



Clinical trial results:

A long term, randomised, double blind, placebo-controlled study to determine the effect of albiglutide, when added to standard blood glucose lowering therapies, on major cardiovascular events in patients with Type 2 diabetes mellitus

Summary

EudraCT number	2014-001824-32
Trial protocol	IT DE CZ GB SE NL HU BE DK ES BG GR
Global end of trial date	12 March 2018

Results information

Result version number	v1 (current)
This version publication date	27 February 2019
First version publication date	27 February 2019

Trial information

Trial identification

Sponsor protocol code	116174
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02465515
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
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	25 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of albiglutide with respect to MACE when added to glycemic standard of care versus standard of care alone

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 1015
Country: Number of subjects enrolled	Belgium: 124
Country: Number of subjects enrolled	Bulgaria: 65
Country: Number of subjects enrolled	Canada: 364
Country: Number of subjects enrolled	Czech Republic: 154
Country: Number of subjects enrolled	Denmark: 136
Country: Number of subjects enrolled	France: 83
Country: Number of subjects enrolled	Germany: 866
Country: Number of subjects enrolled	Greece: 191
Country: Number of subjects enrolled	Hong Kong: 33
Country: Number of subjects enrolled	Hungary: 289
Country: Number of subjects enrolled	Italy: 310
Country: Number of subjects enrolled	Korea, Republic of: 226
Country: Number of subjects enrolled	Mexico: 407
Country: Number of subjects enrolled	Netherlands: 132
Country: Number of subjects enrolled	Norway: 62
Country: Number of subjects enrolled	Peru: 281
Country: Number of subjects enrolled	Philippines: 14
Country: Number of subjects enrolled	Poland: 393
Country: Number of subjects enrolled	Russian Federation: 750
Country: Number of subjects enrolled	South Africa: 240
Country: Number of subjects enrolled	Spain: 704

Country: Number of subjects enrolled	Sweden: 259
Country: Number of subjects enrolled	Taiwan: 67
Country: Number of subjects enrolled	Thailand: 36
Country: Number of subjects enrolled	Ukraine: 396
Country: Number of subjects enrolled	United Kingdom: 285
Country: Number of subjects enrolled	United States: 1581
Worldwide total number of subjects	9463
EEA total number of subjects	4053

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)	4714
From 65 to 84 years	4705
85 years and over	44

Subject disposition

Recruitment

Recruitment details:

This was a randomized, double-blind, parallel group, placebo-controlled study in participants with Type 2 diabetes having a previous history of cardiovascular disease and not having optimal glycemic control.

Pre-assignment

Screening details:

A total of 10793 participants were screened of which 1330 failed screening and 9463 participants were randomized in a 1:1 ratio to receive either once weekly albiglutide or matching placebo subcutaneous injections. The study was conducted in 28 countries.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Albiglutide matching placebo was administered once weekly as subcutaneous injection in the abdomen, thigh or upper arm region in addition to the standard of care therapy for diabetes and cardiovascular health.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Albiglutide matching placebo was provided as fixed-dose, fully disposable pen injector system for self-administration as subcutaneous injection in the abdomen, thigh or upper arm region.

Arm title	Albiglutide
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Arm description:

Albiglutide was administered once weekly as subcutaneous injection in the abdomen, thigh or upper arm region. Participants were administered albiglutide at a dose of 30 milligrams (mg) or 50 mg once weekly in addition to the standard of care therapy for diabetes and cardiovascular health.

Arm type	Experimental
Investigational medicinal product name	Albiglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Albiglutide was provided as fixed-dose, fully disposable pen injector system for self-administration as subcutaneous injection in the abdomen, thigh or upper arm region.

Number of subjects in period 1	Placebo	Albiglutide
Started	4732	4731
Completed	4578	4620
Not completed	154	111
Consent withdrawn by subject	74	43
Physician decision	8	12
Investigator site closed	4	5
Lost to follow-up	68	51

Baseline characteristics

Reporting groups

Reporting group title	Placebo
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Reporting group description:

Albiglutide matching placebo was administered once weekly as subcutaneous injection in the abdomen, thigh or upper arm region in addition to the standard of care therapy for diabetes and cardiovascular health.

Reporting group title	Albiglutide
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Reporting group description:

Albiglutide was administered once weekly as subcutaneous injection in the abdomen, thigh or upper arm region. Participants were administered albiglutide at a dose of 30 milligrams (mg) or 50 mg once weekly in addition to the standard of care therapy for diabetes and cardiovascular health.

Reporting group values	Placebo	Albiglutide	Total
Number of subjects	4732	4731	9463
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2329	2385	4714
From 65-84 years	2383	2322	4705
85 years and over	20	24	44
Age Continuous Units: Years			
arithmetic mean	64.2	64.1	
standard deviation	± 8.65	± 8.71	-
Sex: Female, Male Units: Subjects			
Female	1467	1427	2894
Male	3265	3304	6569
Race/Ethnicity, Customized Units: Subjects			
American Indian (Amer. Ind.) or Alaska Native	238	280	518
Central/South Asian Heritage (Her.)	27	25	52
Japanese Her./East Asian Her/South East Asian Her.	215	204	419
Black or African American (Amer.)	118	121	239
Native Hawaiian or Other Pacific Islander	2	3	5
White	4024	4006	8030
Amer Ind. or Alaska Native & Black or African Amer	1	3	4
Asian & Black or African Amer.	1	0	1
Asian & White	0	1	1

Black or African Amer. & White	81	67	148
Unknown	1	1	2
Amer. Ind. or Alaska Native & White	24	20	44

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Albiglutide matching placebo was administered once weekly as subcutaneous injection in the abdomen, thigh or upper arm region in addition to the standard of care therapy for diabetes and cardiovascular health.	
Reporting group title	Albiglutide
Reporting group description: Albiglutide was administered once weekly as subcutaneous injection in the abdomen, thigh or upper arm region. Participants were administered albiglutide at a dose of 30 milligrams (mg) or 50 mg once weekly in addition to the standard of care therapy for diabetes and cardiovascular health.	

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

End point title	Time to first occurrence of major adverse cardiovascular events (MACE) during cardiovascular (CV) follow-up time period
End point description: Time to MACE defined as the time to first occurrence of Cardiovascular Endpoint Committee (CEC)-adjudicated MACE (CV death, myocardial infarction [MI] or stroke) was analyzed using a Cox Proportional Hazards regression model with treatment group as the only covariate. The incidence rate per 100 person years (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% confidence interval. 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. The analysis was performed on the Intent to Treat (ITT) Population which comprised of all randomized participants excluding participants who did not provide consent.	
End point type	Primary
End point timeframe: Median of 1.65 person years for CV follow-up time period	

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[1]	4731 ^[2]		
Units: Events per 100 person years				
number (confidence interval 95%)	5.87 (5.33 to 6.45)	4.57 (4.10 to 5.08)		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Hazard ratio is estimated using a Cox proportional hazard regression model with treatment as the only covariate	
Comparison groups	Placebo v Albiglutide

Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
P-value	< 0.0001 ^[4]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.9

Notes:

[3] - Non-inferiority was determined by testing the hypothesis that the observed hazard ratio is significantly different from the null margin of 1.3 (a one-sided p <0.025 for such a test with result in appropriate direction being equivalent to the upper 95% confidence limit for the hazard ratio being less than 1.3)

[4] - One-sided p-value based on Wald test of hazard ratio (HR) ≥ 1.3 versus HR <1.3.

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[5]
Method	Wald test

Notes:

[5] - Two-sided p-value based on Wald test of HR=1 versus HR not equal to 1

Secondary: Time to first occurrence of MACE or urgent revascularization for unstable angina

End point title	Time to first occurrence of MACE or urgent revascularization for unstable angina
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End point description:

Time to first occurrence of CEC-adjudicated MACE (CV death, MI or stroke) or urgent revascularization for unstable angina was analyzed using a Cox Proportional Hazards regression model with treatment group as the only covariate. The incidence rate per 100 person years (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% confidence interval. 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:

Median of 1.65 person years for CV follow-up time period

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[6]	4731 ^[7]		
Units: Events per 100 person years				
number (confidence interval 95%)	6.45 (5.88 to 7.06)	5.06 (4.56 to 5.60)		

Notes:

[6] - ITT Population

[7] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Hazard ratio is estimated using a Cox proportional hazard regression model with treatment as the only covariate.	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[8]
Method	Wald statistic
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.9

Notes:

[8] - Two-sided p-value based on the Wald statistic.

Secondary: Time to adjudicated CV death

End point title	Time to adjudicated CV death
End point description:	
Time to adjudicated CV death was analyzed using a Cox Proportional Hazards regression model with treatment group as the only covariate. The incidence rate per 100 person years (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% confidence interval. 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:	
Median of 1.65 person years for the CV follow-up time period	

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[9]	4731 ^[10]		
Units: Events per 100 person years				
number (confidence interval 95%)	1.72 (1.44 to 2.04)	1.61 (1.33 to 1.92)		

Notes:

[9] - ITT Population

[10] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Hazard ratio is estimated using a Cox proportional hazard regression model with treatment as the only covariate	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.578 ^[11]
Method	Wald statistic
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.19

Notes:

[11] - Two-sided p-value based on the Wald statistic

Secondary: Time to first occurrence of adjudicated MI

End point title	Time to first occurrence of adjudicated MI
End point description:	
Time to first occurrence of adjudicated MI was analyzed using a Cox Proportional Hazards regression model with treatment group as the only covariate. The incidence rate per 100 person years (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% confidence interval. 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:	
Median of 1.65 person years for CV follow-up time period	

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[12]	4731 ^[13]		
Units: Events per 100 person years				
number (confidence interval 95%)	3.26 (2.86 to 3.70)	2.43 (2.09 to 2.81)		

Notes:

[12] - ITT Population

[13] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Hazard ratio is estimated using a Cox proportional hazard regression model with treatment as the only covariate.	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003 ^[14]
Method	Wald statistic
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	0.9

Notes:

[14] - Two-sided p-value based on the Wald statistic.

Secondary: Time to first occurrence of adjudicated stroke

End point title	Time to first occurrence of adjudicated stroke
End point description:	
Time to first occurrence of adjudicated stroke was analyzed using a Cox Proportional Hazards regression model with treatment group as the only covariate. The incidence rate per 100 person years ($100 \times \text{number of participants with at least 1 event} / \text{first event person-years}$) is presented along with 95% confidence interval. 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:	
Median of 1.65 person years for CV follow-up time period	

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[15]	4731 ^[16]		
Units: Events per 100 person years				
number (confidence interval 95%)	1.45 (1.19 to 1.74)	1.25 (1.01 to 1.53)		

Notes:

[15] - ITT Population

[16] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Hazard ratio is estimated using a Cox proportional hazard regression model with treatment as the only covariate.	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3 ^[17]
Method	Wald statistic
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.14

Notes:

[17] - Two-sided p-value based on the Wald statistic.

Secondary: Time to first occurrence of adjudicated CV death or hospitalization for heart failure (HF)

End point title	Time to first occurrence of adjudicated CV death or hospitalization for heart failure (HF)
End point description:	
Time to first occurrence of adjudicated CV death or hospitalization for HF was analyzed using a Cox Proportional Hazards regression model with treatment group as the only covariate. The incidence rate per 100 person years (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% confidence interval. 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:	
Median of 1.65 person years for CV follow-up time period	

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[18]	4731 ^[19]		
Units: Events per 100 person years				
number (confidence interval 95%)	2.92 (2.55 to 3.34)	2.49 (2.15 to 2.88)		

Notes:

[18] - ITT Population

[19] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Hazard ratio is estimated using a Cox proportional hazard regression model with treatment as the only covariate.	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.113 ^[20]
Method	Wald statistic
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.04

Notes:

[20] - Two-sided p-value based on the Wald statistic.

Secondary: Time to initiation of insulin of more than 3 months duration for those participants not treated with insulin at study start

End point title	Time to initiation of insulin of more than 3 months duration for those participants not treated with insulin at study start
End point description:	
Time to initiation of insulin of more than 3 months duration in participants not treated with insulin at study start was analyzed using a Cox Proportional Hazards regression model with treatment group as the only covariate. The incidence rate per 100 person years (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% confidence interval. 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 on-therapy and post-therapy AE time period. The analysis was performed on Non-Insulin Population which comprised of participants in the ITT Population who were not on insulin at Baseline.	
End point type	Secondary
End point timeframe:	
Up to 2.7 years	

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1995 ^[21]	1871 ^[22]		
Units: Events per 100 person years				
number (confidence interval 95%)	8.58 (7.56 to 9.70)	3.56 (2.92 to 4.31)		

Notes:

[21] - Non-Insulin Population

[22] - Non-Insulin Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Hazard ratio is estimated using a Cox proportional hazard regression model with treatment as the only covariate.	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	3866
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[23]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	0.53

Notes:

[23] - Two-sided p-value based on Wald test of HR=1 versus HR not equal to 1.

Secondary: Time to initiation of prandial insulin in those participants on basal insulin at study start

End point title	Time to initiation of prandial insulin in those participants on basal insulin at study start
End point description:	
Time to initiation of prandial insulin in those participants on basal insulin at study start was analyzed using a Cox Proportional Hazards regression model with treatment group as the only covariate. The incidence rate per 100 person years ($100 \times \text{number of participants with at least 1 event} / \text{first event person-years}$) is presented along with 95% confidence interval. 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 on-therapy and post-therapy AE time period. The analysis was performed on Basal Insulin Population which comprised of participants in the ITT Population who were on basal insulin but not on other insulin at Baseline (i.e., will not include a participant on a mixed insulin or on a prandial-only insulin).	
End point type	Secondary
End point timeframe:	
Up to 2.7 years	

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1040 ^[24]	1028 ^[25]		
Units: Events per 100 person years				
number (confidence interval 95%)	5.09 (4.06 to 6.31)	3.59 (2.73 to 4.63)		

Notes:

[24] - Basal Insulin Population

[25] - Basal Insulin Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Hazard ratio is estimated using a Cox proportional hazard regression model with treatment as the only covariate.

Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	2068
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.043 ^[26]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.99

Notes:

[26] - Two-sided p-value based on Wald test of HR=1 versus HR not equal to 1.

Secondary: Percentage of participants achieving composite metabolic endpoint

End point title	Percentage of participants achieving composite metabolic endpoint
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End point description:

Percentage of participants achieving composite metabolic endpoint defined as the percentage of participants achieving glycemic control (glycated hemoglobin [HbA1c] $\leq 7\%$) with no severe hypoglycemic incidents and weight gain $< 5\%$. Final Assessment is the latest post-Baseline assessment of both HbA1c and weight. Only those participants with HbA1c and weight values at Baseline and at the specified visits were analyzed (represented by n=X in category titles)

End point type	Secondary
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End point timeframe:

Months 8, 16, 24 and final assessment (up to 2.7 years)

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[27]	4731 ^[28]		
Units: Percentage of participants				
number (not applicable)				
Month 8, n=4127, 4195	15.4	32.2		
Month 16, n=3026, 3118	16.5	28.7		
Month 24, n=1119, 1173	17.8	28.6		
Final assessment, n=4401, 4455	15.1	26.0		

Notes:

[27] - ITT Population

[28] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Month 8	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[29]
Method	Mantel-Haenszel

Notes:

[29] - P-value based on the covariate-adjusted extended Mantel-Haenszel test. Covariates include Baseline HbA1c (<8.0% versus ≥ 8.0%) and Baseline diabetes therapy (diet and exercise alone versus all other therapies).

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Month 16	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[30]
Method	Mantel-Haenszel

Notes:

[30] - P-value based on the covariate-adjusted extended Mantel-Haenszel test. Covariates include Baseline HbA1c (<8.0% versus ≥ 8.0%) and Baseline diabetes therapy (diet and exercise alone versus all other therapies).

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Month 24	
Comparison groups	Placebo v Albiglutide

Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[31]
Method	Mantel-Haenszel

Notes:

[31] - P-value based on the covariate-adjusted extended Mantel-Haenszel test. Covariates include Baseline HbA1c (<8.0% versus ≥ 8.0%) and Baseline diabetes therapy (diet and exercise alone versus all other therapies).

Statistical analysis title	Statistical analysis 4
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Statistical analysis description:

Final assessment

Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[32]
Method	Mantel-Haenszel

Notes:

[32] - P-value based on the covariate-adjusted extended Mantel-Haenszel test. Covariates include Baseline HbA1c (<8.0% versus ≥ 8.0%) and Baseline diabetes therapy (diet and exercise alone versus all other therapies).

Secondary: Time to first occurrence of a clinically important microvascular event

End point title	Time to first occurrence of a clinically important microvascular event
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End point description:

Clinically important microvascular events were defined as the following: need for renal transplant or dialysis, new diabetes-related blindness, and procedures (laser photocoagulation or anti-vascular endothelial growth factor treatment or vitrectomy for diabetic retinopathy/eye disease). Time to first occurrence of a clinically important microvascular event was analyzed using a Cox Proportional Hazards regression model with treatment group as the only covariate. The incidence rate per 100 person years (100*number of participants with at least 1 event)/first event person-years) is presented along with 95% confidence interval. 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 on-therapy and post-therapy AE time period.

End point type	Secondary
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End point timeframe:

Up to 2.7 years

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[33]	4731 ^[34]		
Units: Events per 100 person years				
number (confidence interval 95%)	0.69 (0.52 to 0.90)	0.46 (0.32 to 0.63)		

Notes:

[33] - ITT Population

[34] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Hazard ratio is estimated using a Cox proportional hazard regression model with treatment as the only covariate.	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.055 ^[35]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.01

Notes:

[35] - Two-sided p-value based on Wald test of HR=1 versus HR not equal to 1

Secondary: Change from Baseline in HbA1c

End point title	Change from Baseline in HbA1c
End point description:	
Change from Baseline in HbA1c was analyzed using mixed model repeated measures (MMRM) including observed case data (does not impute any missing data). Baseline is the last non-missing value assessed on or before treatment start date. Change from Baseline is the value at specified time point minus the Baseline value. Change from Baseline in HbA1c using Baseline data from Local or Central Laboratory, and post-Baseline Central Laboratory data is presented. Only those participants with value at Baseline and at the specified visit is presented (represented by n=X in category titles)	
End point type	Secondary
End point timeframe:	
Baseline and Months 8 and 16	

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[36]	4731 ^[37]		
Units: Percentage of HbA1c				
least squares mean (standard error)				
Month 8, n=4211, 4289	-0.28 (± 0.020)	-0.92 (± 0.019)		
Month 16, n=3066, 3163	-0.31 (± 0.023)	-0.83 (± 0.022)		

Notes:

[36] - ITT Population

[37] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Based on MMRM model: Change=Baseline HbA1c+Treatment+Visit+Treatment-by-Visit Interaction+Baseline HbA1c-by-Visit Interaction. Difference of least squares means (Albiglutide-Placebo) is from MMRM model for Month 8

Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[38]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.58

Notes:

[38] - P-value from a two-sided t-test to test whether the difference of least square means (Albiglutide - Placebo) is equal to zero

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

Based on MMRM model: Change=Baseline HbA1c+Treatment+Visit+Treatment-by-Visit Interaction+Baseline HbA1c-by-Visit Interaction. Difference of least squares means (Albiglutide-Placebo) is from MMRM model for Month 16

Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[39]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	-0.45

Notes:

[39] - P-value from a two-sided t-test to test whether the difference of least square means (Albiglutide - Placebo) is equal to zero

Secondary: Change from Baseline in body weight

End point title	Change from Baseline in body weight
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End point description:

Change from Baseline in body weight was analyzed using mixed model repeated measures including observed case data (does not impute any missing data). Baseline is the last non-missing value assessed on or before treatment start date. Change from Baseline is the value at specified time point minus the Baseline value. Only those participants with value at Baseline and at the specified visit is presented (represented by n=X in category titles)

End point type	Secondary
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End point timeframe:

Baseline and Months 8 and 16

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[40]	4731 ^[41]		
Units: Kilograms				
least squares mean (standard error)				
Month 8, n=4217, 4286	-0.36 (± 0.062)	-1.02 (± 0.061)		
Month 16, n=3068, 3173	-0.53 (± 0.084)	-1.36 (± 0.083)		

Notes:

[40] - ITT Population

[41] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Based on MMRM model: Change=Baseline Body Weight+Treatment+Visit+Treatment-by-Visit Interaction+Baseline Body Weight-by-Visit Interaction. Difference of least squares means (Albiglutide-Placebo) is from MMRM model for Month 8

Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[42]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.83
upper limit	-0.49

Notes:

[42] - P-value from a two-sided t-test to test whether the difference of least square means (Albiglutide-Placebo) is equal to zero

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

Based on MMRM model: Change=Baseline Body Weight+Treatment+Visit+Treatment-by-Visit Interaction+Baseline Body weight-by-Visit Interaction. Difference of least squares means (Albiglutide-Placebo) is from MMRM model for Month 16

Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[43]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.83

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	-0.6

Notes:

[43] - P-value from a two-sided t-test to test whether the difference of least square means (Albiglutide - Placebo) is equal to zero

Secondary: Change from Baseline in Treatment Related Impact Measures-Diabetes (TRIM-D) total score

End point title	Change from Baseline in Treatment Related Impact Measures-Diabetes (TRIM-D) total score
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End point description:

TRIM-D is a 28 item treatment satisfaction measure with 5 domains assessing Treatment Burden, Daily Life, Diabetes Management, Compliance and Psychological Health. Raw score ranges for each subscale were: treatment burden (6 to 30), daily life (5 to 25), diabetes management (5 to 25), compliance (4 to 20) and psychological health (8 to 40), higher scores indicating better health state. Total raw score was determined by summing the raw scores for each of the subscales and the total score (transformed) was determined as [(raw score minus lowest possible raw score)/possible raw score range] x100. The possible total (transformed) score range is 0–100, where higher scores indicated better health state. Baseline is the last non-missing value assessed on or before treatment start date. Change from Baseline is the value at specified time point minus the Baseline value. Only those participants with value at Baseline and at specified visit is presented (represented by n=X in category titles).

End point type	Secondary
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End point timeframe:

Baseline and Months 8 and 16

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[44]	4731 ^[45]		
Units: Scores on a scale				
least squares mean (standard error)				
Month 8, n=3013, 3041	4.53 (± 0.194)	6.92 (± 0.193)		
Month 16, n=1738, 1840	4.80 (± 0.247)	7.13 (± 0.241)		

Notes:

[44] - ITT Population

[45] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Based on MMRM model: Change=Baseline Total Score+Treatment+Visit+Treatment-by-Visit Interaction+Baseline Total Score-by-Visit Interaction. Difference of least squares means (Albiglutide-Placebo) is from MMRM model for Month 8

Comparison groups	Placebo v Albiglutide
-------------------	-----------------------

Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[46]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	2.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.85
upper limit	2.93

Notes:

[46] - P-value from a two-sided t-test to test whether the difference of least square means (Albiglutide - Placebo) is equal to zero.

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

Based on MMRM model: Change=Baseline Total Score+Treatment+Visit+Treatment-by-Visit Interaction+Baseline Total Score-by-Visit Interaction. Difference of least squares means (Albiglutide-Placebo) is from MMRM model for Month 16

Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[47]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	2.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.66
upper limit	3.01

Notes:

[47] - P-value from a two-sided t-test to test whether the difference of least square means (Albiglutide-Placebo) is equal to zero

Secondary: Change from Baseline in EuroQol- 5 Dimension (EQ-5D) visual analogue scale (VAS) Score

End point title	Change from Baseline in EuroQol- 5 Dimension (EQ-5D) visual analogue scale (VAS) Score
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End point description:

The EQ-5D is a standardized instrument used to evaluate generic health-related quality of life, comprising 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It provides a simple descriptive profile and a single index value for health status. The EQ-5D self-reported questionnaire includes a visual analog scale (VAS), which records the respondent's self-rated health status on a graduated (0–100) scale, where 0 represents the worst imaginable health state and 100 represents the best imaginable health state. Baseline is the last non-missing value assessed on or before treatment start date. Change from Baseline is the value at specified time point minus the Baseline value. Only those participants with value at Baseline and at the specified visit is presented (represented by n=X in category titles)

End point type	Secondary
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End point timeframe:

Baseline and Months 8 and 16

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[48]	4731 ^[49]		
Units: Scores on a scale				
least squares mean (standard error)				
Month 8, n=3982, 4014	1.36 (± 0.217)	2.83 (± 0.216)		
Month 16, n=2347, 2481	1.87 (± 0.287)	2.39 (± 0.279)		

Notes:

[48] - ITT Population

[49] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Based on MMRM model: Change=Baseline Score+Treatment+Visit+Treatment-by-Visit Interaction+Baseline Score-by-Visit Interaction. Difference of least squares means (Albiglutide-Placebo) is from MMRM model for Month 8.	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 ^[50]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	2.07

Notes:

[50] - P-value from a two-sided t-test to test whether the difference of least square means (Albiglutide-Placebo) is equal to zero.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Based on MMRM model: Change=Baseline Score+Treatment+Visit+Treatment-by-Visit Interaction+Baseline Score-by-Visit Interaction. Difference of least squares means (Albiglutide - Placebo) is from MMRM model for Month 16	
Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.192 ^[51]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	1.31

Notes:

[51] - P-value from a two-sided t-test to test whether the difference of least square means (Albiglutide - Placebo) is equal to zero

Secondary: Time to death

End point title	Time to death
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End point description:

Time to death was analyzed using a Cox Proportional Hazards regression model with treatment group as the only covariate. The incidence rate per 100 person years (100*number of participants who died/endpoint person-years) is presented along with 95% confidence interval. Endpoint person-years=(cumulative total time to event for participants who have the event+cumulative total of censored time for participants without the event)/365.25, based on the Vital Status follow-up time period.

End point type	Secondary
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End point timeframe:

Median of 1.73 years for the Vital Status follow-up time period

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4732 ^[52]	4731 ^[53]		
Units: Events per 100 person years				
number (confidence interval 95%)	2.56 (2.22 to 2.93)	2.44 (2.11 to 2.81)		

Notes:

[52] - ITT Population

[53] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Hazard ratio is estimated using a Cox proportional hazard regression model with treatment as the only covariate.

Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9463
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.644 ^[54]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.16

Notes:

[54] - Two-sided p-value based on Wald test of HR=1 versus HR not equal to 1.

Secondary: Number of participants with non-fatal serious adverse events (SAEs)

End point title	Number of participants with non-fatal serious adverse events (SAEs)
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End point description:

SAE is defined as any untoward medical occurrence that, at any dose: results in death; is life-threatening; requires hospitalization or prolongation of existing hospitalization; results in disability/incapacity; is a congenital anomaly/birth defect; other important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed before; is associated with liver injury and impaired liver function. Number of participants with on-therapy non-fatal SAEs are presented. Safety Population comprised of all randomized participants who received at least one dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to 2.7 years

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4715 ^[55]	4717 ^[56]		
Units: Participants	974	891		

Notes:

[55] - Safety Population

[56] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs) leading to discontinuation of investigational product (AELD)

End point title	Number of participants with adverse events (AEs) leading to discontinuation of investigational product (AELD)
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End point description:

The number of participants with on-therapy AEs leading to discontinuation of investigational product is reported.

End point type	Secondary
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End point timeframe:

Up to 2.7 years

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4715 ^[57]	4717 ^[58]		
Units: Participants	334	427		

Notes:

[57] - Safety Population

[58] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with AEs of special interest

End point title	Number of participants with AEs of special interest
-----------------	---

End point description:

The protocol defined AEs of special interest included: development of thyroid cancer; hematologic malignancy; pancreatic cancer; pancreatitis (investigator reported and pancreatitis positively adjudicated by the Pancreatic Adjudication Committee [PAC]); investigational product injection site reactions; immunological reactions; severe hypoglycemic events; hepatic events; hepatic enzyme elevations (including gamma glutamyl transferase [GGT]); serious gastrointestinal (GI) events; appendicitis; atrial fibrillation/flutter; pneumonia; worsening renal function and diabetic retinopathy. The number of participants with on-therapy AEs of special interest is reported.

End point type	Secondary
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End point timeframe:

Up to 2.7 years

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4715 ^[59]	4717 ^[60]		
Units: Participants				
Thyroid cancer diagnosis	0	0		
Hematologic malignancy	5	9		
Pancreatic cancer	5	6		
Investigational product injection site reaction	29	86		
Hypersensitivity	48	45		
Severe hypoglycemic events	55	31		
Hepatic events	74	98		
Hepatic enzyme elevations (including GGT)	34	51		
Serious GI Events	87	92		
Appendicitis	8	3		
Atrial fibrillation/atrial flutter	131	108		
Pneumonia	138	131		
Renal impairment	319	279		
Diabetic retinopathy	89	78		
Investigator-reported pancreatitis	13	14		
Pancreatitis positively adjudicated by PAC	7	10		

Notes:

[59] - Safety Population

[60] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change in estimated glomerular filtration rate (eGFR) calculated using Modification of Diet in Renal Disease (MDRD) formula

End point title	Change in estimated glomerular filtration rate (eGFR) calculated using Modification of Diet in Renal Disease (MDRD) formula
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End point description:

Blood samples were collected for the measurement of serum creatinine. Serum creatinine values were used to calculate eGFR using the MDRD formula, $eGFR = 175 \times (\text{serum creatinine})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$. Baseline is the last non-missing value assessed on or before treatment start date. Change from Baseline is the value at specified time point minus the Baseline value. Change from Baseline in eGFR using Baseline data from Local or Central Laboratory, and post-Baseline Central Laboratory data for the on-treatment time period is presented. Only those participants with a value at Baseline and specified visit were analyzed (represented by n=X in category titles)

End point type	Secondary
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End point timeframe:

Baseline and Months 8 and 16

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4715 ^[61]	4717 ^[62]		
Units: Milliliter/minute/1.73 meter square				
least squares mean (standard error)				
Month 8; n=3977,4008	1.22 (± 0.264)	0.10 (± 0.262)		
Month 16; n=2354,2496	-0.90 (± 0.303)	-1.33 (± 0.296)		

Notes:

[61] - Safety Population

[62] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

Based on MMRM model: Change=Baseline eGFR+Treatment+Visit+Treatment-by-Visit Interaction+Baseline eGFR-by-Visit Interaction. Difference of least squares means (Albiglutide-Placebo) is from MMRM model for Month 8.

Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9432
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003 ^[63]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-1.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.84
upper limit	-0.39

Notes:

[63] - P-value from a two-sided t-test to test whether the difference of least square means (Albiglutide-Placebo) is equal to zero.

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

Based on MMRM model: Change=Baseline eGFR+Treatment+Visit+Treatment-by-Visit Interaction+Baseline eGFR-by-Visit Interaction. Difference of least squares means (Albiglutide-Placebo) is from MMRM model for Month 16.

Comparison groups	Placebo v Albiglutide
Number of subjects included in analysis	9432
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.315 ^[64]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.26
upper limit	0.41

Notes:

[64] - P-value from a two-sided t-test to test whether the difference of least square means (Albiglutide-Placebo) is equal to zero

Secondary: Change from Baseline in blood pressure

End point title	Change from Baseline in blood pressure
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End point description:

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were taken with the participant in a semi-recumbent or seated position after at least a 5-minute rest period. Baseline is the last non-missing value assessed on or before treatment start date. Change from Baseline is the value at specified time point minus the Baseline value. Only those participants with a value at Baseline and specified visit were analyzed (represented n=X in category titles)

End point type	Secondary
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End point timeframe:

Baseline and Months 8,16,24 and end of study (up to 2.7 years)

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4715 ^[65]	4717 ^[66]		
Units: Millimeter of mercury				
arithmetic mean (standard deviation)				
SBP, Month 8; n=4241, 4319	-0.5 (± 17.33)	-1.0 (± 16.80)		
SBP, Month 16; n=3082, 3187	-0.5 (± 17.45)	-0.9 (± 17.58)		

SBP, Month 24; n=1133, 1198	-0.9 (± 18.62)	-1.2 (± 17.51)		
SBP, End of study; n=3897, 4015	0.0 (± 17.68)	-0.4 (± 17.58)		
DBP, Month 8; n=4241, 4319	-0.5 (± 10.26)	-0.4 (± 10.12)		
DBP, Month 16; n=3082, 3187	-0.9 (± 10.74)	-0.5 (± 10.39)		
DBP, Month 24; n=1133, 1198	-1.1 (± 10.87)	-1.0 (± 10.29)		
DBP, End of study; n=3897, 4015	-0.7 (± 10.66)	-0.6 (± 10.57)		

Notes:

[65] - Safety Population

[66] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in heart rate

End point title	Change from Baseline in heart rate
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End point description:

Heart rate was measured with the participant in a semi-recumbent or seated position after at least a 5-minute rest period. Baseline is the last non-missing value assessed on or before treatment start date. Change from Baseline is the value at specified time point minus the Baseline value. Only those participants with a value at Baseline and specified visit were analyzed (represented n=X in category titles)

End point type	Secondary
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End point timeframe:

Baseline and Months 8, 16, 24 and end of study (up to 2.7 years)

End point values	Placebo	Albiglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4715 ^[67]	4717 ^[68]		
Units: Beats per minute				
arithmetic mean (standard deviation)				
Month 8; n=4239, 4312	0.2 (± 9.99)	1.6 (± 10.07)		
Month 16; n=3078, 3181	0.3 (± 10.19)	1.6 (± 10.16)		
Month 24; n=1131, 1195	0.6 (± 10.84)	1.7 (± 10.32)		
End of study; n=3892, 4005	0.8 (± 10.64)	1.8 (± 10.50)		

Notes:

[67] - Safety Population

[68] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

On-therapy non-SAEs and SAEs were reported on or after treatment start date and within 56 days after treatment stop date (Up to 2.7 years)

Adverse event reporting additional description:

SAEs, non-SAEs and non-SAEs of pre-specified interest were reported systematically in the Safety Population. Some investigators collected other non-SAEs for some participants (i.e. non-systematically). CV events referred for adjudication as study endpoints were not duplicate reported as AEs. Deaths were reported for ITT Population.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Albiglutide matching placebo was administered once weekly as subcutaneous injection in the abdomen, thigh or upper arm region in addition to the standard of care therapy for diabetes and cardiovascular health.

Reporting group title	Albiglutide
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Reporting group description:

Albiglutide was administered once weekly as subcutaneous injection in the abdomen, thigh or upper arm region. Participants were administered albiglutide at a dose of 30 milligrams (mg) or 50 mg once weekly in addition to the standard of care therapy for diabetes and cardiovascular health.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no non-serious adverse events at the frequency threshold of 5%

Serious adverse events	Placebo	Albiglutide	
Total subjects affected by serious adverse events			
subjects affected / exposed	1022 / 4715 (21.68%)	932 / 4717 (19.76%)	
number of deaths (all causes)	205	196	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	12 / 4715 (0.25%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 12	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	2 / 4715 (0.04%)	9 / 4717 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 2	
Breast cancer			

subjects affected / exposed	5 / 4715 (0.11%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	7 / 4715 (0.15%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	5 / 4715 (0.11%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pancreatic carcinoma metastatic			
subjects affected / exposed	2 / 4715 (0.04%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 2	1 / 4	
deaths causally related to treatment / all	0 / 2	1 / 3	
Lung cancer metastatic			
subjects affected / exposed	2 / 4715 (0.04%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metastases to liver			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
Breast cancer metastatic			
subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Colon cancer			

subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	2 / 4715 (0.04%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Adenocarcinoma			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colon cancer metastatic			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal neoplasm			

subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland neoplasm			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma gastric			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			

subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Gastric cancer			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic cancer			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal papilloma			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung neoplasm			

subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lymphoproliferative disorder			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant neoplasm of unknown primary site			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Meningioma			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic gastric cancer			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Prostatic adenoma			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			

subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adrenal adenoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign gastric neoplasm			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of bladder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign salivary gland neoplasm			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer recurrent			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer stage 0, with cancer in situ			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer stage III			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone cancer			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm malignant			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer stage II			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast fibroma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast neoplasm			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial neoplasm			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac myxoma			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chromophobe renal cell carcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer stage 0			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer stage IV			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneoconjunctival intraepithelial neoplasia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatofibrosarcoma protuberans			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypopharyngeal cancer			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal adenocarcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal metastasis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal squamous cell carcinoma			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip squamous cell carcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocytic leukaemia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to adrenals			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to peritoneum			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic bronchial carcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic neoplasm			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system neoplasm benign			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine carcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine carcinoma metastatic			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer metastatic			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-small cell lung cancer stage II			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal cancer metastatic			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal squamous cell carcinoma			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral papilloma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteosarcoma metastatic			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ovarian adenoma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer stage I			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary cystadenoma lymphomatosum			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycythaemia vera			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer recurrent			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectosigmoid cancer stage II			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal adenoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer metastatic			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal cell carcinoma			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal neoplasm			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine carcinoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the tongue			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the vulva			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular neoplasm			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval cancer			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Peripheral arterial occlusive disease			
subjects affected / exposed	41 / 4715 (0.87%)	33 / 4717 (0.70%)	
occurrences causally related to treatment / all	1 / 48	0 / 37	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	12 / 4715 (0.25%)	11 / 4717 (0.23%)	
occurrences causally related to treatment / all	0 / 12	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	13 / 4715 (0.28%)	7 / 4717 (0.15%)	
occurrences causally related to treatment / all	0 / 13	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	11 / 4715 (0.23%)	8 / 4717 (0.17%)	
occurrences causally related to treatment / all	0 / 11	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	7 / 4715 (0.15%)	10 / 4717 (0.21%)	
occurrences causally related to treatment / all	0 / 7	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	13 / 4715 (0.28%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 19	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	5 / 4715 (0.11%)	7 / 4717 (0.15%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	2 / 4715 (0.04%)	9 / 4717 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			

subjects affected / exposed	6 / 4715 (0.13%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	5 / 4715 (0.11%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	4 / 4715 (0.08%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	6 / 4715 (0.13%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	3 / 4715 (0.06%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism arterial			
subjects affected / exposed	1 / 4715 (0.02%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 4715 (0.02%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	4 / 4715 (0.08%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			

subjects affected / exposed	2 / 4715 (0.04%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 4715 (0.02%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			
subjects affected / exposed	0 / 4715 (0.00%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arterial disorder			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	0 / 4715 (0.00%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subclavian artery stenosis			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic vascular disorder			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Essential hypertension			

subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leriche syndrome			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accelerated hypertension			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial haemorrhage			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bleeding varicose vein			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure inadequately controlled			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic microangiopathy			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry gangrene			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery embolism			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery occlusion			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphorrhoea			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphostasis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant hypertension			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral venous disease			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery occlusion			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous occlusion			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Finger amputation			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	22 / 4715 (0.47%)	15 / 4717 (0.32%)	
occurrences causally related to treatment / all	0 / 23	1 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	14 / 4715 (0.30%)	10 / 4717 (0.21%)	
occurrences causally related to treatment / all	1 / 14	0 / 10	
deaths causally related to treatment / all	1 / 14	0 / 10	

Chest pain			
subjects affected / exposed	10 / 4715 (0.21%)	8 / 4717 (0.17%)	
occurrences causally related to treatment / all	0 / 10	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	6 / 4715 (0.13%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 6	0 / 4	
Asthenia			
subjects affected / exposed	4 / 4715 (0.08%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 4	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 3	1 / 2	
Vascular stent stenosis			
subjects affected / exposed	2 / 4715 (0.04%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site haemorrhage			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
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 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Systemic inflammatory response syndrome			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental death			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac complication associated with device			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication associated with device			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Condition aggravated			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Discomfort			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mass			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrobiosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue inflammation			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Treatment noncompliance			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent occlusion			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.02%)	0 / 4717 (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	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contrast media reaction			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			

Benign prostatic hyperplasia			
subjects affected / exposed	6 / 4715 (0.13%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	2 / 4715 (0.04%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast haematoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystocele			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysfunctional uterine bleeding			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic varices			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	21 / 4715 (0.45%)	21 / 4717 (0.45%)	
occurrences causally related to treatment / all	2 / 33	0 / 30	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	14 / 4715 (0.30%)	7 / 4717 (0.15%)	
occurrences causally related to treatment / all	1 / 16	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	6 / 4715 (0.13%)	10 / 4717 (0.21%)	
occurrences causally related to treatment / all	0 / 6	0 / 10	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pleural effusion			
subjects affected / exposed	10 / 4715 (0.21%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 11	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	7 / 4715 (0.15%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary embolism			

subjects affected / exposed	4 / 4715 (0.08%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	1 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 2	
Dyspnoea			
subjects affected / exposed	4 / 4715 (0.08%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	5 / 4715 (0.11%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthma			
subjects affected / exposed	5 / 4715 (0.11%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	3 / 4715 (0.06%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	1 / 4715 (0.02%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	4 / 4715 (0.08%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sleep apnoea syndrome			

subjects affected / exposed	1 / 4715 (0.02%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic respiratory failure			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottic cyst			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercapnia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract congestion			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal septum deviation			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal ulcer			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal cyst			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary mass			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory depression			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis hypertrophic			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord leukoplakia			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	5 / 4715 (0.11%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			

subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adjustment disorder			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Affective disorder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety disorder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breathing-related sleep disorder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hallucination			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impulse-control disorder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device failure			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device extrusion			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device issue			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.15%)	12 / 4717 (0.25%)	
occurrences causally related to treatment / all	0 / 7	1 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			

subjects affected / exposed	5 / 4715 (0.11%)	7 / 4717 (0.15%)	
occurrences causally related to treatment / all	0 / 5	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	4 / 4715 (0.08%)	7 / 4717 (0.15%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			

subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatic failure			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic steatosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-alcoholic steatohepatitis			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4715 (0.00%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 4715 (0.00%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerular filtration rate decreased			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anticoagulation drug level above therapeutic			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration bronchial			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose abnormal			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood ketone body increased			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial necrosis marker increased			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid function test normal			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight increased			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	6 / 4715 (0.13%)	7 / 4717 (0.15%)	
occurrences causally related to treatment / all	1 / 7	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 4715 (0.04%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	4 / 4715 (0.08%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Upper limb fracture			
subjects affected / exposed	3 / 4715 (0.06%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	4 / 4715 (0.08%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			

subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	2 / 4715 (0.04%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	2 / 4715 (0.04%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 4715 (0.00%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Femur fracture			
subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	2 / 4715 (0.04%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery restenosis			
subjects affected / exposed	4 / 4715 (0.08%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			

subjects affected / exposed	2 / 4715 (0.04%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery restenosis			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 4715 (0.00%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			

subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac procedure complication			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lower limb fracture			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative thoracic procedure complication			

subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound complication			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental overdose			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adjacent segment degeneration			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic stenosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal bite			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial restenosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbon monoxide poisoning			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cartilage injury			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured coccyx			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder postoperative			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft thrombosis			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun shot wound			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney contusion			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament injury			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip injury			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open globe injury			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirenal haematoma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematuria			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-traumatic pain			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative delirium			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pneumothorax			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt stenosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suture related complication			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suture rupture			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haematoma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulnar nerve injury			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound evisceration			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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			
Adenomatous polyposis coli			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic arteriovenous malformation			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertrophic cardiomyopathy			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosi			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	41 / 4715 (0.87%)	45 / 4717 (0.95%)	
occurrences causally related to treatment / all	1 / 47	3 / 48	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	36 / 4715 (0.76%)	37 / 4717 (0.78%)	
occurrences causally related to treatment / all	0 / 39	2 / 38	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	31 / 4715 (0.66%)	24 / 4717 (0.51%)	
occurrences causally related to treatment / all	0 / 31	1 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	14 / 4715 (0.30%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	2 / 15	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			

subjects affected / exposed	5 / 4715 (0.11%)	11 / 4717 (0.23%)	
occurrences causally related to treatment / all	0 / 5	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	9 / 4715 (0.19%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 10	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	4 / 4715 (0.08%)	10 / 4717 (0.21%)	
occurrences causally related to treatment / all	0 / 4	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 2	
Cardiogenic shock			
subjects affected / exposed	4 / 4715 (0.08%)	9 / 4717 (0.19%)	
occurrences causally related to treatment / all	1 / 4	0 / 9	
deaths causally related to treatment / all	1 / 3	0 / 6	
Myocardial ischaemia			
subjects affected / exposed	7 / 4715 (0.15%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 1	
Bradycardia			
subjects affected / exposed	4 / 4715 (0.08%)	8 / 4717 (0.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	9 / 4715 (0.19%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 10	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardio-respiratory arrest			
subjects affected / exposed	5 / 4715 (0.11%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 5	0 / 1	
Arteriosclerosis coronary artery			

subjects affected / exposed	5 / 4715 (0.11%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 2	
Cardiac arrest			
subjects affected / exposed	5 / 4715 (0.11%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 3	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	6 / 4715 (0.13%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 6	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	6 / 4715 (0.13%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	4 / 4715 (0.08%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	3 / 4715 (0.06%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	3 / 4715 (0.06%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 4715 (0.02%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			

subjects affected / exposed	4 / 4715 (0.08%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	2 / 4715 (0.04%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	2 / 4715 (0.04%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Arrhythmia			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Bundle branch block left			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemic cardiomyopathy			

subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia supraventricular			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac asthma			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiomegaly			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiovascular disorder			

subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial fibrosis			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute myocardial infarction			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brugada syndrome			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiorenal syndrome			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery dissection			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary no-reflow phenomenon			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary ostial stenosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracardiac thrombus			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinoatrial block			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Torsade de pointes			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	13 / 4715 (0.28%)	14 / 4717 (0.30%)	
occurrences causally related to treatment / all	0 / 15	1 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	7 / 4715 (0.15%)	9 / 4717 (0.19%)	
occurrences causally related to treatment / all	0 / 7	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	3 / 4715 (0.06%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 4715 (0.02%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	2 / 4715 (0.04%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			

subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	4 / 4715 (0.08%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	2 / 4715 (0.04%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	0 / 4715 (0.00%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dementia			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Encephalopathy			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 4715 (0.00%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			

subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid arteriosclerosis			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral arteriosclerosis			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervicobrachial syndrome			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness postural			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			

subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
IIIrd nerve paresis			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acoustic neuritis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autonomic neuropathy			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basilar artery aneurysm			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery disease			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cauda equina syndrome			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic mononeuropathy			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial nerve disorder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic coma			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic unconsciousness			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
IIIrd nerve disorder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intensive care unit acquired weakness			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbosacral radiculopathy			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mixed dementia			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mononeuritis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mononeuropathy multiplex			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple system atrophy			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve degeneration			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuromyopathy			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normal pressure hydrocephalus			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic intolerance			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post stroke seizure			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radial nerve compression			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus headache			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord herniation			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord ischaemia			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery dissection			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery stenosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord paralysis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 4715 (0.21%)	7 / 4717 (0.15%)	
occurrences causally related to treatment / all	0 / 10	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			

subjects affected / exposed	3 / 4715 (0.06%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic anaemia			
subjects affected / exposed	1 / 4715 (0.02%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy mediastinal			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia of chronic disease			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolysis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph node fibrosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic anaemia			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	5 / 4715 (0.11%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Cataract			
subjects affected / exposed	5 / 4715 (0.11%)	7 / 4717 (0.15%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	6 / 4715 (0.13%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	2 / 4715 (0.04%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 2	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid ptosis			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular degeneration			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choroidal detachment			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye pain			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotony of eye			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior capsule rupture			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinopathy			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinopathy proliferative			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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	10 / 4715 (0.21%)	8 / 4717 (0.17%)	
occurrences causally related to treatment / all	0 / 10	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastritis			
subjects affected / exposed	8 / 4715 (0.17%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	5 / 4715 (0.11%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	3 / 4715 (0.06%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 3	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	2 / 4715 (0.04%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	4 / 4715 (0.08%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	3 / 4715 (0.06%)	4 / 4717 (0.08%)	
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	4 / 4715 (0.08%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			

subjects affected / exposed	3 / 4715 (0.06%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 4715 (0.04%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 2	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 4715 (0.02%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 1	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	4 / 4715 (0.08%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	2 / 4715 (0.04%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	1 / 4715 (0.02%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 4715 (0.02%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			

subjects affected / exposed	2 / 4715 (0.04%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			

subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated umbilical hernia			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal discomfort			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholic pancreatitis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortoenteric fistula			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary ascites			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gastroparesis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer perforation			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.02%)	0 / 4717 (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	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiplonic appendagitis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive oesophagitis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric antral vascular ectasia			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis eosinophilic			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematemesis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia oral			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intestinal polyp			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip oedema			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal stenosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palatal ulcer			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic duct stenosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer perforation			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctalgia			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uvulitis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varices oesophageal			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	22 / 4715 (0.47%)	14 / 4717 (0.30%)	
occurrences causally related to treatment / all	0 / 26	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	7 / 4715 (0.15%)	9 / 4717 (0.19%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urticaria			

subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Actinic keratosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathic ulcer			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hidradenitis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperhidrosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panniculitis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pustular psoriasis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash papular			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical discharge			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	47 / 4715 (1.00%)	42 / 4717 (0.89%)	
occurrences causally related to treatment / all	1 / 52	4 / 46	
deaths causally related to treatment / all	0 / 2	0 / 0	
Renal impairment			
subjects affected / exposed	12 / 4715 (0.25%)	17 / 4717 (0.36%)	
occurrences causally related to treatment / all	0 / 13	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	7 / 4715 (0.15%)	9 / 4717 (0.19%)	
occurrences causally related to treatment / all	0 / 7	0 / 10	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic kidney disease			

subjects affected / exposed	7 / 4715 (0.15%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	3 / 4715 (0.06%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	6 / 4715 (0.13%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	4 / 4715 (0.08%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			

subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neck obstruction			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic nephropathy			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis acute			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertonic bladder			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower urinary tract symptoms			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal cyst			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal haematoma			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal mass			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral obstruction			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal mass			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperparathyroidism			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	16 / 4715 (0.34%)	7 / 4717 (0.15%)	
occurrences causally related to treatment / all	0 / 16	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	6 / 4715 (0.13%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lumbar spinal stenosis			
subjects affected / exposed	4 / 4715 (0.08%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	2 / 4715 (0.04%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 4715 (0.06%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	2 / 4715 (0.04%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle haemorrhage			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			

subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropathy			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Articular calcification			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Costochondritis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibromyalgia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture nonunion			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathic arthropathy			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteolysis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sjogren's syndrome			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	77 / 4715 (1.63%)	74 / 4717 (1.57%)	
occurrences causally related to treatment / all	3 / 81	2 / 79	
deaths causally related to treatment / all	1 / 5	0 / 3	
Sepsis			
subjects affected / exposed	28 / 4715 (0.59%)	23 / 4717 (0.49%)	
occurrences causally related to treatment / all	0 / 29	0 / 23	
deaths causally related to treatment / all	0 / 10	0 / 3	
Urinary tract infection			
subjects affected / exposed	23 / 4715 (0.49%)	26 / 4717 (0.55%)	
occurrences causally related to treatment / all	1 / 27	1 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	20 / 4715 (0.42%)	20 / 4717 (0.42%)	
occurrences causally related to treatment / all	0 / 20	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	11 / 4715 (0.23%)	10 / 4717 (0.21%)	
occurrences causally related to treatment / all	1 / 12	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			

subjects affected / exposed	12 / 4715 (0.25%)	9 / 4717 (0.19%)	
occurrences causally related to treatment / all	0 / 14	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	14 / 4715 (0.30%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 14	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	13 / 4715 (0.28%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 14	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroenteritis			
subjects affected / exposed	8 / 4715 (0.17%)	8 / 4717 (0.17%)	
occurrences causally related to treatment / all	0 / 8	1 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	8 / 4715 (0.17%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			
subjects affected / exposed	9 / 4715 (0.19%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 9	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	7 / 4715 (0.15%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 3	0 / 2	
Postoperative wound infection			
subjects affected / exposed	4 / 4715 (0.08%)	6 / 4717 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			

subjects affected / exposed	5 / 4715 (0.11%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 5	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	7 / 4715 (0.15%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 7	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	5 / 4715 (0.11%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	4 / 4715 (0.08%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	5 / 4715 (0.11%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	1 / 4715 (0.02%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	4 / 4715 (0.08%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	4 / 4715 (0.08%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			

subjects affected / exposed	4 / 4715 (0.08%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 4715 (0.08%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	5 / 4715 (0.11%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bacteraemia			
subjects affected / exposed	2 / 4715 (0.04%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	2 / 4715 (0.04%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	4 / 4715 (0.08%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			

subjects affected / exposed	1 / 4715 (0.02%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 4715 (0.02%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis acute			
subjects affected / exposed	2 / 4715 (0.04%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	3 / 4715 (0.06%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 4715 (0.00%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	2 / 4715 (0.04%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			

subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 4715 (0.02%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess soft tissue			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			

subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intervertebral discitis			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural sepsis			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			

subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 4715 (0.00%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound sepsis			
subjects affected / exposed	2 / 4715 (0.04%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Abdominal abscess			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal sepsis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall abscess			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess oral			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Beta haemolytic streptococcal infection			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain abscess			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candiduria			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis gangrenous			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis of male external genital organ			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Citrobacter infection			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Citrobacter sepsis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridial infection			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis klebsiella			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dacryocystitis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue haemorrhagic fever			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysematous pyelonephritis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter sepsis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural abscess			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gas gangrene			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter gastritis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter infection			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis E			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster infection neurological			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected bite			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site infection			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis pneumococcal			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis externa			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal abscess			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia moraxella			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural cellulitis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic abscess			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoas abscess			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyonephrosis			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal abscess			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sterinitis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic candida			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic infection			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue abscess			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral diarrhoea			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval abscess			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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			
Hyperglycaemia			
subjects affected / exposed	30 / 4715 (0.64%)	16 / 4717 (0.34%)	
occurrences causally related to treatment / all	2 / 42	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	30 / 4715 (0.64%)	12 / 4717 (0.25%)	
occurrences causally related to treatment / all	11 / 34	4 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	13 / 4715 (0.28%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 13	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	9 / 4715 (0.19%)	3 / 4717 (0.06%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	6 / 4715 (0.13%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetic metabolic decompensation			
subjects affected / exposed	8 / 4715 (0.17%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 9	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			

subjects affected / exposed	5 / 4715 (0.11%)	5 / 4717 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	6 / 4715 (0.13%)	4 / 4717 (0.08%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	6 / 4715 (0.13%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	4 / 4715 (0.08%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	4 / 4715 (0.08%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	3 / 4715 (0.06%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	2 / 4715 (0.04%)	2 / 4717 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	3 / 4715 (0.06%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			

subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	1 / 4715 (0.02%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food intolerance			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperosmolar state			

subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 4715 (0.02%)	0 / 4717 (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	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketoacidosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ketosis			
subjects affected / exposed	0 / 4715 (0.00%)	1 / 4717 (0.02%)	
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	Placebo	Albiglutide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 4715 (0.00%)	0 / 4717 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 November 2014	Amendment 1 <ul style="list-style-type: none">- Clarification added regarding follow-up after discontinuation of investigational product.- Addition of safety assessment to dose adjustment visits.- Addition of Country Specific Requirements appendix.- Correction of typographical errors and inconsistent terminology
22 July 2015	Amendment 2 <ul style="list-style-type: none">- Amendment to study phase for participating countries where albiglutide is not licensed.- Update list of Authors.- Update to Sponsor Information- Removal of discrepancy in level of pregnancy testing required for inclusion.- Reformatting of Time and Event table to improve clarity.- Addition of table of visits for participants discontinuing investigational product (previously included in text) as an aid to investigators.- Addition of requirement of Mexican Ministry of Health to report events referred to Clinical Endpoint Committee from Mexican investigators as Serious Adverse Events.- Addition of requirement to record lipid results if they are available from participants routine clinical care outside of the trial.- Clarify that TRIM-D should not be assessed at Baseline in participants whose diabetes is treated by diet and exercise alone.- Simplification of description of safety analyses to properly reflect the planned reports.- Correction of typographical and process errors.
04 April 2017	Amendment 3 <ul style="list-style-type: none">- Addition of requirement that the study achieve a median participant follow up of at least 1.5 years as well as the sample size derived number of primary endpoints.- Specifying that to meet the primary objective of assessing the effect of albiglutide with respect to MACE, the primary analysis will be non-inferiority. If the pre-specified non-inferiority criterion is met then superiority testing will be performed with a closed testing procedure. Previously, superiority testing of MACE was considered a secondary endpoint.- Removal of multiplicity testing strategy for selected secondary endpoints.- Revision of the data collection strategy for the exploratory electronic healthcare record ancillary study with improved clarity for the planned data flow and analytical approach.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported