



Clinical trial results:

A phase 3 randomized, open-label (sponsor-blind), active controlled, parallel-group, multi-center, event driven study in dialysis subjects with anemia associated with chronic kidney disease to evaluate the safety and efficacy of daprodustat compared to recombinant human erythropoietin, following a switch from erythropoietin-stimulating agents

Summary

EudraCT number	2016-000541-31
Trial protocol	HU BE GB DK CZ DE SE PT ES NL AT GR FR IT
Global end of trial date	09 November 2020

Results information

Result version number	v1 (current)
This version publication date	20 November 2021
First version publication date	20 November 2021

Trial information

Trial identification

Sponsor protocol code	200807
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.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	15 April 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To compare daprodustat to recombinant human erythropoetin (rhEPO) for cardiovascular (CV) safety (non-inferiority)
- To compare daprodustat to rhEPO for hemoglobin (Hgb) efficacy (non-inferiority)

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 September 2016
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	India: 70
Country: Number of subjects enrolled	Malaysia: 31
Country: Number of subjects enrolled	Singapore: 12
Country: Number of subjects enrolled	Korea, Republic of: 129
Country: Number of subjects enrolled	Taiwan: 43
Country: Number of subjects enrolled	Bulgaria: 80
Country: Number of subjects enrolled	Czechia: 50
Country: Number of subjects enrolled	Estonia: 11
Country: Number of subjects enrolled	Hungary: 143
Country: Number of subjects enrolled	Poland: 73
Country: Number of subjects enrolled	Romania: 37
Country: Number of subjects enrolled	Russian Federation: 207
Country: Number of subjects enrolled	South Africa: 47
Country: Number of subjects enrolled	Turkey: 24
Country: Number of subjects enrolled	Ukraine: 163
Country: Number of subjects enrolled	Australia: 56
Country: Number of subjects enrolled	Austria: 12
Country: Number of subjects enrolled	Belgium: 39
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Denmark: 23
Country: Number of subjects enrolled	France: 27

Country: Number of subjects enrolled	Germany: 43
Country: Number of subjects enrolled	Greece: 96
Country: Number of subjects enrolled	Italy: 34
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	New Zealand: 44
Country: Number of subjects enrolled	Norway: 6
Country: Number of subjects enrolled	Portugal: 64
Country: Number of subjects enrolled	Spain: 81
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Argentina: 182
Country: Number of subjects enrolled	Brazil: 156
Country: Number of subjects enrolled	Mexico: 88
Country: Number of subjects enrolled	United States: 846
Worldwide total number of subjects	2964
EEA total number of subjects	829

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)	1985
From 65 to 84 years	931
85 years and over	48

Subject disposition

Recruitment

Recruitment details:

This was a randomized, open-label (sponsor blind), active-controlled, parallel-group, event-driven study conducted at 431 centers in 35 countries. Participants were randomized to receive daprodustat and recombinant human erythropoietin (rhEPO) (epoetin alfa or darbepoetin alfa).

Pre-assignment

Screening details:

A total of 2964 participants were randomized in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Daprodustat

Arm description:

Participants received placebo tablets orally once daily in run-in period from Week -4 up to randomization (Day 1) and subsequently received daprodustat tablets at dose levels of 1, 2, 4, 6, 8, 10, 12, 16 and 24 milligrams (mg) orally once daily until the required number of major adverse cardiovascular event (MACE) occurred, at approximately 45.1 months of randomized treatment. Study treatment was dose-titrated to achieve and maintain hemoglobin in the target range (10 to 11 grams per deciliter [g/dL]).

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

Dosage and administration details:

Daprodustat was given orally once daily at dose levels ranging from 1, 2, 4, 6, 8, 10, 12, 16 and 24 milligrams (mg).

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

Dosage and administration details:

Placebo was administered orally, one tablet daily.

Arm title	rhEPO
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Arm description:

Participants received placebo tablets orally once daily in run-in period from Week -4 up to randomization (Day 1) and subsequently received treatment with rhEPO. Participants on hemodialysis received epoetin alfa as intravenous (IV) injection once weekly or three-times weekly with total weekly dose levels ranging from 1500 to 60,000 Units. Participants on peritoneal dialysis received subcutaneous (SC) injection of darbepoetin alfa every 1, 2, or 4 weeks with 4-weekly total dose levels ranging from 20 to 400 microgram (mcg). Darbepoetin could be given by IV injection for peritoneal dialysis participants switching to hemodialysis. Study treatment was dose-titrated to achieve and maintain hemoglobin in the target range (10 to 11 g/dL) and administered until the required number of MACE events occurred, at approximately 45.1 months of randomized treatment.

Arm type	Active comparator
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Investigational medicinal product name	Epoetin alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Epoetin alfa was administered as once weekly or three-times weekly intravenous (IV) injection at total weekly dose levels ranging from 1500 to 60,000 Units .

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

Dosage and administration details:

Placebo was administered orally, one tablet daily.

Investigational medicinal product name	Darbepoetin alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Solution for injection in pre-filled syringe
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Darbepoetin alfa was administered subcutaneously (SC) or as IV injection with 4-weekly total dose levels ranging from 20, 30, 40, 60, 80, 100, 150, 200, 300 and 400 microgram (mcg).

Number of subjects in period 1	Daprodustat	rhEPO
Started	1487	1477
Completed	1370	1366
Not completed	117	111
Consent withdrawn by subject	44	42
Investigator Site Closed	55	57
Unknown	1	-
Lost to follow-up	17	12

Baseline characteristics

Reporting groups

Reporting group title	Daprodustat
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Reporting group description:

Participants received placebo tablets orally once daily in run-in period from Week -4 up to randomization (Day 1) and subsequently received daprodustat tablets at dose levels of 1, 2, 4, 6, 8, 10, 12, 16 and 24 milligrams (mg) orally once daily until the required number of major adverse cardiovascular event (MACE) occurred, at approximately 45.1 months of randomized treatment. Study treatment was dose-titrated to achieve and maintain hemoglobin in the target range (10 to 11 grams per deciliter [g/dL]).

Reporting group title	rhEPO
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Reporting group description:

Participants received placebo tablets orally once daily in run-in period from Week -4 up to randomization (Day 1) and subsequently received treatment with rhEPO. Participants on hemodialysis received epoetin alfa as intravenous (IV) injection once weekly or three-times weekly with total weekly dose levels ranging from 1500 to 60,000 Units. Participants on peritoneal dialysis received subcutaneous (SC) injection of darbepoetin alfa every 1, 2, or 4 weeks with 4-weekly total dose levels ranging from 20 to 400 microgram (mcg). Darbepoetin could be given by IV injection for peritoneal dialysis participants switching to hemodialysis. Study treatment was dose-titrated to achieve and maintain hemoglobin in the target range (10 to 11 g/dL) and administered until the required number of MACE events occurred, at approximately 45.1 months of randomized treatment.

Reporting group values	Daprodustat	rhEPO	Total
Number of subjects	1487	1477	2964
Age categorical			
All Randomized (Intent-to-treat [ITT]) Population comprised of all randomized participants. Participants were analyzed according to the treatment to which they were randomized.			
Units: Participants			
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)	1007	978	1985
From 65-84 years	458	473	931
85 years and over	22	26	48
Age Continuous			
All Randomized (Intent-to-treat [ITT]) Population comprised of all randomized participants. Participants were analyzed according to the treatment to which they were randomized.			
Units: years			
arithmetic mean	57.2	57.3	
standard deviation	± 14.29	± 14.65	-
Sex: Female, Male			
All Randomized (Intent-to-treat [ITT]) Population comprised of all randomized participants. Participants were analyzed according to the treatment to which they were randomized.			
Units: Participants			
Female	636	630	1266
Male	851	847	1698
Race/Ethnicity, Customized			
All Randomized (Intent-to-treat [ITT]) Population comprised of all randomized participants. Participants were analyzed according to the treatment to which they were randomized.			

Units: Subjects			
American Indian or Alaskan Native	19	32	51
Asian - Central/South Asian Heritage	36	46	82
Asian - East Asian Heritage	97	86	183
Asian - Japanese Heritage	3	3	6
Asian - South East Asian Heritage	40	45	85
Black or African American	228	233	461
Native Hawaiian or Other Pacific Islander	26	25	51
White - Arabic/North African Heritage	8	14	22
White - White/Caucasian/European Heritage	987	968	1955
Mixed Asian Race	0	1	1
Mixed Race	43	24	67

End points

End points reporting groups

Reporting group title	Daprodustat
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Reporting group description:

Participants received placebo tablets orally once daily in run-in period from Week -4 up to randomization (Day 1) and subsequently received daprodustat tablets at dose levels of 1, 2, 4, 6, 8, 10, 12, 16 and 24 milligrams (mg) orally once daily until the required number of major adverse cardiovascular event (MACE) occurred, at approximately 45.1 months of randomized treatment. Study treatment was dose-titrated to achieve and maintain hemoglobin in the target range (10 to 11 grams per deciliter [g/dL]).

Reporting group title	rhEPO
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Reporting group description:

Participants received placebo tablets orally once daily in run-in period from Week -4 up to randomization (Day 1) and subsequently received treatment with rhEPO. Participants on hemodialysis received epoetin alfa as intravenous (IV) injection once weekly or three-times weekly with total weekly dose levels ranging from 1500 to 60,000 Units. Participants on peritoneal dialysis received subcutaneous (SC) injection of darbepoetin alfa every 1, 2, or 4 weeks with 4-weekly total dose levels ranging from 20 to 400 microgram (mcg). Darbepoetin could be given by IV injection for peritoneal dialysis participants switching to hemodialysis. Study treatment was dose-titrated to achieve and maintain hemoglobin in the target range (10 to 11 g/dL) and administered until the required number of MACE events occurred, at approximately 45.1 months of randomized treatment.

Primary: Time to first occurrence of adjudicated major adverse cardiovascular event (MACE) during cardiovascular (CV) events follow-up time period: Non-inferiority analysis

End point title	Time to first occurrence of adjudicated major adverse cardiovascular event (MACE) during cardiovascular (CV) events follow-up time period: Non-inferiority analysis
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End point description:

Time to MACE defined as time to first occurrence of Clinical Events Committee (CEC) adjudicated MACE (composite of all-cause mortality, non-fatal myocardial infarction [MI] and non-fatal stroke) was analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to first occurrence was computed as (event date minus randomization date)+1. Incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years) is presented along with 95 percent (%) confidence interval (CI). First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period. All Randomized (Intent-to-treat [ITT]) Population comprised of all randomized participants. Participants were analyzed according to the treatment to which they were randomized.

End point type	Primary
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End point timeframe:

Up to 3.9 person-years for CV follow-up time period

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[1]	1477 ^[2]		
Units: Events per 100 person years				
number (confidence interval 95%)	11.07 (9.98 to 12.26)	11.86 (10.72 to 13.09)		

Notes:

[1] - All Randomized (ITT) Population

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.07

Notes:

[3] - Non-inferiority was achieved if the upper limit of the two-sided 95% CI for the hazard ratio was below the pre-specified non-inferiority margin of 1.25.

Primary: Mean Change from Baseline in Hemoglobin (Hgb) levels During Evaluation Period (Week 28 to Week 52)

End point title	Mean Change from Baseline in Hemoglobin (Hgb) levels During Evaluation Period (Week 28 to Week 52)
End point description:	
Blood samples were collected from participants for hemoglobin measurements. Hemoglobin during the evaluation period was defined as the mean of all available post-randomization hemoglobin values (on and off-treatment) during the evaluation period (Week 28 to Week 52). For the primary analysis, missing post-Baseline hemoglobin values were imputed using pre-specified multiple imputation methods. Change from Baseline was defined as post-Baseline value minus Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date.	
End point type	Primary

End point timeframe:

Baseline (Pre-dose on Day 1) and evaluation period (Week 28 to Week 52)

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[4]	1477 ^[5]		
Units: Grams per deciliter				
least squares mean (standard error)	0.28 (± 0.022)	0.10 (± 0.022)		

Notes:

[4] - All Randomized (ITT) Population

[5] - All Randomized (ITT) Population

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description: Analysis of covariance (ANCOVA) model adjusted for treatment, Baseline Hgb, dialysis type and region along with 95% CI for treatment difference (daprodustat-rhEPO).	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[6]
Parameter estimate	Least square (LS) mean difference
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.24

Notes:

[6] - Non-inferiority was to be established if the lower limit of the two-sided 95% CI for the treatment difference was greater than -0.75 g/dL.

Secondary: Time to first occurrence of adjudicated MACE during CV events follow-up time period: Superiority analysis

End point title	Time to first occurrence of adjudicated MACE during CV events follow-up time period: Superiority analysis
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End point description:

Time to MACE defined as the time to first occurrence of CEC adjudicated MACE was analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariate. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period. This endpoint was adjusted for multiplicity using the Holm-Bonferonni method.

End point type	Secondary
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End point timeframe:

Up to 3.9 person-years for CV follow-up time period

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[7]	1477 ^[8]		
Units: Events per 100 person years				
number (confidence interval 95%)	11.07 (9.98 to 12.26)	11.86 (10.72 to 13.09)		

Notes:

[7] - All Randomized (ITT) Population

[8] - All Randomized (ITT) Population

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group,

dialysis type and region as covariates.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.156123 [9]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.07

Notes:

[9] - The p-value was compared against 0.0125 based on the Holm-Bonferonni adjustment.

Secondary: Time to first occurrence of adjudicated MACE or thromboembolic event during CV events follow-up time period

End point title	Time to first occurrence of adjudicated MACE or thromboembolic event during CV events follow-up time period
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End point description:

Time to first occurrence of adjudicated MACE or thromboembolic event (vascular access thrombosis, symptomatic deep vein thrombosis or symptomatic pulmonary embolism) was analyzed using a Cox proportional hazards regression model with with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period. This endpoint was adjusted for multiplicity using the Holm-Bonferonni method.

End point type	Secondary
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End point timeframe:

Up to 3.9 person-years for CV follow-up time period

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[10]	1477 ^[11]		
Units: Events per 100 person years				
number (confidence interval 95%)	15.84 (14.48 to 17.30)	17.85 (16.38 to 19.42)		

Notes:

[10] - All Randomized (ITT) Population.

[11] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023539 [12]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1

Notes:

[12] - The p-value was compared against 0.006250 based on the Holm-Bonferonni adjustment.

Secondary: Time to first occurrence of adjudicated MACE or hospitalization for heart failure during CV events follow-up time period

End point title	Time to first occurrence of adjudicated MACE or hospitalization for heart failure during CV events follow-up time period
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End point description:

Time to first occurrence of adjudicated MACE or hospitalization for heart failure was analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period. This endpoint was adjusted for multiplicity using the Holm-Bonferonni method.

End point type	Secondary
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End point timeframe:

Up to 3.9 person-years for CV follow-up time period

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[13]	1477 ^[14]		
Units: Events per 100 person years				
number (confidence interval 95%)	12.98 (11.77 to 14.27)	13.38 (12.15 to 14.70)		

Notes:

[13] - All Randomized (ITT) Population.

[14] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.325797 ^[15]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.11

Notes:

[15] - The p-value was compared against 0.025000 based on the Holm-Bonferonni adjustment.

Secondary: Mean average monthly On-treatment IV iron dose per participant

End point title	Mean average monthly On-treatment IV iron dose per participant
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End point description:

Average monthly IV iron dose (milligrams) per participant from Day 1 to Week 52 was determined by calculating the total IV iron dose per participant from treatment start date + 1 to the earliest of (Week 52 visit date, first blood (red blood cell [RBC] or whole blood) transfusion date, and treatment stop date + 1 day) which corresponds to the time while the participant was on randomized treatment and before receiving a blood transfusion. This total IV iron dose was divided by (the number of days from treatment start date + 1 to the earliest of (Week 52 visit date, first blood transfusion date (RBC or whole blood), and treatment stop date +1) / 30.4375 days). This endpoint was adjusted for multiplicity using the Holm-Bonferonni method. Only those participants with data available at the indicated time points were analyzed.

End point type	Secondary
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End point timeframe:

Day 1 to Week 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1482 ^[16]	1472 ^[17]		
Units: Milligrams				
least squares mean (standard error)	90.8 (± 3.34)	99.9 (± 3.35)		

Notes:

[16] - All Randomized (ITT) Population.

[17] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Analysis was carried out by using ANCOVA model with terms for treatment, Baseline monthly IV iron dose, dialysis type and region.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	2954
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026947 ^[18]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.4
upper limit	0.2

Notes:

[18] - The p-value was compared against 0.008333 based on the Holm-Bonferonni adjustment.

Secondary: Time to First occurrence of Adjudicated All-Cause Mortality during vital status for follow-up time period

End point title	Time to First occurrence of Adjudicated All-Cause Mortality during vital status for follow-up time period
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End point description:

Time to first occurrence of adjudicated all-cause mortality was analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the vital status for follow-up time period.

End point type	Secondary
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End point timeframe:

Up to 3.9 person-years for vital status follow-up time period

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[19]	1477 ^[20]		
Units: Events per 100 person years				
number (confidence interval 95%)	8.32 (7.39 to 9.32)	8.59 (7.65 to 9.62)		

Notes:

[19] - All Randomized (ITT) Population.

[20] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3281
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.13

Secondary: Time to First occurrence of Adjudicated CV Mortality during CV events follow-up time period

End point title	Time to First occurrence of Adjudicated CV Mortality during CV events follow-up time period
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End point description:

Time to first occurrence of adjudicated CV mortality was analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period.

End point type	Secondary
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End point timeframe:

Up to 3.9 person-years for CV follow-up time period

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[21]	1477 ^[22]		
Units: Events per 100 person years				
number (confidence interval 95%)	3.31 (2.74 to 3.97)	3.46 (2.88 to 4.14)		

Notes:

[21] - All Randomized (ITT) Population.

[22] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3553
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.23

Secondary: Time to First occurrence of Adjudicated Myocardial Infarction (MI) (Fatal and Non-Fatal) during CV events follow-up time period

End point title	Time to First occurrence of Adjudicated Myocardial Infarction (MI) (Fatal and Non-Fatal) during CV events follow-up time period
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End point description:

Time to first occurrence of adjudicated MI (fatal and non-fatal) was analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period.

End point type	Secondary
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End point timeframe:

Up to 3.9 person-years for CV follow-up time period

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[23]	1477 ^[24]		
Units: Events per 100 person years				
number (confidence interval 95%)	3.34 (2.76 to 4.01)	4.08 (3.43 to 4.83)		

Notes:

[23] - All Randomized (ITT) Population.

[24] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0524
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.04

Secondary: Time to First occurrence of Adjudicated Stroke (Fatal and Non-Fatal) during CV events follow-up time period

End point title	Time to First occurrence of Adjudicated Stroke (Fatal and Non-Fatal) during CV events follow-up time period
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End point description:

Time to first occurrence of adjudicated stroke (fatal and non-fatal) was analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period.

End point type	Secondary
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End point timeframe:

Up to 3.9 person-years for CV follow-up time period

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[25]	1477 ^[26]		
Units: Events per 100 person years				
number (confidence interval 95%)	1.23 (0.89 to 1.66)	1.48 (1.10 to 1.94)		

Notes:

[25] - All Randomized (ITT) Population.

[26] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1927
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.25

Secondary: Number of participants with Adjudicated MACE or Hospitalization for Heart Failure (Recurrent events analysis)

End point title	Number of participants with Adjudicated MACE or Hospitalization for Heart Failure (Recurrent events analysis)
End point description: Number of participants with adjudicated MACE or hospitalization for heart failure (recurrent events analysis) is presented, categorized by number of occurrences of adjudicated MACE or hospitalization for heart failure per participant.	
End point type	Secondary
End point timeframe: Up to 3.9 person-years for CV follow-up time period	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[27]	1477 ^[28]		
Units: Participants				
Occurrences per participant: 0	1062	1044		
Occurrences per participant: 1	315	300		
Occurrences per participant: 2	72	88		
Occurrences per participant: 3	25	22		
Occurrences per participant: 4	3	11		
Occurrences per participant: 5	4	4		
Occurrences per participant: 6	4	3		
Occurrences per participant: 7	0	2		
Occurrences per participant: 8	0	1		
Occurrences per participant: 9	1	1		
Occurrences per participant: 10	1	1		

Notes:

[27] - All Randomized (ITT) Population.

[28] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Overall HR is presented using Model 1. Model 1 assumed a common treatment effect, regardless of number of events experienced. HR was estimated using a Prentice, Williams and Peterson(PWP) model, with treatment, dialysis type and region as covariates.	
Comparison groups	rhEPO v Daprodustat
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0351
Method	Chi-squared
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.01

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
First Event Hazard ratio is presented using Model 2. Model 2 assumed treatment effect differs by number of events experienced. Hazard Ratio (HR) was estimated using a PWP model, with treatment, dialysis type and region as covariates.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3258
Method	Chi-squared
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.11

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Second Event Hazard ratio is presented using Model 2. Model 2 assumed treatment effect differs by number of events experienced. HR was estimated using a PWP model, with treatment, dialysis type and region as covariates.	
Comparison groups	Daprodustat v rhEPO

Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0158
Method	Chi-squared
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.98

Statistical analysis title	Statistical analysis 4
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Statistical analysis description:

Third Event Hazard ratio is presented using Model 2. Model 2 assumed treatment effect differs by number of events experienced. HR was estimated using a PWP model, with treatment, dialysis type and region as covariates.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0981
Method	Chi-squared
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.17

Statistical analysis title	Statistical analysis 5
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Statistical analysis description:

First Event Hazard ratio is presented using Model 3. Model 3 assumed treatment effect for first event differs from a common effect for subsequent events. HR was estimated using a PWP model, with treatment, dialysis type and region as covariates.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3258
Method	Chi-squared
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.11

Statistical analysis title	Statistical analysis 6
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Statistical analysis description:

Subsequent Event Hazard ratio is presented using Model 3. Model 3 assumed treatment effect for first event differs from a common effect for subsequent events. HR was estimated using a PWP model, with treatment, dialysis type and region as covariates.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0058
Method	Chi-squared
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	0.94

Secondary: Time to First Occurrence of Adjudicated CV Mortality or Non-Fatal MI during CV events follow-up time period

End point title	Time to First Occurrence of Adjudicated CV Mortality or Non-Fatal MI during CV events follow-up time period
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End point description:

Time to first occurrence of adjudicated CV mortality or non-fatal MI was analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period.

End point type	Secondary
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End point timeframe:

Up to 3.9 person-years for CV follow-up time period

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[29]	1477 ^[30]		
Units: Events per 100 person years				
number (confidence interval 95%)	5.98 (5.18 to 6.86)	6.79 (5.94 to 7.73)		

Notes:

[29] - All Randomized (ITT) Population.

[30] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0872
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.06

Secondary: Time to First Occurrence of All-Cause Hospitalization during CV events follow-up time period

End point title	Time to First Occurrence of All-Cause Hospitalization during CV events follow-up time period
End point description:	
All-cause hospitalization events were hospital admissions recorded on the Hospitalization electronic case report form (eCRF) with a hospitalization duration ≥ 24 hours. Time to first occurrence of all-cause hospitalization was analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as $(100 \times \text{number of participants with at least 1 event}) / \text{first event person-years}$ is presented along with 95% CI. First event person years = $(\text{cumulative total time to first event for participants who have the event} + \text{cumulative total of censored time for participants without the event}) / 365.25$, based on the CV follow-up time period.	
End point type	Secondary
End point timeframe:	
Up to 3.9 person-years for CV follow-up time period	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[31]	1477 ^[32]		
Units: Events per 100 person years				
number (confidence interval 95%)	43.92 (41.18 to 46.81)	46.03 (43.17 to 49.04)		

Notes:

[31] - All Randomized (ITT) Population.

[32] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.154
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.04

Secondary: Time to First Occurrence of All-Cause Hospital Re-admission within 30 Days during CV events follow-up time period

End point title	Time to First Occurrence of All-Cause Hospital Re-admission within 30 Days during CV events follow-up time period
End point description:	
All-cause hospital re-admissions within 30days are defined as hospital admissions recorded on hospitalization eCRF with hospitalization duration of ≥ 24 hours and admission date within 30days following previous discharge date of all-cause hospitalization event, where previous hospitalization was ≥ 24 hours. Time to first occurrence of all-cause hospital re-admission within 30days was analyzed using Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date)+1. Incidence rate per 100person years calculated as(100*number of participants with at least 1 event)/first event person-years) is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event+cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period.	
End point type	Secondary
End point timeframe:	
Up to 3.9 person-years for CV follow-up time period	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[33]	1477 ^[34]		
Units: Events per 100 person years				
number (confidence interval 95%)	8.86 (7.85 to 9.95)	9.67 (8.62 to 10.82)		

Notes:

[33] - All Randomized (ITT) Population.

[34] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1244
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.07

Secondary: Time to First Occurrence of Adjudicated MACE or Hospitalization for Heart Failure or Thromboembolic events during CV events follow-up time period

End point title	Time to First Occurrence of Adjudicated MACE or Hospitalization for Heart Failure or Thromboembolic events during CV events follow-up time period
End point description:	
Time to first occurrence of adjudicated MACE or hospitalization for heart failure or thromboembolic events were analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period.	
End point type	Secondary
End point timeframe:	
Up to 3.9 person-years for CV follow-up time period	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[35]	1477 ^[36]		
Units: Events per 100 person years				
number (confidence interval 95%)	17.74 (16.28 to 19.30)	19.50 (17.94 to 21.16)		

Notes:

[35] - All Randomized (ITT) Population.

[36] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.054
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.02

Secondary: Time to First Occurrence of Adjudicated Hospitalization for Heart Failure during CV events follow-up time period

End point title	Time to First Occurrence of Adjudicated Hospitalization for Heart Failure during CV events follow-up time period
End point description:	
Time to first occurrence of adjudicated hospitalization for heart failure was analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period.	
End point type	Secondary
End point timeframe:	
Up to 3.9 person-years for CV follow-up time period	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[37]	1477 ^[38]		
Units: Events per 100 person years				
number (confidence interval 95%)	3.30 (2.72 to 3.97)	3.01 (2.45 to 3.65)		

Notes:

[37] - All Randomized (ITT) Population.

[38] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7658
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.45

Secondary: Time to First Occurrence of Adjudicated Thromboembolic Events during CV events follow-up time period

End point title	Time to First Occurrence of Adjudicated Thromboembolic Events during CV events follow-up time period
End point description:	
Time to first occurrence of adjudicated thromboembolic events were analyzed using a Cox proportional hazards regression model with treatment group, dialysis type and region as covariates. Time to the first occurrence was computed as (event date minus randomization date) + 1. The incidence rate per 100 person years calculated as (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% CI. First event person years=(cumulative total time to first event for participants who have the event + cumulative total of censored time for participants without the event)/365.25, based on the CV follow-up time period.	
End point type	Secondary
End point timeframe:	
Up to 3.9 person-years for CV follow-up time period	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[39]	1477 ^[40]		
Units: Events per 100 person years				
number (confidence interval 95%)	5.66 (4.87 to 6.54)	6.75 (5.88 to 7.72)		

Notes:

[39] - All Randomized (ITT) Population.

[40] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Hazard ratio was estimated using a Cox proportional hazard regression model with treatment group, dialysis type and region as covariates.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0425
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.02

Secondary: Change From Baseline in Post-randomization Hemoglobin levels at Week 52

End point title	Change From Baseline in Post-randomization Hemoglobin levels at Week 52
End point description:	
Blood samples were collected from participants for hemoglobin measurements. Change from Baseline was defined as post-Baseline value minus Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date. Analysis was performed using mixed model repeated measures (MMRM) model fitted from Baseline up to Week 52, excluding values collected during the stabilization period, with factors for treatment, time, dialysis type, region, Baseline hemoglobin and Baseline hemoglobin by time and treatment by time interactions. Only those participants with data available at the indicated time points were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Pre-dose on Day 1) and Week 52	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1358 ^[41]	1347 ^[42]		
Units: Grams per deciliter				
least squares mean (standard error)	0.26 (± 0.032)	0.14 (± 0.032)		

Notes:

[41] - All Randomized (ITT) Population.

[42] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2705
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[43]
Parameter estimate	LS mean difference
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.21

Notes:

[43] - Non-inferiority was to be established if the lower limit of the two-sided 95% CI for the treatment difference was greater than the pre-specified non-inferiority margin of -0.75 g/dL.

Secondary: Number of Hgb Responders in the Hgb Analysis Range (10 to 11.5 Grams/Deciliter) During Evaluation Period (Week 28 to Week 52)

End point title	Number of Hgb Responders in the Hgb Analysis Range (10 to 11.5 Grams/Deciliter) During Evaluation Period (Week 28 to Week 52)
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End point description:

Mean Hgb during the evaluation period was defined as the mean of all evaluable Hgb values during the evaluation period (Week 28 to Week 52) including any evaluable unscheduled Hgb values that were taken during this time period. Hemoglobin responders were defined as participants with a mean Hgb during the evaluation period that falls within the Hgb analysis range of 10-11.5 g/dL. Only those participants with data available at the indicated time points were analyzed.

End point type	Secondary
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End point timeframe:

Week 28 to Week 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1238 ^[44]	1247 ^[45]		
Units: Participants	903	866		

Notes:

[44] - All Randomized (ITT) Population.

[45] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description: Cochran-Mantel-Haenszel (CMH) test adjusted for dialysis type, and region was used to compare the number of responders between the treatment groups.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2485
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0367
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rate
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	7.1

Secondary: Percentage of Time With Hemoglobin in the Analysis Range (10 to 11.5 Grams/Deciliter) During Evaluation Period (Week 28 to Week 52): Non-inferiority analysis

End point title	Percentage of Time With Hemoglobin in the Analysis Range (10 to 11.5 Grams/Deciliter) During Evaluation Period (Week 28 to Week 52): Non-inferiority analysis
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End point description:

Percentage of days for which a participant's Hgb was within the analysis range of 10-11.5 g/dL (both inclusive) during the evaluation period (Week 28 to Week 52), including any unscheduled evaluable Hgb values that were taken during this time period was calculated. Percentage of time in the analysis range during evaluation period is calculated as time in range during the evaluation period / [Earlier of (Date of the last evaluable Hgb value, Week 52 visit date) - Later of (Date of the first evaluable Hgb value that between Week 16 and Week 52 inclusive, Week 28 visit date)]. Only those participants with data available at the indicated time points were analyzed.

End point type	Secondary
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End point timeframe:

Week 28 to Week 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1202 ^[46]	1224 ^[47]		
Units: Percentage of days				
median (full range (min-max))	60.9 (0.0 to 100.0)	59.4 (0.0 to 100.0)		

Notes:

[46] - All Randomized (ITT) Population.

[47] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description: Hodges-Lehmann estimate of the treatment difference (daprodustat-rhEPO) and associated two-sided asymptotic 95% CI is presented.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2426
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[48]
Parameter estimate	Median difference (final values)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3.86

Notes:

[48] - Non-inferiority was to be established if the lower limit of the two-sided 95% confidence interval for the treatment difference was greater than non-inferiority margin of -15%.

Secondary: Percentage of Time With Hemoglobin in the Analysis Range (10 to 11.5 Grams/Deciliter) During Evaluation Period (Week 28 to Week 52): Superiority analysis

End point title	Percentage of Time With Hemoglobin in the Analysis Range (10 to 11.5 Grams/Deciliter) During Evaluation Period (Week 28 to Week 52): Superiority analysis
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End point description:

Percentage of days for which a participant's Hgb was within the analysis range of 10-11.5 g/dL (both inclusive) during the evaluation period (Week 28 to Week 52), including any unscheduled evaluable Hgb values that were taken during this time period was calculated. Percentage of time in the analysis range during evaluation period is calculated as time in range during the evaluation period / [Earlier of (Date of the last evaluable Hgb value, Week 52 visit date) – Later of (Date of the first evaluable Hgb value that between Week 16 and Week 52 inclusive, Week 28 visit date)]. Only those participants with data available at the indicated time points were analyzed.

End point type	Secondary
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End point timeframe:

Week 28 to Week 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1202 ^[49]	1224 ^[50]		
Units: Percentage of days				
median (full range (min-max))	60.9 (0.0 to 100.0)	59.4 (0.0 to 100.0)		

Notes:

[49] - All Randomized (ITT) Population.

[50] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Mann-Whitney estimate (Probability) of the treatment effect has been presented.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2426
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0805
Method	van Elteren test
Parameter estimate	Probability
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.54

Secondary: Percentage of Time With Hemoglobin in the Analysis Range (10 to 11.5 Grams/Deciliter) During Maintenance Period (Week 28 to End of study): Non-inferiority analysis

End point title	Percentage of Time With Hemoglobin in the Analysis Range (10 to 11.5 Grams/Deciliter) During Maintenance Period (Week 28 to End of study): Non-inferiority analysis
End point description:	Percentage of days for which a participant's Hgb was within the analysis range of 10-11.5 g/dL (both inclusive) during the maintenance period (Week 28 to end of study), including any unscheduled evaluable Hgb values that were taken during this time period was calculated. Percentage of time in the analysis range during maintenance period is calculated as time in range during the maintenance period / [Earlier of (Date of the last evaluable Hgb value, End of study date)- Later of (Date of the first evaluable Hgb value that is on or after week 16, Week 28 visit date)]. Only those participants with data available at the indicated time points were analyzed.
End point type	Secondary
End point timeframe:	Week 28 to end of study (3.9 person-years for follow-up time period)

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1203 ^[51]	1224 ^[52]		
Units: Percentage of days				
median (full range (min-max))	60.9 (0.0 to 100.0)	57.7 (0.0 to 100.0)		

Notes:

[51] - All Randomized (ITT) Population.

[52] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	Hodges-Lehmann estimate of the treatment difference (daprodustat-rhEPO) and associated two-sided asymptotic 95% CI is presented.
Comparison groups	Daprodustat v rhEPO

Number of subjects included in analysis	2427
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[53]
Parameter estimate	Median difference (final values)
Point estimate	2.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	4.05

Notes:

[53] - Non-inferiority was to be established if the lower limit of the two-sided 95% confidence interval for the treatment difference was greater than non-inferiority margin of -15%.

Secondary: Percentage of Time With Hemoglobin in the Analysis Range (10 to 11.5 Grams/Deciliter) During Maintenance Period (Week 28 to End of study): Superiority analysis

End point title	Percentage of Time With Hemoglobin in the Analysis Range (10 to 11.5 Grams/Deciliter) During Maintenance Period (Week 28 to End of study): Superiority analysis
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End point description:

Percentage of days for which a participant's Hgb was within the analysis range of 10-11.5 g/dL (both inclusive) during the maintenance period (Week 28 to end of study), including any unscheduled evaluable Hgb values that were taken during this time period was calculated. Percentage of time in the analysis range during maintenance period is calculated as time in range during the maintenance period / [Earlier of (Date of the last evaluable Hgb value, End of study date)- Later of (Date of the first evaluable Hgb value that is on or after week 16, Week 28 visit date)]. Only those participants with data available at the indicated time points were analyzed.

End point type	Secondary
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End point timeframe:

Week 28 to end of study (3.9 person-years for follow-up time period)

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1203 ^[54]	1224 ^[55]		
Units: Percentage of days				
median (full range (min-max))	60.9 (0.0 to 100.0)	57.7 (0.0 to 100.0)		

Notes:

[54] - All Randomized (ITT) Population.

[55] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Mann-Whitney estimate (Probability) of the treatment effect has been presented.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	2427
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0139
Method	van Elteren test
Parameter estimate	Probability
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.55

Secondary: Change from Baseline in Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Blood Pressure (MAP) at Week 52

End point title	Change from Baseline in Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Blood Pressure (MAP) at Week 52
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End point description:

SBP, DBP and MAP were measured in a semi-supine or seated position in the dialysis chair after at least a 5-minutes of rest. MAP is the average BP in an individual's arteries during a single cardiac cycle. Change from Baseline was calculated as on-treatment visit value minus Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date. Analysis was performed using MMRM model with treatment group + time + dialysis type + region + Baseline value + Baseline value*time + treatment group*time, using an unstructured covariance matrix. Data for post-dialysis BP measurements have been presented. Only those participants with data available at the indicated time points were analyzed.

End point type	Secondary
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End point timeframe:

Baseline (Week -4) and Week 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1455 ^[56]	1442 ^[57]		
Units: Millimeter of mercury				
least squares mean (standard error)				
SBP	-0.61 (± 0.582)	-0.93 (± 0.578)		
DBP	-1.04 (± 0.326)	-0.58 (± 0.324)		
MAP	-0.89 (± 0.370)	-0.71 (± 0.368)		

Notes:

[56] - All Randomized (ITT) Population.

[57] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

The difference in change from Baseline in SBP at Week 52 was analyzed with a MMRM approach with an unstructured covariance matrix to compare the difference in means between arms.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2897
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6551
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	1.94

Statistical analysis title Statistical analysis 2**Statistical analysis description:**

The difference in change from Baseline in DBP at Week 52 was analyzed with a MMRM approach with an unstructured covariance matrix to compare the difference in means between arms.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2897
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1586
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.36
upper limit	0.44

Statistical analysis title Statistical analysis 3**Statistical analysis description:**

The difference in change from Baseline in MAP at Week 52 was analyzed with a MMRM approach with an unstructured covariance matrix to compare the difference in means between arms.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2897
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3646
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.84

Secondary: Change from Baseline in SBP, DBP, MAP at End of Treatment

End point title	Change from Baseline in SBP, DBP, MAP at End of Treatment
End point description:	
<p>SBP, DBP and MAP were measured in a semi-supine or seated position in the dialysis chair after at least a 5-minutes of rest. MAP is an average BP in an individual's arteries during a single cardiac cycle. Change from Baseline was calculated as on-treatment visit value minus Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date. This analysis was carried out by using ANCOVA model with terms for treatment group, dialysis type, region and Baseline value. Data for post-dialysis BP measurements have been presented. Only those participants with data available at the indicated time points were analyzed.</p>	
End point type	Secondary
End point timeframe:	
Baseline (Week -4) and 45.1 months	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1468 ^[58]	1454 ^[59]		
Units: Millimeter of mercury				
least squares mean (standard error)				
SBP	-0.43 (± 0.554)	-0.43 (± 0.557)		
DBP	-0.92 (± 0.310)	-1.37 (± 0.312)		
MAP	-0.75 (± 0.350)	-1.06 (± 0.351)		

Notes:

[58] - All Randomized (ITT) Population.

[59] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
<p>For SBP: Treatment group comparisons were based on an ANCOVA model with terms for treatment group, dialysis type, region and Baseline value.</p>	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2922
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5012
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.54
upper limit	1.54

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

For DBP: Treatment group comparisons were based on an ANCOVA model with terms for treatment group, dialysis type, region and Baseline value.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2922
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8451
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	1.31

Statistical analysis title	Statistical analysis 3
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Statistical analysis description:

For MAP: Treatment group comparisons were based on an ANCOVA model with terms for treatment group, dialysis type, region and Baseline value.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2922
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7312
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.67
upper limit	1.28

Secondary: Blood Pressure (BP) Exacerbation Event Rate per 100 Participant Years

End point title	Blood Pressure (BP) Exacerbation Event Rate per 100 Participant Years
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End point description:

BP exacerbation was defined (based on post-dialysis) as: SBP \geq 25 millimeter of mercury (mmHg) increased from Baseline or SBP \geq 180 mmHg; DBP \geq 15 mmHg increased from Baseline or DBP \geq 110 mmHg. The BP exacerbation events per 100 participant years was estimated using the negative binomial model with treatment, dialysis type and region as covariates and the logarithm of time on-treatment as an offset variable. Data for post-dialysis BP measurements have been presented. Only those participants with data available at the indicated time points were analyzed.

End point type	Secondary
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End point timeframe:

Day 1 to end of study (3.9 person-years for follow-up time period)

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1470 ^[60]	1458 ^[61]		
Units: Events per 100 participant years				
number (confidence interval 95%)	207.13 (188.83 to 227.21)	206.38 (187.88 to 226.71)		

Notes:

[60] - All Randomized (ITT) Population.

[61] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
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Statistical analysis description:

Ratio of model estimated exacerbation rates and CIs were estimated using a negative binomial model for the treatment group comparison.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2928
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.529
Method	Negative binomial model
Parameter estimate	Ratio of exacerbation rate
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.11

Secondary: Number of Participants with at Least one BP Exacerbation Event During Study

End point title	Number of Participants with at Least one BP Exacerbation Event During Study
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End point description:

BP exacerbation was defined as: SBP \geq 25 mmHg increased from Baseline or SBP \geq 180 mmHg; DBP \geq 15 mmHg increased from Baseline or DBP \geq 110 mmHg. Number of participants with at least one BP exacerbation event is presented. Only those participants with data available at the indicated time points

were analyzed.

End point type	Secondary
End point timeframe:	
Day 1 to end of study (3.9 person-years for follow-up time period)	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1480 ^[62]	1470 ^[63]		
Units: Participants	1191	1186		

Notes:

[62] - All Randomized (ITT) Population.

[63] - All Randomized (ITT) Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Permanently Stopping Randomized Treatment Due to Meeting Rescue Criteria

End point title	Percentage of Participants Permanently Stopping Randomized Treatment Due to Meeting Rescue Criteria
End point description:	
Percentage of participants permanently stopping randomized treatment due to meeting rescue criteria has been presented.	
End point type	Secondary
End point timeframe:	
Day 1 to 45.1 months	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1487 ^[64]	1477 ^[65]		
Units: Percentage of participants				
number (not applicable)	3.6	3.6		

Notes:

[64] - All Randomized (ITT) Population.

[65] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Hazard ratio was estimated using a Cox proportional hazard regression model adjusted for treatment group, dialysis type and region.	
Comparison groups	Daprodustat v rhEPO

Number of subjects included in analysis	2964
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5772
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.52

Secondary: Change from Baseline in On-Treatment Physical Component Score (PCS) using Short Form (SF)-36 Health-related Quality of Life (HRQoL) Questionnaire at Weeks 8, 12, 28, 52

End point title	Change from Baseline in On-Treatment Physical Component Score (PCS) using Short Form (SF)-36 Health-related Quality of Life (HRQoL) Questionnaire at Weeks 8, 12, 28, 52
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End point description:

SF-36 acute version 2 is a 36-item generic quality of life instrument designed to measure a participant's level of performance in following 8 health domains: physical functioning, role-physical (role limitations caused by physical problems), social functioning, bodily pain, mental health, role-emotional (role limitations caused by emotional problems), vitality and general health. Each domain is scored from 0 (poorer health) to 100 (better health). The PCS is an average score derived from 4 domains (physical functioning, role-physical, bodily pain and general health) representing overall physical health. PCS ranges from 0 to 100; higher scores represent better health. Change from Baseline was calculated as on-treatment visit value minus Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline (Pre-dose on Day 1), Weeks 8, 12, 28 and 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	990 ^[66]	943 ^[67]		
Units: Scores on a scale				
least squares mean (standard error)				
Week 8, n=982,936	0.30 (± 0.205)	0.01 (± 0.210)		
Week 12, n=990,943	0.33 (± 0.203)	-0.27 (± 0.207)		
Week 28, n=836,819	-0.23 (± 0.229)	-0.57 (± 0.232)		
Week 52, n=729,707	-0.52 (± 0.248)	-1.05 (± 0.252)		

Notes:

[66] - All Randomized (ITT) Population.

[67] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Week 8: Model was fitted from Baseline up to Week 52 and the model adjusted Week 8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.162
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.86

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Week 12: Model was fitted from Baseline up to Week 52 and the model adjusted Week 12 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	1.18

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Week 28: Model was fitted from Baseline up to Week 52 and the model adjusted Week 28 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO

Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.153
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	0.97

Statistical analysis title	Statistical analysis 4
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Statistical analysis description:

Week 52: Model was fitted from Baseline up to Week 52 and the model adjusted Week 52 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0686
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	1.22

Secondary: Change from Baseline in On-Treatment Mental Component Score (MCS) using SF-36 HRQoL Questionnaire at Weeks 8, 12, 28, 52

End point title	Change from Baseline in On-Treatment Mental Component Score (MCS) using SF-36 HRQoL Questionnaire at Weeks 8, 12, 28, 52
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End point description:

The SF-36 acute version 2 is a 36-item generic quality of life instrument designed to measure a participant's level of performance in the following 8 health domains: physical functioning, role-physical (role limitations caused by physical problems), social functioning, bodily pain, mental health, role-emotional (role limitations caused by emotional problems), vitality and general health. Each domain is scored from 0 (poorer health) to 100 (better health). MCS is an average score derived from 4 domains (vitality, social functioning, role-emotional and mental health) representing overall mental health. MCS ranges from 0 to 100; higher scores represent better health. Change from Baseline was calculated as on-treatment visit value minus Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline (Pre-dose on Day 1), Weeks 8, 12, 28 and 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	990 ^[68]	943 ^[69]		
Units: Scores on a scale				
least squares mean (standard error)				
Week 8, n=982,936	-0.38 (± 0.254)	-0.21 (± 0.260)		
Week 12, n=990,943	-0.55 (± 0.262)	-0.72 (± 0.268)		
Week 28, n=836,819	-1.25 (± 0.286)	-1.23 (± 0.290)		
Week 52, n=729,707	-1.63 (± 0.311)	-1.03 (± 0.316)		

Notes:

[68] - All Randomized (ITT) Population.

[69] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Week 8: Model was fitted from Baseline up to Week 52 and the model adjusted Week 8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6807
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	0.54

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

Week 12: Model was fitted from Baseline up to Week 52 and the model adjusted Week 12 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3256
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.91

Statistical analysis title	Statistical analysis 3
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Statistical analysis description:

Week 28: Model was fitted from Baseline up to Week 52 and the model adjusted Week 28 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5144
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	0.78

Statistical analysis title	Statistical analysis 4
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Statistical analysis description:

Week 52: Model was fitted from Baseline up to Week 52 and the model adjusted Week 52 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.912
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	0.27

Secondary: Change from Baseline in On-Treatment SF-36 HRQoL Scores for Bodily Pain, General Health, Mental Health, Role-Emotional, Role-Physical, Social Functioning at Weeks 8, 12, 28, 52

End point title	Change from Baseline in On-Treatment SF-36 HRQoL Scores for Bodily Pain, General Health, Mental Health, Role-Emotional, Role-Physical, Social Functioning at Weeks 8, 12, 28, 52
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End point description:

The SF-36 acute version 2 is a 36-item generic quality of life instrument designed to measure a participant's level of performance in the following 8 health domains: bodily pain, general health, mental health, role-emotional (role limitations caused by emotional problems), role-physical (role limitations caused by physical problems), social functioning (Social fun), physical functioning (Phy. fun) and vitality. Each domain is scored from 0 (poorer health) to 100 (better health). Each domain score ranges from 0 to 100, higher score indicates a better health state and better functioning. Change from Baseline was calculated as on-treatment visit value minus Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline (Pre-dose on Day 1), Weeks 8, 12, 28 and 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	990 ^[70]	943 ^[71]		
Units: Scores on a scale				
least squares mean (standard error)				
Bodily pain: Week 8, n=982,936	-0.13 (± 0.265)	0.12 (± 0.272)		
Bodily pain: Week 12, n=990,943	0.20 (± 0.267)	-0.39 (± 0.274)		
Bodily pain: Week 28, n=836,819	-0.70 (± 0.297)	-0.74 (± 0.301)		
Bodily pain: Week 52, n=729,707	-1.12 (± 0.313)	-1.39 (± 0.318)		
General health: Week 8, n=982,936	-0.39 (± 0.208)	-0.65 (± 0.213)		
General health: Week 12, n=990,943	-0.59 (± 0.210)	-1.04 (± 0.215)		
General health: Week 28, n=836,819	-1.32 (± 0.232)	-0.99 (± 0.235)		
General health: Week 52, n=729,707	-1.51 (± 0.251)	-1.22 (± 0.255)		
Mental health: Week 8, n=982,936	-0.43 (± 0.238)	-0.47 (± 0.244)		
Mental health: Week 12, n=990,943	-0.86 (± 0.247)	-0.81 (± 0.253)		
Mental health: Week 28, n=836,819	-1.30 (± 0.267)	-1.43 (± 0.270)		

Mental health: Week 52, n=729,707	-1.97 (± 0.296)	-1.16 (± 0.301)		
Role-emotional: Week 8, n=982,936	-0.10 (± 0.310)	-0.02 (± 0.317)		
Role-emotional: Week 12, n=990,943	-0.17 (± 0.311)	-0.53 (± 0.318)		
Role-emotional: Week 28, n=836,819	-0.95 (± 0.335)	-0.90 (± 0.339)		
Role-emotional: Week 52, n=729,707	-0.83 (± 0.358)	-0.92 (± 0.363)		
Role-physical: Week 8, n=982,936	0.40 (± 0.241)	0.32 (± 0.246)		
Role-physical: Week 12, n=990,943	0.48 (± 0.239)	0.08 (± 0.245)		
Role-physical: Week 28, n=836,819	-0.10 (± 0.257)	-0.39 (± 0.260)		
Role-physical: Week 52, n=729,707	-0.21 (± 0.285)	-0.60 (± 0.289)		
Social functioning: Week 8, n=982,936	0.24 (± 0.241)	0.38 (± 0.247)		
Social functioning: Week 12, n=990,943	0.25 (± 0.255)	-0.44 (± 0.261)		
Social functioning: Week 28, n=836,819	-0.61 (± 0.280)	-0.94 (± 0.283)		
Social functioning: Week 52, n=729,707	-1.12 (± 0.315)	-1.14 (± 0.320)		

Notes:

[70] - All Randomized (ITT) Population.

[71] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Bodily pain,Week8: Model was fitted from Baseline up to Week52 and model adjusted Week8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7432
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	0.5

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Bodily pain,Week12: Model was fitted from Baseline up to Week52 and model adjusted Week12 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO

Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0631
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	1.33

Statistical analysis title	Statistical analysis 3
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Statistical analysis description:

Bodily pain,Week28: Model was fitted from Baseline up to Week52 and model adjusted Week28 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4604
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	0.87

Statistical analysis title	Statistical analysis 4
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Statistical analysis description:

Bodily pain,Week52: Model was fitted from Baseline up to Week52 and model adjusted Week52 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2688
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.28

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.15

Statistical analysis title	Statistical analysis 5
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Statistical analysis description:

General health,Week8:Model was fitted from Baseline up to Week52 and model adjusted Week8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1918
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.84

Statistical analysis title	Statistical analysis 6
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Statistical analysis description:

General health,Week12:Model was fitted from Baseline up to Week52 and model adjusted Week12 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0677
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	1.04

Statistical analysis title	Statistical analysis 7
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Statistical analysis description:

General health,Week28:Model was fitted from Baseline up to Week52 and model adjusted Week28 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8386
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	0.32

Statistical analysis title	Statistical analysis 8
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Statistical analysis description:

General health,Week52:Model was fitted from Baseline up to Week52 and model adjusted Week52 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7928
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	0.41

Statistical analysis title	Statistical analysis 9
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Statistical analysis description:

Mental health,Week8:Model was fitted from Baseline up to Week52 and model adjusted Week8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4537
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	0.71

Statistical analysis title	Statistical analysis 10
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Statistical analysis description:

Mental health,Week12:Model was fitted from Baseline up to Week52 and model adjusted Week12 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5548
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	0.65

Statistical analysis title	Statistical analysis 11
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Statistical analysis description:

Mental health,Week28:Model was fitted from Baseline up to Week52 and model adjusted Week28 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3626
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.13

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.88

Statistical analysis title	Statistical analysis 12
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Statistical analysis description:

Mental health,Week52:Model was fitted from Baseline up to Week52 and model adjusted Week52 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9721
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.64
upper limit	0.02

Statistical analysis title	Statistical analysis 13
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Statistical analysis description:

Role-emotional,Week8:Model was fitted from Baseline up to Week52 and model adjusted Week8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5789
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	0.78

Statistical analysis title	Statistical analysis 14
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Statistical analysis description:

Role-emotional,Week12:Model was fitted from Baseline up to Week52 and model adjusted Week12 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2054
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	1.24

Statistical analysis title	Statistical analysis 15
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Statistical analysis description:

Role-emotional,Week28:Model was fitted from Baseline up to Week52 and model adjusted Week28 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5389
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.98
upper limit	0.89

Statistical analysis title	Statistical analysis 16
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Statistical analysis description:

Role-emotional,Week52:Model was fitted from Baseline up to Week52 and model adjusted Week52 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4289
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	1.09

Statistical analysis title	Statistical analysis 17
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Statistical analysis description:

Role-physical,Week8:Model was fitted from Baseline up to Week52 and model adjusted Week8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4096
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.75

Statistical analysis title	Statistical analysis 18
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Statistical analysis description:

Role-physical,Week12:Model was fitted from Baseline up to Week52 and model adjusted Week12 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1196
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	1.07

Statistical analysis title	Statistical analysis 19
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Statistical analysis description:

Role-physical,Week28:Model was fitted from Baseline up to Week52 and model adjusted Week28 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2093
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	1.01

Statistical analysis title	Statistical analysis 20
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Statistical analysis description:

Role-physical,Week52:Model was fitted from Baseline up to Week52 and model adjusted Week52 data has been presented, with factors for treatment, time, dialysis type, region,Baseline value and Baseline value by time and treatment by time interactions

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1674
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	1.19

Statistical analysis title	Statistical analysis 21
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Statistical analysis description:

Social fun, Week 8: Model was fitted from Baseline up to Week52 and model adjusted Week8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6585
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	0.54

Statistical analysis title	Statistical analysis 22
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Statistical analysis description:

Social fun, Week 12: Model was fitted from Baseline up to Week52 and model adjusted Week12 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0293
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	1.4

Statistical analysis title	Statistical analysis 23
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Statistical analysis description:

Social fun, Week 28: Model was fitted from Baseline up to Week52 and model adjusted Week28 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2057
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	1.11

Statistical analysis title	Statistical analysis 24
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Statistical analysis description:

Social fun, Week 52: Model was fitted from Baseline up to Week52 and model adjusted Week52 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4849
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	0.9

Secondary: Change from Baseline in On-Treatment Vitality scores using SF-36 HRQoL Questionnaire at Weeks 8, 12, 28, 52

End point title	Change from Baseline in On-Treatment Vitality scores using SF-36 HRQoL Questionnaire at Weeks 8, 12, 28, 52
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End point description:

The SF-36 acute version 2 is a 36-item generic quality of life instrument designed to measure a participant's level of performance in the following 8 health domains: physical functioning, role-physical (role limitations caused by physical problems), social functioning, bodily pain, mental health, role-emotional (role limitations caused by emotional problems), vitality and general health. Each domain is scored from 0 (poorer health) to 100 (better health). Vitality score ranges from 0 to 100; higher scores represent better health. Change from Baseline was calculated as on-treatment visit value minus Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline (Pre-dose on Day 1), Weeks 8, 12, 28 and 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	990 ^[72]	943 ^[73]		
Units: Scores on a scale				
least squares mean (standard error)				
Week 8, n=982,936	-0.23 (± 0.219)	-0.26 (± 0.224)		
Week 12, n=990,943	-0.17 (± 0.227)	-0.51 (± 0.232)		
Week 28, n=836,819	-0.79 (± 0.242)	-1.03 (± 0.245)		
Week 52, n=729,707	-1.19 (± 0.268)	-1.04 (± 0.272)		

Notes:

[72] - All Randomized (ITT) Population.

[73] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Week 8: Model was fitted from Baseline up to Week 52 and model adjusted Week 8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4621
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.64

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Week 12: Model was fitted from Baseline up to Week 52 and model adjusted Week 12 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO

Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1439
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.98

Statistical analysis title	Statistical analysis 3
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Statistical analysis description:

Week 28: Model was fitted from Baseline up to Week 52 and model adjusted Week 28 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2392
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	0.92

Statistical analysis title	Statistical analysis 4
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Statistical analysis description:

Week 52: Model was fitted from Baseline up to Week 52 and model adjusted Week 52 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6545
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.6

Secondary: Change from Baseline in On-Treatment Physical Functioning domain scores using SF-36 HRQoL Questionnaire at Weeks 8, 12, 28, 52

End point title	Change from Baseline in On-Treatment Physical Functioning domain scores using SF-36 HRQoL Questionnaire at Weeks 8, 12, 28, 52
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End point description:

The SF-36 acute version 2 is a 36-item generic quality of life instrument designed to measure a participant's level of performance in the following 8 health domains: physical functioning, role-physical (role limitations caused by physical problems), social functioning, bodily pain, mental health, role-emotional (role limitations caused by emotional problems), vitality and general health. Each domain is scored from 0 (poorer health) to 100 (better health). Physical functioning score ranges from 0 to 100; higher scores represent better health. Change from Baseline was calculated as on-treatment visit value minus (-) Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).

End point type	Secondary
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End point timeframe:

Baseline (Pre-dose on Day 1), Weeks 8, 12, 28 and 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	990 ^[74]	943 ^[75]		
Units: Scores on a scale				
least squares mean (standard error)				
Week 8, n=982,936	0.48 (± 0.237)	-0.16 (± 0.243)		
Week 12, n=990,943	0.11 (± 0.240)	-0.45 (± 0.246)		
Week 28, n=836,819	-0.20 (± 0.273)	-0.97 (± 0.277)		
Week 52, n=729,707	-0.61 (± 0.291)	-1.19 (± 0.296)		

Notes:

[74] - All Randomized (ITT) Population.

[75] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Week 8: Model was fitted from Baseline up to Week 52 and model adjusted Week 8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
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Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	1.31

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

Week 12: Model was fitted from Baseline up to Week 52 and model adjusted Week 12 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0509
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	1.24

Statistical analysis title	Statistical analysis 3
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Statistical analysis description:

Week 28: Model was fitted from Baseline up to Week 52 and model adjusted Week 28 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0237
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.77

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	1.53

Statistical analysis title	Statistical analysis 4
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Statistical analysis description:

Week 52: Model was fitted from Baseline up to Week 52 and model adjusted Week 52 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	1933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0828
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	1.39

Secondary: Change from Baseline in On-Treatment Health Utility EuroQol 5 Dimensions 5 Level (EQ-5D-5L) Questionnaire Score at Week 52

End point title	Change from Baseline in On-Treatment Health Utility EuroQol 5 Dimensions 5 Level (EQ-5D-5L) Questionnaire Score at Week 52
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End point description:

EQ-5D-5L is self-assessment questionnaire, consisting of 5 items covering 5 dimensions (mobility, self care, usual activities, pain/discomfort and anxiety/depression). Each dimension is measured by 5-point Likert scale (1=no problems, 2=slight problems, 3=moderate problems, 4=severe problems and 5=extreme problems). Responses for 5 dimensions together formed a 5-figure description of health state (e.g. 11111 indicates no problems in all 5 dimensions). Each of these 5 figure health states were converted to a single index score by applying country-specific value set formula that attaches weights to dimensions and levels. Range for EQ-5D-5L index score is -0.594 (worst health) to 1 (full health state). Change from Baseline was calculated as on-treatment visit value-Baseline value. Baseline was latest non-missing pre-dose assessment on or before randomization date. Only those participants with data available at the indicated time points were analyzed.

End point type	Secondary
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End point timeframe:

Baseline (Pre-dose on Day 1) and Week 52

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333 ^[76]	329 ^[77]		
Units: Scores on a scale				
least squares mean (standard error)	-0.0198 (± 0.01179)	-0.0201 (± 0.01187)		

Notes:

[76] - All Randomized (ITT) Population.

[77] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
MMRM model was fitted from Baseline up to Week 52 with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	662
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4939
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	0.0003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0326
upper limit	0.0331

Secondary: Change from Baseline in On-Treatment EuroQol Visual Analogue Scale (EQ-VAS) at Week 52

End point title	Change from Baseline in On-Treatment EuroQol Visual Analogue Scale (EQ-VAS) at Week 52
End point description:	
The EQ VAS records the respondent's self-rated health on a vertical VAS, ranging from 0 to 100, where 0 represents the worst health one can imagine and 100 represents the best health one can imagine. Change from Baseline was calculated as on-treatment visit value minus Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date. Only those participants with data available at the indicated time points were analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Pre-dose on Day 1) and Week 52	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333 ^[78]	329 ^[79]		
Units: Scores on a scale				
least squares mean (standard error)	-1.0 (± 0.86)	0.8 (± 0.87)		

Notes:

[78] - All Randomized (ITT) Population.

[79] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
MMRM model was fitted from Baseline up to Week 52 with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	662
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9292
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	0.6

Secondary: Change from Baseline in On-Treatment Patient Global Impression of Severity (PGI-S) at Weeks 8, 12, 28, 52

End point title	Change from Baseline in On-Treatment Patient Global Impression of Severity (PGI-S) at Weeks 8, 12, 28, 52
End point description:	
The PGI-S is a 1-item questionnaire designed to assess participant's impression of disease severity on a 5-point disease severity scale (0=absent, 1=mild, 2=moderate, 3=severe, or 4=very severe). A higher score indicated worse outcome. Change from Baseline was calculated as on-treatment visit value minus Baseline value. Baseline was defined as the latest non-missing pre-dose assessment on or before the randomization date. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).	
End point type	Secondary
End point timeframe:	
Baseline (Pre-dose on Day 1), Weeks 8, 12, 28 and 52	

End point values	Daprodustat	rhEPO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1102 ^[80]	1073 ^[81]		
Units: Scores on a scale				
least squares mean (standard error)				
Week 8, n=1102,1064	-0.03 (± 0.024)	0.02 (± 0.025)		
Week 12, n=1102,1073	0.02 (± 0.025)	0.06 (± 0.025)		
Week 28, n=934,933	0.04 (± 0.027)	0.08 (± 0.027)		
Week 52, n=826,814	0.06 (± 0.029)	0.11 (± 0.030)		

Notes:

[80] - All Randomized (ITT) Population.

[81] - All Randomized (ITT) Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Week 8: Model was fitted from Baseline up to Week 52 and model adjusted Week 8 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0428
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.01

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Week 12: Model was fitted from Baseline up to Week 52 and model adjusted Week 12 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.	
Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1155
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.03

Statistical analysis title	Statistical analysis 3
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Statistical analysis description:

Week 28: Model was fitted from Baseline up to Week 52 and model adjusted Week 28 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1426
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.03

Statistical analysis title	Statistical analysis 4
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Statistical analysis description:

Week 52: Model was fitted from Baseline up to Week 52 and model adjusted Week 52 data has been presented, with factors for treatment, time, dialysis type, region, Baseline value and Baseline value by time and treatment by time interactions.

Comparison groups	Daprodustat v rhEPO
Number of subjects included in analysis	2175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1152
Method	MMRM
Parameter estimate	LS mean difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.03

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality, treatment emergent serious adverse events (TESAEs) and non-serious treatment emergent adverse events (TEAEs) were collected up to 3.9 person-years for CV follow-up time period

Adverse event reporting additional description:

All-cause mortality used All Randomized (ITT) Population, which comprised of all randomized participants and treatment to which the participant was randomized. TESAEs and non-serious TEAEs used the Safety Population, which included all randomized participants who received at least 1 dose of randomized treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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Reporting groups

Reporting group title	rhEPO
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Reporting group description:

Participants received placebo tablets orally once daily in run-in period from Week -4 up to randomization (Day 1) and subsequently received treatment with rhEPO. Participants on hemodialysis received epoetin alfa as intravenous (IV) injection once weekly or three-times weekly with total weekly dose levels ranging from 1500 to 60,000 Units. Participants on peritoneal dialysis received subcutaneous (SC) injection of darbepoetin alfa every 1, 2, or 4 weeks with 4-weekly total dose levels ranging from 20 to 400 microgram (mcg). Darbepoetin could be given by IV injection for peritoneal dialysis participants switching to hemodialysis. Study treatment was dose-titrated to achieve and maintain hemoglobin in the target range (10 to 11 g/dL) and administered until the required number of MACE events occurred, at approximately 45.1 months of randomized treatment.

Reporting group title	Daprodustat
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Reporting group description:

Participants received placebo tablets orally once daily in run-in period from Week -4 up to randomization (Day 1) and subsequently received daprodustat tablets at dose levels of 1, 2, 4, 6, 8, 10, 12, 16 and 24 milligrams (mg) orally once daily until the required number of major adverse cardiovascular event (MACE) occurred, at approximately 45.1 months of randomized treatment. Study treatment was dose-titrated to achieve and maintain hemoglobin in the target range (10 to 11 grams per deciliter [g/dL]).

Serious adverse events	rhEPO	Daprodustat	
Total subjects affected by serious adverse events			
subjects affected / exposed	748 / 1474 (50.75%)	773 / 1482 (52.16%)	
number of deaths (all causes)	300	294	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal cancer			
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			

subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder cancer		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Hepatic cancer		
subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0
Parathyroid tumour benign		
subjects affected / exposed	0 / 1474 (0.00%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Renal neoplasm		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Breast cancer		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Colon adenoma		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Papillary renal cell carcinoma		

subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Papillary thyroid cancer		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Plasma cell myeloma		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cell carcinoma		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Squamous cell carcinoma of skin		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Transitional cell carcinoma		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Thyroid adenoma		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Uterine leiomyoma		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Acute myeloid leukaemia		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Adenocarcinoma gastric		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Adrenal adenoma		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
B-cell type acute leukaemia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Benign neoplasm of ampulla of Vater		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Benign renal neoplasm		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bile duct cancer		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Bladder cancer stage 0, with cancer in situ		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder papilloma		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder transitional cell carcinoma		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Bone neoplasm		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Breast cancer stage II		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Carcinoid tumour pulmonary		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Carcinoma in situ of eye		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac valve fibroelastoma		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer metastatic		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Endometrial adenocarcinoma		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
External ear neoplasm malignant		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Inflammatory pseudotumour		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lung cancer metastatic		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Lung adenocarcinoma		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Malignant melanoma		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Meningioma		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Metastases to lung		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Metastases to bone		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ovarian cancer		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ovarian cancer metastatic		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Pancreatic carcinoma		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Papilloma		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Prostate cancer		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Prostate cancer metastatic		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal adenocarcinoma		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Refractory cytopenia with unilineage dysplasia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cell carcinoma stage I		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Salivary gland cancer		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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 lung		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Urinary tract neoplasm		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ureteric cancer regional		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 1474 (0.75%)	16 / 1482 (1.08%)	
occurrences causally related to treatment / all	0 / 14	1 / 18	
deaths causally related to treatment / all	0 / 0	1 / 1	
Hypotension			
subjects affected / exposed	19 / 1474 (1.29%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 19	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	7 / 1474 (0.47%)	12 / 1482 (0.81%)	
occurrences causally related to treatment / all	0 / 7	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypertensive urgency			
subjects affected / exposed	8 / 1474 (0.54%)	6 / 1482 (0.40%)	
occurrences causally related to treatment / all	2 / 10	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	6 / 1474 (0.41%)	6 / 1482 (0.40%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dialysis hypotension			
subjects affected / exposed	5 / 1474 (0.34%)	6 / 1482 (0.40%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	8 / 1474 (0.54%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			

subjects affected / exposed	7 / 1474 (0.47%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 9	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0
Haematoma		
subjects affected / exposed	5 / 1474 (0.34%)	5 / 1482 (0.34%)
occurrences causally related to treatment / all	0 / 6	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Aortic stenosis		
subjects affected / exposed	7 / 1474 (0.47%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 9	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0
Hypertensive crisis		
subjects affected / exposed	4 / 1474 (0.27%)	5 / 1482 (0.34%)
occurrences causally related to treatment / all	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Orthostatic hypotension		
subjects affected / exposed	3 / 1474 (0.20%)	5 / 1482 (0.34%)
occurrences causally related to treatment / all	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Accelerated hypertension		
subjects affected / exposed	5 / 1474 (0.34%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Brachiocephalic vein stenosis		
subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Peripheral vascular disorder		
subjects affected / exposed	1 / 1474 (0.07%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Subclavian vein stenosis		

subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0
Deep vein thrombosis		
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Dry gangrene		
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Hypovolaemic shock		
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Haemorrhage		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Peripheral artery occlusion		
subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Shock haemorrhagic		
subjects affected / exposed	0 / 1474 (0.00%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1
Steal syndrome		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Arterial haemorrhage		

subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Jugular vein thrombosis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Vena cava thrombosis		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Venous stenosis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Venous thrombosis limb		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Aortic dissection		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Arterial disorder		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Arterial occlusive disease		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetic microangiopathy		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetic vascular disorder		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Granulomatosis with polyangiitis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ischaemic limb pain		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Peripheral artery thrombosis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Peripheral vein occlusion		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Peripheral artery stenosis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Shock		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subclavian vein thrombosis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava occlusion			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Non-cardiac chest pain			
subjects affected / exposed	16 / 1474 (1.09%)	10 / 1482 (0.67%)	
occurrences causally related to treatment / all	0 / 23	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	8 / 1474 (0.54%)	7 / 1482 (0.47%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthenia			
subjects affected / exposed	6 / 1474 (0.41%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Death			
subjects affected / exposed	2 / 1474 (0.14%)	9 / 1482 (0.61%)	
occurrences causally related to treatment / all	0 / 2	0 / 9	
deaths causally related to treatment / all	0 / 2	0 / 9	
Chest pain			
subjects affected / exposed	5 / 1474 (0.34%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	4 / 1474 (0.27%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Sudden cardiac death			
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Fatigue			

subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Impaired healing		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Catheter site haemorrhage		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Complication associated with device		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Device related thrombosis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Generalised oedema		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
General physical health deterioration		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (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 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1
Peripheral swelling		

subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent stenosis			
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site oedema			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site thrombosis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug withdrawal syndrome			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Serositis			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling face			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcer haemorrhage			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcer			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent thrombosis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amyloidosis			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney transplant rejection			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal transplant failure			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Loss of personal independence in daily activities			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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			
Prostatitis			
subjects affected / exposed	2 / 1474 (0.14%)	4 / 1482 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometriosis			
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Menorrhagia			
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acquired hydrocele			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenomyosis			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian disorder			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal oedema			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular infarction			

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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 respiratory failure			
subjects affected / exposed	13 / 1474 (0.88%)	14 / 1482 (0.94%)	
occurrences causally related to treatment / all	0 / 14	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary oedema			
subjects affected / exposed	15 / 1474 (1.02%)	11 / 1482 (0.74%)	
occurrences causally related to treatment / all	0 / 17	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	15 / 1474 (1.02%)	10 / 1482 (0.67%)	
occurrences causally related to treatment / all	0 / 16	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dyspnoea			
subjects affected / exposed	12 / 1474 (0.81%)	13 / 1482 (0.88%)	
occurrences causally related to treatment / all	0 / 12	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pleural effusion			
subjects affected / exposed	11 / 1474 (0.75%)	13 / 1482 (0.88%)	
occurrences causally related to treatment / all	0 / 11	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	9 / 1474 (0.61%)	11 / 1482 (0.74%)	
occurrences causally related to treatment / all	0 / 10	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	10 / 1474 (0.68%)	10 / 1482 (0.67%)
occurrences causally related to treatment / all	0 / 10	0 / 10
deaths causally related to treatment / all	0 / 6	0 / 3
Pulmonary embolism		
subjects affected / exposed	9 / 1474 (0.61%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	3 / 9	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0
Epistaxis		
subjects affected / exposed	4 / 1474 (0.27%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia aspiration		
subjects affected / exposed	2 / 1474 (0.14%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Interstitial lung disease		
subjects affected / exposed	3 / 1474 (0.20%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Asthma		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	1 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary hypertension		
subjects affected / exposed	4 / 1474 (0.27%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pleuritic pain		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary congestion		

subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Dyspnoea exertional		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Haemoptysis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypoxia		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Obstructive airways disorder		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Respiratory distress		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Apnoea		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Aspiration		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dysphonia		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Haemothorax		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hydrothorax		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pleurisy		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonitis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumothorax		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary thrombosis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary arterial hypertension		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Respiratory acidosis		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory arrest			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 1474 (0.07%)	4 / 1482 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	3 / 1474 (0.20%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic attack			
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adjustment disorder with mixed disturbance of emotion and conduct			

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Anorexia nervosa		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bipolar disorder		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Delirium		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Disorientation		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hallucination, visual		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Major depression		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Psychotic disorder		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Suicidal ideation		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device malfunction			
subjects affected / exposed	11 / 1474 (0.75%)	7 / 1482 (0.47%)	
occurrences causally related to treatment / all	0 / 11	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis in device			
subjects affected / exposed	4 / 1474 (0.27%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	1 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	3 / 1474 (0.20%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device expulsion			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device kink			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device leakage			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	7 / 1474 (0.47%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	3 / 1474 (0.20%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	1 / 1474 (0.07%)	4 / 1482 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bile duct stone			
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			

subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic ischaemia		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bile duct stenosis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Biliary dyskinesia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gallbladder polyp		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gallbladder rupture		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic failure		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Hepatic mass		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hydrocholecystis		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Transaminases increased			
subjects affected / exposed	4 / 1474 (0.27%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			

subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Anticoagulation drug level below therapeutic		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Aspartate aminotransferase increased		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Blood pressure decreased		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Blood urine present		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
C-reactive protein increased		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Electrocardiogram T wave inversion		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic enzyme increased		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Oxygen saturation decreased		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus test positive			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcus test positive			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin I increased			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin T increased			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Arteriovenous fistula thrombosis			
subjects affected / exposed	57 / 1474 (3.87%)	36 / 1482 (2.43%)	
occurrences causally related to treatment / all	11 / 74	4 / 43	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site haemorrhage			
subjects affected / exposed	12 / 1474 (0.81%)	12 / 1482 (0.81%)	
occurrences causally related to treatment / all	0 / 12	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous graft thrombosis			
subjects affected / exposed	15 / 1474 (1.02%)	7 / 1482 (0.47%)	
occurrences causally related to treatment / all	0 / 25	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fall			
subjects affected / exposed	7 / 1474 (0.47%)	14 / 1482 (0.94%)	
occurrences causally related to treatment / all	0 / 7	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site complication			
subjects affected / exposed	8 / 1474 (0.54%)	9 / 1482 (0.61%)	
occurrences causally related to treatment / all	0 / 10	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	5 / 1474 (0.34%)	8 / 1482 (0.54%)	
occurrences causally related to treatment / all	0 / 5	0 / 9	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular access site thrombosis			
subjects affected / exposed	5 / 1474 (0.34%)	7 / 1482 (0.47%)	
occurrences causally related to treatment / all	0 / 7	4 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula aneurysm			
subjects affected / exposed	5 / 1474 (0.34%)	6 / 1482 (0.40%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access malfunction			
subjects affected / exposed	5 / 1474 (0.34%)	6 / 1482 (0.40%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula occlusion			
subjects affected / exposed	5 / 1474 (0.34%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	5 / 1474 (0.34%)	4 / 1482 (0.27%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	4 / 1474 (0.27%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	5 / 1474 (0.34%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 5	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	2 / 1474 (0.14%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula site pseudoaneurysm			
subjects affected / exposed	5 / 1474 (0.34%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 1474 (0.07%)	6 / 1482 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	4 / 1474 (0.27%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriovenous graft site stenosis			
subjects affected / exposed	2 / 1474 (0.14%)	4 / 1482 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	6 / 1474 (0.41%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			

subjects affected / exposed	1 / 1474 (0.07%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Rib fracture		
subjects affected / exposed	4 / 1474 (0.27%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tibia fracture		
subjects affected / exposed	1 / 1474 (0.07%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular access complication		
subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1
Arteriovenous graft site haemorrhage		
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Foot fracture		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Peritoneal dialysis complication		
subjects affected / exposed	3 / 1474 (0.20%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Shunt thrombosis		
subjects affected / exposed	3 / 1474 (0.20%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Thermal burn		

subjects affected / exposed	3 / 1474 (0.20%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Acetabulum fracture		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Clavicle fracture		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Contusion		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Dialysis related complication		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Hand fracture		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Limb injury		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Patella fracture		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural haematoma		

subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Procedural haemorrhage		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Shunt blood flow excessive		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Spinal compression fracture		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Toxicity to various agents		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular access steal syndrome		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Arteriovenous fistula site haematoma		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Facial bones fracture		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Graft thrombosis		

subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Humerus fracture		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Joint dislocation		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Joint injury		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Lower limb fracture		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Poisoning		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Postoperative wound complication		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Radius fracture		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular access site haemorrhage		

subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular graft occlusion		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular pseudoaneurysm		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular pseudoaneurysm ruptured		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Anaemia postoperative		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Aortic pseudoaneurysm		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Arteriovenous graft aneurysm		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Bronchial injury		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Burns second degree		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cervical vertebral fracture		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Delayed recovery from anaesthesia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Delayed graft function		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Fractured sacrum		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Foreign body in gastrointestinal tract		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Graft loss		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Implantation complication		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Keratorhexis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lumbar vertebral fracture		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Meniscus injury		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Muscle rupture		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Multiple injuries		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Multiple fractures		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Periorbital haematoma		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural hypotension		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural inflammation		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural swelling		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural urine leak		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Postoperative hypertension		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Procedural pain		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Restenosis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Road traffic accident		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Shunt aneurysm		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Skeletal injury		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Skin laceration		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Skull fracture		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Spinal fracture		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Spinal cord injury		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sternal fracture		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Subdural haemorrhage		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Tendon injury		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Thoracic vertebral fracture		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Traumatic fracture		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular access site swelling		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular graft complication		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular graft thrombosis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular pseudoaneurysm thrombosis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Vena cava injury		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound necrosis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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			
Atrial septal defect			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital cystic kidney disease			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Protein C deficiency			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	31 / 1474 (2.10%)	30 / 1482 (2.02%)	
occurrences causally related to treatment / all	3 / 40	4 / 33	
deaths causally related to treatment / all	0 / 1	0 / 1	
Atrial fibrillation			
subjects affected / exposed	35 / 1474 (2.37%)	23 / 1482 (1.55%)	
occurrences causally related to treatment / all	0 / 44	1 / 26	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac arrest			
subjects affected / exposed	15 / 1474 (1.02%)	20 / 1482 (1.35%)	
occurrences causally related to treatment / all	0 / 15	1 / 20	
deaths causally related to treatment / all	0 / 8	1 / 18	

Angina pectoris			
subjects affected / exposed	16 / 1474 (1.09%)	18 / 1482 (1.21%)	
occurrences causally related to treatment / all	1 / 18	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	15 / 1474 (1.02%)	18 / 1482 (1.21%)	
occurrences causally related to treatment / all	0 / 15	1 / 23	
deaths causally related to treatment / all	0 / 1	0 / 4	
Cardiac failure congestive			
subjects affected / exposed	15 / 1474 (1.02%)	18 / 1482 (1.21%)	
occurrences causally related to treatment / all	1 / 19	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	17 / 1474 (1.15%)	11 / 1482 (0.74%)	
occurrences causally related to treatment / all	1 / 17	2 / 11	
deaths causally related to treatment / all	1 / 4	0 / 2	
Angina unstable			
subjects affected / exposed	13 / 1474 (0.88%)	14 / 1482 (0.94%)	
occurrences causally related to treatment / all	1 / 15	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	16 / 1474 (1.09%)	10 / 1482 (0.67%)	
occurrences causally related to treatment / all	1 / 16	2 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	10 / 1474 (0.68%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 10	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	5 / 1474 (0.34%)	8 / 1482 (0.54%)	
occurrences causally related to treatment / all	0 / 5	1 / 8	
deaths causally related to treatment / all	0 / 2	1 / 6	
Bradycardia			

subjects affected / exposed	8 / 1474 (0.54%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 8	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Acute left ventricular failure		
subjects affected / exposed	5 / 1474 (0.34%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	1 / 6	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Atrial flutter		
subjects affected / exposed	5 / 1474 (0.34%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac failure acute		
subjects affected / exposed	1 / 1474 (0.07%)	8 / 1482 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 1
Aortic valve stenosis		
subjects affected / exposed	5 / 1474 (0.34%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pericardial effusion		
subjects affected / exposed	4 / 1474 (0.27%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Atrioventricular block complete		
subjects affected / exposed	4 / 1474 (0.27%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Mitral valve incompetence		
subjects affected / exposed	2 / 1474 (0.14%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	1 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Myocardial ischaemia		

subjects affected / exposed	2 / 1474 (0.14%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1
Pericarditis		
subjects affected / exposed	3 / 1474 (0.20%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac tamponade		
subjects affected / exposed	3 / 1474 (0.20%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Congestive cardiomyopathy		
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Right ventricular failure		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Sinus bradycardia		
subjects affected / exposed	3 / 1474 (0.20%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Supraventricular tachycardia		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Ventricular tachycardia		
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Atrioventricular block		

subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiogenic shock		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Cardiomyopathy		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Coronary artery stenosis		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Sinus node dysfunction		
subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Coronary artery occlusion		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ischaemic cardiomyopathy		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Nodal arrhythmia		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pericarditis uraemic		

subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
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 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Stress cardiomyopathy		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (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 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ventricular fibrillation		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Aortic valve incompetence		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Atrial thrombosis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Atrial tachycardia		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Atrioventricular block second degree		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac discomfort		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiomegaly		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Chronic left ventricular failure		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Endocarditis noninfective		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Left ventricular dysfunction		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Left ventricular failure		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Mitral valve calcification		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Myocarditis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Nodal rhythm		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Palpitations		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pericardial haemorrhage		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Sinus tachycardia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Subendocardial ischaemia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ventricular arrhythmia		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	11 / 1474 (0.75%)	11 / 1482 (0.74%)	
occurrences causally related to treatment / all	1 / 11	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	11 / 1474 (0.75%)	9 / 1482 (0.61%)	
occurrences causally related to treatment / all	2 / 13	1 / 11	
deaths causally related to treatment / all	0 / 5	0 / 3	
Syncope			
subjects affected / exposed	13 / 1474 (0.88%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 13	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	10 / 1474 (0.68%)	7 / 1482 (0.47%)	
occurrences causally related to treatment / all	0 / 12	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	9 / 1474 (0.61%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 10	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	5 / 1474 (0.34%)	4 / 1482 (0.27%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	4 / 1474 (0.27%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			

subjects affected / exposed	3 / 1474 (0.20%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0
Hypertensive encephalopathy		
subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Carotid artery stenosis		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Cerebral haemorrhage		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 2
Carpal tunnel syndrome		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dizziness		
subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Facial paralysis		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Sciatica		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Toxic encephalopathy		

subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Epilepsy		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Generalised tonic-clonic seizure		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Haemorrhagic stroke		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2
Headache		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic encephalopathy		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Hypocalcaemic seizure		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Nervous system disorder		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Thalamus haemorrhage		

subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uraemic encephalopathy			
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Altered state of consciousness			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem infarction			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem ischaemia			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cerebral artery stenosis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cerebral circulatory failure		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cognitive disorder		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Coma		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Dysarthria		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dyskinesia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Embolic stroke		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Focal dyscognitive seizures		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Haemorrhage intracranial		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
IIIrd nerve paralysis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Intraventricular haemorrhage		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Intracranial aneurysm		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Loss of consciousness		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lumbar radiculopathy		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Myelopathy		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Neuropathy peripheral		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Neurotoxicity		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pachymeningitis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Paraesthesia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Parkinson's disease		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Partial seizures		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Post herpetic neuralgia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Polyneuropathy		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Postictal state		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure cluster			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
VIth nerve paralysis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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	41 / 1474 (2.78%)	26 / 1482 (1.75%)	
occurrences causally related to treatment / all	3 / 52	0 / 29	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood loss anaemia			
subjects affected / exposed	3 / 1474 (0.20%)	4 / 1482 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			

subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pancytopenia		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Aplastic anaemia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Coagulopathy		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cytopenia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Leukocytosis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Leukopenia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lymphadenopathy		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Non-immune heparin associated thrombocytopenia		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normocytic anaemia			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness bilateral			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness unilateral			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoacusis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inner ear disorder			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	5 / 1474 (0.34%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			

subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract nuclear			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye pain			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye haemorrhage			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid ptosis			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Macular fibrosis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ophthalmoplegia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Retinopathy		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Retinal detachment		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Retinal artery embolism		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sympathetic ophthalmia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Tolosa-Hunt syndrome		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ulcerative keratitis		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	11 / 1474 (0.75%)	12 / 1482 (0.81%)	
occurrences causally related to treatment / all	0 / 12	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	7 / 1474 (0.47%)	6 / 1482 (0.40%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	4 / 1474 (0.27%)	4 / 1482 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	5 / 1474 (0.34%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 1474 (0.07%)	7 / 1482 (0.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	6 / 1474 (0.41%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	4 / 1474 (0.27%)	4 / 1482 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	2 / 1474 (0.14%)	5 / 1482 (0.34%)
occurrences causally related to treatment / all	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Duodenal ulcer		
subjects affected / exposed	4 / 1474 (0.27%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Inguinal hernia		
subjects affected / exposed	3 / 1474 (0.20%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Colitis		
subjects affected / exposed	3 / 1474 (0.20%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Colitis ischaemic		
subjects affected / exposed	4 / 1474 (0.27%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Gastritis		
subjects affected / exposed	3 / 1474 (0.20%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroesophageal reflux disease		
subjects affected / exposed	5 / 1474 (0.34%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Chronic gastritis		
subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Constipation		

subjects affected / exposed	4 / 1474 (0.27%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Haemorrhoids		
subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Intestinal ischaemia		
subjects affected / exposed	3 / 1474 (0.20%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0
Small intestinal obstruction		
subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Umbilical hernia		
subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetic gastroparesis		
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Duodenal ulcer haemorrhage		
subjects affected / exposed	0 / 1474 (0.00%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1
Gastric ulcer haemorrhage		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Lower gastrointestinal haemorrhage		

subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	0 / 1474 (0.00%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			

subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Vomiting		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Abdominal adhesions		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Abdominal hernia		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Abdominal pain upper		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dieulafoy's vascular malformation		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Diverticulum intestinal		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Faecaloma		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric polyps		

subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroduodenal ulcer		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal angiectasia		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal polyp haemorrhage		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal vascular malformation haemorrhagic		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Haematochezia		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ileus		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Obstructive pancreatitis		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophageal ulcer haemorrhage		

subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophagitis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumoperitoneum		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Retroperitoneal haemorrhage		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Abdominal wall haemorrhage		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Alcoholic pancreatitis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Anal inflammation		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Anal fissure		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Crohn's disease		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Discoloured vomit		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Duodenal ulcer perforation		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Duodenitis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Dysphagia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Epiplonic appendagitis		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Enterocolitis haemorrhagic		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Erosive oesophagitis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric dysplasia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric disorder		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric mucosa erythema		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric perforation		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal erosion		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal obstruction		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gingival bleeding		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Haemorrhagic necrotic pancreatitis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Haemoperitoneum		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hiatus hernia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ileus paralytic		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Incarcerated umbilical hernia		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Intestinal perforation		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Intussusception		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Irritable bowel syndrome		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Large intestine polyp		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Large intestinal haemorrhage		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lumbar hernia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Mallory-Weiss syndrome		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Mechanical ileus		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophageal perforation		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophageal motility disorder		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophageal ulcer		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophagitis ulcerative		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal ulcer		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Retroperitoneal haematoma		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Small intestinal perforation		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcerative gastritis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	3 / 1474 (0.20%)	8 / 1482 (0.54%)	
occurrences causally related to treatment / all	0 / 3	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 1474 (0.07%)	7 / 1482 (0.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	3 / 1474 (0.20%)	3 / 1482 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blister			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic wound			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkeratosis			

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic skin ulcer			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin weeping			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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			
Chronic kidney disease			
subjects affected / exposed	5 / 1474 (0.34%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Azotaemia			
subjects affected / exposed	4 / 1474 (0.27%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			
subjects affected / exposed	1 / 1474 (0.07%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 3	
Haematuria			
subjects affected / exposed	4 / 1474 (0.27%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			

subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cystitis haemorrhagic		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hydronephrosis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lupus nephritis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Renal artery thrombosis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Renal disorder		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cyst ruptured		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cyst haemorrhage		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Renal failure		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Stag horn calculus			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcapsular renal haematoma			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract disorder			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperparathyroidism secondary			
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal insufficiency			
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperparathyroidism tertiary			

subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Secondary adrenocortical insufficiency			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	6 / 1474 (0.41%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	6 / 1474 (0.41%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	4 / 1474 (0.27%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Costochondritis			

subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Haematoma muscle		
subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hungry bone syndrome		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Osteonecrosis		
subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pathological fracture		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Spinal stenosis		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cervical spinal stenosis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (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	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Intervertebral disc protrusion		

subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Arthritis reactive		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Chondropathy		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Chest wall haematoma		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Compartment syndrome		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
High turnover osteopathy		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lumbar spinal stenosis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Muscular weakness		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Myalgia		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Musculoskeletal pain		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Myositis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Neuropathic arthropathy		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Osteitis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Osteoporosis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sacroiliitis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Rhabdomyolysis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Rheumatoid arthritis		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon disorder			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	81 / 1474 (5.50%)	86 / 1482 (5.80%)	
occurrences causally related to treatment / all	0 / 96	1 / 97	
deaths causally related to treatment / all	0 / 2	0 / 4	
Sepsis			

subjects affected / exposed	37 / 1474 (2.51%)	29 / 1482 (1.96%)
occurrences causally related to treatment / all	0 / 37	0 / 31
deaths causally related to treatment / all	0 / 4	0 / 11
Peritonitis		
subjects affected / exposed	24 / 1474 (1.63%)	31 / 1482 (2.09%)
occurrences causally related to treatment / all	0 / 34	0 / 42
deaths causally related to treatment / all	0 / 1	0 / 2
COVID-19		
subjects affected / exposed	22 / 1474 (1.49%)	22 / 1482 (1.48%)
occurrences causally related to treatment / all	0 / 22	0 / 22
deaths causally related to treatment / all	0 / 3	0 / 5
Cellulitis		
subjects affected / exposed	21 / 1474 (1.42%)	16 / 1482 (1.08%)
occurrences causally related to treatment / all	0 / 26	0 / 18
deaths causally related to treatment / all	0 / 0	0 / 0
Gangrene		
subjects affected / exposed	19 / 1474 (1.29%)	15 / 1482 (1.01%)
occurrences causally related to treatment / all	0 / 28	0 / 19
deaths causally related to treatment / all	0 / 0	0 / 1
Osteomyelitis		
subjects affected / exposed	13 / 1474 (0.88%)	15 / 1482 (1.01%)
occurrences causally related to treatment / all	0 / 16	0 / 18
deaths causally related to treatment / all	0 / 0	0 / 0
Septic shock		
subjects affected / exposed	16 / 1474 (1.09%)	8 / 1482 (0.54%)
occurrences causally related to treatment / all	0 / 17	0 / 9
deaths causally related to treatment / all	0 / 5	0 / 3
Urinary tract infection		
subjects affected / exposed	11 / 1474 (0.75%)	13 / 1482 (0.88%)
occurrences causally related to treatment / all	0 / 16	0 / 14
deaths causally related to treatment / all	0 / 0	0 / 0
Device related infection		

subjects affected / exposed	9 / 1474 (0.61%)	13 / 1482 (0.88%)
occurrences causally related to treatment / all	0 / 10	0 / 14
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis		
subjects affected / exposed	13 / 1474 (0.88%)	9 / 1482 (0.61%)
occurrences causally related to treatment / all	0 / 15	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
Lower respiratory tract infection		
subjects affected / exposed	11 / 1474 (0.75%)	9 / 1482 (0.61%)
occurrences causally related to treatment / all	0 / 11	0 / 10
deaths causally related to treatment / all	0 / 1	0 / 0
Staphylococcal sepsis		
subjects affected / exposed	10 / 1474 (0.68%)	10 / 1482 (0.67%)
occurrences causally related to treatment / all	0 / 10	0 / 10
deaths causally related to treatment / all	0 / 1	0 / 0
Influenza		
subjects affected / exposed	11 / 1474 (0.75%)	8 / 1482 (0.54%)
occurrences causally related to treatment / all	0 / 11	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0
Arteriovenous fistula site infection		
subjects affected / exposed	6 / 1474 (0.41%)	12 / 1482 (0.81%)
occurrences causally related to treatment / all	0 / 6	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 0
Bronchitis		
subjects affected / exposed	7 / 1474 (0.47%)	8 / 1482 (0.54%)
occurrences causally related to treatment / all	0 / 8	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0
Staphylococcal bacteraemia		
subjects affected / exposed	7 / 1474 (0.47%)	8 / 1482 (0.54%)
occurrences causally related to treatment / all	0 / 9	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
Peritonitis bacterial		

subjects affected / exposed	8 / 1474 (0.54%)	6 / 1482 (0.40%)
occurrences causally related to treatment / all	0 / 14	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0
Device related sepsis		
subjects affected / exposed	6 / 1474 (0.41%)	7 / 1482 (0.47%)
occurrences causally related to treatment / all	0 / 7	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetic foot infection		
subjects affected / exposed	6 / 1474 (0.41%)	7 / 1482 (0.47%)
occurrences causally related to treatment / all	0 / 6	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0
Upper respiratory tract infection		
subjects affected / exposed	8 / 1474 (0.54%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 9	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Urosepsis		
subjects affected / exposed	5 / 1474 (0.34%)	7 / 1482 (0.47%)
occurrences causally related to treatment / all	0 / 5	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 1
Bacteraemia		
subjects affected / exposed	7 / 1474 (0.47%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Staphylococcal infection		
subjects affected / exposed	3 / 1474 (0.20%)	8 / 1482 (0.54%)
occurrences causally related to treatment / all	0 / 3	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
Postoperative wound infection		
subjects affected / exposed	4 / 1474 (0.27%)	6 / 1482 (0.40%)
occurrences causally related to treatment / all	0 / 4	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 1
Arteriovenous graft site infection		

subjects affected / exposed	5 / 1474 (0.34%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Clostridium difficile colitis		
subjects affected / exposed	4 / 1474 (0.27%)	5 / 1482 (0.34%)
occurrences causally related to treatment / all	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Endocarditis		
subjects affected / exposed	3 / 1474 (0.20%)	6 / 1482 (0.40%)
occurrences causally related to treatment / all	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 1	0 / 1
Gastroenteritis viral		
subjects affected / exposed	6 / 1474 (0.41%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Abscess limb		
subjects affected / exposed	3 / 1474 (0.20%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Catheter site infection		
subjects affected / exposed	2 / 1474 (0.14%)	5 / 1482 (0.34%)
occurrences causally related to treatment / all	0 / 2	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0
Localised infection		
subjects affected / exposed	5 / 1474 (0.34%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Arthritis bacterial		
subjects affected / exposed	3 / 1474 (0.20%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural infection		

subjects affected / exposed	5 / 1474 (0.34%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular device infection		
subjects affected / exposed	4 / 1474 (0.27%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Diverticulitis		
subjects affected / exposed	4 / 1474 (0.27%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Herpes zoster		
subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Infected skin ulcer		
subjects affected / exposed	3 / 1474 (0.20%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Intervertebral discitis		
subjects affected / exposed	2 / 1474 (0.14%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia viral		
subjects affected / exposed	3 / 1474 (0.20%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Vascular access site infection		
subjects affected / exposed	1 / 1474 (0.07%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Wound infection		

subjects affected / exposed	3 / 1474 (0.20%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Anal abscess		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetic gangrene		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Escherichia sepsis		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Fungal peritonitis		
subjects affected / exposed	0 / 1474 (0.00%)	4 / 1482 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Infection		
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia influenzal		
subjects affected / exposed	4 / 1474 (0.27%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Suspected COVID-19		
subjects affected / exposed	1 / 1474 (0.07%)	3 / 1482 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Device related bacteraemia		

subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Cystitis		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Enterobacter sepsis		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Endocarditis bacterial		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	1 / 2
Erysipelas		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Escherichia infection		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatitis C		
subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Klebsiella infection		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia streptococcal		

subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary tuberculosis		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pyelonephritis		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pyelonephritis chronic		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Respiratory tract infection		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Streptococcal sepsis		
subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Subcutaneous abscess		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Viral upper respiratory tract infection		
subjects affected / exposed	1 / 1474 (0.07%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Abdominal wall abscess		

subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Abdominal sepsis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Acute hepatitis B		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Appendicitis		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Appendicitis perforated		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Arthritis infective		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Atypical pneumonia		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Bacterial infection		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Carbuncle		

subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Cholecystitis infective		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Clostridium difficile infection		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Colonic abscess		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Endocarditis staphylococcal		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gas gangrene		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic cyst infection		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Infectious pleural effusion		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Klebsiella bacteraemia		

subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Klebsiella sepsis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Large intestine infection		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Lung abscess		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lymph node tuberculosis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Nasopharyngitis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Otitis externa		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Parainfluenzae virus infection		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pharyngitis		

subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Proteus infection		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pseudomonal sepsis		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary sepsis		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Pyelonephritis acute		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Renal cyst infection		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Rhinovirus infection		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Scrotal abscess		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Tuberculosis		

subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Varicella		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Abdominal abscess		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Abscess neck		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Acinetobacter bacteraemia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Arteriovenous graft site abscess		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bacterial sepsis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Biliary sepsis		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Bone abscess		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bone tuberculosis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Boutonneuse fever		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Burn infection		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Candida pneumonia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bursitis infective		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Campylobacter gastroenteritis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Catheter site abscess		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Complicated appendicitis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dengue fever		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Diarrhoea infectious		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Douglas' abscess		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Enteritis infectious		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Enterobacter bacteraemia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Enterobacter infection		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Endophthalmitis		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Enterococcal sepsis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Enterococcal bacteraemia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Enterobacter pneumonia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Escherichia peritonitis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Escherichia bacteraemia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Febrile infection		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Furuncle		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Fungaemia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis bacterial		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis staphylococcal		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Graft infection		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Groin infection		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Groin abscess		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic echinococcosis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (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	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatitis B		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Herpes zoster meningitis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Herpes ophthalmic		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Infected cyst		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Infected fistula		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Infective aneurysm		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Kidney infection		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Listeraemia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Listeria sepsis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Liver abscess		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Mastoiditis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Measles		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Meningitis aseptic		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Meningitis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Mesenteric abscess		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Metapneumovirus infection		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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 / 1474 (0.00%)	1 / 1482 (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	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Osteomyelitis acute		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Orchitis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Otitis media		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Paronychia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pericarditis infective		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pelvic infection		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Parotitis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia bacterial		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia haemophilus		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Post procedural sepsis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Postoperative abscess		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pyuria		

subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Respiratory syncytial virus infection		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Respiratory tract infection viral		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Retroperitoneal infection		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Salmonella sepsis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Septic embolus		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Septic encephalopathy		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Shigella infection		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Shunt infection		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sinusitis		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Skin infection		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Soft tissue infection		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Staphylococcal osteomyelitis		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (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 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tooth infection		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tooth abscess		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tonsillitis		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheitis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibulitis			
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	45 / 1474 (3.05%)	42 / 1482 (2.83%)	
occurrences causally related to treatment / all	0 / 57	0 / 53	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	36 / 1474 (2.44%)	19 / 1482 (1.28%)	
occurrences causally related to treatment / all	0 / 41	0 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	9 / 1474 (0.61%)	11 / 1482 (0.74%)	
occurrences causally related to treatment / all	0 / 10	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypervolaemia			
subjects affected / exposed	3 / 1474 (0.20%)	5 / 1482 (0.34%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	2 / 1474 (0.14%)	5 / 1482 (0.34%)
occurrences causally related to treatment / all	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Hyponatraemia		
subjects affected / exposed	4 / 1474 (0.27%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Dehydration		
subjects affected / exposed	4 / 1474 (0.27%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypocalcaemia		
subjects affected / exposed	3 / 1474 (0.20%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetic ketoacidosis		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Malnutrition		
subjects affected / exposed	2 / 1474 (0.14%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 1
Diabetes mellitus inadequate control		
subjects affected / exposed	2 / 1474 (0.14%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypokalaemia		
subjects affected / exposed	3 / 1474 (0.20%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Calciphylaxis		

subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetes mellitus		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetic metabolic decompensation		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Fluid retention		
subjects affected / exposed	2 / 1474 (0.14%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Metabolic acidosis		
subjects affected / exposed	1 / 1474 (0.07%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Type 1 diabetes mellitus		
subjects affected / exposed	0 / 1474 (0.00%)	2 / 1482 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Diabetic complication		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Electrolyte imbalance		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypercalcaemia		

subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypovolaemia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypophagia		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypoalbuminaemia		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Insulin-requiring type 2 diabetes mellitus		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Obesity		
subjects affected / exposed	1 / 1474 (0.07%)	0 / 1482 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Vitamin B12 deficiency		
subjects affected / exposed	0 / 1474 (0.00%)	1 / 1482 (0.07%)
occurrences causally related to treatment / all	0 / 0	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	rhEPO	Daprodustat	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	827 / 1474 (56.11%)	830 / 1482 (56.01%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	84 / 1474 (5.70%)	73 / 1482 (4.93%)	
occurrences (all)	119	96	
Arteriovenous fistula site complication			
subjects affected / exposed	89 / 1474 (6.04%)	61 / 1482 (4.12%)	
occurrences (all)	121	90	
Vascular disorders			
Hypertension			
subjects affected / exposed	232 / 1474 (15.74%)	235 / 1482 (15.86%)	
occurrences (all)	356	366	
Dialysis hypotension			
subjects affected / exposed	105 / 1474 (7.12%)	135 / 1482 (9.11%)	
occurrences (all)	206	254	
Hypotension			
subjects affected / exposed	92 / 1474 (6.24%)	115 / 1482 (7.76%)	
occurrences (all)	130	140	
Nervous system disorders			
Headache			
subjects affected / exposed	139 / 1474 (9.43%)	115 / 1482 (7.76%)	
occurrences (all)	216	176	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	176 / 1474 (11.94%)	161 / 1482 (10.86%)	
occurrences (all)	228	225	
Nausea			
subjects affected / exposed	84 / 1474 (5.70%)	83 / 1482 (5.60%)	
occurrences (all)	106	95	
Vomiting			
subjects affected / exposed	76 / 1474 (5.16%)	83 / 1482 (5.60%)	
occurrences (all)	98	103	
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	101 / 1474 (6.85%) 133	101 / 1482 (6.82%) 128	
Dyspnoea subjects affected / exposed occurrences (all)	74 / 1474 (5.02%) 88	58 / 1482 (3.91%) 67	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	111 / 1474 (7.53%) 138	101 / 1482 (6.82%) 120	
Pain in extremity subjects affected / exposed occurrences (all)	76 / 1474 (5.16%) 99	85 / 1482 (5.74%) 105	
Back pain subjects affected / exposed occurrences (all)	88 / 1474 (5.97%) 103	64 / 1482 (4.32%) 87	
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	104 / 1474 (7.06%) 188	113 / 1482 (7.62%) 188	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	92 / 1474 (6.24%) 125	99 / 1482 (6.68%) 144	
Bronchitis subjects affected / exposed occurrences (all)	97 / 1474 (6.58%) 124	87 / 1482 (5.87%) 116	
Urinary tract infection subjects affected / exposed occurrences (all)	79 / 1474 (5.36%) 97	73 / 1482 (4.93%) 99	
Metabolism and nutrition disorders			
Hyperkalaemia subjects affected / exposed occurrences (all)	62 / 1474 (4.21%) 72	76 / 1482 (5.13%) 92	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2016	Amendment 1: Applies to Austria, Belgium, Czech Republic, Denmark, Estonia, Germany, Hungary, Italy, Norway, Poland, Portugal, Romania, Spain, Sweden and UK. Clarified end of the study; removal of requirement to reduce ESA dose if W-8 Hgb is >11.5 g/dL; guidance to iron management; new exploratory objective to compare daprodustat to rhEPO on delayed graft function after deceased donor kidney transplantation
12 October 2016	Amendment 2: Main changes include new timepoints at Run-in (Week -4) and Week 2 for collection of iron therapy and at Week 52 for Kt/Vurea. Changes to ABPM assessments and prompts for recording awaking and sleeping times; clarification for those randomized to rhEPO who transition from HD to PD will change from epoetin alfa to darbepoetin alfa.
08 February 2017	Amendment 2/France1: Additional ultrasound added to France; PD participants are not eligible for France.
05 October 2017	Amendment 3: Added retest for Hgb and TSAT to determine eligibility; broadened exclusion to include participation in interventional study with investigational agent or device; revised statistical section to change from two-sided testing at the 5% level to one-sided testing at the 2.5% level; correct the comparator for the Null and Alternative hypotheses; changed significance levels to p-values; added description of the adjustments to statistical model; updated hyporesponder analyses; added text regarding the interim analysis process; added exploratory endpoints around Hgb variability, iron parameters, transfusions and dose adjustment scheme; provision for possible adjustment to Dose Adjustment Algorithm triggers for Hgb values 7.5 g/dL to <9.5 g/dL based on the review of blinded instream aggregate Hgb data
09 October 2017	Amendment 3/France1: Changes from amendment 3 to France
30 July 2020	Amendment 4: Revised MACE non-inferiority margin NI margin; revised target MACE as a result of the change to the NI margin; updated the analysis of the hemoglobin co-primary endpoint based on FDA feedback; multiplicity adjustment strategy updated from Hommel to Holm-Bonferroni based on FDA feedback; added AESI of worsening of hypertension
30 July 2020	Amendment 4/France1: changes from amendment 4 to France

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported