intent-to-treat (ITT) population included all enrolled participants who had taken at least one dose of study medication.

End point type	Secondary
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End point timeframe:

52 weeks

End point values	Valganciclovir			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: participants				
number (not applicable)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With CMV Disease in the First 52 Weeks Post-Transplant as Assessed by the Investigator

End point title	Number of Participants With CMV Disease in the First 52 Weeks Post-Transplant as Assessed by the Investigator
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End point description:

A PCR based assay or antigenaemia assay was used for the qualitative assessment of CMV viremia by each study center as part of the clinical assessment required for diagnosis of CMV infection. CMV disease included CMV syndrome or tissue invasive CMV. CMV syndrome required fever greater than or equal to (\geq) 38 degrees Celsius, severe malaise, leukopenia on 2 separate measurements, atypical lymphocytosis \geq 5%, thrombocytopenia, elevation of hepatic transaminases and presence of CMV in blood. Tissue Invasive CMV required evidence of localized CMV infection in a biopsy or other appropriate symptom and relevant symptoms or signs of organ dysfunction.

ITT population included all enrolled participants who had taken at least one dose of study medication.

End point type	Secondary
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End point timeframe:

52 weeks

End point values	Valganciclovir			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: participants				
number (not applicable)				
CMV Syndrome	1			
Tissue Invasive CMV	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Peak CMV Viral Load up to Week 52 Post-Transplant

End point title	Number of Participants With Peak CMV Viral Load up to Week 52 Post-Transplant
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End point description:

Blood samples were sent to a central laboratory for the quantitative assessment of CMV viral load (amount of CMV in the blood) by a Food and Drug Administration (FDA)-approved molecular-based assay. The number of participants in each category is reported in copies/milliliter (CP/mL). CMV deoxy ribonucleic acid (DNA) is detected in all categories < 150 CP/mL and above.

ITT population included all enrolled participants who had taken at least one dose of study medication

End point type	Secondary
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End point timeframe:

52 weeks

End point values	Valganciclovir			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: participants				
number (not applicable)				
No CMV DNA Detected	30			
<150 CP/mL	16			
150 to 1,000 CP/mL	6			
1,001 to 5,000 CP/mL	3			
> 5,000 CP/mL	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Biopsy Proven Rejection

End point title	Number of Participants With Biopsy Proven Rejection
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End point description:

Renal biopsies were performed as medically indicated. Biopsies were assessed histologically using the

updated Banff criteria 1997.

ITT population included all enrolled participants who had taken at least one dose of study medication.

End point type	Secondary
End point timeframe:	
52 weeks	

End point values	Valganciclovir			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: participants				
number (not applicable)				
≤ 2 Years	1			
>2 to <12 Years	1			
≥ 12 Years	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Graft Loss

End point title	Number of Participants With Graft Loss
End point description:	
Graft loss was defined as the institution of chronic dialysis (at least 6 consecutive weeks), transplant nephrectomy, or retransplantation.	
ITT population included all enrolled participants who had taken at least one dose of study medication.	
End point type	Secondary
End point timeframe:	
52 weeks	

End point values	Valganciclovir			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Death

End point title	Number of Participants With Death
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End point description:	
ITT population included all enrolled participants who had taken at least one dose of study medication.	
End point type	Secondary
End point timeframe:	
52 weeks	

End point values	Valganciclovir			
Subject group type	Reporting group			
Number of subjects analysed	56			
Units: participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Known Ganciclovir Resistance (Mutations in Either UL54 or UL97 Genes)

End point title	Number of Participants With Known Ganciclovir Resistance (Mutations in Either UL54 or UL97 Genes)
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End point description:

All participants with measurable CMV had both UL54 and UL97 genes sequenced to assess for known CMV resistance to ganciclovir. All participants meeting the resistance analysis criteria are included into the resistance analysis.

End point type	Secondary
End point timeframe:	
52 weeks	

End point values	Valganciclovir			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: participants				
number (not applicable)				
UL54	0			
UL97	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 28 days after last dose of study medication

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Valganciclovir
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Reporting group description:

Participants received a once daily oral dose (solution or tablets) of valganciclovir starting within 10 days of kidney transplant for up to 200 days post-transplant. Dose (in mg) was calculated using the algorithm [7 * Body Surface Area * Creatinine Clearance].

Serious adverse events	Valganciclovir		
Total subjects affected by serious adverse events			
subjects affected / exposed	41 / 56 (73.21%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Vesicoureteral reflux surgery			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Device leakage			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Transplant rejection			

subjects affected / exposed	3 / 56 (5.36%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Kidney transplant rejection			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Tonsillar hypertrophy			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatine increased			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
HLA marker study positive			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Complications of transplant surgery			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Complications of transplanted kidney			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			

subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Benign intracranial hypertension			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bicytopenia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

Papilloedema			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Aphthous stomatitis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Ureteric obstruction			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Bladder dysfunction			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urethral obstruction			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Urinary tract obstruction			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vesicoureteric reflux			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neurogenic bladder			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Proteinuria			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	7 / 56 (12.50%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Bacterial pyelonephritis			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Peritonitis			

subjects affected / exposed	2 / 56 (3.57%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	2 / 56 (3.57%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis norovirus				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal protozoal infection				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal viral infection				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rotavirus infection				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection bacterial				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urosepsis				

subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Varicella				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	4 / 56 (7.14%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Chronic sinusitis				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea infectious				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia mycoplasmal				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				

subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Valganciclovir		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 56 (98.21%)		
Investigations			
Blood creatine increased			
subjects affected / exposed	7 / 56 (12.50%)		
occurrences (all)	9		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 56 (14.29%)		
occurrences (all)	9		
Nervous system disorders			

Headache			
subjects affected / exposed	12 / 56 (21.43%)		
occurrences (all)	15		
Tremor			
subjects affected / exposed	10 / 56 (17.86%)		
occurrences (all)	12		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	12 / 56 (21.43%)		
occurrences (all)	15		
Neutropenia			
subjects affected / exposed	12 / 56 (21.43%)		
occurrences (all)	15		
Anaemia			
subjects affected / exposed	10 / 56 (17.86%)		
occurrences (all)	10		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	9 / 56 (16.07%)		
occurrences (all)	15		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	18 / 56 (32.14%)		
occurrences (all)	27		
Abdominal pain			
subjects affected / exposed	9 / 56 (16.07%)		
occurrences (all)	11		
Vomiting			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	8		
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	10 / 56 (17.86%)		
occurrences (all)	10		
Haematuria			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	6		
Renal tubular acidosis			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	5		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	20 / 56 (35.71%)		
occurrences (all)	26		
Urinary tract infection			
subjects affected / exposed	13 / 56 (23.21%)		
occurrences (all)	17		
Nasopharyngitis			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	7		
BK virus infection			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 January 2011	The protocol amendment documented an increase in the number of participants, added a Per Protocol analysis population, clarified the assessments for CMV and acute rejection, deleted the analysis for treatment failures because this was already planned in a separate analysis, deleted the urinalysis and simplified a number of terms that were identified as confusing or unclear.
02 September 2011	The protocol amendment corrected an inconsistency between the synopsis and protocol exclusion criteria and incorporated a request from Agence Française de Sécurité Sanitaire des Produits de Santé (AFSAPPS) regarding hypersensitivity to valganciclovir excipients, and specifically stated that tablets were not recommended in children under the age of 6 years due to the risk of choking in this age group. This protocol amendment also added newer methods for the measurement of serum creatinine, added pregnancy testing for post-pubescent girls throughout the prophylaxis period (request from the Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM, Germany), for pregnancy testing throughout the prophylaxis period), added the need for adequate contraception throughout the prophylaxis period (added at the request of the BfArM), modified the study medication storage details to be consistent with the product package insert and removed red blood cell count (RBC) from the hematology assessment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported