

**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 glycemc 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	Abiglutide
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 ($100 \times \text{number of participants with at least 1 event} / \text{first event person-years}$) is presented along with 95% confidence interval. $\text{First event person-years} = (\text{cumulative total time to first event for participants who have the event} + \text{cumulative total of censored time for participants without the event}) / 365.25$, based on the CV follow-up time period. 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 ($100 \times \text{number of participants with at least 1 event} / \text{first event person-years}$) is presented along with 95% confidence interval. First event person-years = $(\text{cumulative total time to first event for participants who have the event} + \text{cumulative total of censored time for participants without the event}) / 365.25$, based on the CV follow-up time period.

End point type	Secondary
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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 ($100 \times \text{number of participants with at least 1 event} / \text{first event person-years}$) is presented along with 95% confidence interval. $\text{First event person-years} = (\text{cumulative total time to first event for participants who have the event} + \text{cumulative total of censored time for participants without the event}) / 365.25$, based on the CV follow-up time period.	
End point type	Secondary
End point timeframe: 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*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 ^[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 ($100 \times \text{number of participants with at least 1 event} / \text{first event person-years}$) is presented along with 95% confidence interval. $\text{First event person-years} = (\text{cumulative total time to first event for participants who have the event} + \text{cumulative total of censored time for participants without the event}) / 365.25$, based on the CV follow-up time period.	
End point type	Secondary
End point timeframe: 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 ($100 \times \text{number of participants with at least 1 event} / \text{first event person-years}$) 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 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*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 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
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
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
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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
Dictionary version	21.0

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	
Phimosis			
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
Sternitis		
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