



Clinical trial results:

A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of Roxadustat for the Treatment of Anemia in Chronic Kidney Disease Patients not on Dialysis Summary

EudraCT number	2014-000770-19
Trial protocol	CZ SK HU DE ES BG PL RO
Global end of trial date	04 October 2018

Results information

Result version number	v1
This version publication date	31 October 2019
First version publication date	31 October 2019

Trial information

Trial identification

Sponsor protocol code	D5740C00001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02174627
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	101 Orchard Ridge Drive, Gaithersburg, Maryland, United States, 20878
Public contact	Global Clinical Lead, AstraZeneca, +1 302 885 1180, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 302 885 1180, ClinicalTrialTransparency@astrazeneca.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	04 October 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of roxadustat compared with placebo for the treatment of anemia in chronic kidney disease (CKD) participants not on dialysis.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation/Good Clinical Practice (GCP), applicable regulatory requirements, and the AstraZeneca policy on Bioethics and Human Biological Sample.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 June 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 74
Country: Number of subjects enrolled	Brazil: 85
Country: Number of subjects enrolled	Bulgaria: 78
Country: Number of subjects enrolled	Canada: 50
Country: Number of subjects enrolled	Colombia: 4
Country: Number of subjects enrolled	Czech Republic: 20
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Hungary: 50
Country: Number of subjects enrolled	India: 205
Country: Number of subjects enrolled	Korea, Republic of: 245
Country: Number of subjects enrolled	Malaysia: 15
Country: Number of subjects enrolled	Mexico: 101
Country: Number of subjects enrolled	Peru: 147
Country: Number of subjects enrolled	Philippines: 97
Country: Number of subjects enrolled	Poland: 38
Country: Number of subjects enrolled	Romania: 3
Country: Number of subjects enrolled	Russian Federation: 102
Country: Number of subjects enrolled	Slovakia: 9
Country: Number of subjects enrolled	Spain: 15

Country: Number of subjects enrolled	Taiwan: 129
Country: Number of subjects enrolled	Thailand: 89
Country: Number of subjects enrolled	Turkey: 32
Country: Number of subjects enrolled	Ukraine: 222
Country: Number of subjects enrolled	United States: 683
Country: Number of subjects enrolled	Vietnam: 263
Worldwide total number of subjects	2761
EEA total number of subjects	218

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	1526
From 65 to 84 years	1137
85 years and over	98

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 385 centers in 25 countries worldwide across the United States (US), Canada, Latin America, Asia and Europe between 26 June 2014 and 04 October 2018. Participants with CKD who were not on dialysis were recruited in this study.

Pre-assignment

Screening details:

Study had a screening period (up to 6 weeks), treatment period (up to 4 years) and follow-up period (4 weeks after treatment period for those who completed treatment). 2781 participants were randomized, of which 2761 were included in the analysis and 20 were excluded. Only participants included in the analysis are presented in the participant flow.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Roxadustat

Arm description:

Participants received roxadustat tablets orally times a week (TIW). The initial dose was 70 milligrams (mg) TIW and was titrated to achieve and maintain haemoglobin (Hb) 11 ± 1 grams per deciliter (g/dL). Treatment started on Day 1 and treatment duration was variable for individual participants (estimated up to 4 years). Dose adjustments were permitted starting at Week 4 and at intervals of every 4 weeks until Week 52, every 8 weeks thereafter using a dose adjustment algorithm; all dose adjustments were based on Hb values.

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

Dosage and administration details:

The initial dose was 70 mg orally TIW. Dosing continued TIW throughout the treatment period (up to 4 years) unless downward dose adjustment required a change to twice or once weekly.

Arm title	Placebo
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Arm description:

Participants received treatment with placebo tablets orally TIW. Dosing instructions were matched to instructions provided for roxadustat (ie, initial dose matched 70 mg TIW). Treatment started on Day 1 and treatment duration was variable for individual participants (estimated up to 4 years). Dose adjustments were permitted starting at Week 4 and at intervals of every 4 weeks until Week 52, every 8 weeks thereafter using a dose adjustment algorithm; all dose adjustments were based on Hb values.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets matched to size and strength of roxadustat tablets, orally TIW. Dosing continued TIW

throughout the treatment period (up to 4 years) unless downward dose adjustment required a change to twice or once weekly.

Number of subjects in period 1	Roxadustat	Placebo
Started	1384	1377
Received treatment	1384	1376
Completed	1300	1247
Not completed	84	130
Incorrect enrolment before randomization	-	1
Consent withdrawn by subject	84	128
Missing	-	1

Baseline characteristics

Reporting groups

Reporting group title	Roxadustat
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Reporting group description:

Participants received roxadustat tablets orally times a week (TIW). The initial dose was 70 milligrams (mg) TIW and was titrated to achieve and maintain haemoglobin (Hb) 11 ± 1 grams per deciliter (g/dL). Treatment started on Day 1 and treatment duration was variable for individual participants (estimated up to 4 years). Dose adjustments were permitted starting at Week 4 and at intervals of every 4 weeks until Week 52, every 8 weeks thereafter using a dose adjustment algorithm; all dose adjustments were based on Hb values.

Reporting group title	Placebo
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Reporting group description:

Participants received treatment with placebo tablets orally TIW. Dosing instructions were matched to instructions provided for roxadustat (ie, initial dose matched 70 mg TIW). Treatment started on Day 1 and treatment duration was variable for individual participants (estimated up to 4 years). Dose adjustments were permitted starting at Week 4 and at intervals of every 4 weeks until Week 52, every 8 weeks thereafter using a dose adjustment algorithm; all dose adjustments were based on Hb values.

Reporting group values	Roxadustat	Placebo	Total
Number of subjects	1384	1377	2761
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	796	730	1526
From 65-84 years	547	590	1137
85 years and over	41	57	98
Age Continuous Units: years			
arithmetic mean	60.9	62.4	
standard deviation	± 14.67	± 14.14	-
Sex: Female, Male Units: Subjects			
Female	820	774	1594
Male	564	603	1167
Race/Ethnicity, Customized Units: Subjects			
White	623	611	1234
Black or African American	112	115	227
Asian	544	538	1082
Native Hawaiian or other Pacific Islander	0	2	2
American Indian or Alaska Native	24	29	53
Other	81	82	163
Ethnicity (NIH/OMB)			

Units: Subjects			
Hispanic or Latino	344	357	701
Not Hispanic or Latino	1040	1020	2060
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Roxadustat
Reporting group description:	
Participants received roxadustat tablets orally times a week (TIW). The initial dose was 70 milligrams (mg) TIW and was titrated to achieve and maintain haemoglobin (Hb) 11±1 grams per deciliter (g/dL). Treatment started on Day 1 and treatment duration was variable for individual participants (estimated up to 4 years). Dose adjustments were permitted starting at Week 4 and at intervals of every 4 weeks until Week 52, every 8 weeks thereafter using a dose adjustment algorithm; all dose adjustments were based on Hb values.	
Reporting group title	Placebo
Reporting group description:	
Participants received treatment with placebo tablets orally TIW. Dosing instructions were matched to instructions provided for roxadustat (ie, initial dose matched 70 mg TIW). Treatment started on Day 1 and treatment duration was variable for individual participants (estimated up to 4 years). Dose adjustments were permitted starting at Week 4 and at intervals of every 4 weeks until Week 52, every 8 weeks thereafter using a dose adjustment algorithm; all dose adjustments were based on Hb values.	

Primary: US Food and Drug Administration (FDA) Analysis: Mean Change From Baseline in Hb Averaged Over Week 28 to Week 52

End point title	US Food and Drug Administration (FDA) Analysis: Mean Change From Baseline in Hb Averaged Over Week 28 to Week 52
End point description:	
Baseline Hb was defined as the mean of the last 3 central laboratory Hb values from the screening and randomization visits. Mean change in Hb from baseline to mean value from Week 28 to Week 52 was analyzed using a missing at random (MAR) based multiple imputation analysis of covariance (ANCOVA) model with baseline Hb, baseline estimated glomerular filtration rate (eGFR), cardiovascular (CV) history, geographic region and treatment group as fixed effect covariates. The adjusted least squares (LS) mean estimates of change from baseline to mean during Week 28 to Week 52 are presented. The Intention-To-Treat (ITT) analysis set included all participants who were randomized to investigational product (IP) irrespective of their protocol adherence and continued participation in the study, except for those excluded from analysis.	
End point type	Primary
End point timeframe:	
Baseline (Day 1, Week 0) and Week 28 to Week 52.	

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1334	1330		
Units: g/dL				
least squares mean (standard error)	1.75 (± 0.033)	0.40 (± 0.034)		

Statistical analyses

Statistical analysis title	Treatment Difference in Hb
Statistical analysis description:	
Difference between groups (roxadustat minus placebo) in LS mean changes; MAR-based multiple	

imputation ANCOVA model.

Comparison groups	Roxadustat v Placebo
Number of subjects included in analysis	2664
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	1.43
Variability estimate	Standard error of the mean
Dispersion value	0.041

Notes:

[1] - Superiority of roxadustat compared with placebo would be declared if the lower bound of the 2-sided 95% confidence interval (CI) of the difference between roxadustat and placebo exceeded 0 g/dL.

Primary: European Union (EU) Health Authorities Analysis: Percentage of Participants With Hb Response During the First 24 Weeks of Treatment

End point title	European Union (EU) Health Authorities Analysis: Percentage of Participants With Hb Response During the First 24 Weeks of Treatment
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End point description:

Hb response was defined as: - Hb \geq 11.0 g/dL and Hb increase from baseline by \geq 1.0 g/dL for participants with baseline Hb > 8.0 g/dL; or - Hb increase from baseline by \geq 2.0 g/dL, for participants with baseline Hb \leq 8.0 g/dL at 2 consecutive visits (with available data) separated at least 5 days during the first 24 weeks of treatment without having received rescue therapy (red blood cell [RBC] transfusion, erythropoietin analogue, or intravenous [IV] iron) prior to Hb response. The percentage of participants with an Hb response during the first 24 weeks of treatment is presented. The Full Analysis Set (FAS) included all participants in the ITT analysis set who received at least 1 dose of IP and had baseline Hb and at least 1 post-dose Hb assessment. Participants from the FAS, with data available for analysis are presented.

End point type	Primary
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End point timeframe:

Baseline (Day 1, Week 0) up to Week 24.

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1371	1357		
Units: Percentage of participants				
number (not applicable)	77.0	8.5		

Statistical analyses

Statistical analysis title	Treatment difference in Hb responders
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Statistical analysis description:

Comparison of the percentage of responders for roxadustat versus placebo was analysed using a Cochran-Mantel-Haenszel test adjusting for baseline Hb, baseline eGFR, geographic region and CV history.

Comparison groups	Roxadustat v Placebo
Number of subjects included in analysis	2728
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Relative Risk
Point estimate	9.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.63
upper limit	10.89

Secondary: Mean Change From Baseline in Hb Averaged Over Week 28 to Week 52 in Participants With Baseline High Sensitivity C-Reactive Protein (hsCRP) Greater Than the Upper Limit of Normal (ULN)

End point title	Mean Change From Baseline in Hb Averaged Over Week 28 to Week 52 in Participants With Baseline High Sensitivity C-Reactive Protein (hsCRP) Greater Than the Upper Limit of Normal (ULN)
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End point description:

Baseline hsCRP was quantified from stored biomarker samples obtained at randomization. Baseline Hb was defined as the mean of the last 3 central laboratory Hb values from the screening and randomization visits. Mean change in Hb from baseline to mean value during Week 28 to Week 52 was analyzed using a MAR based multiple imputation ANCOVA model with baseline Hb, baseline eGFR, CV history, geographic region and treatment group as fixed effect covariates. The adjusted LS mean estimates of change from baseline in participants with baseline hsCRP >ULN to mean during Week 28 to Week 52 are presented. The ITT analysis set included all participants who were randomized to IP irrespective of their protocol adherence and continued participation in the study, except for those excluded from analysis. Only participants who consented to the use of donated biomarker samples and had baseline hsCRP >ULN were included in the analysis.

End point type	Secondary
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End point timeframe:

Baseline (Day 1, Week 0) and Week 28 to Week 52.

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	198		
Units: g/dL				
least squares mean (standard error)	1.75 (± 0.087)	0.62 (± 0.091)		

Statistical analyses

Statistical analysis title	Treatment Difference in Hb
Statistical analysis description: Difference between groups (roxadustat minus placebo) in LS mean changes; MAR-based multiple imputation ANCOVA model.	
Comparison groups	Roxadustat v Placebo
Number of subjects included in analysis	411
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.35
Variability estimate	Standard error of the mean
Dispersion value	0.112

Notes:

[2] - Superiority of roxadustat compared with placebo would be declared if the lower bound of the 2-sided 95% CI of the difference between roxadustat and placebo exceeded 0 g/dL.

Secondary: Proportion of Total Time of Interpolated Hb Values Greater Than or Equal To 10 g/dL From Week 28 to Week 52

End point title	Proportion of Total Time of Interpolated Hb Values Greater Than or Equal To 10 g/dL From Week 28 to Week 52
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End point description:

Proportion of total time of interpolated Hb values ≥ 10 g/dL was calculated as the time the linearly interpolated curve between measurements ≥ 10 g/dL divided by the time between measurements from Week 28 to Week 52. Proportion of total time was analyzed using an ANCOVA model with baseline Hb and baseline eGFR as covariates, and CV history, geographic region and treatment group as fixed effects. The adjusted LS mean estimates of change from Week 28 to Week 52 are presented. The ITT analysis set included all participants who were randomized to IP irrespective of their protocol adherence and continued participation in the study, except for those excluded from analysis. Participants without any Hb measurements from Week 28 were not included in the analysis.

End point type	Secondary
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End point timeframe:

Week 28 up to Week 52.

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1220	1145		
Units: proportion of total time				
least squares mean (standard error)	0.82 (\pm 0.011)	0.33 (\pm 0.011)		

Statistical analyses

Statistical analysis title	Treatment Difference in Total Time of Hb
Statistical analysis description: Difference between groups (roxadustat minus placebo) in LS mean changes; ANCOVA model.	
Comparison groups	Roxadustat v Placebo
Number of subjects included in analysis	2365
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.52
Variability estimate	Standard error of the mean
Dispersion value	0.013

Notes:

[3] - Superiority of roxadustat compared with placebo would be declared if the lower bound of the 2-sided 95% CI of the difference between roxadustat and placebo exceeded 0.

Secondary: Proportion of Total Time of Interpolated Hb Values Within the Interval of 10 to 12 g/dL From Week 28 to Week 52

End point title	Proportion of Total Time of Interpolated Hb Values Within the Interval of 10 to 12 g/dL From Week 28 to Week 52
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End point description:

Proportion of total time of interpolated Hb values within the interval of 10 to 12 g/dL was calculated as the time the linearly interpolated curve between measurements were within 10 to 12 g/dL divided by the time between measurements from Week 28 to Week 52. Proportion of total time was analyzed using an ANCOVA model with baseline Hb and baseline eGFR as covariates, and CV history, geographic region and treatment group as fixed effects. The adjusted LS mean estimates of change from Week 28 to Week 52 are presented. The ITT analysis set included all participants who were randomized to IP irrespective of their protocol adherence and continued participation in the study, except for those excluded from analysis. Participants without any Hb measurements from Week 28 were not included in the analysis.

End point type	Secondary
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End point timeframe:

Week 28 up to Week 52.

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1220	1145		
Units: proportion of total time				
least squares mean (standard error)	0.70 (± 0.010)	0.28 (± 0.010)		

Statistical analyses

Statistical analysis title	Treatment Difference in Total Time of Hb
Statistical analysis description: Difference between groups (roxadustat minus placebo) in LS mean changes; ANCOVA model.	
Comparison groups	Roxadustat v Placebo
Number of subjects included in analysis	2365
Analysis specification	Pre-specified
Analysis type	superiority ^[4]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.45
Variability estimate	Standard error of the mean
Dispersion value	0.013

Notes:

[4] - Superiority of roxadustat compared with placebo would be declared if the lower bound of the 2-sided 95% CI of the difference between roxadustat and placebo exceeded 0.

Secondary: Mean Change in Low-Density Lipoprotein (LDL) Cholesterol From Baseline to Week 24

End point title	Mean Change in Low-Density Lipoprotein (LDL) Cholesterol From Baseline to Week 24
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End point description:

Baseline LDL was defined as the last result obtained prior to randomization. Mean changes in LDL cholesterol from baseline to Week 24 was analyzed using an ANCOVA model with baseline LDL, baseline Hb and baseline eGFR as covariates, and CV history, geographic region and treatment group as fixed effects. The adjusted LS mean estimates of change from baseline to Week 24 are presented. The ITT analysis set included all participants who were randomized to IP irrespective of their protocol adherence and continued participation in the study, except for those excluded from analysis.

End point type	Secondary
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End point timeframe:

Baseline (Day 1, Week 0) and Week 24

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1147	1133		
Units: millimole per liter				
least squares mean (standard error)	-0.38 (± 0.028)	-0.02 (± 0.027)		

Statistical analyses

Statistical analysis title	Treatment Difference in LDL Cholesterol
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Statistical analysis description:

Difference between groups (roxadustat minus placebo) in LS mean changes; ANCOVA model.

Comparison groups	Roxadustat v Placebo
Number of subjects included in analysis	2280
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	-0.29
Variability estimate	Standard error of the mean
Dispersion value	0.033

Notes:

[5] - Superiority of roxadustat compared with placebo would be declared if the lower bound of the 2-sided 95% CI of the difference between roxadustat and placebo exceeded 0.

Secondary: Time-To-First Instance of Receiving IV Iron, RBC Transfusion or Erythropoietin Analogue as Rescue Therapy

End point title	Time-To-First Instance of Receiving IV Iron, RBC Transfusion or Erythropoietin Analogue as Rescue Therapy
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End point description:

Time-to-first rescue therapy (IV iron, RBC transfusion or erythropoietin analogue) was calculated as (date of first rescue therapy, or date of censoring if no rescue therapy was taken) minus (date of first dose of IP) +1. Event rate was calculated as (number of participants with event) divided by (the total number of days at risk for event across all participants in given group divided by 365.25) multiplied by 100. The event rate is presented for participants with events. The on-treatment plus 28 days (OT+28) analysis set included all participants who received at least 1 dose of randomized IP, except for those excluded from analysis. Participants were censored 28 days after last intake of IP.

End point type	Secondary
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End point timeframe:

Baseline (Day1, Week 0) up to End of Study (EOS) visit (4 weeks after the treatment period) (or up to date of first rescue therapy), with treatment duration up to 4 years.

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1384	1376		
Units: Event rate				
number (not applicable)	11.90	39.76		

Statistical analyses

Statistical analysis title	Treatment Difference in Rescue Therapy
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Statistical analysis description:

Treatments were compared using a Cox proportional hazards model, with baseline Hb and baseline eGFR

as continuous variables used as covariates, and treatment group, CV history and geographic region as fixed effects. The Efron method was used for ties and p-values were calculated using the Wald test.

Comparison groups	Roxadustat v Placebo
Number of subjects included in analysis	2760
Analysis specification	Pre-specified
Analysis type	superiority ^[6]
P-value	< 0.001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.31

Notes:

[6] - Superiority of roxadustat compared with placebo would be declared if the upper limit of the 2-sided 95% CI for the HR was ≤ 1.0 .

Secondary: Time-To-First Instance of Receiving a RBC Transfusion As Rescue Therapy

End point title	Time-To-First Instance of Receiving a RBC Transfusion As Rescue Therapy
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End point description:

Time-to-first RBC rescue therapy was calculated as (date of first RBC rescue therapy, or date of censoring if no rescue therapy was taken) minus (date of first dose of IP) +1. Event rate was calculated as (number of participants with event) divided by (the total number of days at risk for event across all participants in given group divided by 365.25) multiplied by 100. The event rate is presented for participants with events. The OT+28 analysis set included all participants who received at least 1 dose of randomized IP, except for those excluded from analysis. Participants were censored 28 days after last intake of IP.

End point type	Secondary
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End point timeframe:

Baseline (Day1, Week 0) up to EOS visit (4 weeks after the treatment period) (or up to date of first RBC rescue therapy), with treatment duration up to 4 years.

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1384	1376		
Units: Event rate				
number (not applicable)	7.98	19.61		

Statistical analyses

Statistical analysis title	Treatment Difference in RBC Transfusion
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Statistical analysis description:

Treatments were compared using a Cox proportional hazards model, with baseline Hb and baseline eGFR as continuous variables used as covariates, and treatment group, CV history and geographic region as fixed effects. The Efron method was used for ties and p-values were calculated using the Wald test.

Comparison groups	Roxadustat v Placebo
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Number of subjects included in analysis	2760
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	< 0.001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.44

Notes:

[7] - Superiority of roxadustat compared with placebo would be declared if the upper limit of the 2-sided 95% CI for the HR was ≤ 1.0 .

Secondary: Mean Change From Baseline in Short Form 36 (SF-36) Vitality Sub-Score From Week 12 to Week 28

End point title	Mean Change From Baseline in Short Form 36 (SF-36) Vitality Sub-Score From Week 12 to Week 28
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End point description:

SF-36 is a Quality of Life (QoL) scale comprising 8 domains of health status: Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional and Mental Health. Each domain score is on a scale from 0-100 (worst health possible to best health possible); higher scores indicate better health status. Mean change in SF-36 Vitality sub-score from baseline to mean from Week 12 to Week 28 was analyzed using a mixed model for repeated measures (MMRM) with terms for baseline score, treatment group, baseline Hb, baseline eGFR, CV history, geographic region, visit and treatment-by-visit interaction as fixed effects and participant as random effect. The adjusted LS mean estimates of change from baseline to mean score from Week 12 to Week 28 are presented. The ITT analysis set included all participants who were randomized to IP irrespective of their protocol adherence and continued participation in the study, except for those excluded from analysis.

End point type	Secondary
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End point timeframe:

Baseline (Day 1, Week 0) and Week 12 to Week 28.

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1279	1235		
Units: scores on a scale				
least squares mean (standard error)	1.59 (\pm 0.231)	1.15 (\pm 0.233)		

Statistical analyses

Statistical analysis title	Treatment Difference in SF-36 Vitality
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Statistical analysis description:

Difference between groups (roxadustat minus placebo) in LS mean changes; MMRM analysis.

Comparison groups	Roxadustat v Placebo
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Number of subjects included in analysis	2514
Analysis specification	Pre-specified
Analysis type	superiority ^[8]
P-value	= 0.12
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.99
Variability estimate	Standard error of the mean
Dispersion value	0.283

Notes:

[8] - Superiority of roxadustat compared with placebo would be declared if the lower bound of the 2-sided 95% CI of the difference between roxadustat and placebo exceeded 0.

Secondary: Annual Rate of eGFR Change From Baseline Prior to the Initiation of Dialysis or Kidney Transplant

End point title	Annual Rate of eGFR Change From Baseline Prior to the Initiation of Dialysis or Kidney Transplant
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End point description:

Baseline eGFR was defined as the mean of all available central laboratory values prior to or at randomization. Rate of change in eGFR from baseline during the entire treatment period (in milliliters/minute/1.73 meters squared/years [mL/min/1.73m²/years]) was estimated using a random effects model using all post baseline eGFR values prior to initiation of dialysis/transplant. Baseline eGFR, baseline Hb, geographic region, CV history, treatment group and post baseline eGFR measurement time were used as fixed effects and participant and time (years) as random effects, ie, random intercept and slope. The ITT analysis set included all participants who were randomized to IP irrespective of their protocol adherence and continued participation in the study, except for those excluded from analysis.

End point type	Secondary
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End point timeframe:

Baseline (Day1, Week 0) up to EOS visit (4 weeks after the treatment period), with treatment duration up to 4 years.

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1326	1314		
Units: eGFR rate (mL/min/1.73m ² /years)				
number (not applicable)	-3.70	-3.19		

Statistical analyses

Statistical analysis title	Treatment Difference in eGFR Rate
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Statistical analysis description:

Difference between groups (roxadustat minus placebo) in rate of change in eGFR; random effects analysis.

Comparison groups	Roxadustat v Placebo
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Number of subjects included in analysis	2640
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.046 ^[9]
Method	Random Effects Analysis
Parameter estimate	Rate of Change Difference
Point estimate	-0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.254

Notes:

[9] - Nominal p-value (as prior sequential outcome measure p-value did not meet < 0.05).

Secondary: Mean Change From Baseline in SF-36 Physical Functioning Sub-Score From Week 12 to Week 28

End point title	Mean Change From Baseline in SF-36 Physical Functioning Sub-Score From Week 12 to Week 28
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End point description:

SF-36 is a QoL scale comprising 8 domains of health status: Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional and Mental Health. Each domain score is on a scale from 0-100 (worst health possible to best health possible); higher scores indicate better health status. Mean change in SF-36 Physical Functioning sub-score from baseline to mean from Week 12 to Week 28 was analyzed using a MMRM with terms for baseline score, treatment group, baseline Hb, baseline eGFR, CV history, geographic region, visit and treatment-by-visit interaction as fixed effects and participant as random effect. The adjusted LS mean estimates of change from baseline to mean score from Week 12 to Week 28 are presented. The ITT analysis set included all participants who were randomized to IP irrespective of their protocol adherence and continued participation in the study, except for those excluded from analysis.

End point type	Secondary
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End point timeframe:

Baseline (Day 1, Week 0) and Week 12 to Week 28.

End point values	Roxadustat	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1279	1234		
Units: scores on a scale				
least squares mean (standard error)	0.14 (± 0.222)	-0.39 (± 0.224)		

Statistical analyses

Statistical analysis title	Treatment Difference in SF-36 Physical Functioning
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Statistical analysis description:

Difference between groups (roxadustat minus placebo) in LS mean changes; MMRM analysis.

Comparison groups	Roxadustat v Placebo
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Number of subjects included in analysis	2513
Analysis specification	Pre-specified
Analysis type	superiority ^[10]
P-value	= 0.051 ^[11]
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1.05
Variability estimate	Standard error of the mean
Dispersion value	0.269

Notes:

[10] - Superiority of roxadustat compared with placebo would be declared if the lower bound of the 2-sided 95% CI of the difference between roxadustat and placebo exceeded 0.

[11] - Nominal p-value (as prior sequential outcome measure p-value did not meet < 0.05).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of randomization up to EOS visit (4 weeks after the treatment period), with treatment duration up to 4 years.

Adverse event reporting additional description:

The ITT analysis set included all participants who were randomized to IP irrespective of their protocol adherence and continued participation in the study, except for those excluded from analysis. Higher IP discontinuation in placebo participants (58.2%) versus in roxadustat participants (36.1%) was observed.

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	Placebo
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Reporting group description:

Participants received placebo tablets orally TIW. Dosing instructions were matched to instructions provided for roxadustat (ie, initial dose matched to 70 mg TIW). Treatment started on Day 1 and treatment duration was variable for individual participants (estimated up to 4 years). Dose adjustments were permitted starting at Week 4 and at intervals of every 4 weeks until Week 52, every 8 weeks thereafter using a dose adjustment algorithm; all dose adjustments were based on Hb values.

Reporting group title	Roxadustat
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Reporting group description:

Participants received roxadustat tablets orally TIW. The initial dose was 70 mg TIW and was titrated to achieve and maintain Hb 11±1 g/dL. Treatment started on Day 1 and treatment duration was variable for individual participants (estimated up to 4 years). Dose adjustments were permitted starting at Week 4 and at intervals of every 4 weeks until Week 52, every 8 weeks thereafter using a dose adjustment algorithm; all dose adjustments were based on Hb values.

Serious adverse events	Placebo	Roxadustat	
Total subjects affected by serious adverse events			
subjects affected / exposed	749 / 1377 (54.39%)	795 / 1384 (57.44%)	
number of deaths (all causes)	245	284	
number of deaths resulting from adverse events	213	262	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bladder cancer			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer female			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer metastatic			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast neoplasm			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon neoplasm			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer metastatic			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottic carcinoma			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric adenoma			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric neoplasm			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal tract adenoma			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			

subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyoma			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip squamous cell carcinoma			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung carcinoma cell type unspecified stage IV			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung neoplasm			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 1377 (0.07%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 3	
Malignant melanoma			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelofibrosis			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm of appendix			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour of the lung			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ovarian cancer			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	4 / 1377 (0.29%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prostate cancer			
subjects affected / exposed	0 / 1377 (0.00%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the vagina			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm rupture			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aortic rupture			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	4 / 1377 (0.29%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriosclerosis			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriovenous fistula			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	4 / 1377 (0.29%)	15 / 1384 (1.08%)	
occurrences causally related to treatment / all	0 / 4	1 / 15	
deaths causally related to treatment / all	0 / 0	0 / 1	
Distributive shock			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dry gangrene			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism venous			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	4 / 1377 (0.29%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	16 / 1377 (1.16%)	17 / 1384 (1.23%)	
occurrences causally related to treatment / all	1 / 16	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	27 / 1377 (1.96%)	33 / 1384 (2.38%)	
occurrences causally related to treatment / all	0 / 31	0 / 51	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	21 / 1377 (1.53%)	21 / 1384 (1.52%)	
occurrences causally related to treatment / all	0 / 23	0 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	8 / 1377 (0.58%)	6 / 1384 (0.43%)	
occurrences causally related to treatment / all	0 / 8	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	6 / 1377 (0.44%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Iliac artery perforation			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant hypertension			

subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paget-Schroetter syndrome			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pallor			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	2 / 1377 (0.15%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peripheral artery occlusion			
subjects affected / exposed	3 / 1377 (0.22%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			

subjects affected / exposed	2 / 1377 (0.15%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral venous disease			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post thrombotic syndrome			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	4 / 1377 (0.29%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Steal syndrome			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery thrombosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose ulceration			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular occlusion			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visceral congestion			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	9 / 1377 (0.65%)	13 / 1384 (0.94%)	
occurrences causally related to treatment / all	0 / 9	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	

Catheter site haemorrhage			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site pain			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	28 / 1377 (2.03%)	43 / 1384 (3.11%)	
occurrences causally related to treatment / all	1 / 28	0 / 43	
deaths causally related to treatment / all	1 / 28	0 / 43	
Device related thrombosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	7 / 1377 (0.51%)	17 / 1384 (1.23%)	
occurrences causally related to treatment / all	0 / 11	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia pain			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site extravasation			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site necrosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Non-cardiac chest pain			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	7 / 1377 (0.51%)	7 / 1384 (0.51%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema due to renal disease			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	5 / 1377 (0.36%)	7 / 1384 (0.51%)	
occurrences causally related to treatment / all	0 / 10	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pacemaker generated arrhythmia			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	5 / 1377 (0.36%)	6 / 1384 (0.43%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stenosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sudden death			
subjects affected / exposed	11 / 1377 (0.80%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 11	0 / 5	
deaths causally related to treatment / all	0 / 11	0 / 5	
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device allergy			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney transplant rejection			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal transplant failure			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant rejection			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysfunctional uterine bleeding			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst ruptured			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst torsion			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian mass			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic prolapse			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic fibrosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic mass			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatomegaly			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			

subjects affected / exposed	22 / 1377 (1.60%)	13 / 1384 (0.94%)	
occurrences causally related to treatment / all	0 / 25	0 / 13	
deaths causally related to treatment / all	0 / 2	0 / 1	
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	20 / 1377 (1.45%)	12 / 1384 (0.87%)	
occurrences causally related to treatment / all	0 / 20	0 / 13	
deaths causally related to treatment / all	0 / 5	0 / 5	
Aspiration			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthma			
subjects affected / exposed	3 / 1377 (0.22%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial fistula			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	8 / 1377 (0.58%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dyspnoea			
subjects affected / exposed	12 / 1377 (0.87%)	11 / 1384 (0.79%)	
occurrences causally related to treatment / all	0 / 14	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 2	
Dyspnoea exertional			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Laryngeal stenosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal pain			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	16 / 1377 (1.16%)	15 / 1384 (1.08%)	
occurrences causally related to treatment / all	0 / 20	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural thickening			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pneumonitis			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			

subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary embolism			
subjects affected / exposed	3 / 1377 (0.22%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary hypertension			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	16 / 1377 (1.16%)	17 / 1384 (1.23%)	
occurrences causally related to treatment / all	0 / 16	0 / 17	
deaths causally related to treatment / all	0 / 1	0 / 1	
Respiratory alkalosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	9 / 1377 (0.65%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 6	0 / 2	
Tracheal stenosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Confusional state			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			

subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insomnia			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paranoia			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular cognitive impairment			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device failure			

subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			
subjects affected / exposed	2 / 1377 (0.15%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	1 / 1377 (0.07%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			

subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 1377 (0.07%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic hepatic failure			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cirrhosis alcoholic			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemorrhagic hepatic cyst			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hepatitis acute			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis alcoholic			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Anticoagulation drug level increased			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bicarbonate decreased			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine increased			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose abnormal			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure decreased			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood urine present			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulation factor decreased			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			

subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anastomotic stenosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula occlusion			
subjects affected / exposed	4 / 1377 (0.29%)	7 / 1384 (0.51%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site complication			
subjects affected / exposed	4 / 1377 (0.29%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site haemorrhage			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula thrombosis			
subjects affected / exposed	9 / 1377 (0.65%)	18 / 1384 (1.30%)	
occurrences causally related to treatment / all	1 / 9	1 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cervical vertebral fracture			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chemical peritonitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chemical poisoning			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Comminuted fracture			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complications of transplanted kidney			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compression fracture			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dialysis disequilibrium syndrome			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dialysis related complication			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	3 / 1377 (0.22%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	2 / 1377 (0.15%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heat stroke			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	6 / 1377 (0.44%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Joint dislocation			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			

subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip injury			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle injury			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital haemorrhage			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal dialysis complication			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Post procedural complication			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural complication			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural hypotension			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt malfunction			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt occlusion			

subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin injury			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury cervical			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Spinal fracture			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spleen contusion			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma obstruction			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site haemorrhage			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			

subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subdural haematoma			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant dysfunction			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic liver injury			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access malfunction			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access site thrombosis			
subjects affected / exposed	2 / 1377 (0.15%)	6 / 1384 (0.43%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft complication			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound haematoma			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Congenital cystic kidney disease			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocele			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	5 / 1377 (0.36%)	8 / 1384 (0.58%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	4 / 1377 (0.29%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute myocardial infarction			
subjects affected / exposed	27 / 1377 (1.96%)	26 / 1384 (1.88%)	
occurrences causally related to treatment / all	1 / 31	0 / 28	
deaths causally related to treatment / all	0 / 6	0 / 6	
Angina pectoris			
subjects affected / exposed	9 / 1377 (0.65%)	10 / 1384 (0.72%)	
occurrences causally related to treatment / all	0 / 9	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	10 / 1377 (0.73%)	10 / 1384 (0.72%)	
occurrences causally related to treatment / all	0 / 11	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	3 / 1377 (0.22%)	6 / 1384 (0.43%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 3	
Arteriosclerosis coronary artery			

subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	12 / 1377 (0.87%)	10 / 1384 (0.72%)	
occurrences causally related to treatment / all	1 / 15	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	3 / 1377 (0.22%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block left			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	4 / 1377 (0.29%)	9 / 1384 (0.65%)	
occurrences causally related to treatment / all	0 / 4	0 / 9	
deaths causally related to treatment / all	0 / 3	0 / 6	
Cardiac asthma			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	32 / 1377 (2.32%)	25 / 1384 (1.81%)	
occurrences causally related to treatment / all	0 / 35	0 / 31	
deaths causally related to treatment / all	0 / 5	0 / 6	
Cardiac failure acute			
subjects affected / exposed	14 / 1377 (1.02%)	8 / 1384 (0.58%)	
occurrences causally related to treatment / all	0 / 16	0 / 8	
deaths causally related to treatment / all	0 / 7	0 / 3	
Cardiac failure chronic			
subjects affected / exposed	5 / 1377 (0.36%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	31 / 1377 (2.25%)	33 / 1384 (2.38%)	
occurrences causally related to treatment / all	1 / 42	0 / 41	
deaths causally related to treatment / all	0 / 5	0 / 7	
Cardiac tamponade			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	4 / 1377 (0.29%)	6 / 1384 (0.43%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 3	0 / 5	
Cardiogenic shock			

subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Cardiomegaly			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Chronic left ventricular failure			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	7 / 1377 (0.51%)	12 / 1384 (0.87%)	
occurrences causally related to treatment / all	0 / 7	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery insufficiency			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery stenosis			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart valve incompetence			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart valve stenosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive cardiomyopathy			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Left ventricular failure			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular hypertrophy			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic cardiomyopathy			

subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	13 / 1377 (0.94%)	14 / 1384 (1.01%)	
occurrences causally related to treatment / all	0 / 13	0 / 14	
deaths causally related to treatment / all	0 / 9	0 / 6	
Myocardial ischaemia			
subjects affected / exposed	8 / 1377 (0.58%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 4	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinoatrial block			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			

subjects affected / exposed	3 / 1377 (0.22%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar stroke			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haematoma			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral haemorrhage			
subjects affected / exposed	3 / 1377 (0.22%)	9 / 1384 (0.65%)	
occurrences causally related to treatment / all	0 / 3	1 / 9	
deaths causally related to treatment / all	0 / 3	0 / 4	
Cerebral infarction			
subjects affected / exposed	8 / 1377 (0.58%)	13 / 1384 (0.94%)	
occurrences causally related to treatment / all	1 / 9	0 / 14	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	11 / 1377 (0.80%)	15 / 1384 (1.08%)	
occurrences causally related to treatment / all	0 / 11	0 / 15	
deaths causally related to treatment / all	0 / 2	0 / 2	
Cerebrovascular disorder			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebrovascular insufficiency			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical cord compression			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Coma uraemic			

subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Dementia			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Demyelination			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic hyperglycaemic coma			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic hyperosmolar coma			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidotic hyperglycaemic coma			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diabetic neuropathy			

subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	2 / 1377 (0.15%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 1377 (0.00%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial spasm			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhagic stroke			

subjects affected / exposed	6 / 1377 (0.44%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 3	0 / 2	
Headache			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive encephalopathy			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intercostal neuralgia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	3 / 1377 (0.22%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemic stroke			
subjects affected / exposed	7 / 1377 (0.51%)	9 / 1384 (0.65%)	
occurrences causally related to treatment / all	0 / 7	1 / 9	
deaths causally related to treatment / all	0 / 2	0 / 0	
Lacunar infarction			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke			

subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	3 / 1377 (0.22%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Migraine			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myoclonus			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurodegenerative disorder			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neuroleptic malignant syndrome			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neuropathy peripheral			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Occipital neuralgia			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post stroke seizure			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 1377 (0.15%)	6 / 1384 (0.43%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Senile dementia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Somnolence			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	3 / 1377 (0.22%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamic infarction			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thalamus haemorrhage			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Transient ischaemic attack			
subjects affected / exposed	5 / 1377 (0.36%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uraemic encephalopathy			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
VIth nerve paralysis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular encephalopathy			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo CNS origin			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular migraine			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Evans syndrome			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic uraemic syndrome			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic anaemia			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Histiocytosis haematophagic			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocoagulable state			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 1377 (0.22%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular ataxia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			
subjects affected / exposed	1 / 1377 (0.07%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blindness unilateral			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcerative keratitis			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Abdominal discomfort			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	4 / 1377 (0.29%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall haematoma			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal incontinence			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gastroparesis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gastropathy			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	5 / 1377 (0.36%)	9 / 1384 (0.65%)	
occurrences causally related to treatment / all	0 / 5	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dieulafoy's vascular malformation			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 1377 (0.07%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis haemorrhagic			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	2 / 1377 (0.15%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis haemorrhagic			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive duodenitis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral hernia incarcerated			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	2 / 1377 (0.15%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			

subjects affected / exposed	3 / 1377 (0.22%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	15 / 1377 (1.09%)	18 / 1384 (1.30%)	
occurrences causally related to treatment / all	1 / 18	0 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroduodenitis haemorrhagic			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	15 / 1377 (1.09%)	20 / 1384 (1.45%)	
occurrences causally related to treatment / all	0 / 16	1 / 20	
deaths causally related to treatment / all	0 / 0	1 / 3	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic ascites			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic erosive gastritis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal perforation			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	3 / 1377 (0.22%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia strangulated			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			

subjects affected / exposed	5 / 1377 (0.36%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery thrombosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis ulcerative			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic cyst			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 1377 (0.00%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	4 / 1377 (0.29%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	3 / 1377 (0.22%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer haemorrhage			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer perforation			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal adhesions			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal cloudy effluent			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumatosis intestinalis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal haemorrhage			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	4 / 1377 (0.29%)	11 / 1384 (0.79%)	
occurrences causally related to treatment / all	0 / 4	0 / 11	
deaths causally related to treatment / all	0 / 1	0 / 2	
Uraemic gastropathy			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 1377 (0.15%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis atopic			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	5 / 1377 (0.36%)	6 / 1384 (0.43%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diabetic ulcer			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrobiosis lipoidica diabetorum			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papule			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic epidermal necrolysis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	32 / 1377 (2.32%)	41 / 1384 (2.96%)	
occurrences causally related to treatment / all	0 / 33	0 / 48	
deaths causally related to treatment / all	0 / 1	0 / 1	
Anuria			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Azotaemia			
subjects affected / exposed	60 / 1377 (4.36%)	61 / 1384 (4.41%)	
occurrences causally related to treatment / all	0 / 79	0 / 73	
deaths causally related to treatment / all	0 / 10	0 / 14	
Chronic kidney disease			

subjects affected / exposed	7 / 1377 (0.51%)	8 / 1384 (0.58%)	
occurrences causally related to treatment / all	0 / 7	0 / 8	
deaths causally related to treatment / all	0 / 5	0 / 7	
Cystitis haemorrhagic			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic nephropathy			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
End stage renal disease			
subjects affected / exposed	201 / 1377 (14.60%)	199 / 1384 (14.38%)	
occurrences causally related to treatment / all	0 / 211	1 / 211	
deaths causally related to treatment / all	0 / 11	0 / 11	
Glomerulonephritis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis chronic			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Haematuria			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritic syndrome			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			

subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive uropathy			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedematous kidney			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oliguria			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyuria			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelocaliectasis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal atrophy			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst haemorrhage			
subjects affected / exposed	3 / 1377 (0.22%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 1377 (0.07%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal pain			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal papillary necrosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal pelvis fistula			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ureteric obstruction			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric stenosis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary fistula			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 1377 (0.07%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract inflammation			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperparathyroidism			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperparathyroidism secondary			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			

subjects affected / exposed	1 / 1377 (0.07%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	3 / 1377 (0.22%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	3 / 1377 (0.22%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatitis B			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	5 / 1377 (0.36%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site infection			

subjects affected / exposed	3 / 1377 (0.22%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous graft site infection			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 1377 (0.07%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone tuberculosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	9 / 1377 (0.65%)	7 / 1384 (0.51%)	
occurrences causally related to treatment / all	0 / 9	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbuncle			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve abscess			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site cellulitis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			
subjects affected / exposed	8 / 1377 (0.58%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	13 / 1377 (0.94%)	24 / 1384 (1.73%)	
occurrences causally related to treatment / all	0 / 13	0 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis gangrenous			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridial infection			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	2 / 1377 (0.15%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Clostridium difficile infection			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis bacterial			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus nephritis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	5 / 1377 (0.36%)	14 / 1384 (1.01%)	
occurrences causally related to treatment / all	0 / 6	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	5 / 1377 (0.36%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetic foot infection			
subjects affected / exposed	4 / 1377 (0.29%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			

subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	4 / 1377 (0.29%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	3 / 1377 (0.22%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysematous cystitis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysematous pyelonephritis			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endotoxic shock			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Enteritis infectious			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter sepsis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal sepsis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungaemia			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal oesophagitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal peritonitis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Furuncle			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	7 / 1377 (0.51%)	10 / 1384 (0.72%)	
occurrences causally related to treatment / all	0 / 9	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	8 / 1377 (0.58%)	13 / 1384 (0.94%)	
occurrences causally related to treatment / all	0 / 8	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis bacterial			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 1377 (0.07%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			

subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter gastritis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B reactivation			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes virus infection			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected lymphocyte			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective aneurysm			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	5 / 1377 (0.36%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal tuberculosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Localised infection			

subjects affected / exposed	5 / 1377 (0.36%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	3 / 1377 (0.22%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph node tuberculosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal candidiasis			
subjects affected / exposed	0 / 1377 (0.00%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			

subjects affected / exposed	2 / 1377 (0.15%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis acute			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis chronic			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media chronic			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parvovirus infection			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perinephric abscess			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	14 / 1377 (1.02%)	15 / 1384 (1.08%)	
occurrences causally related to treatment / all	0 / 19	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peritonitis bacterial			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural infection			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	88 / 1377 (6.39%)	113 / 1384 (8.16%)	
occurrences causally related to treatment / all	1 / 107	0 / 149	
deaths causally related to treatment / all	0 / 10	0 / 12	
Pneumonia bacterial			
subjects affected / exposed	3 / 1377 (0.22%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
Pneumonia influenzal			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural cellulitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural pneumonia			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			

subjects affected / exposed	2 / 1377 (0.15%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Purulence			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	5 / 1377 (0.36%)	8 / 1384 (0.58%)	
occurrences causally related to treatment / all	0 / 5	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	4 / 1377 (0.29%)	6 / 1384 (0.43%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	11 / 1377 (0.80%)	11 / 1384 (0.79%)	
occurrences causally related to treatment / all	0 / 14	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyoderma			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyonephrosis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst infection			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	23 / 1377 (1.67%)	49 / 1384 (3.54%)	
occurrences causally related to treatment / all	0 / 24	0 / 51	
deaths causally related to treatment / all	0 / 8	0 / 26	
Septic shock			
subjects affected / exposed	15 / 1377 (1.09%)	18 / 1384 (1.30%)	
occurrences causally related to treatment / all	0 / 15	0 / 19	
deaths causally related to treatment / all	0 / 9	0 / 14	
Sinusitis			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Staphylococcal sepsis			
subjects affected / exposed	3 / 1377 (0.22%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stenotrophomonas sepsis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal endocarditis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	4 / 1377 (0.29%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Taeniasis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	3 / 1377 (0.22%)	5 / 1384 (0.36%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Typhoid fever			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	26 / 1377 (1.89%)	36 / 1384 (2.60%)	
occurrences causally related to treatment / all	0 / 32	0 / 38	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 1377 (0.00%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	6 / 1377 (0.44%)	8 / 1384 (0.58%)	
occurrences causally related to treatment / all	0 / 6	0 / 11	
deaths causally related to treatment / all	0 / 1	0 / 1	
Vascular access site infection			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	3 / 1377 (0.22%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adult failure to thrive			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calciophylaxis			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	4 / 1377 (0.29%)	8 / 1384 (0.58%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetes mellitus			
subjects affected / exposed	3 / 1377 (0.22%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetes mellitus inadequate control			
subjects affected / exposed	3 / 1377 (0.22%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	10 / 1377 (0.73%)	6 / 1384 (0.43%)	
occurrences causally related to treatment / all	0 / 12	0 / 10	
deaths causally related to treatment / all	0 / 2	0 / 1	
Diabetic metabolic decompensation			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Electrolyte imbalance			
subjects affected / exposed	3 / 1377 (0.22%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			

subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	22 / 1377 (1.60%)	20 / 1384 (1.45%)	
occurrences causally related to treatment / all	0 / 27	0 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid retention			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food aversion			
subjects affected / exposed	2 / 1377 (0.15%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	1 / 1377 (0.07%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	3 / 1377 (0.22%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	9 / 1377 (0.65%)	16 / 1384 (1.16%)	
occurrences causally related to treatment / all	0 / 10	0 / 17	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperinsulinaemic hypoglycaemia			

subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	25 / 1377 (1.82%)	41 / 1384 (2.96%)	
occurrences causally related to treatment / all	0 / 35	2 / 53	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hypernatraemia			
subjects affected / exposed	0 / 1377 (0.00%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricaemia			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypervolaemia			
subjects affected / exposed	0 / 1377 (0.00%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	2 / 1377 (0.15%)	2 / 1384 (0.14%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	26 / 1377 (1.89%)	32 / 1384 (2.31%)	
occurrences causally related to treatment / all	0 / 27	0 / 38	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 1377 (0.07%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hyponatraemia			

subjects affected / exposed	6 / 1377 (0.44%)	7 / 1384 (0.51%)	
occurrences causally related to treatment / all	0 / 9	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hypovolaemia			
subjects affected / exposed	4 / 1377 (0.29%)	3 / 1384 (0.22%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketoacidosis			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketosis			
subjects affected / exposed	1 / 1377 (0.07%)	0 / 1384 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	4 / 1377 (0.29%)	4 / 1384 (0.29%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 0	
Metabolic acidosis			
subjects affected / exposed	3 / 1377 (0.22%)	7 / 1384 (0.51%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 3	
Type 1 diabetes mellitus			
subjects affected / exposed	2 / 1377 (0.15%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			

subjects affected / exposed	1 / 1377 (0.07%)	1 / 1384 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Roxadustat	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	757 / 1377 (54.97%)	839 / 1384 (60.62%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	117 / 1377 (8.50%)	148 / 1384 (10.69%)	
occurrences (all)	151	190	
Nervous system disorders			
Dizziness			
subjects affected / exposed	86 / 1377 (6.25%)	74 / 1384 (5.35%)	
occurrences (all)	113	91	
Headache			
subjects affected / exposed	82 / 1377 (5.95%)	93 / 1384 (6.72%)	
occurrences (all)	96	122	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	106 / 1377 (7.70%)	144 / 1384 (10.40%)	
occurrences (all)	135	192	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	88 / 1377 (6.39%)	91 / 1384 (6.58%)	
occurrences (all)	101	126	
Diarrhoea			
subjects affected / exposed	117 / 1377 (8.50%)	138 / 1384 (9.97%)	
occurrences (all)	156	190	
Nausea			
subjects affected / exposed	103 / 1377 (7.48%)	124 / 1384 (8.96%)	
occurrences (all)	127	171	
Vomiting			

subjects affected / exposed occurrences (all)	67 / 1377 (4.87%) 85	75 / 1384 (5.42%) 90	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	69 / 1377 (5.01%) 91	105 / 1384 (7.59%) 123	
Dyspnoea subjects affected / exposed occurrences (all)	64 / 1377 (4.65%) 80	70 / 1384 (5.06%) 85	
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	80 / 1377 (5.81%) 89	68 / 1384 (4.91%) 84	
Renal and urinary disorders End stage renal disease subjects affected / exposed occurrences (all)	85 / 1377 (6.17%) 86	93 / 1384 (6.72%) 93	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	53 / 1377 (3.85%) 61	73 / 1384 (5.27%) 85	
Back pain subjects affected / exposed occurrences (all)	57 / 1377 (4.14%) 69	70 / 1384 (5.06%) 87	
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	64 / 1377 (4.65%) 76	72 / 1384 (5.20%) 80	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	75 / 1377 (5.45%) 100	95 / 1384 (6.86%) 137	
Urinary tract infection subjects affected / exposed occurrences (all)	94 / 1377 (6.83%) 135	152 / 1384 (10.98%) 205	
Viral upper respiratory tract infection			

subjects affected / exposed occurrences (all)	106 / 1377 (7.70%) 152	101 / 1384 (7.30%) 159	
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all)	75 / 1377 (5.45%) 86	86 / 1384 (6.21%) 105	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2014	<p>Tiered weight-based start doses changed to fixed 70 mg TIW start dose: 120 and 350 mg dose steps removed. Dose algorithm adjusted to reflect results of pharmacometric modeling and simulation using the simplified dosing regimen. Dose cap lowered as additional modeling/simulation indicated this dose would be sufficient. Definition of excessive erythropoiesis simplified. Visit 1 changed to a phone call. Removed visits at Weeks 3, 5, and 7. Visits every 8 weeks (not 4 weeks) after Week 52. Visit window from ± 2 days to -4 days to 2 days. Priority order of secondary objectives changed. Rescue therapy objective prioritized before self-reported health status. Inclusion criteria: #3 reworded to clarify that qualifying eGFR was by central laboratory calculation; #5 and #6: Ferritin raised to ≥ 50 nanograms/mL and transferrin saturation raised to $\geq 15\%$. Exclusion criteria: #9 changed from Bosniak category II to IIF; #13 added "that is determined to be the principal cause of anemia". Removed "or their guardian/legal representative" for participant consent. Deleted IP discontinuation for thrombocytopenia or bleeding. Rescue medication: IV iron guidance adjusted to align with guidelines. Added recommendation for oral iron supplementation. Inclusion of statins text to ask Investigators to consider roxadustat-statin interactions and local prescribing information when deciding on appropriate statin dose for individual participants. Inclusion of text on phosphate binders. Efficacy analysis set: Participants were not to be censored 96 hours after their last dose in the OT+28 population; ITT analysis set for major adverse cardiovascular event (MACE) instead. ANCOVA changed to MMRM for efficacy analysis. Added: "In subjects who do not experience a MACE event, the time-to-event will be censored at the EOT visit for analyses based both on the safety analysis population and on FAS". Removed annual study discontinuation rate of 8.5% and changed estimated time from 1.5 years to 1.4 years.</p>
31 August 2018	<p>To harmonize D5740C00001 with other studies in the CKD-non-dialysis-dependent Phase 3 program, to serve as a pivotal study for confirming efficacy and safety and to facilitate assessment of pooled efficacy and safety data across the Phase 3 program, the following changes were implemented: Previous primary objective changed to primary safety objective (with CV safety analyses now being pooled across the study program). Addition of 2 primary efficacy objectives: one objective for the US FDA and one for the EU health authority. Previous primary objective text moved to new sub-section. Inclusion of text on pooled CV safety analyses and the pooled statistical analysis plan. Previous secondary objectives split out by objective type (efficacy and safety) and updated and new secondary objectives added. Study duration extended. Enrollment anticipated to occur over approximately a 3 year period. Text on sample size determination revised, including addition of text on sample size estimation for the primary efficacy objective. Study end date changed (extension of study into Q3 2018) to reflect a common end date across the Phase 3 studies when the required number of participants with adjudicated CV endpoints was anticipated. Additional criteria (participants requiring a third course of erythropoietin analogue rescue therapy, or those initiating dialysis who required erythropoietin analogue rescue therapy) for permanent discontinuation from the IP were added. Text added to state that hepcidin and hsCRP were to be analyzed from biomarker samples. Added definition of treatment emergent AE. FAS was renamed to the ITT and a new sub-section was added describing the new FAS. Changes were made to the criteria, treatment groups and censoring rules of the analysis sets. A new sub-section was added on participants who will not be included in any analysis set.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

20 participants were excluded from the analysis due to GCP violations or system technical issues (9 in the roxadustat group and 11 in the placebo group).

Notes: