Clinical trial results:
A Multicenter Single-arm Extension Study to Characterize the Long-term Safety of Cinacalcet Hydrochloride in the Treatment of Secondary Hyperparathyroidism in Pediatric Subjects With Chronic Kidney Disease on Dialysis

Summary

EudraCT number	2014-003563-38
Trial protocol	IT HU CZ ES BE SK FR Outside EU/EEA GR
Global end of trial date	15 March 2017

Results information

Result version number	v1 (current)
This version publication date	14 October 2017
First version publication date	14 October 2017

Trial information

Trial identification

Sponsor protocol code	20140159

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02341417
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)	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	15 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to characterize the long-term safety and tolerability of cinacalcet in pediatric subjects with chronic kidney disease (CKD) receiving dialysis.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.
Before a subject's participation in the clinical study, the investigator obtained written informed consent from the subject or the subject's legally acceptable representative after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study and before any protocol-specific screening procedures or any investigational product was administered. In this study, assent was obtained from the child, except if the child was very young, and consent was obtained from the parents or legally authorized representative as defined by local law.
A copy of the protocol, proposed informed consent form, other written subject information, and any proposed advertising materials was submitted to the Independent Ethics Committee (IEC)/Institutional Review Board (IRB) for written approval. A copy of the written approval of the protocol and informed consent form must have been received by Amgen before recruitment of subjects into the study and shipment of investigational product.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 June 2015
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	Belgium: 2
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Ukraine: 7
Country: Number of subjects enrolled	Russian Federation: 6
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	28
EEA total number of subjects	8

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

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 16 centers in United States, Russian Federation, Ukraine, Belgium, Czech Republic, Greece, France, and Poland.

Pre-assignment

Screening details:

This extension study enrolled participants who completed one of the parent studies 20110100 or 20130356.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	20130356 SOC

Arm description:

Participants who received standard of care (SOC) in parent study 20130356 received cinacalcet daily for 28 weeks in this extension study. The starting dose was 0.20 mg/kg/day. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.

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

Dosage and administration details:

Cinacalcet was provided as 5 mg capsules for sprinkling or as film-coated tablets for swallowing. The protocol-specified doses were: 1, 2.5, 5, 7.5, 10, 15, 30, 60, 90, 120, and 180 mg.

Arm title	20130356 SOC + Cinacalcet

Arm description:

Participants who received SOC and cinacalcet in parent study 20130356 received cinacalcet daily for 28 weeks in this extension study. The starting dose was either the same as the last dose received in the parent study or 0.20 mg/kg/day if the last dose of cinacalcet in the parent study was received > 14 days before day 1 of this study. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.

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

Dosage and administration details:

Cinacalcet was provided as 5 mg capsules for sprinkling or as film-coated tablets for swallowing. The protocol-specified doses were: 1, 2.5, 5, 7.5, 10, 15, 30, 60, 90, 120, and 180 mg.

Arm title	20110100 SOC + Cinacalcet

Arm description:

Participants who received SOC and cinacalcet in parent study 2011100 received cinacalcet daily for 28

weeks in this extension study. The starting dose was either the same as the last dose received in the parent study or 0.20 mg/kg/day if the last dose of cinacalcet in the parent study was received > 14 days before day 1 of this study. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.

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

Dosage and administration details:

Cinacalcet was provided as 5 mg capsules for sprinkling or as film-coated tablets for swallowing. The protocol-specified doses were: 1, 2.5, 5, 7.5, 10, 15, 30, 60, 90, 120, and 180 mg.

Number of subjects in period 1	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet
Started	13	14	1
Completed	11	12	0
Not completed	2	2	1
Consent withdrawn by subject	-	2	-
Death	-	-	1
Decision by sponsor	2	-	-

Baseline characteristics

Reporting groups	
Reporting group title	20130356 SOC
Reporting group description:	
Participants who received standard of care (SOC) in parent study 20130356 received cinacalcet daily for 28 weeks in this extension study. The starting dose was 0.20 mg/kg/day. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.	
Reporting group title	20130356 SOC + Cinacalcet
Reporting group description:	
Participants who received SOC and cinacalcet in parent study 20130356 received cinacalcet daily for 28 weeks in this extension study. The starting dose was either the same as the last dose received in the parent study or 0.20 mg/kg/day if the last dose of cinacalcet in the parent study was received > 14 days before day 1 of this study. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.	
Reporting group title	20110100 SOC + Cinacalcet
Reporting group description:	
Participants who received SOC and cinacalcet in parent study 2011100 received cinacalcet daily for 28 weeks in this extension study. The starting dose was either the same as the last dose received in the parent study or 0.20 mg/kg/day if the last dose of cinacalcet in the parent study was received > 14 days before day 1 of this study. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.	

Reporting group values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet
Number of subjects	13	14	1
Age Categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	4	6	1
Adolescents (12-17 years)	9	8	0
Age Continuous Units: years			
median	14	14	2
full range (min-max)	11 to 16	9 to 16	2 to 2
Gender Categorical Units: Subjects			
Female	8	10	0
Male	5	4	1
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black (or African American)	1	4	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	12	9	1
Other	0	1	0
Ethnicity Units: Subjects			

Hispanic/Latino	1	0	0
Not Hispanic/Latino	12	14	1

Intact Parathyroid Hormone (iPTH)			
Units: pg/mL			
median	1432.69	1001.35	907.74
inter-quartile range (Q1-Q3)	800.19 to 1695.48	525.76 to 1292.08	907.74 to 907.74
Corrected Total Serum Calcium			
Units: mg/dL			
median	9.56	9.93	10.29
inter-quartile range (Q1-Q3)	9.4 to 10	9.02 to 10.16	10.29 to 10.29
Ionized Calcium			
Units: mmol/L			
median	1.13	1.145	1.39
inter-quartile range (Q1-Q3)	1.11 to 1.23	1.1 to 1.28	1.39 to 1.39
Serum Phosphorus			
Units: mg/dL			
median	5.57	6.05	8.08
inter-quartile range (Q1-Q3)	4.86 to 6.19	5.31 to 6.67	8.08 to 8.08
Calcium Phosphorus product (Ca x P)			
Units: mg^2/dL^2			
median	54.42	57.8	82.28
inter-quartile range (Q1-Q3)	48.59 to 58.82	50.94 to 65.65	82.28 to 82.28

Reporting group values	Total		
Number of subjects	28		
Age Categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	11		
Adolescents (12-17 years)	17		
Age Continuous			
Units: years			
median			
full range (min-max)	-		
Gender Categorical			
Units: Subjects			
Female	18		
Male	10		
Race			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Black (or African American)	5		
Native Hawaiian or Other Pacific Islander	0		
White	22		
Other	1		
Ethnicity			
Units: Subjects			
Hispanic/Latino	1		

Not Hispanic/Latino	27		

Intact Parathyroid Hormone (iPTH) Units: pg/mL median inter-quartile range (Q1-Q3)	- -		
Corrected Total Serum Calcium Units: mg/dL median inter-quartile range (Q1-Q3)	- -		
Ionized Calcium Units: mmol/L median inter-quartile range (Q1-Q3)	- -		
Serum Phosphorus Units: mg/dL median inter-quartile range (Q1-Q3)	- -		
Calcium Phosphorus product (Ca x P) Units: mg^2/dL^2 median inter-quartile range (Q1-Q3)	- -		

End points

End points reporting groups

Reporting group title	20130356 SOC

Reporting group description:

Participants who received standard of care (SOC) in parent study 20130356 received cinacalcet daily for 28 weeks in this extension study. The starting dose was 0.20 mg/kg/day. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.

Reporting group title	20130356 SOC + Cinacalcet

Reporting group description:

Participants who received SOC and cinacalcet in parent study 20130356 received cinacalcet daily for 28 weeks in this extension study. The starting dose was either the same as the last dose received in the parent study or 0.20 mg/kg/day if the last dose of cinacalcet in the parent study was received > 14 days before day 1 of this study. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.

Reporting group title	20110100 SOC + Cinacalcet

Reporting group description:

Participants who received SOC and cinacalcet in parent study 2011100 received cinacalcet daily for 28 weeks in this extension study. The starting dose was either the same as the last dose received in the parent study or 0.20 mg/kg/day if the last dose of cinacalcet in the parent study was received > 14 days before day 1 of this study. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.

Primary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events[1]

End point description:

Adverse events (AEs) were graded according to the Common Terminology Criteria for Adverse Events (CTCAE, v4.0).
The investigator assessed whether the adverse event was possibly related to the study drug as indicated by a "yes" or "no" response to the question: Is there a reasonable possibility that the event may have been caused by the study drug?

End point type	Primary

End point timeframe:

From first dose of study drug up to 4 weeks after the last dose; 32 weeks.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary, secondary, and safety endpoints was descriptive in nature.

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: participants				
Any adverse event (AE)	9	10	1	
AE Grade ≥ 2	2	7	1	
AE Grade ≥ 3	2	6	1	
AE Grade ≥ 4	0	0	1	
Serious adverse event (SAE)	2	6	1	
AE leading to discontinuation of study drug	0	0	0	

Fatal adverse events	0	0	1	
Treatment-related adverse events (TRAE)	5	4	0	
Treatment-related AE Grade ≥ 2	0	1	0	
Treatment-related AE Grade ≥ 3	0	0	0	
Treatment-related AE Grade ≥ 4	0	0	0	
Treatment-related serious adverse events	0	0	0	
TRAE leading to discontinuation of study drug	0	0	0	
Fatal treatment-related adverse events	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ≥ 30% Reduction in iPTH from Baseline to Mean Value During Weeks 11 and 15

End point title	Percentage of Participants Achieving ≥ 30% Reduction in iPTH from Baseline to Mean Value During Weeks 11 and 15[2]

End point description:

This endpoint was analyzed in participants who received SOC only in parent study 20130356.
Subjects who had no iPTH values during weeks 11 to 15 were considered as non-responders.

End point type	Secondary

End point timeframe:

Baseline and weeks 11 to 15

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed for participants who received SOC treatment in study 20130356.

End point values	20130356 SOC			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: percentage of participants				
number (confidence interval 95%)	30.8 (9.1 to 61.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ≥ 30% Reduction in iPTH from Baseline to Mean Value During Weeks 12 and 28

End point title	Percentage of Participants Achieving ≥ 30% Reduction in iPTH from Baseline to Mean Value During Weeks 12 and 28[3]

End point description:

This endpoint was analyzed in participants who received SOC only in parent study 20130356.
For subjects who had no values during week 23 and 28, the mean of the last 2 available postbaseline

values collected in the dose-titration phase was used. If only 1 postbaseline value was available, this single value was used. If no postbaseline value was available, the subject was considered a non-responder.

End point type	Secondary

End point timeframe:

Baseline and week 23 to 28

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed for participants who received SOC treatment in study 20130356.

End point values	20130356 SOC			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: percentage of participants				
number (confidence interval 95%)	23.1 (5 to 53.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in iPTH to the Mean Value During Weeks 23 and 28

End point title	Percent Change From Baseline in iPTH to the Mean Value During Weeks 23 and 28[4]

End point description:

This endpoint was analyzed in participants who received SOC only in parent study 20130356.
For subjects who had no values during week 23 and 28, the mean of the last 2 available postbaseline values collected in the dose-titration phase was used. If only 1 postbaseline value was available, this single value was used. If no postbaseline value was available, the subject was excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline and weeks 23 to 28

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed for participants who received SOC treatment in study 20130356.

End point values	20130356 SOC			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: percent change				
median (inter-quartile range (Q1-Q3))	11.43 (-20.64 to 27.27)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved Mean iPTH ≤ 300 pg/mL During Weeks 23 and 28

End point title	Percentage of Participants who Achieved Mean iPTH ≤ 300 pg/mL During Weeks 23 and 28

End point description:

This endpoint was analyzed in the efficacy analysis set which includes all enrolled subjects in Study 20140159 who received at least one dose of cinacalcet during Study 20140159 and had at least one assessment after Study Day 1.
For subjects who had no values during week 23 and 28, the mean of the last 2 available postbaseline values collected in the dose-titration phase was used. If only 1 postbaseline value was available, this single value was used. If no postbaseline value was available, the subject was considered a non-responder.

End point type	Secondary

End point timeframe:

Weeks 23 to 28

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: percentage of participants				
number (confidence interval 95%)	7.7 (0.2 to 36)	21.4 (4.7 to 50.8)	0 (0 to 97.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Corrected Serum Calcium to the Mean Value During Weeks 23 to 28

End point title	Change From Baseline in Corrected Serum Calcium to the Mean Value During Weeks 23 to 28

End point description:

This analysis was conducted in the Efficacy Analysis Set. For subjects who had no values during week 23 and 28, the mean of the last 2 available postbaseline values collected in the dose-titration phase was used. If only 1 postbaseline value was available, this single value was used. If no postbaseline value was available, the subject was excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline and weeks 23 to 28

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: mg/dL				
median (inter-quartile range (Q1-Q3))	-0.24 (-0.46 to -0.06)	-0.24 (-0.81 to 0.58)	-0.74 (-0.74 to -0.74)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Phosphorus to the Mean Value During Weeks 23 to 28

End point title	Change From Baseline in Serum Phosphorus to the Mean Value During Weeks 23 to 28

End point description:

This analysis was conducted in the Efficacy Analysis Set. For subjects who had no values during week 23 and 28, the mean of the last 2 available postbaseline values collected in the dose-titration phase was used. If only 1 postbaseline value was available, this single value was used. If no postbaseline value was available, the subject was excluded from the analysis.

End point type	Secondary

End point timeframe:

Baseline and weeks 23 to 28

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: mg/dL				
median (inter-quartile range (Q1-Q3))	0.19 (-0.52 to 0.56)	-0.08 (-1.41 to 0.17)	0.82 (0.82 to 0.82)	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Corrected Calcium at Baseline, Week 11, and Week 28

End point title	Serum Corrected Calcium at Baseline, Week 11, and Week 28

End point description:

This endpoint was analyzed using the Efficacy Analysis Set. "99999" indicates no data available.

End point type	Secondary

End point timeframe:

Baseline, weeks 11 and 28

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: mg/dL				
median (inter-quartile range (Q1-Q3))				
Baseline	9.56 (9.4 to 10)	9.93 (9.02 to 10.16)	10.29 (10.29 to 10.29)	
Week 11 (n = 12, 12, 0)	9.35 (9.2 to 9.6)	9.85 (9.3 to 10.65)	99999 (99999 to 99999)	
Week 28 (n = 9, 12, 0)	9.5 (9.3 to 10)	9.9 (9.1 to 10.25)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Phosphorus at Baseline, Week 11, and Week 28

End point title	Serum Phosphorus at Baseline, Week 11, and Week 28

End point description:

This endpoint was analyzed using the Efficacy Analysis Set. "99999" indicates no data available.

End point type	Secondary

End point timeframe:

Baseline and weeks 11 and 28

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: mg/dL				
median (inter-quartile range (Q1-Q3))				
Baseline	5.57 (4.86 to 6.19)	6.05 (5.31 to 6.67)	8.08 (8.08 to 8.08)	
Week 11 (n = 12, 12, 0)	5.25 (4.55 to 5.8)	6.2 (5.55 to 7.3)	99999 (99999 to 99999)	
Week 28 (n = 9, 10, 0)	5 (4.3 to 5.6)	5.95 (5.7 to 6.8)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ≥ 30% Reduction in iPTH from Day

1 of Cinacalcet Treatment to Mean Value During Weeks 11 and 15

End point title	Percentage of Participants Achieving ≥ 30% Reduction in iPTH from Day 1 of Cinacalcet Treatment to Mean Value During Weeks 11 and 15

End point description:

This analysis was conducted in the Efficacy Analysis Set. Subjects who had no iPTH values during weeks 11 and 15 were considered as non-responders.

End point type	Secondary

End point timeframe:

Day 1 of cinacalcet treatment (the date that the initial dose of cinacalcet treatment was administered in study 20130356, 20110100 or 20140159) and weeks 11 to 15

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: percentage of participants				
number (confidence interval 95%)	30.8 (9.1 to 61.4)	35.7 (12.8 to 64.9)	100 (2.5 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving ≥ 30% Reduction in iPTH from Day 1 of Cinacalcet Treatment to Mean Value During Weeks 23 and 28

End point title	Percentage of Participants Achieving ≥ 30% Reduction in iPTH from Day 1 of Cinacalcet Treatment to Mean Value During Weeks 23 and 28

End point description:

This analysis was conducted in the Efficacy Analysis Set. For subjects who did not have an iPTH value during weeks 23 and 28, the mean of the last two available post-baseline values collected at protocol-specified visits was used. If only one post-baseline value was available, this single value was used. If no post-baseline value was available, the subject was considered a non-responder.

End point type	Secondary

End point timeframe:

Day 1 of cinacalcet treatment (the date that the initial dose of cinacalcet treatment was administered in study 20130356, 20110100 or 20140159) and weeks 23 to 28

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: percentage of participants				
number (confidence interval 95%)	23.1 (5 to 53.8)	35.7 (12.8 to 64.9)	0 (0 to 97.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Day 1 of Cinacalcet Treatment in iPTH Over Time

End point title	Percent Change From Day 1 of Cinacalcet Treatment in iPTH Over Time

End point description:

This analysis was conducted in the Efficacy Analysis Set with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline (the date that the initial dose of cinacalcet treatment was administered in study 20130356, 20110100 or 20140159), and weeks 3, 7, 11, 15, 17, 18, 19, 20, 23, 27, 31, 35, 39, 43, 48, 52, 56, and 60

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: percent change				
median (inter-quartile range (Q1-Q3))				
Week 3 (n = 13, 14, 1)	10.16 (-4.42 to 20.24)	-6.88 (-30.86 to 41.81)	55.54 (55.54 to 55.54)	
Week 7 (n = 13, 13, 1)	1.99 (-37.82 to 17.42)	-4.96 (-40.93 to 32.44)	9.78 (9.78 to 9.78)	
Week 11 (n = 12, 13, 1)	19.75 (-27.88 to 84.96)	-7.64 (-30.77 to 13.37)	-7 (-7 to -7)	
Week 15 (n = 12, 14, 1)	-7.67 (-59.96 to 51.23)	-13.04 (-68.59 to 10.74)	-73.85 (-73.85 to -73.85)	
Week 17 (n = 2, 12, 1)	-23.93 (-59.61 to 11.75)	-3.09 (-40.52 to 21.4)	-20.02 (-20.02 to -20.02)	
Week 18 (n = 0, 12, 1)	99999 (99999 to 99999)	-29.85 (-54.42 to 31.15)	-7.49 (-7.49 to -7.49)	
Week 19 (n = 10, 12, 0)	-37.17 (-69.24 to 21.47)	-3.5 (-50.02 to 19.16)	99999 (99999 to 99999)	
Week 20 (n = 1, 11, 1)	-13.12 (-13.12 to -13.12)	0.44 (-35.1 to 66.13)	160.8 (160.8 to 160.8)	
Week 23 (n = 10, 14, 0)	-9.05 (-52.43 to 28.64)	-6.65 (-35.13 to 83.11)	99999 (99999 to 99999)	
Week 27 (n = 10, 13, 0)	-8.5 (-69.2 to 18.78)	16.36 (-59.79 to 50.23)	99999 (99999 to 99999)	
Week 31 (n = 0, 13, 0)	99999 (99999 to 99999)	32.3 (-58.73 to 75.48)	99999 (99999 to 99999)	
Week 35 (n = 0, 12, 0)	99999 (99999 to 99999)	16.82 (-70.15 to 82.83)	99999 (99999 to 99999)	
Week 39 (n = 0, 12, 0)	99999 (99999 to 99999)	0.09 (-58.27 to 86.94)	99999 (99999 to 99999)	

Week 43 (n = 0, 12, 0)	99999 (99999 to 99999)	-17.13 (-47.15 to 47.3)	99999 (99999 to 99999)	
Week 48 (n = 0, 10, 0)	99999 (99999 to 99999)	-45.67 (-66.01 to 33.64)	99999 (99999 to 99999)	
Week 52 (n = 0, 1, 0)	99999 (99999 to 99999)	86.5 (86.5 to 86.5)	99999 (99999 to 99999)	
End of treatment (n = 10, 12, 0)	-8.5 (-69.2 to 18.78)	-45.67 (-74.62 to 34.62)	99999 (99999 to 99999)	
End of study (n = 1, 1, 0)	105.27 (105.27 to 105.27)	20.21 (20.21 to 20.21)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Day 1 of Cinacalcet Treatment in Serum Corrected Calcium Over Time

End point title	Change From Day 1 of Cinacalcet Treatment in Serum Corrected Calcium Over Time

End point description:

This analysis was conducted in the Efficacy Analysis Set with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline (the date that the initial dose of cinacalcet treatment was administered in study 20130356, 20110100 or 20140159), and weeks 3, 7, 11, 15, 17, 18, 19, 20, 23, 27, 31, 35, 39, 43, 48, 52, 56, and 60

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: mg/dL				
median (inter-quartile range (Q1-Q3))				
Week 3 (n = 13, 14, 1)	-0.18 (-0.26 to -0.11)	0.19 (0.05 to 0.32)	-0.1 (-99999 to 99999)	
Week 7 (n = 13, 13, 1)	-0.34 (-0.44 to -0.24)	-0.01 (-0.23 to 0.21)	-0.5 (-99999 to 99999)	
Week 11 (n = 12, 13, 1)	-0.35 (-0.46 to -0.24)	-0.06 (-0.19 to 0.07)	-0.5 (-99999 to 99999)	
Week 15 (n = 12, 14, 1)	-0.37 (-0.62 to -0.12)	0.06 (-0.18 to 0.3)	0.5 (-99999 to 99999)	
Week 17 (n = 2, 12, 1)	-0.02 (-0.24 to 0.2)	-0.11 (-0.45 to 0.22)	-0.8 (-99999 to 99999)	
Week 18 (n = 0, 12, 1)	99999 (99999 to 99999)	-0.17 (-0.35 to 0.02)	-0.3 (-99999 to 99999)	
Week 19 (n = 10, 12, 1)	-0.43 (-0.6 to -0.26)	-0.2 (-0.37 to -0.03)	-0.1 (-99999 to 99999)	
Week 20 (n = 0, 12, 0)	99999 (99999 to 99999)	-0.01 (-0.18 to 0.16)	99999 (-99999 to 99999)	
Week 21 (n = 0, 9, 1)	99999 (99999 to 99999)	-0.36 (-0.63 to -0.09)	-2.6 (-99999 to 99999)	

Week 23 (n = 9, 12, 0)	-0.18 (-0.24 to -0.12)	-0.2 (-0.47 to 0.08)	99999 (99999 to 99999)	
Week 27 (n = 9, 13, 0)	-0.14 (-0.25 to -0.02)	-0.24 (-0.41 to -0.07)	99999 (99999 to 99999)	
Week 31 (n = 0, 13, 0)	99999 (99999 to 99999)	0 (-0.2 to 0.19)	99999 (99999 to 99999)	
Week 35 (n = 0, 12, 0)	99999 (99999 to 99999)	-0.42 (-0.57 to -0.26)	99999 (99999 to 99999)	
Week 39 (n = 0, 12, 0)	99999 (99999 to 99999)	-0.63 (-0.84 to -0.43)	99999 (99999 to 99999)	
Week 43 (n = 0, 12, 0)	99999 (99999 to 99999)	-0.37 (-0.63 to -0.11)	99999 (99999 to 99999)	
Week 48 (n = 0, 10, 0)	99999 (99999 to 99999)	-0.55 (-0.87 to -0.23)	99999 (99999 to 99999)	
Week 52 (n = 0, 1, 0)	99999 (99999 to 99999)	-0.16 (-99999 to 99999)	99999 (99999 to 99999)	
End of treatment (n = 9, 12, 0)	0.18 (0.02 to 0.34)	-0.04 (-0.26 to 0.18)	99999 (99999 to 99999)	
End of study (n = 1, 0, 0)	1 (-99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Day 1 of Cinacalcet Treatment in Serum Phosphorus Over Time

End point title	Percent Change From Day 1 of Cinacalcet Treatment in Serum Phosphorus Over Time

End point description:

This analysis was conducted in the Efficacy Analysis Set with available data at each time point.

End point type	Secondary

End point timeframe:

Baseline (the date that the initial dose of cinacalcet treatment was administered in study 20130356, 20110100 or 20140159), and weeks 3, 7, 11, 15, 17, 18, 19, 20, 23, 27, 31, 35, 39, 43, 48, 52, 56, and 60

End point values	20130356 SOC	20130356 SOC + Cinacalcet	20110100 SOC + Cinacalcet	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	14	1	
Units: mg/dL				
median (inter-quartile range (Q1-Q3))				
Week 3 (n = 13, 14, 1)	-0.24 (-0.56 to -0.08)	0.81 (-0.54 to 1.07)	5.6 (-99999 to 99999)	
Week 7 (n = 13, 13, 1)	-0.16 (-0.5 to 0.17)	0.37 (0.1 to 0.64)	0.3 (-99999 to 99999)	
Week 11 (n = 12, 12, 1)	0.01 (-0.33 to 0.36)	1.17 (0.87 to 1.47)	0 (-99999 to 99999)	
Week 15 (n = 12, 14, 1)	-0.52 (-0.79 to -0.25)	0.96 (0.71 to 1.2)	-1.9 (-99999 to 99999)	
Week 17 (n = 2, 12, 0)	-0.08 (-0.19 to 0.03)	1.57 (0.96 to 2.19)	99999 (99999 to 99999)	

Week 18 (n = 0, 12, 1)	99999 (99999 to 99999)	0.61 (0.3 to 0.93)	-0.9 (-99999 to 99999)	
Week 19 (n = 10, 12, 1)	-0.45 (-0.74 to -0.16)	0.91 (0.37 to 1.44)	-0.3 (-99999 to 99999)	
Week 20 (n = 0, 11, 0)	99999 (99999 to 99999)	0.84 (0.16 to 1.51)	99999 (99999 to 99999)	
Week 21 (n = 0, 9, 1)	99999 (99999 to 99999)	0.17 (-0.67 to 1.01)	0.1 (-99999 to 99999)	
Week 23 (n = 9, 12, 0)	-0.37 (-0.78 to 0.05)	0.55 (0.12 to 0.98)	99999 (99999 to 99999)	
Week 27 (n = 9, 13, 0)	-0.18 (-0.53 to 0.18)	0.76 (0.27 to 1.24)	99999 (99999 to 99999)	
Week 31 (n = 0, 13, 0)	99999 (99999 to 99999)	0.83 (0.24 to 1.42)	99999 (99999 to 99999)	
Week 35 (n = 0, 12, 0)	99999 (99999 to 99999)	-0.03 (-0.51 to 0.45)	99999 (99999 to 99999)	
Week 39 (n = 0, 12, 0)	99999 (99999 to 99999)	0.4 (-0.11 to 0.91)	99999 (99999 to 99999)	
Week 43 (n = 0, 12, 0)	99999 (99999 to 99999)	0.33 (-0.21 to 0.86)	99999 (99999 to 99999)	
Week 48 (n = 0, 8, 0)	99999 (99999 to 99999)	0.6 (-0.21 to 1.42)	99999 (99999 to 99999)	
Week 52 (n = 0, 1, 0)	99999 (99999 to 99999)	0.61 (-99999 to 99999)	99999 (99999 to 99999)	
End of treatment (n = 9, 10, 0)	-0.18 (-0.53 to 0.18)	0.43 (-0.25 to 1.11)	99999 (99999 to 99999)	
End of study (n = 1, 0, 0)	1.2 (-99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

32 Weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	20130356 SOC

Reporting group description:

Participants who received standard of care (SOC) in parent study 20130356 received cinacalcet daily for 28 weeks in this extension study. The starting dose was 0.20 mg/kg/day. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.

Reporting group title	20130356 SOC+Cinacalcet

Reporting group description:

Participants who received SOC and cinacalcet in parent study 20130356 received cinacalcet daily for 28 weeks in this extension study. The starting dose was either the same as the last dose received in the parent study or 0.20 mg/kg/day if the last dose of cinacalcet in the parent study was received > 14 days before day 1 of this study. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.

Reporting group title	20110100 SOC+Cinacalcet

Reporting group description:

Participants who received SOC and cinacalcet in parent study 2011100 received cinacalcet daily for 28 weeks in this extension study. The starting dose was either the same as the last dose received in the parent study or 0.20 mg/kg/day if the last dose of cinacalcet in the parent study was received > 14 days before day 1 of this study. Dose adjustments and withholding were based on weekly assessments of ionized calcium as well as plasma intact parathyroid hormone (iPTH) and corrected serum calcium levels assessed monthly.

Reporting group title	Total

Reporting group description:

All participants who received cinacalcet in study 20140159.

Serious adverse events	20130356 SOC	20130356 SOC+Cinacalcet	20110100 SOC+Cinacalcet
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 13 (15.38%)	6 / 14 (42.86%)	1 / 1 (100.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Vascular disorders			
Venous occlusion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Surgical and medical procedures			

Catheter placement			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (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			
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Local swelling			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Gastrointestinal disorders			
Gastroduodenitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Respiratory, thoracic and mediastinal disorders			
Tachypnoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Endocrine disorders			
Goitre			

subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (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
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Device related infection			
subjects affected / exposed	0 / 13 (0.00%)	2 / 14 (14.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis infective			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Staphylococcal infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Product issues			
Device damage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (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
Device dislocation			

subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Total		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 28 (32.14%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Vascular disorders			
Venous occlusion			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Catheter placement			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Local swelling			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastroduodenitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Tachypnoea			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pericarditis infective			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Staphylococcal infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device damage			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device dislocation			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	20130356 SOC	20130356 SOC+Cinacalcet	20110100 SOC+Cinacalcet
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 13 (69.23%)	10 / 14 (71.43%)	1 / 1 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 14 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Venous haemorrhage			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			

Catheter placement			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Complication associated with device			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Local swelling			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Mass			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nodule			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 14 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0

Pulmonary calcification			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Major depression			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Staring			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Investigations			
Adjusted calcium decreased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Blood calcium decreased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Blood parathyroid hormone decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Red blood cell sedimentation rate			

increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Arteriovenous fistula site complication			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Heat exhaustion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Ulna fracture			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Left ventricular hypertrophy			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Headache			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Loss of consciousness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Tremor			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 13 (7.69%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Duodenogastric reflux			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastritis erosive			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Gastroduodenitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Nausea			

subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)	2 / 14 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hyperparathyroidism secondary			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Joint swelling			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	2 / 13 (15.38%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal stiffness			

subjects affected / exposed	1 / 13 (7.69%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Osteoarthritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Herpes virus infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 14 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pyelonephritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 14 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			

subjects affected / exposed	2 / 13 (15.38%)	1 / 14 (7.14%)	0 / 1 (0.00%)
occurrences (all)	4	4	0

Non-serious adverse events	Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 28 (71.43%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Venous haemorrhage			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Surgical and medical procedures			
Catheter placement			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Complication associated with device			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Local swelling			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Mass			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nodule			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pyrexia			

subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Pulmonary calcification subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		
Psychiatric disorders Major depression subjects affected / exposed occurrences (all) Staring subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		
Investigations Adjusted calcium decreased subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	 2 / 28 (7.14%) 2 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		

Blood calcium decreased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Blood parathyroid hormone decreased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Haemoglobin decreased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Red blood cell sedimentation rate increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arteriovenous fistula site complication			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Heat exhaustion			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		

Ulna fracture			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Cardiac disorders			
Left ventricular hypertrophy			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Loss of consciousness			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Tremor			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Diarrhoea			

subjects affected / exposed occurrences (all) Duodenogastric reflux subjects affected / exposed occurrences (all) Gastritis erosive subjects affected / exposed occurrences (all) Gastroduodenitis subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 2 2 / 28 (7.14%) 4		
Skin and subcutaneous tissue disorders Pain of skin subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		
Endocrine disorders Goitre subjects affected / exposed occurrences (all) Hyperparathyroidism secondary subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Joint swelling			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Musculoskeletal pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Musculoskeletal stiffness			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Osteoarthritis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Infections and infestations			
Herpes virus infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pyelonephritis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Upper respiratory tract infection			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hypocalcaemia			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2014	• Language regarding the transition of eligible subjects from the parent Study 20130356 was incorporated. • Updates were also made to study procedures for consistency with the cinacalcet pediatric program.
22 July 2015	• Eligible subjects from Study 20110100 were included in this study. • Dosing procedures were revised to: 1) include withholding criteria for adverse events, 2) make restarting criteria consistent across dose holds, 3) clarify dose adjustments, and 4) clarify day 1 ionized calcium criteria. • Eligibility of subjects who turned 18 years of age while participating in Study 20130356 was clarified. • Language was added to allow standard of care therapy that is commercially available to be provided by Amgen if required by local regulation, since these therapeutics would need to be provided to Russian sites.
16 March 2016	• Eligibility criteria and study procedures were revised to allow eligible subjects who were ongoing at the time an administrative decision was made to end Studies 20130356 and 20110100 to enroll in this study. • Inclusion criteria for iPTH and corrected serum calcium were added for subjects in the Study 20130356 SOC group. • Subjects who had a new onset of seizure or worsening of pre-existing seizure disorder were excluded. • Additional secondary efficacy and exploratory endpoints were included. • The statistical methods were also revised to clarify that interim analyses could be conducted and the timing of the primary analysis, as well as to add the definition of the efficacy analysis set.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported