Clinical trial results:
A Randomized, Double-blind, Placebo controlled Study to Assess the Efficacy and Safety of Cinacalcet HCl in Pediatric Subjects with Chronic Kidney Disease and Secondary Hyperparathyroidism Receiving Dialysis

Summary

EudraCT number	2010-023150-37
Trial protocol	ES HU BE SK DE Outside EU/EEA
Global end of trial date	30 April 2014

Results information

Result version number	v1 (current)
This version publication date	20 June 2016
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	20070208

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01277510
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen, Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000078-PIP01-07
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	30 April 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the safety and efficacy of adding cinacalcet to the current treatment of secondary hyperparathyroidism in children currently receiving dialysis compared to a treatment regimen that does not include cinacalcet.

Protection of trial subjects:

This study was conducted in accordance with applicable country regulations and International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.
All parents or legally acceptable representatives provided written informed consent before the subject underwent any study-related procedures, including screening procedures.
The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy:

All participants, regardless of treatment assignment, eceived standard of care with vitamin D sterols (calcitriol and its analogs), as prescribed by the treating physician.

Evidence for comparator: -

Actual start date of recruitment	28 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 23
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Mexico: 1
Worldwide total number of subjects	43
EEA total number of subjects	11

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)	11
Adolescents (12-17 years)	32
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was enrolled on 28 June 2011 and the last patient enrolled was on 15 January 2013. Eligible participants were between the ages of 6 to less than 18 years old who had chronic kidney (CKD) and secondary hyperparathyroidism treated with either hemodialysis or peritoneal dialysis for ≥ 2 months.

Pre-assignment

Screening details:

This study consisted of a 30-week randomized, double-blind phase followed by a 30-week open-label phase. Participants were randomized 1:1 to receive either cinacalcet or placebo in the double-blind phase. All participants received cinacalcet in the open-label phase.

Period 1

Period 1 title	Double-blind Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received standard of care and placebo once daily for 30 weeks during the double-blind phase.

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

Dosage and administration details:

Placebo tablets and capsules for sprinkling identical to active treatment.

Arm title	Cinacalcet

Arm description:

Participants received standard of care and cinacalcet once daily for 30 weeks during the double-blind phase. The starting dose of cinacalcet was ≤ 0.20 mg/kg based on dry weight, and could be titrated up according to plasma iPTH and serum calcium levels every 4 weeks until Week 24 to a maximum dose of 4.2 mg/kg.

Arm type	Experimental
Investigational medicinal product name	Cinacalcet
Investigational medicinal product code	
Other name	Sensipar, Mimpara
Pharmaceutical forms	Capsule, Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Cinacalcet was prepared for oral administration as both capsules for sprinkling and film coated tablets for swallowing.

Number of subjects in period 1	Placebo	Cinacalcet
Started	21	22
Received Investigational Product	21	22
Completed	8	4
Not completed	13	18
Consent withdrawn by subject	2	-
Administrative decision	7	9
Other	1	1
Death	-	1
Adverse event	1	-
Non-compliance	-	1
Protocol-specified criteria	2	6

Period 2

Period 2 title	Open-label Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Cinacalcet

Arm description:

Participants who received standard of care and placebo during the double-blind phase received cinacalcet with standard of care for 30 weeks during the open-label phase. The starting dose of cinacalcet was ≤ 0.20 mg/kg based on dry weight, and could be titrated up according to plasma iPTH and serum calcium levels every 4 weeks up to Week 54 to a maximum dose of 4.2 mg/kg.

Arm type	Open-label
Investigational medicinal product name	Cinacalcet
Investigational medicinal product code	
Other name	Sensipar, Mimpara
Pharmaceutical forms	Capsule, Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Cinacalcet was prepared for oral administration as both capsules for sprinkling and film coated tablets for swallowing.

Arm title	Cinacalcet/Cinacalcet

Arm description:

Participants who received standard of care and cinacalcet during the double-blind phase continued to receive cinacalcet with standard of care for an additional 30 weeks during the open-label phase. Regardless of the titration level reached at the last dose of IP in the double-blind phase, all participants started titration at ≤ 0.20 mg/kg based on dry weight and could be titrated up according to plasma iPTH and serum calcium levels every 4 weeks up to Week 54 to a maximum dose of 4.2 mg/kg.

Arm type	Experimental

Investigational medicinal product name	Cinacalcet
Investigational medicinal product code	
Other name	Sensipar, Mimpara
Pharmaceutical forms	Capsule, Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Cinacalcet was prepared for oral administration as both capsules for sprinkling and film coated tablets for swallowing.

Number of subjects in period 2	Placebo/Cinacalcet	Cinacalcet/Cinacalcet
Started	8	4
Received investigational product	6	4
Completed	1	1
Not completed	7	3
Never received investigational product	2	-
Administrative decision	4	3
Protocol-specified criteria	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received standard of care and placebo once daily for 30 weeks during the double-blind phase.	
Reporting group title	Cinacalcet
Reporting group description:	
Participants received standard of care and cinacalcet once daily for 30 weeks during the double-blind phase. The starting dose of cinacalcet was ≤ 0.20 mg/kg based on dry weight, and could be titrated up according to plasma iPTH and serum calcium levels every 4 weeks until Week 24 to a maximum dose of 4.2 mg/kg.	

Reporting group values	Placebo	Cinacalcet	Total
Number of subjects	21	22	43
Age, Customized Units: participants			
6 to < 12 years	5	6	11
12 to < 18 years	16	16	32
Age Continuous Units: years			
arithmetic mean	13.2	13.3	
standard deviation	± 2.9	± 3.6	-
Gender, Male/Female Units: participants			
Female	10	12	22
Male	11	10	21
Race/Ethnicity, Customized Units: Subjects			
White	15	16	31
Black or African American	6	5	11
Other	0	1	1
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	5	3	8
Not Hispanic or Latino	16	19	35
Intact Parathyroid Hormone (iPTH) Units: pg/mL			
arithmetic mean	795.8	757.1	
standard deviation	± 537.9	± 440.1	-
Corrected Total Serum Calcium			
Serum calcium was reported as a corrected value by the central laboratory based on calcium and albumin concentrations: Corrected total calcium (mg/dL) = measured total serum calcium (mg/dL) + 0.8 (4.0 – Serum albumin (g/dL)).			
Units: mg/dL			
arithmetic mean	9.88	9.91	
standard deviation	± 0.62	± 0.54	-
Serum Phosphorous Units: mg/dL			

arithmetic mean	6.37	6.68	
standard deviation	± 1.48	± 1.78	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received standard of care and placebo once daily for 30 weeks during the double-blind phase.	
Reporting group title	Cinacalcet
Reporting group description:	
Participants received standard of care and cinacalcet once daily for 30 weeks during the double-blind phase. The starting dose of cinacalcet was ≤ 0.20 mg/kg based on dry weight, and could be titrated up according to plasma iPTH and serum calcium levels every 4 weeks until Week 24 to a maximum dose of 4.2 mg/kg.	
Reporting group title	Placebo/Cinacalcet
Reporting group description:	
Participants who received standard of care and placebo during the double-blind phase received cinacalcet with standard of care for 30 weeks during the open-label phase. The starting dose of cinacalcet was ≤ 0.20 mg/kg based on dry weight, and could be titrated up according to plasma iPTH and serum calcium levels every 4 weeks up to Week 54 to a maximum dose of 4.2 mg/kg.	
Reporting group title	Cinacalcet/Cinacalcet
Reporting group description:	
Participants who received standard of care and cinacalcet during the double-blind phase continued to receive cinacalcet with standard of care for an additional 30 weeks during the open-label phase. Regardless of the titration level reached at the last dose of IP in the double-blind phase, all participants started titration at ≤ 0.20 mg/kg based on dry weight and could be titrated up according to plasma iPTH and serum calcium levels every 4 weeks up to Week 54 to a maximum dose of 4.2 mg/kg.	

Primary: Percentage of Participants Achieving ≥ 30% Reduction in Mean iPTH From Baseline to the Efficacy Assessment Phase

End point title	Percentage of Participants Achieving ≥ 30% Reduction in Mean iPTH From Baseline to the Efficacy Assessment Phase
End point description:	
The efficacy assessment value is based on the scheduled assessment(s) taken during the efficacy assessment phase (EAP; Weeks 25 - 30). When multiple assessments were available, the average of those was used. If an efficacy measurement during the EAP was missing, the mean of the last 2 available post-baseline values in the dose-titration phase was used. If only one post-baseline value was available, this single value was used. The full analysis set, which includes all randomized participants with at least 1 post-baseline assessment, was used for the analysis.	
End point type	Primary
End point timeframe:	
From Baseline to the Efficacy Assessment Phase, Weeks 25-30	

End point values	Placebo	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: percentage of participants				
number (not applicable)	19	54.5		

Statistical analyses

Statistical analysis title	Primary Analysis

Statistical analysis description:

A hierarchical testing procedure was used to test the primary and biochemical secondary endpoints (Endpoints 1-5). The primary endpoint was tested at a significance level of 0.05. The four biochemical secondary endpoints were to be tested using Holm's method at 0.05 should the primary endpoint achieve a significant result.

Comparison groups	Placebo v Cinacalcet
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference (Cinacalcet - Placebo)
Point estimate	35.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.76
upper limit	62.24

Notes:

[1] - Cochran- Mantel-Haenszel (CMH) test stratified by baseline age group (6 -<12 years old or 12 - <18 years old).

Secondary: Percentage of Participants Achieving Mean iPTH ≤ 300 pg/mL (31.8 pmol/L) During the Efficacy Assessment Phase

End point title	Percentage of Participants Achieving Mean iPTH ≤ 300 pg/mL (31.8 pmol/L) During the Efficacy Assessment Phase

End point description:

The efficacy assessment value is based on the scheduled assessment(s) taken during the efficacy assessment phase. When multiple assessments were available, the average of those was used. If an efficacy measurement during the EAP was missing, the mean of the last 2 available postbaseline values in the dose-titration phase was used. If only one post-baseline value was available, this single value was used.

End point type	Secondary

End point timeframe:

From Baseline to the Efficacy Assessment Phase (EAP), Weeks 25-30

End point values	Placebo	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: percentage of participants				
number (not applicable)	23.8	27.3		

Statistical analyses

Statistical analysis title	Statistical Analysis

Statistical analysis description:

The secondary endpoint with the smallest p-value was first compared at a significance level of 0.0125. If the p-value was > 0.0125, all 4 secondary endpoints were non-significant; if ≤ 0.0125, the null hypothesis for that endpoint was rejected. Next, the 2nd smallest p-value was compared at a level of 0.0167; if > 0.0167, the remaining 3 endpoints were not significant, or, the null hypothesis of that endpoint was rejected. The other 2 endpoints were analyzed similarly, at 0.025 and 0.05.

Comparison groups	Placebo v Cinacalcet
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.826 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference (Cinacalcet - Placebo)
Point estimate	3.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.58
upper limit	29.51

Notes:

[2] - Cochran- Mantel-Haenszel (CMH) test stratified by baseline age group (6 -<12 years old or 12 - <18 years old).

Secondary: Percent Change From Baseline in Mean Corrected Total Serum Calcium During the Efficacy Assessment Period

End point title	Percent Change From Baseline in Mean Corrected Total Serum Calcium During the Efficacy Assessment Period

End point description:

Serum calcium was reported as a corrected value by the central laboratory based on calcium and albumin concentrations: Corrected total calcium (mg/dL) = measured total serum calcium (mg/dL) + 0.8 (4.0 – Serum albumin (g/dL)). The efficacy assessment value is based on the scheduled assessment(s) taken during the efficacy assessment phase. When multiple assessments were available, the average of those was used. If an efficacy measurement during the EAP was missing, the mean of the last 2 available postbaseline values in the dose-titration phase was used. If only one post-baseline value was available, this single value was used.

End point type	Secondary

End point timeframe:

From Baseline to the Efficacy Assessment Phase, Weeks 25-30.

End point values	Placebo	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: percent change				
least squares mean (confidence interval 95%)	-1 (-4.9 to 2.9)	-4.6 (-8.4 to -0.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis

Statistical analysis description:

The secondary endpoint with the smallest p-value was first compared at a significance level of 0.0125. If the p-value was > 0.0125, all 4 secondary endpoints were non-significant; if ≤ 0.0125, the null hypothesis for that endpoint was rejected. Next, the 2nd smallest p-value was compared at a level of 0.0167; if > 0.0167, the remaining 3 endpoints were not significant, or, the null hypothesis of that endpoint was rejected. The other 2 endpoints were analyzed similarly, at 0.025 and 0.05.

Comparison groups	Placebo v Cinacalcet
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.147 [3]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.6
upper limit	1.3

Notes:

[3] - Baseline age group was used as covariate.

Secondary: Percent Change From Baseline in Mean Serum Phosphorus During the Efficacy Assessment Phase

End point title	Percent Change From Baseline in Mean Serum Phosphorus During the Efficacy Assessment Phase

End point description:

The efficacy assessment value is based on the scheduled assessment(s) taken during the efficacy assessment phase. When multiple assessments were available, the average of those was used. If an efficacy measurement during the EAP was missing, the mean of the last 2 available postbaseline values in the dose-titration phase was used. If only one post-baseline value was available, this single value was used.

End point type	Secondary

End point timeframe:

From Baseline to the Efficacy Assessment Phase, Weeks 25-30.

End point values	Placebo	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	22		
Units: percent change				
least squares mean (confidence interval 95%)	10.2 (-0.8 to 21.2)	4.9 (-5.5 to 15.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis

Statistical analysis description:

The secondary endpoint with the smallest p-value was first compared at a significance level of 0.0125. If the p-value was > 0.0125, all 4 secondary endpoints were non-significant; if ≤ 0.0125, the null hypothesis for that endpoint was rejected. Next, the 2nd smallest p-value was compared at a level of 0.0167; if > 0.0167, the remaining 3 endpoints were not significant, or, the null hypothesis of that endpoint was rejected. The other 2 endpoints were analyzed similarly, at 0.025 and 0.05.

Comparison groups	Placebo v Cinacalcet
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.454 [4]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.4
upper limit	8.9

Notes:

[4] - Baseline age group was used as covariate.

Secondary: Percent Change From Baseline in Mean Phosphorous Product (Ca x P) During the Efficacy Assessment Phase

End point title	Percent Change From Baseline in Mean Phosphorous Product (Ca x P) During the Efficacy Assessment Phase

End point description:

The efficacy assessment value is based on the scheduled assessment(s) taken during the efficacy assessment phase. When multiple assessments were available, the average of those was used. If an efficacy measurement during the EAP was missing, the mean of the last 2 available postbaseline values in the dose-titration phase was used. If only one post-baseline value was available, this single value was used.

End point type	Secondary

End point timeframe:

From Baseline to end of Efficacy Assessment Period, assessed up to 30 weeks

End point values	Placebo	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: percent change				
least squares mean (confidence interval 95%)	8 (-1.8 to 17.7)	-2 (-11.4 to 7.4)		

Statistical analyses

Statistical analysis title	Statistical Analysis

Statistical analysis description:

The secondary endpoint with the smallest p-value was first compared at a significance level of 0.0125. If the p-value was > 0.0125, all 4 secondary endpoints were non-significant; if ≤ 0.0125, the null hypothesis for that endpoint was rejected. Next, the 2nd smallest p-value was compared at a level of 0.0167; if > 0.0167, the remaining 3 endpoints were not significant, or, the null hypothesis of that endpoint was rejected. The other 2 endpoints were analyzed similarly, at 0.025 and 0.05.

Comparison groups	Placebo v Cinacalcet
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.117 [5]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.5
upper limit	2.6

Notes:

[5] - Baseline age group was used as covariate.

Secondary: Growth Velocity from Baseline to End of Double-blind Phase

End point title	Growth Velocity from Baseline to End of Double-blind Phase

End point description:

Linear growth velocity (cm/year) = 52 x change in height (cm) / number of weeks between the two assessments. End of double-blind phase visit was at Week 30 by design but the last assessment in the double-blind phase was used due to the early termination of the study.

End point type	Secondary

End point timeframe:

From Baseline to end of Efficacy Assessment at Week 30

End point values	Placebo	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[6]	17[7]		
Units: cm/year				
least squares mean (confidence interval 95%)	3.1 (0.7 to 5.6)	3.3 (0.8 to 5.8)		

Notes:

[6] - Full analysis set. Only participants with available data were included in the analysis.

[7] - Full analysis set. Only participants with available data were included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Cinacalcet
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.896 [8]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	3.6

Notes:

[8] - No adjustments for multiplicity were made. Baseline age group was used as covariate.

Secondary: Growth Velocity From End of Double-blind Phase to End of Open-label Phase

End point title	Growth Velocity From End of Double-blind Phase to End of Open-label Phase

End point description:

Linear growth velocity (cm/year) = 52 x change in height (cm) / number of weeks between the two assessments. End of open-label phase visit was at Week 60 by design but the last assessment in the open-label phase was used due to the early termination of the study.

End point type	Secondary

End point timeframe:

End of double-blind phase (Week 30) until end of the open-label phase (Week 60)

End point values	Placebo/Cinacalcet	Cinacalcet/Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7[9]	3[10]		
Units: cm/year				
arithmetic mean (standard deviation)	2.75 (± 3.23)	1.21 (± 1.31)		

Notes:

[9] - Full analysis set. Only participants with available data were included in the analysis.

[10] - Full analysis set. Only participants with available data were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Mean Ionized Calcium During the Efficacy Assessment Phase

End point title	Percent Change From Baseline in Mean Ionized Calcium During the Efficacy Assessment Phase

End point description:

The efficacy assessment value is based on the scheduled assessment(s) taken during the efficacy assessment phase. When multiple assessments were available, the average of those was used. If an efficacy measurement during the EAP was missing, the mean of the last 2 available postbaseline values in the dose-titration phase was used. If only one post-baseline value was available, this single value was used.

End point type	Secondary

End point timeframe:

From Baseline to the Efficacy Assessment Phase, Weeks 25-30.

End point values	Placebo	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12[11]	18[12]		
Units: percent change				
least squares mean (confidence interval 95%)	-1.5 (-8.6 to 5.6)	-2.3 (-8.2 to 3.5)		

Notes:

[11] - Full analysis set. Only participants with available data were included in the analysis.

[12] - Full analysis set. Only participants with available data were included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v Cinacalcet
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.854 [13]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	7.9

Notes:
[13] - Baseline age group was used as covariate.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

60 Weeks + 30 Days

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Double-blind Phase: Placebo

Reporting group description:

Participants received standard of care and placebo once daily for 30 weeks during the double-blind phase.

Reporting group title	Double-blind Phase: Cinacalcet

Reporting group description:

Participants received standard of care and cinacalcet once daily for 30 weeks during the double-blind phase. The starting dose of cinacalcet was ≤ 0.20 mg/kg based on dry weight, and could be titrated up according to plasma iPTH and serum calcium levels every 4 weeks until Week 24 to a maximum dose of 4.2 mg/kg.

Reporting group title	Open-label Phase: Placebo/Cinacalcet

Reporting group description:

Participants who received standard of care and placebo during the double-blind phase received cinacalcet with standard of care for 30 weeks during the open-label phase. The starting dose of cinacalcet was ≤ 0.20 mg/kg based on dry weight, and could be titrated up according to plasma iPTH and serum calcium levels every 4 weeks up to Week 54 to a maximum dose of 4.2 mg/kg.

Reporting group title	Open-label Phase: Cinacalcet/Cinacalcet

Reporting group description:

Participants who received standard of care and cinacalcet during the double-blind phase continued to receive cinacalcet with standard of care for an additional 30 weeks during the open-label phase. Regardless of the titration level reached at the last dose of IP in the double-blind phase, all participants started titration at ≤ 0.20 mg/kg based on dry weight and could be titrated up according to plasma iPTH and serum calcium levels every 4 weeks up to Week 54 to a maximum dose of 4.2 mg/kg.

Serious adverse events	Double-blind Phase: Placebo	Double-blind Phase: Cinacalcet	Open-label Phase: Placebo/Cinacalcet
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 21 (42.86%)	9 / 22 (40.91%)	3 / 6 (50.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 21 (4.76%)	2 / 22 (9.09%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			

subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Medical device complication			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thirst			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis in device			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Rubber sensitivity			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplant rejection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood pressure increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Arteriovenous fistula site complication			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft complication			

subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular graft complication			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiopulmonary failure			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Nervous system disorders			
Hypertensive encephalopathy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Neutropenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Papilloedema			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Glycosuria			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Catheter site cellulitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Measles			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sepsis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food intolerance			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperphosphataemia			

subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Open-label Phase: Cinacalcet/Cinacalcet		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Medical device complication			

subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thirst				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombosis in device				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Rubber sensitivity				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transplant rejection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Blood creatinine increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood pressure increased				

subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoglobin increased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Arteriovenous fistula site complication				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Graft complication				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular graft complication				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiopulmonary failure				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Nervous system disorders			
Hypertensive encephalopathy			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Papilloedema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			

subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Varices oesophageal				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Glycosuria				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Catheter site cellulitis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				

subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Measles				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 4 (25.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Acidosis				
subjects affected / exposed	0 / 4 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fluid overload			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Food intolerance			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperphosphataemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Double-blind Phase: Placebo	Double-blind Phase: Cinacalcet	Open-label Phase: Placebo/Cinacalcet
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 21 (80.95%)	16 / 22 (72.73%)	6 / 6 (100.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	4 / 21 (19.05%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	4	1	0
Hypotension			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Catheter site pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Catheter site pruritus			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Catheter site related reaction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	2 / 21 (9.52%)	1 / 22 (4.55%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Device breakage			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Device leakage			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Face oedema			

subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Feeling cold			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Local swelling			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Oedema peripheral			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	2 / 21 (9.52%)	1 / 22 (4.55%)	2 / 6 (33.33%)
occurrences (all)	5	1	2
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 21 (14.29%)	1 / 22 (4.55%)	1 / 6 (16.67%)
occurrences (all)	4	3	2
Dyspnoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	3 / 21 (14.29%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	2
Oropharyngeal pain			

subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Daydreaming			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Staring			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood calcium abnormal			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood phosphorus increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haematocrit decreased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			

subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haemoglobin increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Arteriovenous fistula site complication			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Arthropod bite			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dialysis related complication			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Femur fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Overdose			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Procedural hypotension			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Procedural nausea			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vascular graft complication			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Mitral valve stenosis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Palpitations			

subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Tachycardia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Epilepsy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 21 (9.52%)	3 / 22 (13.64%)	1 / 6 (16.67%)
occurrences (all)	4	4	1
Hypoaesthesia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Paraesthesia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Syncope			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 21 (0.00%)	3 / 22 (13.64%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Eye disorders			

Keratitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	2 / 21 (9.52%)	3 / 22 (13.64%)	2 / 6 (33.33%)
occurrences (all)	2	4	2
Abdominal pain upper			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	3 / 21 (14.29%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Dry mouth			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	2 / 21 (9.52%)	2 / 22 (9.09%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Dyspepsia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia oral			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Stomatitis			

subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	2 / 21 (9.52%)	4 / 22 (18.18%)	2 / 6 (33.33%)
occurrences (all)	2	6	2
Vomiting			
subjects affected / exposed	5 / 21 (23.81%)	7 / 22 (31.82%)	1 / 6 (16.67%)
occurrences (all)	9	10	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dandruff			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hirsutism			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Rash			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin irritation			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Urticaria			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Leukocyturia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Knee deformity			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 21 (4.76%)	3 / 22 (13.64%)	0 / 6 (0.00%)
occurrences (all)	2	5	0
Musculoskeletal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 21 (4.76%)	3 / 22 (13.64%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	1 / 6 (16.67%)
occurrences (all)	0	1	1

Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Catheter site infection			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	0 / 6 (0.00%)
occurrences (all)	0	6	0
Cellulitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Device related infection			
subjects affected / exposed	1 / 21 (4.76%)	2 / 22 (9.09%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 21 (4.76%)	3 / 22 (13.64%)	1 / 6 (16.67%)
occurrences (all)	1	3	1
Nasopharyngitis			
subjects affected / exposed	1 / 21 (4.76%)	2 / 22 (9.09%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Oral herpes			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Otitis media acute			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Peritonitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			

subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 21 (19.05%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	5	0	0
Viral infection			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Fluid overload			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Hyperkalaemia			
subjects affected / exposed	3 / 21 (14.29%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Hyperuricaemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	4 / 21 (19.05%)	5 / 22 (22.73%)	2 / 6 (33.33%)
occurrences (all)	8	12	8
Hypokalaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	0 / 6 (0.00%)
occurrences (all)	1	1	0

Hyponatraemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Open-label Phase: Cinacalcet/Cinacalcet		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	3		
General disorders and administration site conditions			
Catheter site pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Catheter site pruritus			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Catheter site related reaction			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Device breakage subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Device leakage subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Face oedema subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Fatigue subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Feeling cold subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Local swelling subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pain subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Pyrexia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Dyspnoea			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Daydreaming			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Staring			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Investigations			
Blood calcium abnormal			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood phosphorus increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Electrocardiogram T wave abnormal			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haematocrit decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haemoglobin increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Arteriovenous fistula site complication			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Arthropod bite			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dialysis related complication			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Femur fracture			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Overdose			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Procedural hypotension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Procedural nausea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Vascular graft complication			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Mitral valve stenosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Epilepsy			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tremor			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Ocular hyperaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoaesthesia oral			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dandruff			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dermatitis contact			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hirsutism			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Swelling face subjects affected / exposed occurrences (all) Skin irritation subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
Renal and urinary disorders Hydronephrosis subjects affected / exposed occurrences (all) Leukocyturia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		
Endocrine disorders Hyperparathyroidism subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Knee deformity subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0		

Musculoskeletal stiffness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Catheter site infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Device related infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Otitis media acute			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Peritonitis			

subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Pharyngitis streptococcal			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Fluid overload			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypercholesterolaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		

Hypokalaemia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 February 2011	The following changes were made to address FDA comments: - changed PK samples from being an optional study for hemodialysis subjects only to being mandatory for both hemodialysis and peritoneal dialysis subjects - amended the post-dose collection windows for hemodialysis subjects - specified that approximately 35% of enrolled subjects were to be in the younger age group of 6 to less than12 years - changed growth velocity endpoints from exploratory endpoints to secondary endpoints - included infections as an adverse event of interest
31 January 2012	- replaced Appendix E with a newly written Investigational Product Instruction Manual - assisted with enrollment challenges by changing the entry criterion for iPTH to a value that better accommodated regional differences in iPTH thresholds for initiating treatment - at the request of EMA, the exploratory endpoint of assessing the percent change in ionized calcium from baseline to the mean value during the EAP was changed to a secondary endpoint
20 June 2012	- added worksheet on adverse events as Appendix E - clarified/updated definition of standard of care, entry criteria, and concomitant therapy - updated safety reporting language to comply with the European Union Clinical Trial Directive

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 study was terminated early with a smaller sample size. However, the study was still sufficiently powered for the double-blind phase. The data collected in the open-label phase is very sparse.

Notes: