Clinical trial results:
A Randomized, Open-label, Controlled Study to Assess the Efficacy and Safety of Cinacalcet HCl in Pediatric Subjects With Secondary Hyperparathyroidism and Chronic Kidney Disease Receiving Dialysis

Summary

EudraCT number	2013-004958-18
Trial protocol	LT SK IT HU ES BE CZ PT DE Outside EU/EEA GR FR
Global end of trial date	23 June 2016

Results information

Result version number	v1
This version publication date	31 December 2016
First version publication date	31 December 2016

Trial information

Trial identification

Sponsor protocol code	20130356

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02138838
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000078-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 June 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 June 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy of cinacalcet for reducing the plasma intact parathyroid hormone (iPTH) level by ≥ 30%.

Protection of trial subjects:

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

Background therapy:

Vitamin D sterols, calcium supplementation and/or phosphate binders were administered as appropriate per individual clinic practice as standard of care.

Evidence for comparator: -

Actual start date of recruitment	07 November 2014
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: 3
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Lithuania: 2
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Ukraine: 9
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	United States: 19

Worldwide total number of subjects	55
EEA total number of subjects	20

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)	18
Adolescents (12-17 years)	37
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 32 centers in Belgium, Czech Republic, France, Germany, Greece, Hungary, Lithuania, Poland, Portugal, Russia Federation, Slovakia, Spain, Ukraine, and the US.

Pre-assignment

Screening details:

Following the completion of a screening period of up to 14 days, eligible subjects were randomized to 1 of 2 treatment groups in a 1:1 ratio administration of cinacalcet daily in addition to standard of care (SOC) therapy or SOC therapy alone. Subjects remained on treatment for 20 weeks or until the time of renal transplant or parathyroidectomy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard of Care

Arm description:

Standard of care therapy included the use of vitamin D sterols, calcium supplementation, and phosphate binders.

Arm type	Active comparator
Investigational medicinal product name	Standard of Care
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Standard of care therapy included the use of vitamin D sterols, calcium supplementation, and phosphate binders.

Arm title	Cinacalcet

Arm description:

In addition to standard of care participants received cinacalcet at a starting dose (based on dry body weight) of 0.20 mg/kg administered once a day by mouth. Dose adjustments and withholding were based on ionized calcium levels, plasma iPTH, and corrected calcium levels.

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

Dosage and administration details:

Capsules were opened and either sprinkled onto soft food (≥ 5 mg dose) or suspended into a sucrose syrup (≥ 2.5 mg dose) to create a liquid suspension for administration. Tablets were used for doses of 30 mg and higher in subjects who could swallow tablets.

Investigational medicinal product name	Standard of Care
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Standard of care therapy included the use of vitamin D sterols, calcium supplementation, and phosphate binders.

Number of subjects in period 1	Standard of Care	Cinacalcet
Started	28	27
Received Study Drug	28	25
Completed	20	16
Not completed	8	11
Consent withdrawn by subject	1	5
Study closure	7	6

Baseline characteristics

Reporting groups	
Reporting group title	Standard of Care
Reporting group description:	
Standard of care therapy included the use of vitamin D sterols, calcium supplementation, and phosphate binders.	
Reporting group title	Cinacalcet
Reporting group description:	
In addition to standard of care participants received cinacalcet at a starting dose (based on dry body weight) of 0.20 mg/kg administered once a day by mouth. Dose adjustments and withholding were based on ionized calcium levels, plasma iPTH, and corrected calcium levels.	

Reporting group values	Standard of Care	Cinacalcet	Total
Number of subjects	28	27	55
Age Categorical			
Units: Subjects			
6 to < 12 years	9	9	18
12 to < 18 years	19	18	37
Age Continuous			
Units: years			
arithmetic mean	12.4	12.8	
standard deviation	± 3.5	± 3.9	-
Gender Categorical			
Units: Subjects			
Female	15	12	27
Male	13	15	28
Race			
Units: Subjects			
Black (or African American)	4	5	9
White	23	19	42
Mixed Race	0	1	1
Other	1	2	3
Ethnicity			
Units: Subjects			
Hispanic/Latino	4	0	4
Not Hispanic/Latino	24	27	51

End points

End points reporting groups

Reporting group title	Standard of Care
Reporting group description:	
Standard of care therapy included the use of vitamin D sterols, calcium supplementation, and phosphate binders.	
Reporting group title	Cinacalcet
Reporting group description:	
In addition to standard of care participants received cinacalcet at a starting dose (based on dry body weight) of 0.20 mg/kg administered once a day by mouth. Dose adjustments and withholding were based on ionized calcium levels, plasma iPTH, and corrected calcium levels.	

Primary: Percentage of Participants Who Achieved a ≥ 30% Reduction From Baseline In Mean Plasma Intact Parathyroid Hormone (iPTH) During the Efficacy Assessment Period

End point title	Percentage of Participants Who Achieved a ≥ 30% Reduction From Baseline In Mean Plasma Intact Parathyroid Hormone (iPTH) During the Efficacy Assessment Period
End point description:	
This endpoint was the primary endpoint in all countries except the US. The analysis was performed using the full analysis set, which included all randomized subjects. Missing data were handled using the last value carried forward method.	
End point type	Primary
End point timeframe:	
Baseline and the efficacy assessment period, weeks 17 to 20	

End point values	Standard of Care	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: percentage of participants				
number (not applicable)	32.1	22.2		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Standard of Care v Cinacalcet
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.42 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	-9.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.3
upper limit	13.4

Notes:

[1] - A hierarchical testing procedure was used to test the primary and biochemical secondary endpoints. The primary endpoint was tested at a 2-sided significance level of 0.05. The secondary endpoints were tested using Holm's method at 0.05 (2-sided) should the primary endpoint achieve a significant result.
[2] - Cochran-Mantel-Haenszel stratified by baseline age group

Primary: Percentage of Participants Who Achieved a ≥ 30% Reduction From Baseline In Mean Plasma iPTH During Weeks 11 to 15

End point title	Percentage of Participants Who Achieved a ≥ 30% Reduction From Baseline In Mean Plasma iPTH During Weeks 11 to 15

End point description:

This endpoint was the primary endpoint in the US only.
The analysis was performed in the full analysis set using non-responder imputation.

End point type	Primary

End point timeframe:

Baseline and weeks 11-15

End point values	Standard of Care	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: percentage of participants				
number (not applicable)	17.9	25.9		

Statistical analyses

Statistical analysis title	Primary nalysis
Comparison groups	Standard of Care v Cinacalcet
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.48 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.7
upper limit	29.9

Notes:

[3] - Cochran-Mantel-Haenszel test stratified by baseline age group

Secondary: Percentage of Participants Who Achieved a Mean iPTH ≤ 300 pg/mL (31.8 pmol/L) During Weeks 17 to 20

End point title	Percentage of Participants Who Achieved a Mean iPTH ≤ 300 pg/mL (31.8 pmol/L) During Weeks 17 to 20

End point description:

This analysis was performed in the full analysis set using last value carried forward imputation.

End point type	Secondary

End point timeframe:

Weeks 17 - 20

End point values	Standard of Care	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: percentage of participants				
number (not applicable)	17.9	7.4		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Standard of Care v Cinacalcet
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	-10.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.7
upper limit	6.8

Notes:

[4] - Cochran-Mantel-Haenszel test stratified by baseline age group

Secondary: Percent Change in iPTH from Baseline to the Mean Value During Weeks 17 to 20

End point title	Percent Change in iPTH from Baseline to the Mean Value During Weeks 17 to 20

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 17-20

End point values	Standard of Care	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	24		
Units: percent change				
least squares mean (standard error)	-11.3 (± 11.1)	7.7 (± 11.73)		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Standard of Care v Cinacalcet
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.23 [5]
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.5
upper limit	50.5

Notes:

[5] - Analysis of covariance (ANCOVA) with baseline age group as the covariate.

Secondary: Percent Change in Corrected Serum Calcium From Baseline to the Mean Value During Weeks 17 to 20

End point title	Percent Change in Corrected Serum Calcium From Baseline to the Mean Value During Weeks 17 to 20

End point description:

This analysis was performed in the full analysis set using last value carried forward imputation.

End point type	Secondary

End point timeframe:

Baseline and weeks 17-20

End point values	Standard of Care	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	24		
Units: percent change				
least squares mean (standard error)	0.06 (± 0.126)	-0.28 (± 0.135)		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Standard of Care v Cinacalcet
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.059 [6]
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.01

Notes:

[6] - Analysis of covariance (ANCOVA) with baseline age group as the covariate.

Secondary: Percent Change in Serum Phosphorous from Baseline to the Mean Value During Weeks 17 to 20

End point title	Percent Change in Serum Phosphorous from Baseline to the Mean Value During Weeks 17 to 20

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 17-20

End point values	Standard of Care	Cinacalcet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	24		
Units: percent change				
least squares mean (standard error)	-0.09 (± 0.258)	0.67 (± 0.266)		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Standard of Care v Cinacalcet
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.039 [7]
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	1.48

Notes:

[7] - Analysis of covariance (ANCOVA) with baseline age group as the covariate.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
24 Weeks	
Adverse event reporting additional description:	
20130356 Final	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Cinacalcet
Reporting group description:	
In addition to standard of care participants received cinacalcet at a starting dose (based on dry body weight) of 0.20 mg/kg administered once a day by mouth. Dose adjustments and withholding were based on ionized calcium levels, plasma iPTH, and corrected calcium levels.	
Reporting group title	Standard of Care
Reporting group description:	
Standard of care therapy included the use of vitamin D sterols, calcium supplementation, and phosphate binders.	

Serious adverse events	Cinacalcet	Standard of Care	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 25 (16.00%)	2 / 30 (6.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Arteriovenous fistula site haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Renovascular hypertension			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ileus			

subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Product issues			
Device dislocation			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cinacalcet	Standard of Care	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 25 (80.00%)	17 / 30 (56.67%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Venous stenosis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Catheter placement			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Catheter removal			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			

subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Vessel puncture site pain			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Dysphonia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Nasal discharge discolouration			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Rhinitis allergic			

subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Product issues			
Device occlusion			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Blood calcium decreased			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Blood parathyroid hormone decreased			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Blood phosphorus decreased			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Blood phosphorus increased			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Weight increased			
subjects affected / exposed	0 / 25 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			

Arteriovenous fistula site complication			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Ligament sprain			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Overdose			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Post procedural oedema			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Procedural headache			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	0 / 25 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness postural			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 25 (4.00%)	4 / 30 (13.33%)	
occurrences (all)	5	4	
Hypoaesthesia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Neurological symptom			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Paraesthesia			

subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Nephrogenic anaemia			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Motion sickness			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Abdominal pain upper			
subjects affected / exposed	1 / 25 (4.00%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	1 / 25 (4.00%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Lip blister			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	3 / 25 (12.00%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
Vomiting			
subjects affected / exposed	0 / 25 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	4	
Skin and subcutaneous tissue disorders			

Dermatitis atopic			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Acne			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Hypertonic bladder			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Endocrine disorders			
Precocious puberty			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Joint swelling			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	3 / 25 (12.00%)	2 / 30 (6.67%)	
occurrences (all)	4	7	
Myalgia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 25 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	

Infections and infestations			
Bronchitis bacterial			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Cellulitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Hepatitis B			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Lip infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	2 / 25 (8.00%)	2 / 30 (6.67%)	
occurrences (all)	2	2	
Peritonitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Respiratory tract infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection viral			

subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 25 (4.00%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Sinusitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Viral pharyngitis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hyperphosphataemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Hypocalcaemia			
subjects affected / exposed	6 / 25 (24.00%)	2 / 30 (6.67%)	
occurrences (all)	7	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 November 2014	•to incorporate information regarding the transition of eligible subjects to an open label extension study (Amgen Study 20140159) at the conclusion of the treatment period in this study. Language regarding the potential to conduct an interim analysis was also incorporated.
06 August 2015	•US-specific primary and secondary endpoints were added to the protocol to satisfy a request from the US FDA •Language was added to allow IP holding for other adverse events that warrant IP dose withhold. The original protocol only specified hold criteria for corrected calcium, ionized calcium, iPTH, and symptomatic hypocalcemia •Restart criteria was made consistent for all IP holds •The dose adjustments section was revised for clarity •The wording to indicate SOC therapy that is commercially available will not usually be provided or reimbursed by Amgen (except if required by local regulation) and will need to be provided to study centers in Russia was added. •An ECG at week 20/end of IP was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported