Clinical trial results:
A Phase 3, Open-Label, Multicenter Study to Evaluate the Safety of Paricalcitol Capsules in Pediatric Subjects Ages 10 to 16 with Stage 5 Chronic Kidney Disease Receiving Peritoneal Dialysis or Hemodialysis

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2013-002610-13
Trial protocol	PT DE GB
Global end of trial date	24 April 2015

Results information

Result version number	v1 (current)
This version publication date	18 May 2016
First version publication date	18 May 2016

Trial information

Trial identification

Sponsor protocol code	M11-612

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01382212
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	1 North Waukegan Road, North Chicago, IL, United States, 60064
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	Ann Eldred, MD, AbbVie, ann.eldred@abbvie.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 April 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to evaluate the safety of paricalcitol capsules for the treatment of secondary hyperparathyroidism in pediatric subjects ages 10 to 16 years with Stage 5 chronic kidney disease (CKD), receiving peritoneal dialysis or hemodialysis through the evaluation of the incidence of hypercalcemia.

Protection of trial subjects:

Subject and/or parent or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 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	United States: 11
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	13
EEA total number of subjects	2

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)	13
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 total of 26 subjects were screened and 13 pediatric subjects (between 10 and 16 years of age) were enrolled; 1 subject was 16 years of age at the time of Screening and turned 17 by the time treatment began.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Paricalcitol

Arm description:

Open-label paricalcitol (maximum dose of 16 µg), 3 times weekly (no more frequently than every other day) for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	paricalcitol 1 µg capsule, soft
Investigational medicinal product code	
Other name	ABT-358, Zemplar
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Starting dose of paricalcitol was determined by the intact parathyroid hormone (iPTH) value (iPTH/120) from prior to Day 1, rounded down to the nearest whole number, not to exceed 16 µg 3 times weekly, no more frequently than every other day. Decisions to hold, maintain, increase, or decrease a dose were based on the iPTH, phosphorus, and calcium results generated from the most recent visit and within target Kidney Dialysis Outcomes Quality Initiatives (KDOQI) levels.

Investigational medicinal product name	paricalcitol 2 µg capsule, soft
Investigational medicinal product code	
Other name	ABT-358, Zemplar
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Starting dose of paricalcitol was determined by the iPTH/120 from prior to Day 1, rounded down to the nearest whole number, not to exceed 16 µg 3 times weekly, no more frequently than every other day. Decisions to hold, maintain, increase, or decrease a dose were based on the iPTH, phosphorus, and calcium results generated from the most recent visit and within target KDOQI levels.

Number of subjects in period 1	Paricalcitol
Started	13
Completed	11
Not completed	2
Withdrew consent	1

Kidney transplant	1

Baseline characteristics

Reporting groups	
Reporting group title	Paricalcitol
Reporting group description:	
Open-label paricalcitol (maximum dose of 16 µg), 3 times weekly (no more frequently than every other day) for 12 weeks.	

Reporting group values	Paricalcitol	Total	
Number of subjects	13	13	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	14.5		
standard deviation	± 1.76	-	
Gender categorical			
Units: Subjects			
Female	8	8	
Male	5	5	

End points

End points reporting groups

Reporting group title	Paricalcitol

Reporting group description:

Open-label paricalcitol (maximum dose of 16 µg), 3 times weekly (no more frequently than every other day) for 12 weeks.

Primary: Percentage of Subjects With Hypercalcemia

End point title	Percentage of Subjects With Hypercalcemia[1]

End point description:

The percentage of subjects with hypercalcemia, defined as at least 2 consecutive post-baseline corrected calcium values > 10.2 mg/dL (2.55 mmol/L).

End point type	Primary

End point timeframe:

Day 1 to Week 12

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 data were summarized for this end point per protocol.

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[2]			
Units: percentage of subjects				
number (confidence interval 95%)	15.3 (1.9 to 45.4)			

Notes:

[2] - All-treated data set: all subjects enrolled and administered at least 1 dose of paricalcitol

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With 2 Consecutive iPTH/120 Between 150 and 300 pg/mL

End point title	Percentage of Subjects With 2 Consecutive iPTH/120 Between 150 and 300 pg/mL

End point description:

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Week 12

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[3]			
Units: percentage of subjects				
number (confidence interval 95%)	38.5 (13.9 to 68.4)			

Notes:

[3] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With 2 Consecutive iPTH Reductions of at Least 30% From Baseline

End point title	Percentage of Subjects With 2 Consecutive iPTH Reductions of at Least 30% From Baseline

End point description:

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Week 12

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[4]			
Units: percentage of subjects				
number (confidence interval 95%)	61.5 (31.6 to 86.1)			

Notes:

[4] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Hemoglobin: Mean Change from Baseline to Final Visit

End point title	Hemoglobin: Mean Change from Baseline to Final Visit

End point description:

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	11[5]			
Units: g/dL				
arithmetic mean (standard deviation)	-0.1 (± 1.263)			

Notes:

[5] - All subjects in the all -treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Hematocrit: Mean Change from Baseline to Final Visit

End point title	Hematocrit: Mean Change from Baseline to Final Visit

End point description:

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	11[6]			
Units: percent				
arithmetic mean (standard deviation)	-1.08 (± 5.066)			

Notes:

[6] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Red Blood Cells: Mean Change from Baseline to Final Visit

End point title	Red Blood Cells: Mean Change from Baseline to Final Visit

End point description:

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	11[7]			
Units: x10^6/µL				
arithmetic mean (standard deviation)	-0.09 (± 0.496)			

Notes:

[7] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: White Blood Cells (WBC) and Platelet Count: Mean Change from Baseline to Final Visit

End point title	White Blood Cells (WBC) and Platelet Count: Mean Change from Baseline to Final Visit

End point description:

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	11[8]			
Units: x10^3/µL				
arithmetic mean (standard deviation)				
WBC	-0.06 (± 2.982)			
Platelet Count	19.2 (± 47.03)			

Notes:

[8] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Neutrophils, Lymphocytes, Monocytes, Eosinophils, and Basophils: Mean Change from Baseline to Final Visit

End point title	Neutrophils, Lymphocytes, Monocytes, Eosinophils, and Basophils: Mean Change from Baseline to Final Visit

End point description:

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	11[9]			
Units: x10^9/µL				
arithmetic mean (standard deviation)				
Neutrophils	0.11 (± 2.6812)			
Lymphocytes	-0.294 (± 0.597)			
Monocytes	0.032 (± 0.1276)			
Eosinophils	0.059 (± 0.1522)			
Basophils	-0.01 (± 0.0322)			

Notes:

[9] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Lactic Dehydrogenase (LDH), and Bone-Specific Alkaline Phosphatase (BSAP): Mean Change from Baseline to Final Visit

End point title	Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Lactic Dehydrogenase (LDH), and Bone-Specific Alkaline Phosphatase (BSAP): Mean Change from Baseline to Final Visit

End point description:

n=subjects with evaluable Baseline and Post-baseline data for each parameter.

End point type	Secondary

End point timeframe:

End point timeframe Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	11[10]			
Units: U/L				
arithmetic mean (standard deviation)				
ALT (n=11)	-4.55 (± 16.501)			
AST (n=11)	-4.45 (± 12.25)			
LDH (n=11)	-6.5 (± 33.22)			
BSAP (n=9)	-49.4 (± 86.95)			

Notes:

[10] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Bilirubin, Blood Urea Nitrogen (BUN), Uric Acid, Magnesium, Glucose, Cholesterol, Triglycerides, High sensitivity C-Reactive Protein (hsCRP), Inorganic phosphate, Corrected Calcium, and Creatinine: Mean Change from Baseline to Final Visit

End point title	Bilirubin, Blood Urea Nitrogen (BUN), Uric Acid, Magnesium, Glucose, Cholesterol, Triglycerides, High sensitivity C-Reactive Protein (hsCRP), Inorganic phosphate, Corrected Calcium, and Creatinine: Mean Change from Baseline to Final Visit

End point description:

n=subjects with evaluable Baseline and Post-baseline data for each parameter.

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	11[11]			
Units: mg/dL				
arithmetic mean (standard deviation)				
Total bilirubin (n=11)	0.032 (± 0.3165)			
Direct Bilirubin (n=11)	0.013 (± 0.0785)			
Indirect Bilirubin (n=9)	0.056 (± 0.3035)			
BUN (n=11)	1.33 (± 11.614)			
Uric Acid (n=11)	0.31 (± 1.245)			
Magnesium (n=11)	0.082 (± 0.3649)			
Glucose (n=11)	4.36 (± 10.172)			
Cholesterol (n=11)	-16.4 (± 27.37)			
Triglycerides (n=11)	9.2 (± 40.32)			
hsCRP (n=11)	0.061 (± 0.1967)			
Inorganic phosphate (n=13)	0.64 (± 1.188)			
Corrected Calcium (n=7)	0.31 (± 0.421)			
Creatinine (n=11)	0.48 (± 1.592)			

Notes:
[11] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Alkaline phosphatase: Mean Change from Baseline to Final Visit

End point title	Alkaline phosphatase: Mean Change from Baseline to Final Visit

End point description:

End point type	Secondary

End point timeframe:
Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	11[12]			
Units: IU/L				
arithmetic mean (standard deviation)	-61.8 (± 117.34)			

Notes:
[12] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Sodium, Potassium, Chloride, Bicarbonate: Mean Change from Baseline to Final Visit

End point title	Sodium, Potassium, Chloride, Bicarbonate: Mean Change from Baseline to Final Visit

End point description:

End point type	Secondary

End point timeframe:
Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	11[13]			
Units: mEq/L				
arithmetic mean (standard deviation)				
Sodium	-0.5 (± 2.02)			
Potassium	0.25 (± 0.746)			
Chloride	0.5 (± 3.21)			
Bicarbonate	-0.45 (± 3.446)			

Notes:

[13] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Total Protein and Albumin: Mean Change from Baseline to Final Visit

End point title	Total Protein and Albumin: Mean Change from Baseline to Final Visit

End point description:

n=subjects with evaluable Baseline and Post-baseline data for each parameter.

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[14]			
Units: g/dL				
arithmetic mean (standard deviation)				
Total protein (n=11)	0.15 (± 0.43)			
Albumin (n=13)	0.04 (± 0.325)			

Notes:

[14] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Fibroblast Growth Factor-23 (FGF-23), 1,25-Hydroxy Vitamin D, 25-Hydroxy Vitamin D, and Intact Parathyroid Hormone (iPTH): Mean Change from Baseline to Final Visit

End point title	Fibroblast Growth Factor-23 (FGF-23), 1,25-Hydroxy Vitamin D, 25-Hydroxy Vitamin D, and Intact Parathyroid Hormone (iPTH): Mean Change from Baseline to Final Visit

End point description:

n=subjects with evaluable Baseline and Post-baseline data for each parameter.

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[15]			
Units: pg/mL				
arithmetic mean (standard deviation)				
FGF-23 (n=10)	1990.7 (± 3317.79)			
1,25-Hydroxy Vitamin D (n=11)	15.65 (± 29.296)			
25-Hydroxy Vitamin D (n=11)	5.8 (± 10.38)			
iPTH (n=13)	-437.5 (± 491.83)			

Notes:

[15] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Osteocalcin: Mean Change from Baseline to Final Visit

End point title	Osteocalcin: Mean Change from Baseline to Final Visit

End point description:

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	10[16]			
Units: ng/mL				
arithmetic mean (standard deviation)	117.21 (± 223.075)			

Notes:

[16] - All subjects in the all-treated data set with evaluable data

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events

End point title	Number of Subjects With Adverse Events

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. The investigator assessed the relationship of each event to the use of study drug as either probably related, possibly related, probably not related or not related. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs/TESAEs) are defined as any event that began or worsened in severity after the first dose of study drug. For more details on adverse events please see the Adverse Event section.

End point type	Secondary

End point timeframe:

From first dose of study drug until 30 days following last dose of study drug (up to 16 weeks).

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[17]			
Units: subjects				
Any TEAE	11			
TESAE	2			

Notes:

[17] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Potentially Clinically Significant Electrocardiogram (ECG) Findings

End point title	Number of Subjects with Potentially Clinically Significant Electrocardiogram (ECG) Findings

End point description:

12-lead ECGs were recorded after the subject had been in the supine position for at least 5 minutes. The number of subjects with potentially clinically significant ECG findings, as determined by the investigator, is presented.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[18]			
Units: subjects	0			

Notes:

[18] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP): Mean Change from Baseline to Final Visit

End point title	Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP): Mean Change from Baseline to Final Visit

End point description:

Blood pressure was measured after the subject had been sitting for at least 3 minutes.

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[19]			
Units: mm Hg				
arithmetic mean (standard deviation)				
SBP	7.5 (± 15.66)			
DBP	3.7 (± 12.98)			

Notes:

[19] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Heart Rate: Mean Change from Baseline to Final Visit

End point title	Heart Rate: Mean Change from Baseline to Final Visit

End point description:

Heart rate was measured after the subject had been sitting for at least 3 minutes.

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[20]			
Units: bpm				
arithmetic mean (standard deviation)	1.8 (± 17.43)			

Notes:

[20] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Oral Body Temperature: Mean Change from Baseline to Final Visit

End point title	Oral Body Temperature: Mean Change from Baseline to Final Visit

End point description:

End point type	Secondary

End point timeframe:

Baseline (last measurement collected prior to the first dose) to Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[21]			
Units: degrees Celsius				
arithmetic mean (standard deviation)	0.03 (± 0.338)			

Notes:

[21] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Potentially Clinically Significant Physical Examination Findings

End point title	Number of Subjects with Potentially Clinically Significant Physical Examination Findings

End point description:

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Final Visit (up to Week 12)

End point values	Paricalcitol			
Subject group type	Reporting group			
Number of subjects analysed	13[22]			
Units: subjects	0			

Notes:

[22] - All-treated data set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were collected from first dose of study drug until 30 days following last dose of study drug (up to 16 weeks); serious adverse events were collected from the time when informed consent was obtained (up to 28 weeks).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Paricalcitol

Reporting group description:

Open-label paricalcitol (maximum dose of 16 µg), 3 times weekly (no more frequently than every other day) for 12 weeks.

Serious adverse events	Paricalcitol		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 13 (15.38%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Peritoneal dialysis complication			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Paricalcitol		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 13 (76.92%)		

Investigations			
Blood calcium increased			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Haemoglobin decreased			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arteriovenous fistula site complication			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Procedural vomiting			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		

Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Nausea subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3		
Vomiting subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2		
Throat irritation subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Pain in extremity subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Metabolism and nutrition disorders			

Hyperphosphataemia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 May 2011	The purpose of the amendment was to revise the definition of full immunosuppressant therapy, so otherwise eligible transplant patients were not excluded.
21 August 2012	The purpose of the amendment was to add a maximum iPTH value for entry into the Washout Period and increased the upper limit for corrected calcium for entry into the Dosing Period. In addition, the fasting requirement for blood draws was removed at all points in the study at the request of the investigators.
29 August 2012	The purpose of the amendment was to clarify that positive drug test results, due to controlled drugs prescribed for a medical need, were not exclusionary
19 June 2013	The purpose of the amendment was to revise the number of study sites to accommodate additional sites outside of the United States and add equivalent values in the units mmol/L for current calcium and phosphorus in the units mg/dL to comply with local standards.
31 October 2013	The purpose of the amendment was to modify the protocol so that subjects on hemodialysis could be included in the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The sample size of the study was limited to 13 subjects and there was no comparator group, so the study was not designed to analyze efficacy.

Notes: