

**Clinical trial results:****A Multicenter Single-arm Extension Study to Describe the Long-term Safety of AMG 416 in the Treatment of Secondary Hyperparathyroidism in Subjects With Chronic Kidney Disease on Hemodialysis****Summary**

EudraCT number	2013-004136-30
Trial protocol	SE IT BE AT ES PT LT PL CZ DK LV DE GR HU NL
Global end of trial date	26 June 2017

**Results information**

Result version number	v1 (current)
This version publication date	06 July 2018
First version publication date	06 July 2018

**Trial information****Trial identification**

Sponsor protocol code	20130213
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02102204
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	26 June 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	26 June 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study was to characterize the long-term safety and tolerability of etelcalcetide in the treatment of secondary hyperparathyroidism in subjects with chronic kidney disease (CKD) receiving hemodialysis.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH), Good Clinical Practice (GCP), and country-specific regulations/guidelines.

The study protocol and all amendments, the proposed informed consent form, other written subject information, and any proposed advertising materials were reviewed by the applicable independent ethics committee (IEC) or institutional review board (IRB) at each study center. The applicable IEC/IRB provided written approval, and a copy of the approval was received by Amgen before recruitment of subjects into the study and shipment of etelcalcetide.

Before a subject's participation in the clinical study, the investigator at each study center obtained written informed consent from the subject after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study, and before any protocol-specific screening procedures or etelcalcetide was administered.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 March 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	Australia: 11
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Belgium: 33
Country: Number of subjects enrolled	Czech Republic: 34
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 20
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Greece: 17
Country: Number of subjects enrolled	Hungary: 71
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Italy: 35
Country: Number of subjects enrolled	Lithuania: 10
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	New Zealand: 4

Country: Number of subjects enrolled	Poland: 33
Country: Number of subjects enrolled	Portugal: 29
Country: Number of subjects enrolled	Russian Federation: 117
Country: Number of subjects enrolled	Spain: 56
Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	Switzerland: 10
Country: Number of subjects enrolled	Turkey: 11
Country: Number of subjects enrolled	Canada: 27
Country: Number of subjects enrolled	United States: 326
Worldwide total number of subjects	902
EEA total number of subjects	386

Notes:

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### 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)	589
From 65 to 84 years	294
85 years and over	19

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 229 study centers in Europe, Australia, New Zealand, and North America.

### Pre-assignment

Screening details:

A total of 902 participants were enrolled in Study 20130213: 215 and 200 participants from the cinacalcet and etelcalcetide groups of the double-blind parent Study 20120360 (2013-000192-33), respectively, and 487 participants from the open-label parent Studies 20120231 (2012-002808-41) and 20120334 (NCT01576146).

### Period 1

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

### Arms

<b>Arm title</b>	Etelcalcetide
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Arm description:

Participants received etelcalcetide three times a week (TIW) by bolus injection at the end of hemodialysis. The minimum etelcalcetide dose in this study was 2.5 mg and the maximum dose was 15 mg. Etelcalcetide dose was titrated to maintain parathyroid hormone levels within 2x to 9x the upper limit of normal based on the reference range of the assay used at the individual study center.

Arm type	Experimental
Investigational medicinal product name	Etelcalcetide
Investigational medicinal product code	AMG 416
Other name	KAI-4169 Parsabiv
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Etelcalcetide was administered TIW by bolus injection into the venous line of the dialysis circuit at the end of hemodialysis.

<b>Number of subjects in period 1</b>	Etelcalcetide
Started	902
Received Etelcalcetide	884
Completed	603
Not completed	299
Consent withdrawn by subject	137
Death	92
Lost to follow-up	65
Sponsor decision	5



## Baseline characteristics

### Reporting groups

Reporting group title	Overall Study
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Reporting group description:

Participants were enrolled to receive etelcalcetide three times a week (TIW) by bolus injection at the end of hemodialysis. The minimum etelcalcetide dose in this study was 2.5 mg and the maximum dose was 15 mg. Etelcalcetide dose was titrated to maintain parathyroid hormone levels within 2x to 9x the upper limit of normal based on the reference range of the assay used at the individual study center.

Reporting group values	Overall Study	Total	
Number of subjects	902	902	
Age Categorical			
Units: Subjects			
Adults (18-64 years)	589	589	
From 65-84 years	294	294	
85 years and over	19	19	
Age Continuous			
Units: years			
arithmetic mean	57.8	-	
standard deviation	± 14.3		
Gender Categorical			
Units: Subjects			
Female	365	365	
Male	537	537	
Race			
Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	16	16	
Black (or African American)	195	195	
Native Hawaiian or Other Pacific Islander	9	9	
White	670	670	
Other	11	11	
Ethnicity			
Units: Subjects			
Hispanic/Latino	79	79	
Not Hispanic/Latino	823	823	
Baseline Parathyroid Hormone Level			
Data are reported for 871 participants with available data.			
Units: pg/mL			
arithmetic mean	522.1	-	
standard deviation	± 563.9		

## End points

### End points reporting groups

Reporting group title	Etelcalcetide
Reporting group description:	
Participants received etelcalcetide three times a week (TIW) by bolus injection at the end of hemodialysis. The minimum etelcalcetide dose in this study was 2.5 mg and the maximum dose was 15 mg. Etelcalcetide dose was titrated to maintain parathyroid hormone levels within 2x to 9x the upper limit of normal based on the reference range of the assay used at the individual study center.	

### Primary: Number of Participants With Adverse Events

End point title	Number of Participants With Adverse Events <sup>[1]</sup>
End point description:	
A serious adverse event is an AE that met at least 1 of the following criteria:	
<ul style="list-style-type: none"><li>• fatal</li><li>• life threatening</li><li>• required in-patient hospitalization or prolongation of existing hospitalization</li><li>• resulted in persistent or significant disability/incapacity</li><li>• congenital anomaly/birth defect</li><li>• other medically important serious event.</li></ul>	
The relationship of each AE to study treatment was assessed by the investigator.	
The following AE grading scale was used:	
Mild: Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required	
Moderate: Mild to moderate limitation in activity-some assistance may be needed; no or minimal medical intervention/therapy required	
Severe: Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalization possible	
Life-threatening: Extreme limitation in activity, significant assistance required, significant medical intervention/therapy required, hospitalization probable.	
End point type	Primary

End point timeframe:

From the date of first dose of etelcalcetide (in the current study) and up to 30 days after the last dose as of the final analysis data cut-off date of 26 June 2017; median duration of treatment was 563 days.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The study was descriptive; no formal hypothesis was tested.

End point values	Etelcalcetide			
Subject group type	Reporting group			
Number of subjects analysed	884			
Units: participants				
Any adverse event	768			
Serious adverse events	436			
Treatment-related adverse events	288			
Serious treatment-related adverse events	4			
AEs leading to discontinuation of etelcalcetide	41			
Fatal adverse events	89			
Mild adverse events	122			
Moderate adverse events	219			
Severe adverse events	325			
Life-threatening adverse events	102			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Parathyroid Hormone Levels Between Two to Nine-times the Upper Limit of Normal

End point title	Percentage of Participants With Parathyroid Hormone Levels Between Two to Nine-times the Upper Limit of Normal
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End point description:

The percentage of participants who maintained plasma parathyroid hormone (PTH) levels within the Kidney Disease Improving Global Outcomes (KDIGO) recommended range of not less than 2x the upper limit of normal (ULN) and not greater than 9x the ULN at months 6, 12, and 18, with the ULN based on the reference range of the assay used at the individual clinical site.

End point type	Secondary
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End point timeframe:

Months 6, 12, and 18

End point values	Etelcalcetide			
Subject group type	Reporting group			
Number of subjects analysed	884 <sup>[2]</sup>			
Units: percentage of participants				
number (confidence interval 95%)				
Month 6 (N = 770)	67.0 (63.6 to 70.3)			
Month 12 (N = 679)	73.2 (69.7 to 76.5)			
Month 18 (N = 540)	71.9 (67.9 to 75.6)			

Notes:

[2] - Participants who received at least 1 dose of etelcalcetide with available data at each time point.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Serum Phosphorus $\leq$ the ULN

End point title	Percentage of Participants With Serum Phosphorus $\leq$ the ULN
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End point description:

Percentage of participants with serum phosphorus less than or equal to the upper limit of normal for the assay used.

End point type	Secondary
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End point timeframe:

Months 6, 12, and 18

<b>End point values</b>	Etelcalcetide			
Subject group type	Reporting group			
Number of subjects analysed	884			
Units: percentage of participants				
number (confidence interval 95%)				
Month 6 (N = 774)	39.4 (35.9 to 43.0)			
Month 12 (N = 625)	40.0 (36.1 to 44.0)			
Month 18 (N = 478)	36.8 (32.5 to 41.3)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Serum Corrected Calcium < 7.5 mg/dL

End point title	Percentage of Participants With Serum Corrected Calcium < 7.5 mg/dL
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End point description:

The percentage of participants with serum corrected calcium (cCa) reported for cumulative time intervals from day 1 through months 6, 12, and 18, using the participant's lowest recorded corrected calcium value during the time interval.

If serum albumin was less than 4.0 g/dL, serum calcium was corrected according to the following formula:

$cCa \text{ (mg/dL)} = \text{total calcium (mg/dL)} + (4 - \text{albumin [g/dL]}) * 0.8$ . If serum albumin was > 4.0 g/dL no correction was made.

End point type	Secondary
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End point timeframe:

From day 1 to months 6, 12, and 18

<b>End point values</b>	Etelcalcetide			
Subject group type	Reporting group			
Number of subjects analysed	871 <sup>[3]</sup>			
Units: percentage of participants				
number (confidence interval 95%)				
Day 1 to Month 6	9.5 (7.7 to 11.7)			
Day 1 to Month 12	14.1 (11.9 to 16.6)			
Day 1 to Month 18	16.3 (13.9 to 18.9)			

Notes:

[3] - Participants who received at least 1 dose of etelcalcetide with available day 1 data

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Shifts From Baseline Grade 0 or 1 to Postbaseline Grade 3 or 4 for Laboratory Parameters

End point title	Number of Participants With Shifts From Baseline Grade 0 or 1 to Postbaseline Grade 3 or 4 for Laboratory Parameters
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End point description:

The Common Terminology Criteria for Adverse Events (CTCAE) grades for laboratory parameter values were defined based on the upper/lower limit of normal from the local laboratories contracted by the study centers

End point type	Secondary
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End point timeframe:

Baseline to end of treatment; median duration of treatment was 563 days.

End point values	Etelcalcetide			
Subject group type	Reporting group			
Number of subjects analysed	884 <sup>[4]</sup>			
Units: participants				
Increased Alanine Aminotransferase Grade 1 to 3	1			
Increased Alkaline Phosphatase Grade 1 to 3	2			
Increased Aspartate Aminotransferase Grade 1 to 3	1			
Decreased Corrected Calcium Grade 1 to 3	18			
Decreased Corrected Calcium Grade 1 to 4	2			
Decreased ionized Calcium Grade 1 to 3	1			
Decreased ionized Calcium Grade 1 to 4	2			
Decreased Phosphorous Grade 1 to 3	1			

Notes:

[4] - Participants who received at least 1 dose of etelcalcetide

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants Who Developed Positive Binding Anti-Etelcalcetide Antibodies

End point title	Number of Participants Who Developed Positive Binding Anti-Etelcalcetide Antibodies
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End point description:

The number of participants who were binding antibody positive post-baseline with a negative or no result at baseline (where baseline for participants previously treated with etelcalcetide is Day 1 of the first study in which they were exposed to etelcalcetide and for participants previously treated with cinacalcet is the ending time point for study 20120360).

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End point type	Secondary
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End point timeframe:

Baseline and every 6 months (up to 24 months)

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<b>End point values</b>	Etelcalcetide			
Subject group type	Reporting group			
Number of subjects analysed	808 <sup>[5]</sup>			
Units: participants	111			

Notes:

[5] - Participants who received at least 1 dose of etelcalcetide and a post-baseline antibody result

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the date of first dose of etelcalcetide (in the current study) and up to 30 days after the last dose as of the final analysis data cut-off date of 26 June 2017; median duration of treatment was 563 days.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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### Reporting groups

Reporting group title	Etelcalcetide
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Reporting group description:

Participants received etelcalcetide three times a week (TIW) by bolus injection at the end of hemodialysis. The minimum etelcalcetide dose in this study was 2.5 mg and the maximum dose was 15 mg. Etelcalcetide dose was titrated to maintain parathyroid hormone levels within 2x to 9x the upper limit of normal based on the reference range of the assay used at the individual study center.

<b>Serious adverse events</b>	Etelcalcetide		
Total subjects affected by serious adverse events			
subjects affected / exposed	436 / 884 (49.32%)		
number of deaths (all causes)	89		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Benign neoplasm			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Benign neoplasm of bladder			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder cancer			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Bladder papilloma</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Breast cancer</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Carcinoid tumour of the small bowel</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Endometrial adenocarcinoma</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Lung adenocarcinoma</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Malignant melanoma</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Prostate cancer</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Renal cell carcinoma</b>			

subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Vascular disorders</b>			
<b>Accelerated hypertension</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Aortic aneurysm</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Aortic dissection</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
<b>Aortic stenosis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Arterial occlusive disease</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Arteriosclerosis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Arteriovenous fistula</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Axillary vein thrombosis</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Exsanguination			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Extremity necrosis			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Haematoma			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	9 / 884 (1.02%)		
occurrences causally related to treatment / all	0 / 13		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	6 / 884 (0.68%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Hypertensive emergency			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			

subjects affected / exposed	8 / 884 (0.90%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Hypovolaemic shock			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Iliac artery occlusion			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant hypertension			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Peripheral artery aneurysm			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral artery occlusion			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral artery stenosis			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral artery thrombosis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral ischaemia			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Peripheral vascular disorder			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Shock haemorrhagic			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Steal syndrome			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Superior vena cava stenosis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Superior vena cava syndrome			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombophlebitis			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular calcification			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular compression			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous occlusion			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 884 (0.57%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Chest pain			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	1 / 4		
Drowning			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Hyperpyrexia			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Impaired healing			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Ischaemic ulcer			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Non-cardiac chest pain			
subjects affected / exposed	11 / 884 (1.24%)		
occurrences causally related to treatment / all	0 / 14		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			

subjects affected / exposed	11 / 884 (1.24%)		
occurrences causally related to treatment / all	0 / 11		
deaths causally related to treatment / all	0 / 0		
<b>Sudden death</b>			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 4		
<b>Systemic inflammatory response syndrome</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Immune system disorders</b>			
<b>Chronic allograft nephropathy</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Transplant rejection</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Reproductive system and breast disorders</b>			
<b>Benign prostatic hyperplasia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Postmenopausal haemorrhage</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Priapism</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Uterine polyp			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Choking			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Cystic lung disease			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dependence on respirator			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dyspnoea			
subjects affected / exposed	12 / 884 (1.36%)		
occurrences causally related to treatment / all	0 / 14		
deaths causally related to treatment / all	0 / 0		

Epistaxis				
subjects affected / exposed	3 / 884 (0.34%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Haemothorax				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hydrothorax				
subjects affected / exposed	2 / 884 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	6 / 884 (0.68%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Orthopnoea				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	3 / 884 (0.34%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				

subjects affected / exposed	12 / 884 (1.36%)		
occurrences causally related to treatment / all	0 / 13		
deaths causally related to treatment / all	0 / 0		
<b>Respiratory arrest</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Respiratory failure</b>			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 2		
<b>Psychiatric disorders</b>			
<b>Anxiety</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Confusional state</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Delirium</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
<b>Depression</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Depression suicidal</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Insomnia</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	8 / 884 (0.90%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Device failure			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device malfunction			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device occlusion			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stent malfunction			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis in device			

subjects affected / exposed	6 / 884 (0.68%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
<b>Investigations</b>			
Blood potassium decreased			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paracentesis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral pulse decreased			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Injury, poisoning and procedural complications</b>			
Acetabulum fracture			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arteriovenous fistula aneurysm			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arteriovenous fistula occlusion			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Arteriovenous fistula site complication				
subjects affected / exposed	11 / 884 (1.24%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 0			
Arteriovenous fistula site haematoma				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arteriovenous fistula site haemorrhage				
subjects affected / exposed	4 / 884 (0.45%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Arteriovenous fistula thrombosis				
subjects affected / exposed	24 / 884 (2.71%)			
occurrences causally related to treatment / all	0 / 27			
deaths causally related to treatment / all	0 / 1			
Arteriovenous graft site haemorrhage				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arteriovenous graft thrombosis				
subjects affected / exposed	9 / 884 (1.02%)			
occurrences causally related to treatment / all	0 / 14			
deaths causally related to treatment / all	0 / 0			
Cervical vertebral fracture				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Craniocerebral injury				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	7 / 884 (0.79%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	2 / 884 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	2 / 884 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Joint dislocation				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Laceration				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Limb injury				
subjects affected / exposed	4 / 884 (0.45%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar vertebral fracture				

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Overdose</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Patella fracture</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Pelvic fracture</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Post procedural haemorrhage</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Post-traumatic pain</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Procedural hypertension</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Procedural hypotension</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Procedural intestinal perforation</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Procedural pain			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shunt aneurysm			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shunt occlusion			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Shunt stenosis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Subarachnoid haemorrhage</b>			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
<b>Subdural haematoma</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Tendon rupture</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Thermal burn</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Tibia fracture</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Toxicity to various agents</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Tracheostomy malfunction</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Upper limb fracture</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular access complication			
subjects affected / exposed	5 / 884 (0.57%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Vascular access malfunction			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular graft complication			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular graft occlusion			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular injury			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular pseudoaneurysm ruptured			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Wound			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound dehiscence			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Congenital, familial and genetic disorders</b>			
Congenital cystic kidney disease			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic arteriovenous malformation			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Porencephaly			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Cardiac disorders</b>			
Acute coronary syndrome			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	13 / 884 (1.47%)		
occurrences causally related to treatment / all	0 / 13		
deaths causally related to treatment / all	0 / 3		
Angina pectoris			
subjects affected / exposed	8 / 884 (0.90%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		

Aortic valve incompetence				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Aortic valve stenosis				
subjects affected / exposed	2 / 884 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	15 / 884 (1.70%)			
occurrences causally related to treatment / all	0 / 15			
deaths causally related to treatment / all	0 / 1			
Atrial flutter				
subjects affected / exposed	3 / 884 (0.34%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	4 / 884 (0.45%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	3 / 884 (0.34%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	20 / 884 (2.26%)			
occurrences causally related to treatment / all	0 / 21			
deaths causally related to treatment / all	0 / 15			
Cardiac failure				
subjects affected / exposed	2 / 884 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure congestive			
subjects affected / exposed	8 / 884 (0.90%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 0		
Cardiac valve disease			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 3		
Cardiogenic shock			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Cardiomyopathy			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Coronary artery stenosis			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Mitral valve incompetence			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Myocardial infarction</b>			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 3		
<b>Myocardial ischaemia</b>			
subjects affected / exposed	5 / 884 (0.57%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
<b>Pericardial effusion</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Pericarditis uraemic</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Sinus node dysfunction</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Sinus tachycardia</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Supraventricular tachycardia</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Ventricular tachycardia</b>			

subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Nervous system disorders</b>			
Altered state of consciousness			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aphasia			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain injury			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Brain stem stroke			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Carotid artery occlusion			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Carotid artery stenosis			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Carpal tunnel syndrome			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			

subjects affected / exposed	5 / 884 (0.57%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 2		
<b>Cerebral infarction</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Cerebral ischaemia</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Cerebrovascular accident</b>			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 2		
<b>Diabetic neuropathy</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Dizziness</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Dysaesthesia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Dysarthria</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Encephalopathy</b>			

subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Facial paresis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic stroke			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypersomnia			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoaesthesia			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hypoxic-ischaemic encephalopathy			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Loss of consciousness			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Metabolic encephalopathy			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Multiple sclerosis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuritis cranial			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Normal pressure hydrocephalus			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Quadriplegia			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Seizure</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Syncope</b>			
subjects affected / exposed	13 / 884 (1.47%)		
occurrences causally related to treatment / all	0 / 14		
deaths causally related to treatment / all	0 / 0		
<b>Transient global amnesia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Transient ischaemic attack</b>			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
<b>Tremor</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Uraemic neuropathy</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Blood and lymphatic system disorders</b>			
<b>Anaemia</b>			
subjects affected / exposed	19 / 884 (2.15%)		
occurrences causally related to treatment / all	0 / 26		
deaths causally related to treatment / all	0 / 1		
<b>Coagulopathy</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Haemorrhagic anaemia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Nephrogenic anaemia</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Neutropenia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Thrombocytopenia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Ear and labyrinth disorders</b>			
<b>Vertigo</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Eye disorders</b>			
<b>Cataract</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Optic ischaemic neuropathy</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Vision blurred</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Gastrointestinal disorders</b>			
<b>Abdominal hernia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Abdominal pain</b>			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
<b>Abdominal pain upper</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Ascites</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Chronic gastritis</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Colitis</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Colitis ischaemic</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Constipation</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Diarrhoea</b>			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
<b>Diverticulum</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Diverticulum intestinal haemorrhagic</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Duodenal ulcer</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Duodenitis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Enteritis</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Epigastric discomfort</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Gastric ulcer</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis haemorrhagic			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroduodenitis			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	5 / 884 (0.57%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematochezia			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic erosive gastritis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhoidal haemorrhage			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hernial eventration</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Ileus</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Inguinal hernia</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Intestinal ischaemia</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Intestinal obstruction</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Intestinal perforation</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Large intestinal obstruction</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Large intestine perforation</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine polyp			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal haemorrhage			
subjects affected / exposed	5 / 884 (0.57%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatic disorder			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	5 / 884 (0.57%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Pancreatitis chronic			

subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retroperitoneal haemorrhage			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestine polyp			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	6 / 884 (0.68%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	5 / 884 (0.57%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bile duct obstruction			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Bile duct stone</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Biliary colic</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Cholangitis</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Cholecystitis acute</b>			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 1		
<b>Cholecystitis chronic</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Cholelithiasis</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Gallbladder disorder</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hepatic cyst</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic cyst ruptured			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jaundice			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Liver injury			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sphincter of Oddi dysfunction			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Skin discolouration			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin ulcer			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

End stage renal disease				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Haematuria				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal cyst				
subjects affected / exposed	2 / 884 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Renal cyst haemorrhage				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Renal vein thrombosis				

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urethral stenosis			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Goitre			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperparathyroidism secondary			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperparathyroidism tertiary			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 884 (0.68%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Arthritis reactive			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Back pain				
subjects affected / exposed	4 / 884 (0.45%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Cervical spinal stenosis				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chondrocalcinosis				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fracture nonunion				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc degeneration				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Muscle spasms				
subjects affected / exposed	2 / 884 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Muscle swelling				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	1 / 884 (0.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				

subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Musculoskeletal pain</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Myalgia</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Neck pain</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Neuropathic arthropathy</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Pain in extremity</b>			
subjects affected / exposed	6 / 884 (0.68%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
<b>Pseudarthrosis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>SLE arthritis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Spinal column stenosis</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal osteoarthritis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon calcification			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal wall abscess			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abscess limb			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis perforated			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arteriovenous fistula site infection			

subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Arteriovenous graft site abscess</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Arteriovenous graft site infection</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Arthritis bacterial</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Bacteraemia</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Bacterial sepsis</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Bronchitis</b>			
subjects affected / exposed	10 / 884 (1.13%)		
occurrences causally related to treatment / all	0 / 11		
deaths causally related to treatment / all	0 / 1		
<b>Bronchitis bacterial</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Campylobacter gastroenteritis</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Catheter site infection</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Cellulitis</b>			
subjects affected / exposed	9 / 884 (1.02%)		
occurrences causally related to treatment / all	0 / 11		
deaths causally related to treatment / all	0 / 0		
<b>Cellulitis gangrenous</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Cellulitis orbital</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Citrobacter sepsis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Clostridium difficile colitis</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Device related infection</b>			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
<b>Device related sepsis</b>			

subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Diabetic foot infection			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diabetic gangrene			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ear infection			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocarditis			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 2		
Epiglottitis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Escherichia sepsis			

subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Febrile infection</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Gangrene</b>			
subjects affected / exposed	9 / 884 (1.02%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 0		
<b>Gastroenteritis</b>			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
<b>Helicobacter gastritis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hepatitis A</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Herpes zoster</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Infection</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Influenza</b>			

subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Intervertebral discitis</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
<b>Intestinal tuberculosis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Laryngitis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Liver abscess</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Lower respiratory tract infection</b>			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Localised infection</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Lower respiratory tract infection viral</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Mediastinitis</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Meningitis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Muscle abscess</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Orchitis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Osteomyelitis</b>			
subjects affected / exposed	11 / 884 (1.24%)		
occurrences causally related to treatment / all	0 / 11		
deaths causally related to treatment / all	0 / 1		
<b>Osteomyelitis chronic</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Perineal abscess</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Pneumonia</b>			
subjects affected / exposed	40 / 884 (4.52%)		
occurrences causally related to treatment / all	0 / 48		
deaths causally related to treatment / all	0 / 6		
<b>Post procedural infection</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudomembranous colitis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	7 / 884 (0.79%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection viral			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	27 / 884 (3.05%)		
occurrences causally related to treatment / all	0 / 29		
deaths causally related to treatment / all	0 / 8		
Septic shock			

subjects affected / exposed	14 / 884 (1.58%)		
occurrences causally related to treatment / all	0 / 14		
deaths causally related to treatment / all	0 / 5		
<b>Serratia bacteraemia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Sinusitis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Skin infection</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Staphylococcal bacteraemia</b>			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
<b>Staphylococcal sepsis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Stoma site infection</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Subcutaneous abscess</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Systemic infection</b>			

subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tracheitis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tracheobronchitis			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	6 / 884 (0.68%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Vascular access site infection			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vulval abscess			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound infection			

subjects affected / exposed	3 / 884 (0.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Metabolism and nutrition disorders</b>			
<b>  Calciphylaxis</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>  Dehydration</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>  Electrolyte imbalance</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>  Fluid overload</b>			
subjects affected / exposed	16 / 884 (1.81%)		
occurrences causally related to treatment / all	0 / 17		
deaths causally related to treatment / all	0 / 0		
<b>  Fluid retention</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>  Hyperglycaemia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>  Hyperinsulinaemic hypoglycaemia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>  Hyperkalaemia</b>			

subjects affected / exposed	16 / 884 (1.81%)		
occurrences causally related to treatment / all	0 / 17		
deaths causally related to treatment / all	0 / 0		
<b>Hypervolaemia</b>			
subjects affected / exposed	2 / 884 (0.23%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
<b>Hypoglycaemia</b>			
subjects affected / exposed	4 / 884 (0.45%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Hyponatraemia</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Metabolic acidosis</b>			
subjects affected / exposed	1 / 884 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Etelcalcetide		
<b>Total subjects affected by non-serious adverse events</b>			
subjects affected / exposed	537 / 884 (60.75%)		
<b>Investigations</b>			
Blood calcium decreased			
subjects affected / exposed	253 / 884 (28.62%)		
occurrences (all)	408		
<b>Injury, poisoning and procedural complications</b>			
Arteriovenous fistula site complication			
subjects affected / exposed	45 / 884 (5.09%)		
occurrences (all)	71		
<b>Vascular disorders</b>			

Hypertension subjects affected / exposed occurrences (all)	62 / 884 (7.01%) 88		
Hypotension subjects affected / exposed occurrences (all)	60 / 884 (6.79%) 108		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	84 / 884 (9.50%) 112		
Nausea subjects affected / exposed occurrences (all)	58 / 884 (6.56%) 70		
Vomiting subjects affected / exposed occurrences (all)	56 / 884 (6.33%) 71		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	51 / 884 (5.77%) 63		
Dyspnoea subjects affected / exposed occurrences (all)	50 / 884 (5.66%) 63		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	52 / 884 (5.88%) 58		
Muscle spasms subjects affected / exposed occurrences (all)	73 / 884 (8.26%) 122		
Pain in extremity subjects affected / exposed occurrences (all)	59 / 884 (6.67%) 85		
Infections and infestations Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	58 / 884 (6.56%) 73		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	45 / 884 (5.09%) 74		
Metabolism and nutrition disorders Hyperphosphataemia subjects affected / exposed occurrences (all)	82 / 884 (9.28%) 99		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 May 2014	<p>The primary reason for the protocol amendment was both to create greater flexibility in dose titration in a real-world setting while recognizing differences in practice patterns across centers and regions and to standardize certain measurements. Changes to the protocol included:</p> <ul style="list-style-type: none"><li>• A minimum monthly calcium and albumin was mandated because there are slight differences in standards of care globally for frequency of selected laboratory assays. These values allowed for a consistent calcium value to use in analyses.</li><li>• Flexibility was allowed in the type of calcium measurement allowed (ie, corrected calcium or total calcium or ionized calcium equivalent) to inform dose titration.</li><li>• The titration algorithm was modified to allow for increased flexibility for dose reductions in increments of 2.5 mg at the discretion of the investigator, based on corrected calcium values and not just parathyroid hormone values.</li><li>• The titration algorithm was modified to allow for increased flexibility in the use of oral calcium supplements and the dialysate calcium bath.</li><li>• The starting dose was modified only for subjects entering from Study 20120360 to 2.5 mg instead of 5 mg (all other subjects entered without a treatment gap from an open-label study, continuing on the same dose).</li><li>• "Velcalcetide" was replaced with AMG 416.</li></ul>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported