Clinical trial results:
An Open-label, Single-arm Study to Assess the Safety and Tolerability of Cinacalcet HCl in Addition to Standard of Care in Pediatric Subjects Age 28 Days to < 6 years With Chronic Kidney Disease and Secondary Hyperparathyroidism Receiving Dialysis

Summary

EudraCT number	2011-004618-40
Trial protocol	DE NL PL HU CZ IT SK BE Outside EU/EEA
Global end of trial date	03 June 2016

Results information

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

Trial information

Trial identification

Sponsor protocol code	20110100

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01439867
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	03 June 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 June 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To characterize corrected serum calcium levels on treatment with cinacalcet in pediatric subjects with secondary hyperparathyroidism.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) and applicable Food and Drug Administration (FDA) regulations/guidelines set forth in 21 CFR Parts 11, 50, 54, 56, and 312.
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.
Before a subject's participation in the clinical study, the investigator obtained written assent from the subject and/or informed consent from 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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 June 2012
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	Czech Republic: 1
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	18
EEA total number of subjects	9

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	3
Children (2-11 years)	15
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 14 study centers in Czech Republic (1 site), France (1 site), Germany (1 site), Italy (1 site), Slovakia (1 site), Poland (3 sites), and the US (6 sites). The first subject was enrolled on 22 June 2012, and the last subject completed the study on 03 June 2016.

Pre-assignment

Screening details:

Patients between the ages of 28 days to < 6 years of age, who had chronic kidney disease and secondary hyperparathyroidism and were undergoing either hemodialysis or peritoneal dialysis at the time of screening (subjects 6 months or older should have been receiving dialysis for ≥ 1 month).

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	Cohort 1

Arm description:

Cohort 1 consists of subjects enrolled before the partial clinical hold. Participants received cinacalcet administered daily for 24 weeks. The starting dose was 0.25 mg/kg (based on dry weight) with dose adjustments and withholding based on plasma iPTH, corrected serum calcium levels obtained monthly, and adverse signs and symptoms; the maximum allowed daily dose was 4.2 mg/kg.

Arm type	Experimental
Investigational medicinal product name	Cinacalcet hydrochloride
Investigational medicinal product code	AMG 073
Other name	Sensipar®, Mimpara®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Cinacalcet was provided as 5-mg capsules that were opened, and the contents were either sprinkled on soft food or suspended into a sucrose syrup to create a liquid suspension for administration. All doses were administered with food or shortly after a meal at the same time daily.

Arm title	Cohort 2

Arm description:

Cohort 2 consists of subjects enrolled after the partial clinical hold. Participants received cinacalcet administered daily for 24 weeks. The starting dose was 0.20 mg/kg (based on dry weight) with dose adjustments and withholding based on plasma iPTH, corrected serum calcium levels obtained monthly, weekly monitoring of ionized calcium levels, and adverse signs and symptoms; the maximum allowed daily dose was 2.5 mg/kg/day or 60 mg, whichever was lower.

Arm type	Experimental
Investigational medicinal product name	Cinacalcet hydrochloride
Investigational medicinal product code	AMG 073
Other name	Sensipar®, Mimpara®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Cinacalcet was provided as 5-mg capsules that were opened, and the contents were either sprinkled on soft food or suspended into a sucrose syrup to create a liquid suspension for administration. All doses were administered with food or shortly after a meal at the same time daily.

Number of subjects in period 1	Cohort 1	Cohort 2
Started	8	10
Received treatment	7	10
Completed	2	2
Not completed	6	8
Consent withdrawn by subject	1	2
Administrative decision	4	5
Protocol-specified criteria	1	-
Noncompliance	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
Cohort 1 consists of subjects enrolled before the partial clinical hold. Participants received cinacalcet administered daily for 24 weeks. The starting dose was 0.25 mg/kg (based on dry weight) with dose adjustments and withholding based on plasma iPTH, corrected serum calcium levels obtained monthly, and adverse signs and symptoms; the maximum allowed daily dose was 4.2 mg/kg.	
Reporting group title	Cohort 2
Reporting group description:	
Cohort 2 consists of subjects enrolled after the partial clinical hold. Participants received cinacalcet administered daily for 24 weeks. The starting dose was 0.20 mg/kg (based on dry weight) with dose adjustments and withholding based on plasma iPTH, corrected serum calcium levels obtained monthly, weekly monitoring of ionized calcium levels, and adverse signs and symptoms; the maximum allowed daily dose was 2.5 mg/kg/day or 60 mg, whichever was lower.	

Reporting group values	Cohort 1	Cohort 2	Total
Number of subjects	8	10	18
Age Categorical Units: Subjects			
28 days to < 2 years	2	1	3
2 years to < 6 years	6	9	15
Age Continuous Units: months			
arithmetic mean	37.1	35	
standard deviation	± 18.9	± 15.9	-
Gender Categorical Units: Subjects			
Female	3	3	6
Male	5	7	12
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black or African American	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
White	6	9	15
Other	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	1	2	3
Not Hispanic or Latino	7	8	15
Corrected Serum Calcium Units: mg/dL			
arithmetic mean	10.56	9.82	
standard deviation	± 0.75	± 0.61	-
Intact Parathyroid Hormone Units: pg/mL			
arithmetic mean	1414.34	1206.92	

standard deviation	± 699.9	± 597.85	-

Subject analysis sets	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set included all enrolled subjects who had at least 1 post-baseline assessment.	
Subject analysis set title	Calcium Analysis Set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The calcium analysis set includes all subjects who received at least one dose of study drug and had at least one measured serum calcium value while on study drug.	

Reporting group values	Full Analysis Set	Calcium Analysis Set	
Number of subjects	17	17	
Age Categorical Units: Subjects			
28 days to < 2 years 2 years to < 6 years			
Age Continuous Units: months arithmetic mean standard deviation	±	±	
Gender Categorical Units: Subjects			
Female Male			
Race Units: Subjects			
American Indian or Alaska Native Asian Black or African American Native Hawaiian or Other Pacific Islander White Other			
Ethnicity Units: Subjects			
Hispanic or Latino Not Hispanic or Latino			
Corrected Serum Calcium Units: mg/dL arithmetic mean standard deviation	10.08 ± 0.72	±	
Intact Parathyroid Hormone Units: pg/mL arithmetic mean standard deviation	1298.03 ± 653.68	±	

End points

End points reporting groups

Reporting group title	Cohort 1

Reporting group description:

Cohort 1 consists of subjects enrolled before the partial clinical hold. Participants received cinacalcet administered daily for 24 weeks. The starting dose was 0.25 mg/kg (based on dry weight) with dose adjustments and withholding based on plasma iPTH, corrected serum calcium levels obtained monthly, and adverse signs and symptoms; the maximum allowed daily dose was 4.2 mg/kg.

Reporting group title	Cohort 2

Reporting group description:

Cohort 2 consists of subjects enrolled after the partial clinical hold. Participants received cinacalcet administered daily for 24 weeks. The starting dose was 0.20 mg/kg (based on dry weight) with dose adjustments and withholding based on plasma iPTH, corrected serum calcium levels obtained monthly, weekly monitoring of ionized calcium levels, and adverse signs and symptoms; the maximum allowed daily dose was 2.5 mg/kg/day or 60 mg, whichever was lower.

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set included all enrolled subjects who had at least 1 post-baseline assessment.

Subject analysis set title	Calcium Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The calcium analysis set includes all subjects who received at least one dose of study drug and had at least one measured serum calcium value while on study drug.

Primary: Percentage of participants with Hypocalcemia

End point title	Percentage of participants with Hypocalcemia[1]

End point description:

Hypocalcemia was defined as corrected serum calcium levels < 9.0 mg/dL (2.25 mmol/L) for participants aged 28 days to < 2 years, and < 8.4 mg/dL (2.1 mmol/L) for participants aged ≥ 2 years to < 6 years at any time during the study.
The analysis included subjects who received at least 1 dose of cinacalcet and had at least 1 measured serum calcium value while on cinacalcet.

End point type	Primary

End point timeframe:

26 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: There was no formal statistical testing for this study.

End point values	Cohort 1	Cohort 2	Calcium Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7	10	17	
Units: percentage of participants				
number (confidence interval 90%)	0 (0 to 34.8)	0 (0 to 25.9)	0 (0 to 16.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Corrected Serum Calcium Levels < 8.8 mg/dL (2.2 mmol/L) During the Study

End point title	Percentage of Participants With Corrected Serum Calcium Levels < 8.8 mg/dL (2.2 mmol/L) During the Study

End point description:

The analysis included subjects who received at least 1 dose of cinacalcet and had at least 1 measured serum calcium value while on cinacalcet.

End point type	Secondary

End point timeframe:

26 weeks

End point values	Cohort 1	Cohort 2	Calcium Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7	10	17	
Units: percentage of participants				
number (confidence interval 90%)	14.3 (0.7 to 52.1)	10 (0.5 to 39.4)	11.8 (2.1 to 32.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Intact Parathyroid Hormone (iPTH)

End point title	Percent Change From Baseline in Intact Parathyroid Hormone (iPTH)

End point description:

The analysis included all enrolled subjects with at least 1 post-baseline assessment. "99999" indicates data that was not calculated due to low number of patients with available data.

End point type	Secondary

End point timeframe:

Baseline and weeks 3, 7, 11, 15, 19, 22, and 24

End point values	Cohort 1	Cohort 2	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7	10	17	
Units: percent change				
arithmetic mean (standard deviation)				
Week 3 (N = 7, 9, 16)	-22.96 (± 64.67)	-3.37 (± 54.82)	-11.94 (± 58.11)	
Week 7 (n = 4, 9, 13)	3.87 (± 110.94)	-3.13 (± 52.94)	-0.98 (± 70.4)	

Week 11 (n = 4, 8, 12)	-51.7 (± 27.18)	-7.15 (± 75.3)	-22 (± 65.51)	
Week 15 (n = 2, 7, 9)	-65.31 (± 6.83)	-51.69 (± 39.91)	-54.71 (± 35.16)	
Week 19 (n = 1, 3, 4)	-79.02 (± 99999)	-57.35 (± 32.86)	-62.76 (± 28.93)	
Week 22 (n = 0, 1 1)	99999 (± 99999)	-78.04 (± 99999)	-78.04 (± 99999)	
Week 24 (n = 0, 1, 1)	99999 (± 99999)	-67.42 (± 99999)	-67.42 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Corrected Serum Calcium

End point title	Percent Change From Baseline in Corrected Serum Calcium

End point description:

The analysis included all enrolled subjects with at least 1 post-baseline assessment. "99999" indicates data that was not calculated due to low number of patients with available data.

End point type	Secondary

End point timeframe:

Baseline and weeks 3, 7, 11, 15, 19, 22, and 24

End point values	Cohort 1	Cohort 2	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7	10	17	
Units: percent change				
arithmetic mean (standard deviation)				
Week 3 (n = 7, 10, 17)	-0.5 (± 4.47)	3.43 (± 6.38)	1.81 (± 5.86)	
Week 7 (n = 4, 8, 12)	-3.58 (± 12.23)	3.6 (± 9.31)	1.21 (± 10.41)	
Week 11 (n = 4, 8, 12)	-3.23 (± 10.51)	1.46 (± 5.24)	-0.1 (± 7.28)	
Week 15 (n = 2, 7, 9)	-6.86 (± 12.44)	2.99 (± 5.09)	0.8 (± 7.59)	
Week 19 (n = 1, 3, 4)	1.94 (± 99999)	-0.49 (± 6.62)	0.12 (± 5.54)	
Week 22 (n = 0, 1, 1)	99999 (± 99999)	5.88 (± 99999)	5.88 (± 99999)	
Week 24 (n = 0, 1, 1)	99999 (± 99999)	2.94 (± 99999)	2.94 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Serum Phosphorous

End point title	Percent Change From Baseline in Serum Phosphorous

End point description:

The analysis included all enrolled subjects with at least 1 post-baseline assessment. "99999" indicates data that was not calculated due to low number of patients with available data.

End point type	Secondary

End point timeframe:

Baseline and weeks 3, 7, 11, 15, 19, 22, and 24

End point values	Cohort 1	Cohort 2	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7	10	17	
Units: percent change				
arithmetic mean (standard deviation)				
Week 3 (n = 7, 10, 17)	-10.75 (± 32.49)	-5.11 (± 39.32)	-7.43 (± 35.69)	
Week 7 (n = 4, 8, 12)	-8.68 (± 20.88)	-9.6 (± 29.79)	-9.29 (± 26.15)	
Week 11 (n = 4, 8, 12)	14.39 (± 22.18)	4.54 (± 39.08)	7.82 (± 33.61)	
Week 15 (n = 2, 7, 9)	13.99 (± 26.33)	-16.07 (± 28.14)	-9.39 (± 29.26)	
Week 19 (n = 1, 2, 3)	10.87 (± 99999)	3.45 (± 4.88)	5.92 (± 5.5)	
Week 22 (n = 0, 1, 1)	99999 (± 99999)	-1.72 (± 99999)	-1.72 (± 99999)	
Week 24 (n = 0, 1, 1)	99999 (± 99999)	8.62 (± 99999)	8.62 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Calcium Phosphorus Product (Ca x P)

End point title	Percent Change From Baseline in Calcium Phosphorus Product (Ca x P)

End point description:

The analysis included all enrolled subjects with at least 1 post-baseline assessment. "99999" indicates data that was not calculated due to low number of patients with available data.

End point type	Secondary

End point timeframe:

Baseline and weeks 3, 7, 11, 15, 19, 22, and 24

End point values	Cohort 1	Cohort 2	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7	10	17	
Units: percent change				
arithmetic mean (standard deviation)				
Week 3 (n = 7, 10, 17)	-1.89 (± 39)	-2.72 (± 38.08)	-2.37 (± 37.23)	
Week 7 (n = 4, 8, 12)	-11.56 (± 26.35)	-6.83 (± 29.97)	-8.4 (± 27.68)	
Week 11 (n = 4, 8, 12)	9.48 (± 17.84)	5.74 (± 38.78)	6.99 (± 32.36)	
Week 15 (n = 2, 7, 9)	7.58 (± 38.39)	-14.24 (± 28.24)	-9.39 (± 29.58)	
Week 19 (n = 1, 2, 3)	12.34 (± 99999)	6.41 (± 9.06)	8.39 (± 7.27)	
Week 22 (n = 0, 1, 1)	99999 (± 99999)	3.37 (± 99999)	3.37 (± 99999)	
Week 24 (n = 0, 1, 1)	99999 (± 99999)	10.96 (± 99999)	10.96 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved > 30% Reduction in iPTH From Baseline at Any Two Consecutive Measurements

End point title	Percentage of Participants Who Achieved > 30% Reduction in iPTH From Baseline at Any Two Consecutive Measurements

End point description:

A subject was considered to have achieved > 30% reduction in iPTH from baseline at any 2 consecutive measurements if percent change of any two consecutive postbaseline iPTH values were < -30% regardless if there was a missing value in between.
The analysis included all enrolled subjects with at least 1 post-baseline assessment.

End point type	Secondary

End point timeframe:

26 weeks

End point values	Cohort 1	Cohort 2	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7	10	17	
Units: percentage of participants				
number (confidence interval 90%)	57.1 (22.5 to 87.1)	40 (15 to 69.6)	47.1 (26 to 68.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved ≥ 30% Reduction in Intact Parathyroid Hormone From Baseline During the Study

End point title	Percentage of Participants Who Achieved ≥ 30% Reduction in Intact Parathyroid Hormone From Baseline During the Study

End point description:

A subject was considered to have achieved ≥ 30% reduction in iPTH if the percent change of any post-baseline iPTH value was ≤ -30% from baseline.
The analysis included all enrolled subjects with at least 1 post-baseline assessment.

End point type	Secondary

End point timeframe:

26 weeks

End point values	Cohort 1	Cohort 2	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7	10	17	
Units: percentage of participants				
number (confidence interval 90%)	100 (65.2 to 100)	50 (22.2 to 77.8)	70.6 (47.8 to 87.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved iPTH Values Between 200 and 300 pg/mL at Any Two Consecutive Measurements

End point title	Percentage of Participants Who Achieved iPTH Values Between 200 and 300 pg/mL at Any Two Consecutive Measurements

End point description:

A subject was considered to have achieved iPTH between 200 and 300 pg/mL (21.2 and 31.8 pmol/L) at any 2 consecutive measurements if any two consecutive post-baseline iPTH values were within the range regardless if there was a missing value in between.
The analysis included all enrolled subjects with at least 1 post-baseline assessment.

End point type	Secondary

End point timeframe:

26 weeks

End point values	Cohort 1	Cohort 2	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7	10	17	
Units: percentage of participants				
number (confidence interval 90%)	0 (0 to 34.8)	10 (0.5 to 39.4)	5.9 (0.3 to 25)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved iPTH Values < 300 pg/mL During the Study

End point title	Percentage of Participants Who Achieved iPTH Values < 300 pg/mL During the Study

End point description:

A subject was considered to have achieved iPTH < 300 pg/mL (31.8 pmol/L) during the study if any post-baseline iPTH value was < 300 pg/mL.
The analysis included all enrolled subjects with at least 1 post-baseline assessment.

End point type	Secondary

End point timeframe:

26 weeks

End point values	Cohort 1	Cohort 2	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	7	10	17	
Units: percentage of participants				
number (confidence interval 90%)	57.1 (22.5 to 87.1)	50 (22.2 to 77.8)	52.9 (31.1 to 74)	

Statistical analyses

No statistical analyses for this end point

Secondary: Dose- and Weight-Normalized Maximum Plasma Concentration (Cmax) of Cinacalcet

End point title	Dose- and Weight-Normalized Maximum Plasma Concentration (Cmax) of Cinacalcet

End point description:

The Pharmacokinetic/ Pharmacodynamic (PK/PD) analysis set includes all subjects who received at least one dose of study drug and had at least one evaluable PK parameter.

End point type	Secondary

End point timeframe:

Week 12

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	7		
Units: ng/mL/(mgkg)				
arithmetic mean (standard deviation)	15.1 (± 16.6)	17.8 (± 10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dose- and Weight-Normalized Area under the Plasma Concentration-time Curve from Time 0 to the Time of Last Quantifiable Concentration (AUClast) for Cinacalcet

End point title	Dose- and Weight-Normalized Area under the Plasma Concentration-time Curve from Time 0 to the Time of Last Quantifiable Concentration (AUClast) for Cinacalcet

End point description:

The Pharmacokinetic/ Pharmacodynamic (PK/PD) analysis set includes all subjects who received at least one dose of study drug and had at least one evaluable PK parameter.

End point type	Secondary

End point timeframe:

Week 12

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	6		
Units: hr*ng/mL/(mgkg)				
arithmetic mean (standard deviation)	160 (± 195)	176.8 (± 177)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
26 Weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
Cohort 1 consists of subjects enrolled before the partial clinical hold. Participants received cinacalcet administered daily for 24 weeks. The starting dose was 0.25 mg/kg (based on dry weight) and the maximum allowed daily dose was 4.2 mg/kg.	
Reporting group title	Cohort 2
Reporting group description:	
Cohort 2 consists of subjects enrolled after the partial clinical hold. Participants received cinacalcet administered daily for 24 weeks. The starting dose was 0.20 mg/kg (based on dry weight) and the maximum allowed daily dose was 2.5 mg/kg/day or 60 mg, whichever was lower.	
Reporting group title	Total
Reporting group description:	
Participants received cinacalcet administered daily for 24 weeks.	

Serious adverse events	Cohort 1	Cohort 2	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)	5 / 10 (50.00%)	9 / 17 (52.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal dialysis complication			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			

subjects affected / exposed	1 / 7 (14.29%)	1 / 10 (10.00%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Complication associated with device			
subjects affected / exposed	1 / 7 (14.29%)	1 / 10 (10.00%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			

subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device malfunction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1	Cohort 2	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 7 (71.43%)	9 / 10 (90.00%)	14 / 17 (82.35%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 7 (14.29%)	1 / 10 (10.00%)	2 / 17 (11.76%)
occurrences (all)	1	1	2
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Surgical and medical procedures			
Catheter removal			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Complication associated with device			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 10 (20.00%)	3 / 17 (17.65%)
occurrences (all)	1	4	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)	3 / 10 (30.00%)	4 / 17 (23.53%)
occurrences (all)	1	3	4
Nasal congestion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Investigations			

Platelet count decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Nervous system disorders			
Lethargy			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Unresponsive to stimuli			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	4	4
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Eye disorders			
Eye pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	1 / 10 (10.00%)	2 / 17 (11.76%)
occurrences (all)	3	1	4
Nausea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	2 / 7 (28.57%)	2 / 10 (20.00%)	4 / 17 (23.53%)
occurrences (all)	3	2	5
Skin and subcutaneous tissue disorders			

Dermatitis contact			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Erythema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 7 (28.57%)	0 / 10 (0.00%)	2 / 17 (11.76%)
occurrences (all)	2	0	2
Device related sepsis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Laryngitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Peritonitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	2	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	3 / 10 (30.00%)	4 / 17 (23.53%)
occurrences (all)	1	3	4
Viral infection			
subjects affected / exposed	2 / 7 (28.57%)	0 / 10 (0.00%)	2 / 17 (11.76%)
occurrences (all)	2	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			

Acidosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 10 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 10 (10.00%)	1 / 17 (5.88%)
occurrences (all)	0	2	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 March 2014	•Weekly monitoring of ionized calcium with a point-of-care device was added; required prior to weekly IP dispensing to the patient •Criteria for dose adjustments were added to the protocol based on ionized calcium values •Daily cinacalcet compliance monitoring with an electronic diary by the patient/parent/legal guardian was added. •Cinacalcet treatment period was changed to 24 weeks with a 2-week follow-up period for a total of 26 weeks on study •SAE reporting language was modified. Also the time period for AE/SAE collection was modified to 14 days following the last dose of IP •Updated miscellaneous study conduct procedures
21 June 2014	•Aligned the dosing schema being used amongst all studies within the cinacalcet pediatric program. The dosing algorithm in Amendment 2 assigned a dose of cinacalcet across a weight band of several kilograms versus the previous dose assignments based on precise weight increments. The assignment of doses across a weight band in regular increments (eg, 1, 2.5, 5, 7.5, 10 mg, etc) allowed for greater convenience and simplicity for the care-giver administering the drug during the course of the trial. •Changes were made to the study procedures and schedule of clinical laboratory assessments to accommodate the requirements of the revised dosing algorithm.
05 November 2014	•Incorporated language regarding adynamic bone disease •Updated language regarding study procedures for consistency within the cinacalcet pediatric program
21 July 2015	•Revised the dose adjustments section for clarity. •Clarified the ionized calcium value on Day 1 must be ≥ 1.13 mmol/L for subjects < 2 years of age and ≥ 1.05 mmol/L for subjects ≥ 2 years of age prior to initiation of treatment. •Clarified that, with the exception of the predose PK sample on day 1, PK samples are only collected if the subject has been receiving IP prior to the visit. •Changed "Screening serum calcium" to be "Screening corrected calcium" for eligibility criterion 4.1.4. •Changed number of screening attempts permitted from a maximum of 4 to a maximum of 3. •Clarified that the eDiary will capture the number of capsules or milliliters suspension administered. •Added ionized calcium at week 1 in the Schedule of Assessments. Changed the endpoints to match wording provided in a regulatory response from the US FDA. •Added text to specify that subjects who complete this 26-week study may be eligible to participate in an extension study (Study 20140159). •Clarified that Amgen must be contacted prior to dispensing new bottle(s) of IP in the event unused medication or empty bottles have been permanently misplaced.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
07 February 2013	The study and enrollment was placed on partial clinical hold by Amgen and the FDA in February 2013 following the death of a patient in another cinacalcet pediatric study. Following the death, the IRB recommended changes to all of the cinacalcet pediatric studies, which resulted in changes to the protocol; Study 20110100 was restarted in April 2014 following these changes.	23 April 2014

Notes:

Limitations and caveats

None reported