



Clinical trial results:

A Multicenter, Multiple-dose, Two-arm, Active-controlled, Double-blind, Double-dummy Study to Compare the Therapeutic Efficacy and Safety of Oral Doses of Cinacalcet HCl With Intravenous Doses of AMG 416 in Hemodialysis Subjects With Secondary Hyperparathyroidism

Summary

EudraCT number	2013-000192-33
Trial protocol	PT IT CZ LV SE AT BE ES EE DE GR LT DK HU PL
Global end of trial date	08 January 2015

Results information

Result version number	v1 (current)
This version publication date	16 July 2016
First version publication date	16 July 2016

Trial information

Trial identification

Sponsor protocol code	20120360
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01896232
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 January 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstrate that treatment with etelcalcetide (AMG 416) is not inferior to treatment with cinacalcet for lowering plasma intact parathyroid hormone (PTH) levels by > 30% from baseline among subjects with chronic kidney disease (CKD) and secondary hyperparathyroidism (SHPT) who require management with hemodialysis.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines. Essential documents are retained in accordance with ICH GCP.

All subjects provided written informed consent 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: -

Evidence for comparator: -

Actual start date of recruitment	13 August 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 25
Country: Number of subjects enrolled	Portugal: 43
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Austria: 10
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	Denmark: 9
Country: Number of subjects enrolled	Estonia: 2
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Greece: 30
Country: Number of subjects enrolled	Hungary: 50
Country: Number of subjects enrolled	Italy: 35

Country: Number of subjects enrolled	Latvia: 4
Country: Number of subjects enrolled	Lithuania: 28
Country: Number of subjects enrolled	New Zealand: 15
Country: Number of subjects enrolled	Russian Federation: 97
Country: Number of subjects enrolled	Switzerland: 16
Country: Number of subjects enrolled	Turkey: 19
Country: Number of subjects enrolled	Canada: 28
Country: Number of subjects enrolled	United States: 180
Worldwide total number of subjects	683
EEA total number of subjects	328

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	505
From 65 to 84 years	172
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 164 centers in Austria, Belgium, Canada, the Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, New Zealand, Poland, Portugal, Russia, Spain, Sweden, Switzerland, Turkey, and the United States. Participants were enrolled from 13 August 2013 to 16 May 2014.

Pre-assignment

Screening details:

Patients were assessed for eligibility during an 8-week screening phase. Eligible subjects were stratified by screening serum parathyroid hormone (PTH) level (< 900 or ≥ 900 pg/mL) and region (North America or non-North America) and were randomized 1:1 to receive etelcalcetide intravenously (IV) plus oral placebo or oral cinacalcet plus placebo IV.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Cinacalcet

Arm description:

Participants were randomized to receive oral cinacalcet once daily and placebo intravenous bolus injection at the end of each hemodialysis session, three times per week (TIW) for 26 weeks. The starting dose of cinacalcet was 30 mg daily and could have been titrated at weeks 5, 9, 13, and 17 to target predialysis serum PTH ≤ 300 pg/mL but no lower than 100 pg/mL while maintaining corrected calcium (cCa) ≥ 8.3 mg/dL.

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

Dosage and administration details:

Cinacalcet was administered orally once a day. The starting dose was 30 mg daily, titrated up to 180 mg daily based on serum PTH and corrected calcium levels.

Investigational medicinal product name	Intravenous Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Administered intravenously (IV) three times per week.

Arm title	Etelcalcetide
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Arm description:

Participants were randomized to receive etelcalcetide administered by intravenous bolus injection at the end of each hemodialysis session TIW, and daily oral doses of placebo tablets for 26 weeks. The starting dose of etelcalcetide was 5 mg, and could have been titrated at weeks 5, 9, 13, and 17 to target predialysis serum PTH ≤ 300 pg/mL but no lower than 100 pg/mL while maintaining cCa ≥ 8.3 mg/dL.

Arm type	Experimental
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Investigational medicinal product name	Etelcalcetide
Investigational medicinal product code	AMG 416
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Administered intravenously three times per week. The starting dose was 5 mg, titrated up to 15 mg based on serum PTH and corrected calcium levels.

Investigational medicinal product name	Oral Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day.

Number of subjects in period 1	Cinacalcet	Etelcalcetide
Started	343	340
Received Treatment	341	338
Completed	294	287
Not completed	49	53
Consent withdrawn by subject	32	31
Death	6	10
Lost to follow-up	9	12
Sponsor decision	2	-

Baseline characteristics

Reporting groups

Reporting group title	Cinacalcet
Reporting group description:	
Participants were randomized to receive oral cinacalcet once daily and placebo intravenous bolus injection at the end of each hemodialysis session, three times per week (TIW) for 26 weeks. The starting dose of cinacalcet was 30 mg daily and could have been titrated at weeks 5, 9, 13, and 17 to target predialysis serum PTH \leq 300 pg/mL but no lower than 100 pg/mL while maintaining corrected calcium (cCa) \geq 8.3 mg/dL.	
Reporting group title	Etelcalcetide
Reporting group description:	
Participants were randomized to receive etelcalcetide administered by intravenous bolus injection at the end of each hemodialysis session TIW, and daily oral doses of placebo tablets for 26 weeks. The starting dose of etelcalcetide was 5 mg, and could have been titrated at weeks 5, 9, 13, and 17 to target predialysis serum PTH \leq 300 pg/mL but no lower than 100 pg/mL while maintaining cCa \geq 8.3 mg/dL.	

Reporting group values	Cinacalcet	Etelcalcetide	Total
Number of subjects	343	340	683
Age categorical			
Units: Subjects			
< 65 years	243	262	505
\geq 65 years	100	78	178
Age continuous			
Units: years			
arithmetic mean	55.3	54	-
standard deviation	\pm 14.4	\pm 13.8	
Gender categorical			
Units: Subjects			
Female	151	148	299
Male	192	192	384
Race			
Units: Subjects			
Asian	7	9	16
Black (or African American)	52	54	106
Native Hawaiian or Other Pacific Islander	3	6	9
White	277	261	538
Other	4	10	14
Ethnicity			
Units: Subjects			
Hispanic/Latino	41	38	79
Not Hispanic/Latino	302	302	604
Stratification Factor: Screening Serum Parathyroid Hormone (PTH)			
Units: Subjects			
< 900 pg/mL	171	169	340
\geq 900 pg/mL	172	171	343
Stratification Factor: Region			
Units: Subjects			
North America	105	103	208

Non-North America	238	237	475
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Parathyroid Hormone Units: pg/mL arithmetic mean standard deviation	1138.71 ± 706.77	1092.12 ± 622.81	-
Corrected Calcium Units: mg/dL arithmetic mean standard deviation	9.58 ± 0.67	9.67 ± 0.71	-
Phosphorus			
Data available for 341 and 337 in each treatment group respectively.			
Units: mg/dL arithmetic mean standard deviation	5.82 ± 1.58	5.81 ± 1.69	-
Corrected Calcium Phosphorus Product (cCa x P)			
Data available for 341 and 337 participants in each treatment group respectively.			
Units: mg ² /dL ² arithmetic mean standard deviation	55.65 ± 15.37	56.36 ± 17.15	-

End points

End points reporting groups

Reporting group title	Cinacalcet
Reporting group description: Participants were randomized to receive oral cinacalcet once daily and placebo intravenous bolus injection at the end of each hemodialysis session, three times per week (TIW) for 26 weeks. The starting dose of cinacalcet was 30 mg daily and could have been titrated at weeks 5, 9, 13, and 17 to target predialysis serum PTH ≤ 300 pg/mL but no lower than 100 pg/mL while maintaining corrected calcium (cCa) ≥ 8.3 mg/dL.	
Reporting group title	Etelcalcetide
Reporting group description: Participants were randomized to receive etelcalcetide administered by intravenous bolus injection at the end of each hemodialysis session TIW, and daily oral doses of placebo tablets for 26 weeks. The starting dose of etelcalcetide was 5 mg, and could have been titrated at weeks 5, 9, 13, and 17 to target predialysis serum PTH ≤ 300 pg/mL but no lower than 100 pg/mL while maintaining cCa ≥ 8.3 mg/dL.	

Primary: Percentage of Participants With > 30% Reduction From Baseline in Mean Parathyroid Hormone During the Efficacy Assessment Phase

End point title	Percentage of Participants With > 30% Reduction From Baseline in Mean Parathyroid Hormone During the Efficacy Assessment Phase
End point description:	
End point type	Primary
End point timeframe: Baseline and the efficacy assessment phase (EAP; defined as Weeks 20 to 27, inclusive).	

End point values	Cinacalcet	Etelcalcetide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310 ^[1]	298 ^[2]		
Units: percentage of participants				
number (not applicable)	63.9	77.9		

Notes:

[1] - Subjects with PTH data during the EAP

[2] - Subjects with PTH data during the EAP

Statistical analyses

Statistical analysis title	Non-inferiority Analysis
Statistical analysis description: The analysis was conducted on the Full Analysis Set (FAS), defined as all randomized participants. Imputation under the non-inferiority null method was applied to participants who did not have data during the EAP. The actual number of subjects included in the analysis is 683. The Mantel-Haenszel estimator was used to calculate the treatment difference between the proportions (Cinacalcet - Etelcalcetide) stratified by screening PTH level and region.	
Comparison groups	Etelcalcetide v Cinacalcet

Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
Parameter estimate	Stratified Treatment Difference
Point estimate	-10.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.45
upper limit	-3.51

Notes:

[3] - Etelcalcetide was considered non-inferior to cinacalcet if the upper bound of the 2-sided 95% confidence interval (CI) of the treatment difference (cinacalcet - etelcalcetide) was < 12%, the prespecified margin for non-inferiority.

Secondary: Percentage of Participants With > 50% Reduction From Baseline in Mean PTH During the Efficacy Assessment Phase

End point title	Percentage of Participants With > 50% Reduction From Baseline in Mean PTH During the Efficacy Assessment Phase
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End point description:

End point type	Secondary
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End point timeframe:

Baseline and the efficacy assessment phase (Weeks 20 to 27, inclusive).

End point values	Cinacalcet	Etelcalcetide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	343	340		
Units: percentage of participants				
number (not applicable)	40.2	52.4		

Statistical analyses

Statistical analysis title	Superiority Analysis
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Statistical analysis description:

The analysis was conducted on the full analysis set. Participants were considered as non-responders if they did not have PTH data during the EAP (ie, non-responder imputation).

Achievement of > 50% reduction in mean predialysis serum PTH from baseline during the EAP was analyzed using the Cochran-Mantel-Haenszel (CMH) test stratified by screening PTH level and region. The CMH-stratified odds ratio is Etelcalcetide : Cinacalcet.

Comparison groups	Etelcalcetide v Cinacalcet
Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.65

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	2.23

Secondary: Percentage of Participants With > 30% Reduction From Baseline in Mean PTH During the Efficacy Assessment Phase

End point title	Percentage of Participants With > 30% Reduction From Baseline in Mean PTH During the Efficacy Assessment Phase
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End point description:

End point type	Secondary
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End point timeframe:

Baseline and the efficacy assessment phase (Week 20 to Week 27)

End point values	Cinacalcet	Etelcalcetide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	343	340		
Units: percentage of participants				
number (not applicable)	57.7	68.2		

Statistical analyses

Statistical analysis title	Superiority Analysis
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Statistical analysis description:

The analysis was conducted on the full analysis set. Participants were considered as non-responders if they did not have PTH data during the EAP (ie, non-responder imputation). Achievement of > 30% reduction in mean predialysis serum PTH from baseline during the EAP was analyzed using the Cochran-Mantel-Haenszel test stratified by screening PTH level and region. The CMH-stratified odds ratio is Etelcalcetide : Cinacalcet.

Comparison groups	Etelcalcetide v Cinacalcet
Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	2.17

Secondary: Mean Number of Days of Vomiting or Nausea per Week in the First 8 Weeks

End point title	Mean Number of Days of Vomiting or Nausea per Week in the First 8 Weeks
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End point description:

Participants completed the Nausea/Vomiting Symptom Assessment (NVSA) questionnaire daily. This questionnaire asked participants to indicate the severity of nausea on a scale from 0 (no nausea) to 10 (as severe as can be imagined) and if they had vomited in the past 24 hours. A day of vomiting or nausea was defined as those where the severity of nausea score was > 0 or where the episodes of vomiting score was > 0.

For participants providing less than 7 days of responses to NVSA questions in any given week, data from that week did not contribute to the analysis.

End point type	Secondary
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End point timeframe:

First 8 weeks

End point values	Cinacalcet	Etelcalcetide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	324	331		
Units: days/week				
least squares mean (standard error)	0.3 (\pm 0.03)	0.4 (\pm 0.04)		

Statistical analyses

Statistical analysis title	Superiority Analysis
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Statistical analysis description:

Analyzed using a generalized linear mixed model with Poisson regression, including screening value of the number of days of nausea and vomiting, treatment, stratification factors (screening PTH level and region), study weeks, and treatment by study weeks as covariates. The full analysis set with available data was used for this analysis. The treatment rate ratio is Etelcalcetide : Cinacalcet.

Comparison groups	Etelcalcetide v Cinacalcet
Number of subjects included in analysis	655
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.27
Method	Generalized Linear Mixed Model
Parameter estimate	Treatment Rate Ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.49
Variability estimate	Standard error of the mean
Dispersion value	0.15

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

End point title	Percent Change From Baseline in Mean Corrected Calcium During the Efficacy Assessment Phase
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End point description:

End point type	Secondary
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End point timeframe:

Baseline and the efficacy assessment phase (weeks 20 - 27)

End point values	Cinacalcet	Etelcalcetide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310	298		
Units: percent change				
arithmetic mean (standard error)	-6.28 (± 0.44)	-9.83 (± 0.49)		

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference
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Statistical analysis description:

The analysis was conducted on the full analysis set using a repeated measures mixed effects model, including treatment group, randomization stratification factors (screening PTH level and region), study week, and study week by treatment as fixed effects. Treatment difference is Etelcalcetide - Cinacalcet.

Comparison groups	Etelcalcetide v Cinacalcet
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Number of subjects included in analysis	608
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Analysis specification	Pre-specified
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Analysis type	other
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Parameter estimate	Treatment difference
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Point estimate	-3.48
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-4.76
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upper limit	-2.21
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Variability estimate	Standard error of the mean
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Dispersion value	0.65
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Secondary: Percentage of Participants With Mean Predialysis Serum Phosphorus ≤ 4.5 mg/dL During the Efficacy Assessment Phase

End point title	Percentage of Participants With Mean Predialysis Serum Phosphorus ≤ 4.5 mg/dL During the Efficacy Assessment Phase
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End point description:

End point type	Secondary
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End point timeframe:

Efficacy assessment phase (weeks 20 - 27)

End point values	Cinacalcet	Etelcalcetide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	343	340		
Units: percentage of participants				
number (not applicable)	29.2	32.1		

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference
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Statistical analysis description:

The analysis was conducted on the full analysis set using a CMH test stratified by screening PTH level and region. Participants with no phosphorus assessments during the EAP were considered non-responders. The CMH-stratified odds ratio is Etelcalcetide : Cinacalcet.

Comparison groups	Etelcalcetide v Cinacalcet
Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.59

Secondary: Mean Severity of Nausea in the First 8 Weeks

End point title	Mean Severity of Nausea in the First 8 Weeks
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End point description:

Severity of nausea was assessed using the Nausea and Vomiting Symptom Assessment questionnaire which asked participants to rate the severity of nausea on a scale from 0 (no nausea) to 10 (as severe as can be imagined).

For each participant, the mean severity of nausea was calculated by averaging all available daily severities (including zeroes) reported in the first 8 weeks.

End point type	Secondary
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End point timeframe:

First 8 weeks

End point values	Cinacalcet	Etelcalcetide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	339	339		
Units: units on a scale				
least squares mean (standard error)	0.48 (\pm 0.06)	0.45 (\pm 0.06)		

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference
Statistical analysis description:	
Analyzed using an analysis of covariance (ANCOVA) model adjusted for screening PTH level and region. The full analysis set with available data was used for this analysis. Treatment difference is Etelcalcetide - Cinacalcet.	
Comparison groups	Etelcalcetide v Cinacalcet
Number of subjects included in analysis	678
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.08

Secondary: Mean Number of Episodes of Vomiting per Week in the First 8 Weeks

End point title	Mean Number of Episodes of Vomiting per Week in the First 8 Weeks
End point description:	
The number of vomiting episodes was assessed using the Nausea and Vomiting Symptom Assessment questionnaire which asks participants on a daily basis how many times they vomited in the past 24 hours. The number of episodes in a week is the sum of all reported daily episodes in the week. For participants providing less than 7 days of responses to NVSA questions in any given week, data from that week did not contribute to the analysis.	
End point type	Secondary
End point timeframe:	
First 8 weeks	

End point values	Cinacalcet	Etelcalcetide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	324	331		
Units: vomiting episodes				
least squares mean (standard error)	0.1 (\pm 0.02)	0.2 (\pm 0.02)		

Statistical analyses

Statistical analysis title	Analysis of Treatment Rate Ratio
Statistical analysis description:	
This analysis was conducted in the full analysis set using a generalized linear mixed model with Poisson regression including screening value of the number of episodes of vomiting, treatment, stratification factors (screening PTH level and region), study weeks, and treatment by study weeks as covariates. The treatment rate ratio is Etelcalcetide : Cinacalcet.	
Comparison groups	Etelcalcetide v Cinacalcet
Number of subjects included in analysis	655
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Rate Ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.72
Variability estimate	Standard error of the mean
Dispersion value	0.22

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 until 30 days after the last dose; the treatment period was 26 weeks.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Cinacalcet
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Reporting group description:

Participants received oral cinacalcet once daily and placebo intravenous bolus injection at the end of each hemodialysis session, three times per week (TIW) for 26 weeks. The starting dose of cinacalcet was 30 mg daily and could have been titrated at weeks 5, 9, 13, and 17 to target predialysis serum PTH ≤ 300 pg/mL but no lower than 100 pg/mL while maintaining corrected calcium (cCa) ≥ 8.3 mg/dL.

Reporting group title	Etelcalcetide
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Reporting group description:

Participants received etelcalcetide administered by intravenous bolus injection at the end of each hemodialysis session TIW, and daily oral doses of placebo tablets for 26 weeks. The starting dose of etelcalcetide was 5 mg, and could have been titrated at weeks 5, 9, 13, and 17 to target predialysis serum PTH ≤ 300 pg/mL but no lower than 100 pg/mL while maintaining cCa ≥ 8.3 mg/dL.

Serious adverse events	Cinacalcet	Etelcalcetide	
Total subjects affected by serious adverse events			
subjects affected / exposed	93 / 341 (27.27%)	85 / 338 (25.15%)	
number of deaths (all causes)	6	9	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal cancer			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Uterine leiomyoma			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic arteriosclerosis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brachiocephalic vein stenosis			
subjects affected / exposed	2 / 341 (0.59%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial thrombosis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 341 (0.29%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 341 (0.00%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			

subjects affected / exposed	1 / 341 (0.29%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous stenosis			
subjects affected / exposed	2 / 341 (0.59%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			

subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device complication			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 341 (0.29%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			

subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression suicidal			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sopor			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood calcium decreased			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonoscopy			

subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Arteriovenous fistula aneurysm			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site complication			
subjects affected / exposed	2 / 341 (0.59%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site haemorrhage			
subjects affected / exposed	0 / 341 (0.00%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula thrombosis			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous graft site haemorrhage			

subjects affected / exposed	2 / 341 (0.59%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Concussion			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemodialysis complication			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	3 / 341 (0.88%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney rupture			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax traumatic			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural fistula			

subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural hypotension			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access complication			
subjects affected / exposed	3 / 341 (0.88%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft thrombosis			
subjects affected / exposed	3 / 341 (0.88%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			

subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular injury			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Congenital, familial and genetic disorders			
Cerebrovascular arteriovenous malformation			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	2 / 341 (0.59%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	2 / 341 (0.59%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 341 (0.59%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac arrest			
subjects affected / exposed	3 / 341 (0.88%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure acute			
subjects affected / exposed	0 / 341 (0.00%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiac failure congestive			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery disease			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	2 / 341 (0.59%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amputation stump pain			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			

subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological symptom			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	4 / 341 (1.17%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Antiphospholipid syndrome			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Glaucoma			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diarrhoea			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gastroparesis			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis haemorrhagic			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 341 (0.00%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis haemorrhagic			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 341 (0.00%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			

subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Ecchymosis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	0 / 341 (0.00%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Brown tumour			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			

subjects affected / exposed	2 / 341 (0.59%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	2 / 341 (0.59%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	2 / 341 (0.59%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous graft site abscess			

subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	3 / 341 (0.88%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	3 / 341 (0.88%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			

subjects affected / exposed	2 / 341 (0.59%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 341 (0.00%)	4 / 338 (1.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 341 (0.29%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected fistula			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			

subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngolaryngeal abscess			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			

subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	1 / 341 (0.29%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst infection			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	4 / 341 (1.17%)	3 / 338 (0.89%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	2 / 341 (0.59%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Calciphylaxis			
subjects affected / exposed	1 / 341 (0.29%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes with hyperosmolarity			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	1 / 341 (0.29%)	2 / 338 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 341 (0.00%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	5 / 341 (1.47%)	1 / 338 (0.30%)	
occurrences causally related to treatment / all	1 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			

subjects affected / exposed	1 / 341 (0.29%)	0 / 338 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Cinacalcet	Etelcalcetide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	259 / 341 (75.95%)	278 / 338 (82.25%)	
Investigations			
Blood calcium decreased			
subjects affected / exposed	203 / 341 (59.53%)	232 / 338 (68.64%)	
occurrences (all)	347	376	
Vascular disorders			
Hypertension			
subjects affected / exposed	22 / 341 (6.45%)	20 / 338 (5.92%)	
occurrences (all)	26	30	
Hypotension			
subjects affected / exposed	10 / 341 (2.93%)	21 / 338 (6.21%)	
occurrences (all)	11	30	
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 341 (7.04%)	21 / 338 (6.21%)	
occurrences (all)	34	31	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 341 (3.23%)	17 / 338 (5.03%)	
occurrences (all)	14	19	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	34 / 341 (9.97%)	21 / 338 (6.21%)	
occurrences (all)	47	24	
Nausea			
subjects affected / exposed	77 / 341 (22.58%)	62 / 338 (18.34%)	
occurrences (all)	172	150	
Vomiting			

subjects affected / exposed occurrences (all)	46 / 341 (13.49%) 99	44 / 338 (13.02%) 72	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	13 / 341 (3.81%)	17 / 338 (5.03%)	
occurrences (all)	16	19	
Muscle spasms			
subjects affected / exposed	20 / 341 (5.87%)	22 / 338 (6.51%)	
occurrences (all)	32	29	
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	8 / 341 (2.35%)	17 / 338 (5.03%)	
occurrences (all)	9	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2013	<ul style="list-style-type: none">- Allowed initiation of AMG 416 administration Monday to Friday, instead of the previous restriction of Wednesday or Thursday only.- Allowed adjustment of vitamin D for hypocalcemia during the study.- Provided a recommended sequence of interventions for treating hypocalcemia with reference to the modification of oral calcium supplements, dialysate calcium concentration, and then vitamin D.- Clarified that AMG 416 was not to be administered subcutaneously or by any route other than IV, and that it was not to be administered concurrently with other IV medications.- Changed the assay for PTH testing from plasma to serum to be consistent with previous AMG 416 studies.
30 August 2013	<ul style="list-style-type: none">- Addressed 4 main issues:<ul style="list-style-type: none">o Updated inclusion/exclusion criteria to facilitate enrollment challenges and to align with updated male contraception for both investigational products.o Addressed regulatory authority comments on the analysis of the primary endpoint.o Updated serious adverse event reporting language.o Updated miscellaneous study conduct procedures.- Changed the eligibility criteria from 2 consecutive PTH concentrations > 600 pg/mL to 1 PTH concentration > 500 pg/mL.- Changed the inclusion criteria to allow changes (up to 50%) in the maximum dose for protocol-specified concomitant therapies (vitamin D, calcium supplements, and phosphate binders).
17 October 2014	<ul style="list-style-type: none">- Added a key secondary endpoint based on efficacy and reprioritized the order of sequential statistical testing of the key secondary endpoints based on the results of recently-concluded, phase 3, placebo-controlled AMG 416 Studies 20120229 and 20120230, for which an indirect comparison was made to concluded phase 3, placebo-controlled studies of cinacalcet.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported