Clinical trial results:
Ensayo clínico de vacunación fase III, aleatorizado, observador-ciego, controlado con placebo, multicéntrico para evaluar la eficacia profiláctica, seguridad e inmunogenicidad de la vacuna gE/AS01B de GSK Biologicals administrada por vía intramuscular con un esquema de 0, 2 meses en adultos de 70 años y mayores.

Summary

EudraCT number	2009-015791-94
Trial protocol	ES FI DE GB SE EE FR IT CZ
Global end of trial date	24 July 2015
Results information	
Result version number	v2 (current)
This version publication date	03 May 2020
First version publication date	08 August 2016
Version creation reason	• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification	
Sponsor protocol code	113077
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02723773
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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	14 January 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- Zoster-022 study:

To evaluate vaccine efficacy (VE) in the prevention of herpes Zoster (HZ) compared to placebo in adults ≥ 70 years of age (YOA), as measured by the reduction in HZ risk.

- Zoster-006 and Zoster-022 pooled studies:

To evaluate VE in the prevention of postherpetic neuralgia (PHN) compared to placebo in subjects ≥ 70 YOA across both Phase III studies.
To consolidate VE estimation in the prevention of HZ compared to placebo in subjects ≥ 70 YOA across both Phase III studies.

Protection of trial subjects:

The vaccine/product recipients were to be observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccine/product. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed-up for 30 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 August 2010
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	United States: 1879
Country: Number of subjects enrolled	Australia: 309
Country: Number of subjects enrolled	Brazil: 627
Country: Number of subjects enrolled	Canada: 802
Country: Number of subjects enrolled	Czech Republic: 321
Country: Number of subjects enrolled	Estonia: 1015
Country: Number of subjects enrolled	Finland: 1705
Country: Number of subjects enrolled	France: 575
Country: Number of subjects enrolled	Germany: 1202
Country: Number of subjects enrolled	Hong Kong: 180
Country: Number of subjects enrolled	Italy: 109
Country: Number of subjects enrolled	Japan: 511
Country: Number of subjects enrolled	Korea, Republic of: 528
Country: Number of subjects enrolled	Mexico: 453

Country: Number of subjects enrolled	Spain: 934
Country: Number of subjects enrolled	Sweden: 961
Country: Number of subjects enrolled	Taiwan: 1110
Country: Number of subjects enrolled	United Kingdom: 692
Worldwide total number of subjects	13913
EEA total number of subjects	7514

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)	13913
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Only 13900 subjects from the total enrolled number were vaccinated and included in the Total Vaccinated Cohort. In the placebo group, 1 subject had an unknown withdrawal status before the study site closure. This was not identified during database freeze, leading to 1190 subjects in place of 1189 that actually completed the placebo group

Pre-assignment period milestones

Number of subjects started	14819[1]
Number of subjects completed	13900

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Eliminated from statistical analysess: 906
Reason: Number of subjects	No vaccination received: 13

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number started in pre-assignment period are the number of subjects considered for enrollment. However, 906 subjects were excluded for analysis- leading to actual enrolled of 13913, which was considered as the total eligible cohort. This total eligible cohort was considered for further analysis.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Zoster-022 GSK1437173A Group

Arm description:

Subjects receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.

Arm type	Experimental
Investigational medicinal product name	GSK1437173A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The study product was administered according to a 0, 2 month schedule.

Arm title	Zoster-022 Placebo Group

Arm description:

Subjects receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The study product was administered according to a 0, 2 month schedule.

Number of subjects in period 1[2]	Zoster-022 GSK1437173A Group	Zoster-022 Placebo Group
Started	6950	6950
Completed	5770	5760
Not completed	1180	1190
Consent withdrawn by subject	387	396
Non-Serious Adverse Event	47	15
No reason from the subject	108	102
Migrated/moved from study area	51	46
Suspected HZ Episode	2	2
Lost to follow-up	123	133
Serious Adverse Event	456	487
Protocol deviation	6	8
Unknown completion status	-	1

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of the 13913 subjects considered for analysis in the trial, 13 were assigned participant codes but did not receive vaccination, hence were excluded from study start.

Baseline characteristics

Reporting groups	
Reporting group title	Zoster-022 GSK1437173A Group
Reporting group description:	
Subjects receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.	
Reporting group title	Zoster-022 Placebo Group
Reporting group description:	
Subjects receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.	

Reporting group values	Zoster-022 GSK1437173A Group	Zoster-022 Placebo Group	Total
Number of subjects	6950	6950	13900
Age categorical Units: Subjects			
Age continuous			
Age continuous description			
Units: years			
arithmetic mean	75.6	75.6	
standard deviation	± 4.7	± 4.7	-
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	3789	3836	7625
Male	3161	3114	6275

End points

End points reporting groups

Reporting group title	Zoster-022 GSK1437173A Group
Reporting group description:	
Subjects receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.	
Reporting group title	Zoster-022 Placebo Group
Reporting group description:	
Subjects receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.	
Subject analysis set title	Zoster-022 GSK1437173A 70-79YOA Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects between 70 and 79 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.	
Subject analysis set title	Zoster-022 GSK1437173A >=80YOA Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects above 80 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.	
Subject analysis set title	Zoster-022 GSK1437173A >=70YOA Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects above 70 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.	
Subject analysis set title	Zoster-022 Placebo 70-79YOA Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects between 70 and 79 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.	
Subject analysis set title	Zoster-022 Placebo >=80YOA Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects above 80 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.	
Subject analysis set title	Zoster-022 Placebo >=70YOA Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects above 70 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.	
Subject analysis set title	Zoster-022/006 Pooled GSK1437173A 70-79YOA Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects between 70 and 79 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.	
Subject analysis set title	Zoster-022/006 Pooled GSK1437173A >=80YOA Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects above 80 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.	
Subject analysis set title	Zoster-022/006 Pooled GSK1437173A >=70YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects above 70 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled Placebo 70-79YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects between 70 and 79 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled Placebo >=80YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects above 80 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled Placebo >=70YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects above 70 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled GSK1437173A 50-59 YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects between 50 and 59 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled GSK1437173A 60-69 YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects between 60 and 69 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled GSK1437173A 70-79 YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects between 70 and 79 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled GSK1437173A >=80 YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects above 80 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled Placebo 50-59 YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects between 50 and 59 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled Placebo 60-69 YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects between 60 and 69 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled Placebo 70-79 YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects between 70 and 79 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled Placebo >=80 YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects above 80 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled GSK1437173A >=70 YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects above 70 years of age (YOA), receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.

Subject analysis set title	Zoster-022/006 Pooled Placebo >=70 YOA Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects above 70 years of age (YOA), receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.

Primary: Number of subjects with any episodes of herpes zoster (HZ)

End point title	Number of subjects with any episodes of herpes zoster (HZ)

End point description:

Confirmed HZ cases during the study in the modified total vaccinated cohort (mTVc). The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Primary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A 70-79YOA Group	Zoster-022 GSK1437173A >=80YOA Group	Zoster-022 GSK1437173A >=70YOA Group	Zoster-022 Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5114	1427	6541	5189
Units: Subjects	17	6	23	169

End point values	Zoster-022 Placebo >=80YOA Group	Zoster-022 Placebo >=70YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1433	6622		
Units: Subjects	54	223		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of vaccine efficacy in prevention of Herpes Zoster (HZ) disease between Zoster-022 GSK1437173A 70-79 YOA group and Zoster-022 Placebo 70-79 YOA group.

Comparison groups	Zoster-022 GSK1437173A 70-79YOA Group v Zoster-022

	Placebo 70-79YOA Group
Number of subjects included in analysis	10303
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.0001
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	90.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	83.54
upper limit	94.32

Notes:

[1] - The efficacy of Herpes Zoster subunit (HZ/su) vaccine against herpes zoster disease was demonstrated if the lower limit (LL) of the two-sided 95% Confidence Interval (CI) of VE was above 10%.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of vaccine efficacy in prevention of Herpes Zoster (HZ) disease between Zoster-022 GSK1437173A >=80YOA Group and Zoster-022 Placebo Zoster-022 Placebo >=80YOA Group

Comparison groups	Zoster-022 Placebo >=80YOA Group v Zoster-022 GSK1437173A >=80YOA Group
Number of subjects included in analysis	2860
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.0001
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	89.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	74.65
upper limit	96.16

Notes:

[2] - The efficacy of HZ/su vaccine against herpes zoster disease was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 10%

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of vaccine efficacy in prevention of Herpes Zoster (HZ) disease between Zoster-022 GSK1437173A >=70YOA Group and Zoster-022 Placebo >=70YOA Group

Comparison groups	Zoster-022 GSK1437173A >=70YOA Group v Zoster-022 Placebo >=70YOA Group
Number of subjects included in analysis	13163
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.0001
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	89.79

Confidence interval	
level	95 %
sides	2-sided
lower limit	84.29
upper limit	93.66

Notes:

[3] - The efficacy of HZ/su vaccine against herpes zoster disease was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 10%

Primary: Outcome measure for the pooled analysis of combined data from studies ZOSTER-006 (NCT01165177) and ZOSTER-022 (NCT01165229): Number of subjects with post-herpetic neuralgia (PHN)

End point title	Outcome measure for the pooled analysis of combined data from studies ZOSTER-006 (NCT01165177) and ZOSTER-022 (NCT01165229): Number of subjects with post-herpetic neuralgia (PHN)

End point description:

Incidence of PHN calculated using the mTVc during the entire study period in subjects ≥ 70 years of age (YOA). The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Primary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022/006 Pooled GSK1437173A 70-79YOA Group	Zoster-022/006 Pooled GSK1437173A >=80YOA Group	Zoster-022/006 Pooled GSK1437173A >=70YOA Group	Zoster-022/006 Pooled Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6468	1782	8250	6554
Units: Subjects	2	2	4	29

End point values	Zoster-022/006 Pooled Placebo >=80YOA Group	Zoster-022/006 Pooled Placebo >=70YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1792	8346		
Units: Subjects	7	36		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of vaccine efficacy in prevention of Post-Herpetic Neuralgia (PHN) between Zoster-022/006

Pooled GSK1437173A 70-79 YOA Group and Zoster-022/006 Pooled Placebo 70-79YOA Group	
Comparison groups	Zoster-022/006 Pooled GSK1437173A 70-79YOA Group v Zoster-022/006 Pooled Placebo 70-79YOA Group
Number of subjects included in analysis	13022
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	< 0.0001
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	93.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	72.47
upper limit	99.19

Notes:

[4] - The efficacy of HZ/su vaccine against PHN was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 0%

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of vaccine efficacy in prevention of PHN between Zoster-022/006 Pooled GSK1437173A>=80YOA Group and Zoster-022/006 Pooled Placebo >=80YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A >=80YOA Group v Zoster-022/006 Pooled Placebo >=80YOA Group
Number of subjects included in analysis	3574
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.1844
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	71.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.51
upper limit	97.08

Notes:

[5] - The efficacy of HZ/su vaccine against PHN was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 0%

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of vaccine efficacy in prevention of PHN between Zoster-022/006 Pooled GSK1437173A>=70YOA Group and Zoster-022/006 Pooled Placebo >=70YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A >=70YOA Group v Zoster-022/006 Pooled Placebo >=70YOA Group
Number of subjects included in analysis	16596
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	< 0.0001
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	88.78

Confidence interval	
level	95 %
sides	2-sided
lower limit	68.7
upper limit	97.1

Notes:

[6] - The efficacy of HZ/su vaccine against PHN was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 0%

Primary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with confirmed HZ

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with confirmed HZ

End point description:

Occurrence of confirmed HZ during the entire study period in subjects ≥ 70 YOA. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Primary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022/006 Pooled GSK1437173A 70-79YOA Group	Zoster-022/006 Pooled GSK1437173A >=80YOA Group	Zoster-022/006 Pooled GSK1437173A >=70YOA Group	Zoster-022/006 Pooled Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6468	1782	8250	6554
Units: Subjects	19	6	25	216

End point values	Zoster-022/006 Pooled Placebo >=80YOA Group	Zoster-022/006 Pooled Placebo >=70YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1792	8346		
Units: Subjects	68	284		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of vaccine efficacy in prevention of herpes zoster disease between Zoster-022/006 Pooled GSK1437173A 70-79YOA Group and Zoster-022/006 Pooled Placebo 70-79YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A 70-79YOA Group v Zoster-022/006 Pooled Placebo 70-79YOA Group
Number of subjects included in analysis	13022
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	< 0.0001
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	91.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	86.04
upper limit	94.85

Notes:

[7] - The efficacy of HZ/su vaccine against herpes zoster disease was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 10%

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of vaccine efficacy in prevention of herpes zoster disease between Zoster-022/006 Pooled GSK1437173A >=80YOA Group and Zoster-022/006 Pooled Placebo >=80YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A >=80YOA Group v Zoster-022/006 Pooled Placebo >=80YOA Group
Number of subjects included in analysis	3574
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	< 0.0001
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	91.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	80.22
upper limit	96.94

Notes:

[8] - The efficacy of HZ/su vaccine against herpes zoster disease was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 10%

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of vaccine efficacy in prevention of herpes zoster disease between Zoster-022/006 GSK1437173A >=70 YOA Group and Zoster-022/006 Pooled Placebo >=70YOA Group

Comparison groups	Zoster-022/006 Pooled Placebo >=70YOA Group v Zoster-022/006 Pooled GSK1437173A >=70YOA Group

Number of subjects included in analysis	16596
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	< 0.0001
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	91.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	86.88
upper limit	94.46

Notes:

[9] - The efficacy of HZ/su vaccine against herpes zoster disease was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 10%

Secondary: Number of subjects with post-herpetic neuralgia (PHN)

End point title	Number of subjects with post-herpetic neuralgia (PHN)

End point description:

PHN cases in the mTVc. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A 70-79YOA Group	Zoster-022 GSK1437173A >=80YOA Group	Zoster-022 GSK1437173A >=70YOA Group	Zoster-022 Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5114	1427	6541	5189
Units: Subjects	2	2	4	22

End point values	Zoster-022 Placebo >=80YOA Group	Zoster-022 Placebo >=70YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1433	6622		
Units: Subjects	6	28		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of of Vaccine Efficacy (VE) in prevention of PHN between Zoster-022 GSK1437173A 70-79YOA Group and Zoster-022 placebo 70-79YOA Group

Comparison groups	Zoster-022 GSK1437173A 70-79YOA Group v Zoster-022 Placebo 70-79YOA Group
Number of subjects included in analysis	10303
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	< 0.0001
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	90.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	62.57
upper limit	98.95

Notes:

[10] - The efficacy of HZ/su vaccine against PHN was demonstrated if the LL of the two-sided 95% CI of VE was above 0%.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of vaccine efficacy in prevention of PHN between Zoster-022 GSK1437173A >=80YOA Group and Zoster-022 Placebo >=80YOA Group

Comparison groups	Zoster-022 GSK1437173A >=80YOA Group v Zoster-022 Placebo >=80YOA Group
Number of subjects included in analysis	2860
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	= 0.3072
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	65.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-91.58
upper limit	96.62

Notes:

[11] - The efficacy of HZ/su vaccine against PHN was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 0%

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of vaccine efficacy in prevention of PHN between Zoster-022 GSK1437173A >=70YOA Group and Zoster-022 Placebo >=70YOA Group

Comparison groups	Zoster-022 GSK1437173A >=70YOA Group v Zoster-022 Placebo >=70YOA Group

Number of subjects included in analysis	13163
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	< 0.0001
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	85.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	58.52
upper limit	96.3

Notes:

[12] - The efficacy of HZ/su vaccine against PHN was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 0%

Secondary: Number of days with severe 'worst' HZ-associated pain

End point title	Number of days with severe 'worst' HZ-associated pain

End point description:

Duration of severe 'worst' HZ-associated pain following the onset of a confirmed HZ rash over the entire pain reporting period as measured by the Zoster Brief Pain Inventory (ZBPI) in subjects with confirmed HZ. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A 70-79YOA Group	Zoster-022 GSK1437173A >=80YOA Group	Zoster-022 GSK1437173A >=70YOA Group	Zoster-022 Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	3	18	150
Units: Days				
arithmetic mean (standard deviation)	21.8 (± 31.41)	98.7 (± 57.73)	34.6 (± 45.54)	47.9 (± 100.08)

End point values	Zoster-022 Placebo >=80YOA Group	Zoster-022 Placebo >=70YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	198		
Units: Days				
arithmetic mean (standard deviation)	50.4 (± 106.51)	48.5 (± 101.4)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Comparison of VE in reduction of duration of severe worst HZ associated pain between Zoster-022 GSK1437173A 70-79YOA Group and Zoster-022 Placebo 70-79YOA Group	
Comparison groups	Zoster-022 Placebo 70-79YOA Group v Zoster-022 GSK1437173A 70-79YOA Group
Number of subjects included in analysis	165
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	= 0.3749
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.4
upper limit	54.39

Notes:

[13] - The efficacy of HZ/su vaccine against duration of severe worst HZ associated pain was demonstrated if the LL of the two-sided 95% CI of VE derived from the Hazard ratio was above 0%.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Comparison of VE in reduction of duration of severe worst HZ associated pain between Zoster-022 GSK1437173A >=80YOA Group and Zoster-022 Placebo>=80YOA Group	
Comparison groups	Zoster-022 GSK1437173A >=80YOA Group v Zoster-022 Placebo >=80YOA Group
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	= 0.2466
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	51.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-65.55
upper limit	85.95

Notes:

[14] - The efficacy of HZ/su vaccine against duration of severe worst HZ associated pain was demonstrated if the LL of the two-sided 95% CI of VE derived from the Hazard ratio was above 0%.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:	
Comparison of VE in reduction of duration of severe worst HZ associated pain between Zoster-022 GSK1437173A >=70YOA Group and Zoster-022 Placebo>=70YOA Group	
Comparison groups	Zoster-022 GSK1437173A >=70YOA Group v Zoster-022 Placebo >=70YOA Group
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other[15]
P-value	= 0.1877
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	28.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.69
upper limit	56.44

Notes:

[15] - The efficacy of HZ/su vaccine against duration of severe worst HZ associated pain was demonstrated if the LL of the two-sided 95% CI of VE derived from the Hazard ratio was above 0%.

Secondary: Number of subjects with confirmed HZ episode related mortality and hospitalizations

End point title	Number of subjects with confirmed HZ episode related mortality and hospitalizations

End point description:

The number of subjects with confirmed HZ related mortality and hospitalizations were tabulated. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A 70-79YOA Group	Zoster-022 GSK1437173A >=80YOA Group	Zoster-022 GSK1437173A >=70YOA Group	Zoster-022 Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5114	1427	6541	5189
Units: Subjects				
Mortality	0	0	0	0
Hospitalization	0	0	0	3
Mortality or hospitalization	0	0	0	3

End point values	Zoster-022 Placebo >=80YOA Group	Zoster-022 Placebo >=70YOA Group		

Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1433	6622		
Units: Subjects				
Mortality	0	0		
Hospitalization	2	5		
Mortality or hospitalization	2	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with overall mortality and HZ-related mortality

End point title	Number of subjects with overall mortality and HZ-related mortality

End point description:

The number of subjects with overall mortality and HZ related mortality were tabulated. Evaluation of VE in the reduction of overall and HZ related mortality as per study objective was not performed due to low number of events reported. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A 70-79YOA Group	Zoster-022 GSK1437173A >=80YOA Group	Zoster-022 GSK1437173A >=70YOA Group	Zoster-022 Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5114	1427	6541	5189
Units: Subjects	0	0	0	0

End point values	Zoster-022 Placebo >=80YOA Group	Zoster-022 Placebo >=70YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1433	6622		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with confirmed HZ episode related hospitalizations

End point title	Number of subjects with confirmed HZ episode related hospitalizations

End point description:

Incidence of overall and HZ-related hospitalizations during the study. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A 70-79YOA Group	Zoster-022 GSK1437173A >=80YOA Group	Zoster-022 GSK1437173A >=70YOA Group	Zoster-022 Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5114	1427	6541	5189
Units: Subjects	0	0	0	3

End point values	Zoster-022 Placebo >=80YOA Group	Zoster-022 Placebo >=70YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1433	6622		
Units: Subjects	2	5		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of VE in reduction of overall and HZ related hospitalizations between Zoster-022 GSK1437173A 70-79YOA Group and Zoster-022 Placebo 70-79YOA Group

Comparison groups	Zoster-022 GSK1437173A 70-79YOA Group v Zoster-022 Placebo 70-79YOA Group
Number of subjects included in analysis	10303
Analysis specification	Pre-specified
Analysis type	other[16]
P-value	= 0.2533
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	100

Confidence interval	
level	95 %
sides	2-sided
lower limit	-144.13
upper limit	100

Notes:

[16] - Efficacy of the HZ/su vaccine against overall and HZ related hospitalizations was demonstrated if the LL of the two-sided 95% CI of VE was above 0%.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of VE in reduction of overall and HZ related hospitalizations between Zoster-022 GSK1437173A >=80YOA Group and Zoster-022 Placebo >=80YOA Group

Comparison groups	Zoster-022 GSK1437173A >=80YOA Group v Zoster-022 Placebo >=80YOA Group
Number of subjects included in analysis	2860
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	= 0.5024
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-435.14
upper limit	100

Notes:

[17] - Efficacy of the HZ/su vaccine against overall and HZ related hospitalizations was demonstrated if the LL of the two-sided 95% CI of VE was above 0%.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of VE in reduction of overall and HZ related hospitalizations between Zoster-022 GSK1437173A >=70YOA Group and Zoster-022 Placebo >=70YOA Group

Comparison groups	Zoster-022 GSK1437173A >=70YOA Group v Zoster-022 Placebo >=70YOA Group
Number of subjects included in analysis	13163
Analysis specification	Pre-specified
Analysis type	other[18]
P-value	= 0.0636
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.92
upper limit	100

Notes:

[18] - Efficacy of the HZ/su vaccine against overall and HZ related hospitalizations was demonstrated if the LL of the two-sided 95% CI of VE was above 0%.

Secondary: Number of subjects with HZ related complications

End point title	Number of subjects with HZ related complications

End point description:

Incidence of HZ complications during the study in subjects with confirmed HZ. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A 70-79YOA Group	Zoster-022 GSK1437173A >=80YOA Group	Zoster-022 GSK1437173A >=70YOA Group	Zoster-022 Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	6	23	169
Units: Subjects				
At least one complication	1	0	1	6
HZ vasculitis	0	0	0	0
Disseminated Disease	0	0	0	0
Ophthalmic Disease	1	0	1	4
Neurologic Disease	0	0	0	3
Visceral Disease	0	0	0	0
Stroke	0	0	0	0

End point values	Zoster-022 Placebo >=80YOA Group	Zoster-022 Placebo >=70YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	223		
Units: Subjects				
At least one complication	4	10		
HZ vasculitis	0	0		
Disseminated Disease	2	2		
Ophthalmic Disease	2	6		
Neurologic Disease	0	3		
Visceral Disease	0	0		
Stroke	0	0		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of VE in reduction of HZ related complications between Zoster-022 GSK1437173A 70-79YOA Group and Zoster-022 Placebo 70-79YOA Group

Comparison groups	Zoster-022 GSK1437173A 70-79YOA Group v Zoster-022

	Placebo 70-79YOA Group
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	= 0.4947
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	-65.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-827.06
upper limit	73.62

Notes:

[19] - Efficacy of the HZ/su vaccine against HZ related complications was demonstrated if the LL of the VE was above 0%.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of VE in reduction of HZ related complications between Zoster-022 GSK1437173A >=80YOA Group and Zoster-022 Placebo >=80YOA Group

Comparison groups	Zoster-022 GSK1437173A >=80YOA Group v Zoster-022 Placebo >=80YOA Group
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other[20]
P-value	= 1
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-558.05
upper limit	100

Notes:

[20] - Efficacy of the HZ/su vaccine against HZ related complications was demonstrated if the LL of the VE was above 0%

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of VE in reduction of HZ related complications between Zoster-022 GSK1437173A >=70YOA Group and Zoster-022 Placebo >=70YOA Group

Comparison groups	Zoster-022 GSK1437173A >=70YOA Group v Zoster-022 Placebo >=70YOA Group
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	other[21]
P-value	= 1
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	0.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	-433.32
upper limit	83.16

Notes:

[21] - Efficacy of the HZ/su vaccine against HZ related complications was demonstrated if the LL of the VE was above 0%

Secondary: Number of subjects receiving pain medication associated with HZ

End point title	Number of subjects receiving pain medication associated with HZ

End point description:

Incidence of use of pain medications throughout the study. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A 70-79YOA Group	Zoster-022 GSK1437173A >=80YOA Group	Zoster-022 GSK1437173A >=70YOA Group	Zoster-022 Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	6	23	169
Units: Subjects				
At least 1 pain medication	7	3	10	123
1 pain medication only	5	0	5	43
2 pain medications only	0	1	1	30
3 pain medications or more	2	2	4	50

End point values	Zoster-022 Placebo >=80YOA Group	Zoster-022 Placebo >=70YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	223		
Units: Subjects				
At least 1 pain medication	37	160		
1 pain medication only	17	60		
2 pain medications only	4	34		
3 pain medications or more	16	66		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of VE in reduction in use of pain medication between Zoster-022 GSK1437173A 70-79YOA Group and Zoster-022 Placebo 70-79YOA Group

Comparison groups	Zoster-022 GSK1437173A 70-79YOA Group v Zoster-022 Placebo 70-79YOA Group
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other[22]
P-value	= 0.0112
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	43.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.77
upper limit	70.53

Notes:

[22] - Efficacy of the HZ/su vaccine against use of pain medications was demonstrated if the LL of the two-sided 95% CI of VE was above 0%.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of VE in reduction in use of pain medication between Zoster-022 GSK1437173A >=80YOA Group and Zoster-022 Placebo >=80YOA Group

Comparison groups	Zoster-022 GSK1437173A >=80YOA Group v Zoster-022 Placebo >=80YOA Group
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other[23]
P-value	= 0.3903
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	27.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.43
upper limit	73.2

Notes:

[23] - Efficacy of the HZ/su vaccine against use of pain medications was demonstrated if the LL of the two-sided 95% CI of the VE was above 0%

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of VE in reduction in use of pain medication between Zoster-022 GSK1437173A >=70YOA group and Zoster-022 Placebo >=70YOA Group

Comparison groups	Zoster-022 GSK1437173A >=70YOA Group v Zoster-022 Placebo >=70YOA Group

Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	other[24]
P-value	= 0.0083
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	39.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.79
upper limit	64.75

Notes:

[24] - Efficacy of the HZ/su vaccine against use of pain medications was demonstrated if the LL of the two-sided 95% CI of VE was above 0%.

Secondary: Number of days with pain medication associated with HZ

End point title	Number of days with pain medication associated with HZ

End point description:

Incidence of reduction of duration of pain medication associated with HZ throughout the study. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A 70-79YOA Group	Zoster-022 GSK1437173A >=80YOA Group	Zoster-022 GSK1437173A >=70YOA Group	Zoster-022 Placebo 70-79YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	3	10	123
Units: Days				
arithmetic mean (standard deviation)	38.7 (± 56.44)	274.7 (± 337)	109.5 (± 200.88)	218.6 (± 593.8)

End point values	Zoster-022 Placebo >=80YOA Group	Zoster-022 Placebo >=70YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	37	160		
Units: Days				
arithmetic mean (standard deviation)	135 (± 207.31)	199.3 (± 530.6)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Comparison of VE in reduction in duration of pain medication associated with HZ between Zoster-022 GSK1437173A 70-79YOA Group and Zoster-022 Placebo 70-79YOA Group	
Comparison groups	Zoster-022 GSK1437173A 70-79YOA Group v Zoster-022 Placebo 70-79YOA Group
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	other[25]
P-value	= 0.0232
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	58.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.45
upper limit	80.96

Notes:

[25] - Efficacy of the HZ/su vaccine against duration of pain medication associated with HZ was demonstrated if the LL of the two-sided 95% CI of VE derived from the hazard ratio was above 0%.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Comparison of VE in reduction in duration of pain medication associated with HZ between Zoster-022 GSK1437173A >=80YOA Group and Zoster-022 Placebo >=80YOA Group	
Comparison groups	Zoster-022 GSK1437173A >=80YOA Group v Zoster-022 Placebo >=80YOA Group
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[26]
P-value	= 0.8324
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	-14.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-303.3
upper limit	67.46

Notes:

[26] - Efficacy of the HZ/su vaccine against duration of pain medication associated with HZ was demonstrated if the LL of the two-sided 95% CI of VE derived from the hazard ratio was above 0%.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of VE in reduction in duration of pain medication associated with HZ between Zoster-022 GSK1437173A >=70YOA Group and Zoster-022 Placebo >=70YOA Group

Comparison groups	Zoster-022 GSK1437173A >=70YOA Group v Zoster-022 Placebo >=70YOA Group
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	other[27]
P-value	= 0.0404
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	49.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.92
upper limit	73.47

Notes:

[27] - Efficacy of the HZ/su vaccine against duration of pain medication associated with HZ was demonstrated if the LL of the two-sided 95% CI of VE derived from the hazard ratio was above 0%.

Secondary: Number of subjects with any and grade 3 solicited local symptoms

End point title	Number of subjects with any and grade 3 solicited local symptoms

End point description:

Occurrence, intensity of each solicited local symptom within 7 days (Days 0-6) after each vaccination, in subjects included in the 7-day diary card subset; Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site. The analysis was performed on the total vaccinated cohort – Diary Card, which was a subset of subjects from the total vaccinated cohort, who completed diary cards with any solicited symptoms during the 7 days (Day 0 to Day 6) post vaccination period

End point type	Secondary

End point timeframe:

Within the 7 days (Days 0-6) after each vaccination

End point values	Zoster-022 GSK1437173A Group	Zoster-022 Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	505	505		
Units: Subjects				
Any Pain, Dose 1 (N=502;504)	297	26		
Grade 3 Pain, Dose 1 (N=502;504)	12	1		
Any Redness, Dose 1 (N=502;504)	143	3		
Grade 3 Redness, Dose 1 (N=502;504)	9	0		
Any Swelling, Dose 1 (N=502;504)	85	2		
Grade 3 Swelling, Dose 1 (N=502;504)	2	0		
Any Pain, Dose 2 (N=492;491)	282	23		
Grade 3 Pain, Dose 2 (N=492;491)	12	0		
Any Redness, Dose 2 (N=492;491)	137	3		
Grade 3 Redness, Dose 2 (N=492;491)	15	0		

Any Swelling, Dose 2 (N=492;491)	68	0		
Grade 3 Swelling, Dose 2 (N=492;491)	7	0		
Any Pain, Across Doses (N=505;505)	347	43		
Grade 3 Pain, Across Doses (N=505;505)	22	1		
Any Redness, Across Doses (N=505;505)	198	5		
Grade 3 Redness, Across Doses (N=505;505)	20	0		
Any Swelling, Across Doses (N=505;505)	114	2		
Grade 3 Swelling, Across Doses (N=505;505)	8	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms

End point title	Number of subjects with any, grade 3 and related solicited general symptoms

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal symptoms, headache, myalgia, shivering and fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.0 °C. Related = symptom assessed by the investigator as related to the vaccination.The analysis was performed on the total vaccinated cohort – Diary Card, which was a subset of subjects from the total vaccinated cohort, who completed diary cards with any solicited symptoms during the 7 days (Day 0 to Day 6) post vaccination period

End point type	Secondary

End point timeframe:

Within the 7 days (Days 0-6) post-vaccination period following each dose and across doses

End point values	Zoster-022 GSK1437173A Group	Zoster-022 Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	501	505		
Units: Subjects				
Any Fatigue, Dose 1 (N=501;503)	104	56		
Grade 3 Fatigue, Dose 1 (N=501;503)	8	4		
Related Fatigue, Dose 1 (N=501;503)	85	34		
Any Gastrointestinal, Dose 1 (N=501;503)	25	28		
Grade 3 Gastrointestinal, Dose 1 (N=501;503)	3	2		
Related Gastrointestinal, Dose 1 (N=501;503)	16	14		
Any Headache, Dose 1 (N=501;503)	72	42		
Grade 3 Headache, Dose 1 (N=501;503)	2	4		

Related Headache, Dose 1 (N=501;503)	58	27		
Any Myalgia, Dose 1 (N=501;503)	106	27		
Grade 3 Myalgia, Dose 1 (N=501;503)	6	2		
Related Myalgia, Dose 1 (N=501;503)	91	16		
Any Shivering, Dose 1 (N=501;503)	38	17		
Grade 3 Shivering, Dose 1 (N=501;503)	1	1		
Related Shivering, Dose 1 (N=501;503)	32	12		
Any Temperature, Dose 1 (N=501;503)	39	9		
Grade 3 Temperature, Dose 1 (N=501;503)	0	2		
Related Temperature, Dose 1 (N=501;503)	31	4		
Any Fatigue, Dose 2 (N=492;489)	122	39		
Grade 3 Fatigue, Dose 2 (N=492;489)	9	0		
Related Fatigue, Dose 2 (N=492;489)	105	30		
Any Gastrointestinal, Dose 2 (N=492;489)	37	19		
Grade 3 Gastrointestinal, Dose 2 (N=492;489)	3	1		
Related Gastrointestinal, Dose 2 (N=492;489)	26	13		
Any Headache, Dose 2 (N=492;489)	76	26		
Grade 3 Headache, Dose 2 (N=492;489)	4	0		
Related Headache, Dose 2 (N=492;489)	63	20		
Any Myalgia, Dose 2 (N=492;489)	113	18		
Grade 3 Myalgia, Dose 2 (N=492;489)	7	0		
Related Myalgia, Dose 2 (N=492;489)	94	16		
Any Shivering, Dose 2 (N=492;489)	59	11		
Grade 3 Shivering, Dose 2 (N=492;489)	5	1		
Related Shivering, Dose 2 (N=492;489)	47	9		
Any Temperature, Dose 2 (N=492;489)	38	6		
Grade 3 Temperature, Dose 2 (N=492;489)	0	2		
Related Temperature, Dose 2 (N=492;489)	35	2		
Any Fatigue, Across Doses (N=504;505)	166	77		
Grade 3 Fatigue, Across Doses (N=504;505)	16	4		
Related Fatigue, Across Doses (N=504;505)	140	52		
Any Gastrointestinal, Across Doses (N=504;505)	55	40		
Grade 3 Gastrointestinal, Across Doses (N=504;505)	5	2		
Related Gastrointestinal, Across Doses (N=504;505)	38	21		
Any Headache, Across Doses (N=504;505)	124	55		
Grade 3 Headache, Across Doses (N=504;505)	5	4		
Related Headache, Across Doses (N=504;505)	104	37		
Any Myalgia, Across Doses (N=504;505)	157	41		
Grade 3 Myalgia, Across Doses (N=504;505)	12	2		
Related Myalgia, Across Doses (N=504;505)	137	29		

Any Shivering, Across Doses (N=504;505)	75	22		
Grade 3 Shivering, Across Doses (N=504;505)	6	2		
Related Shivering, Across Doses (N=504;505)	64	16		
Any Temperature, Across Doses (N=504;505)	62	13		
Grade 3 Temperature, Across Doses (N=504;505)	0	2		
Related Temperature, Across Doses (N=504;505)	54	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related unsolicited adverse events (AEs)

End point title	Number of subjects with any, grade 3 and related unsolicited adverse events (AEs)

End point description:

Occurrence, intensity and relationship to vaccination of unsolicited AEs during 30 days (Days 0-29) after each vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification in all subjects. An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

Within the 30 days (Days 0-29) after each vaccination

End point values	Zoster-022 GSK1437173A Group	Zoster-022 Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6950	6950		
Units: Subjects				
Any AE(s)	3859	2263		
Grade 3 AE(s)	485	265		
Related AE(s)	2853	529		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and related serious adverse events (SAEs)

End point title	Number of subjects with any and related serious adverse events (SAEs)

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

From Month 0 to Month 14

End point values	Zoster-022 GSK1437173A Group	Zoster-022 Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6950	6950		
Units: Subjects				
Any SAE(s)	891	939		
Related SAE(s)	12	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and related potential immune mediated diseases (pIMDs)

End point title	Number of subjects with any and related potential immune mediated diseases (pIMDs)

End point description:

Occurrence and relationship to vaccination of any potential immune-mediated diseases (pIMDs) during the entire study period in all subjects. This analysis was based on the the total vaccinated cohort, which included all subjects with at least one dose of study vaccine or placebo administered.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A Group	Zoster-022 Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6950	6950		
Units: Subjects				
Any pIMD	92	97		
Related pIMD(s)	8	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and related Medically Attended visits

End point title	Number of subjects with any and related Medically Attended visits

End point description:

Occurrence and relationship to vaccination of medically attended visits other than routine health care visits, from Month 0 to Month 8 in all subjects. Medically attended visits were defined as events for which the subject received medical attention defined as hospitalization, an emergency room visit, or a visit to or from medical personnel (medical doctor) for any reason. Any medically attended visits(s) = Occurrence of any medically attended visits(s) regardless of intensity grade or relation to vaccination. This analysis was based on the the total vaccinated cohort, which included all subjects with at least one dose of study vaccine or placebo administered.

End point type	Secondary

End point timeframe:

From Month 0 to Month 8 post-vaccination

End point values	Zoster-022 GSK1437173A Group	Zoster-022 Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6950	6950		
Units: Subjects				
Any medically attended visits	2882	2911		
Related medically attended visits	165	66		

Statistical analyses

No statistical analyses for this end point

Secondary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Overall number of subjects with PHN in subjects ≥ 50 YOA

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Overall number of subjects with PHN in subjects ≥ 50 YOA

End point description:

Incidence of PHN calculated using the mTVc during the entire study period in subjects ≥ 50 YOA. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022/006 Pooled GSK1437173A 50-59 YOA Group	Zoster-022/006 Pooled GSK1437173A 60-69 YOA Group	Zoster-022/006 Pooled GSK1437173A 70-79 YOA Group	Zoster-022/006 Pooled GSK1437173A >=80 YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3491	2140	6468	1782
Units: Subjects	0	0	2	2

End point values	Zoster-022/006 Pooled Placebo 50-59 YOA Group	Zoster-022/006 Pooled Placebo 60-69 YOA Group	Zoster-022/006 Pooled Placebo 70-79 YOA Group	Zoster-022/006 Pooled Placebo >=80 YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3523	2166	6554	1792
Units: Subjects	8	2	29	7

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of vaccine efficacy in prevention of PHN between Zoster-022/006 Pooled GSK1437173A 50-59YOA Group and Zoster-022/006 Pooled Placebo 50-59YOA Group.Comparison of vaccine efficacy for groups 70-79 and above 80 YOA are presented in outcome measure 2.

Comparison groups	Zoster-022/006 Pooled GSK1437173A 50-59 YOA Group v Zoster-022/006 Pooled Placebo 50-59 YOA Group
Number of subjects included in analysis	7014
Analysis specification	Pre-specified
Analysis type	other[28]
P-value	= 0.0081
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	40.88
upper limit	100

Notes:

[28] - The efficacy of HZ/su vaccine against PHN was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 0%

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of vaccine efficacy in prevention of PHN between Zoster-022/006 Pooled GSK1437173A 60-69YOA Group and Zoster-022/006 Pooled Placebo 60-69YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A 60-69 YOA Group v Zoster-022/006 Pooled Placebo 60-69 YOA Group
Number of subjects included in analysis	4306
Analysis specification	Pre-specified
Analysis type	other[29]
P-value	= 0.5097
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-442.83
upper limit	100

Notes:

[29] - The efficacy of HZ/su vaccine against PHN was demonstrated if the lower limit of the of the 2-sided 95% CI of VE was above 0%

Secondary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with a reduction of PHN incidence in subjects ≥ 50 YOA with confirmed HZ

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with a reduction of PHN incidence in subjects ≥ 50 YOA with confirmed HZ

End point description:

Occurrence of PHN during the entire study period in all subjects with confirmed HZ.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022/006 Pooled GSK1437173A 50-59 YOA Group	Zoster-022/006 Pooled GSK1437173A 60-69 YOA Group	Zoster-022/006 Pooled GSK1437173A 70-79 YOA Group	Zoster-022/006 Pooled GSK1437173A >=80 YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	3	19	6
Units: Subjects	0	0	2	2

End point values	Zoster-022/006 Pooled Placebo 50-59 YOA Group	Zoster-022/006 Pooled Placebo 60-69 YOA Group	Zoster-022/006 Pooled Placebo 70-79 YOA Group	Zoster-022/006 Pooled Placebo >=80 YOA Group

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	103	90	216	68
Units: Subjects	8	2	29	7

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of Vaccine efficacy in reduction of PHN incidence in subjects with confirmed HZ episode in Zoster-022/006 Pooled GSK1437173A 50-59 YOA Group versus Zoster-022/006 Pooled Placebo 50-59 YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A 50-59 YOA Group v Zoster-022/006 Pooled Placebo 50-59 YOA Group
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other[30]
P-value	= 1
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-649.86
upper limit	100

Notes:

[30] - The efficacy of HZ/su vaccine in reduction of PHN in subjects with confirmed HZ episodes was demonstrated if the LL of the two-sided 95% CI of VE was above 0%

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of Vaccine efficacy in reduction of PHN incidence in subjects with confirmed HZ episode in Zoster-022/006 Pooled GSK1437173A 60-69 YOA Group versus Zoster-022/006 Pooled Placebo 60-69 YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A 60-69 YOA Group v Zoster-022/006 Pooled Placebo 60-69 YOA Group
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	other[31]
P-value	= 1
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3938.7
upper limit	100

Notes:

[31] - The efficacy of HZ/su vaccine in reduction of PHN in subjects with confirmed HZ episodes was demonstrated if the LL of the two-sided 95% CI of VE was above 0%

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of Vaccine efficacy in reduction of PHN incidence in subjects with confirmed HZ episode in Zoster-022/006 Pooled GSK1437173A 70-79 YOA Group versus Zoster-022/006 Pooled Placebo 70-79 YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A 70-79 YOA Group v Zoster-022/006 Pooled Placebo 70-79 YOA Group
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	other[32]
P-value	= 1
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	21.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-149.41
upper limit	78.91

Notes:

[32] - The efficacy of HZ/su vaccine in reduction of PHN in subjects with confirmed HZ episodes was demonstrated if the LL of the two-sided 95% CI of VE was above 0%

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Comparison of Vaccine efficacy in reduction of PHN incidence in subjects with confirmed HZ episode in Zoster-022/006 Pooled GSK1437173A >=80 YOA Group versus Zoster-022/006 Pooled Placebo>=80 YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A >=80 YOA Group v Zoster-022/006 Pooled Placebo >=80 YOA Group
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other[33]
P-value	= 0.1528
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	-223.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-883.05
upper limit	18.84

Notes:

[33] - The efficacy of HZ/su vaccine in reduction of PHN in subjects with confirmed HZ episodes was demonstrated if the LL of the two-sided 95% CI of VE was above 0%

Secondary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with reduction of duration of severe 'worst' HZ-associated pain in subjects ≥ 70 YOA with confirmed HZ

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with reduction of duration of severe 'worst' HZ-associated pain in subjects ≥ 70 YOA with confirmed HZ

End point description:

The duration of severe 'worst' HZ-associated pain following the onset of a confirmed HZ rash over the entire pain reporting period was measured by the ZBPI in subjects ≥ 70 YOA with confirmed HZ. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022/006 Pooled GSK1437173A 70-79 YOA Group	Zoster-022/006 Pooled GSK1437173A >=80 YOA Group	Zoster-022/006 Pooled Placebo 70-79 YOA Group	Zoster-022/006 Pooled Placebo >=80 YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	6	216	68
Units: Subjects	17	3	193	61

End point values	Zoster-022/006 Pooled GSK1437173A >=70 YOA Group	Zoster-022/006 Pooled Placebo >=70 YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	284		
Units: Subjects	20	254		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Comparison of VE in reduction of duration of severe worst HZ associated pain between Zoster-022/006 pooled GSK1437173A 70-79YOA Group and Zoster-022/006 pooled Placebo 70-79YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A 70-79 YOA Group v Zoster-022/006 Pooled Placebo 70-79 YOA Group
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	other[34]
P-value	= 0.2885
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	23.75

Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.8
upper limit	53.78

Notes:

[34] - The VE of HZ/su against duration of severe worst pain in subjects with confirmed HZ was demonstrated if the LL of the two-sided 95% CI of VE derived from the Hazard ratio was above 0%.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Comparison of VE in reduction of duration of severe worst HZ associated pain between Zoster-022/006 pooled GSK1437173A >=80 YOA Group and Zoster-022/006 pooled Placebo >=80 YOA Group

Comparison groups	Zoster-022/006 Pooled GSK1437173A >=80 YOA Group v Zoster-022/006 Pooled Placebo >=80 YOA Group
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other[35]
P-value	= 0.194
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	54.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.03
upper limit	86.46

Notes:

[35] - The VE of HZ/su against duration of severe worst pain in subjects with confirmed HZ was demonstrated if the LL of the two-sided 95% CI of VE derived from the Hazard ratio was above 0%.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Comparison of VE in reduction of duration of severe worst HZ associated pain between Zoster-022/006 pooled GSK1437173A >=70 YOA Group and Zoster-022/006 pooled Placebo>=70 YOA Group

Comparison groups	Zoster-022/006 Pooled Placebo >=70 YOA Group v Zoster-022/006 Pooled GSK1437173A >=70 YOA Group
Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	other[36]
P-value	= 0.1243
Method	Poisson exact test
Parameter estimate	Vaccine efficacy
Point estimate	30.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.52
upper limit	56.27

Notes:

[36] - The VE of HZ/su against duration of severe worst pain in subjects with confirmed HZ was demonstrated if the LL of the two-sided 95% CI of VE derived from the Hazard ratio was above 0%.

Secondary: Outcome measure for the pooled analysis of combined data from studies

Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Duration of severe 'worst' HZ-associated pain in subjects ≥ 70 YOA with confirmed HZ

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Duration of severe 'worst' HZ-associated pain in subjects ≥ 70 YOA with confirmed HZ

End point description:

Duration of severe 'worst' HZ-associated pain following the onset of a confirmed HZ rash over the entire pain reporting period was measured by the ZBPI in subjects ≥ 70 YOA with confirmed HZ. The analysis was based on the modified total vaccinated cohort, which included subjects from the total vaccinated cohort, except those who were not administered with the second vaccination or who developed a confirmed case of Herpes Zoster prior to 1 month after the second vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022/006 Pooled GSK1437173A 70-79 YOA Group	Zoster-022/006 Pooled GSK1437173A >=80 YOA Group	Zoster-022/006 Pooled Placebo 70-79 YOA Group	Zoster-022/006 Pooled Placebo >=80 YOA Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17	3	193	61
Units: Days				
arithmetic mean (standard deviation)	20.3 (± 29.71)	98.7 (± 57.73)	48.3 (± 96.34)	45.2 (± 95.58)

End point values	Zoster-022/006 Pooled GSK1437173A >=70 YOA Group	Zoster-022/006 Pooled Placebo >=70 YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	254		
Units: Days				
arithmetic mean (standard deviation)	32.1 (± 43.80)	47.5 (± 95.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any and Grade 3 solicited local symptoms

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any and Grade 3 solicited local symptoms

End point description:

Occurrence, intensity of each solicited local symptom within 7 days (Days 0-6) after each vaccination, in subjects ≥ 70 YOA. Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site. The analysis was performed on the total vaccinated cohort – Diary Card, which was a subset of subjects from the total vaccinated cohort, who completed diary cards with any solicited symptoms during the 7 days (Day 0 to Day 6) post vaccination period.

End point type	Secondary

End point timeframe:

Within 7 days (Days 0-6) post-vaccination period following each dose and across doses

End point values	Zoster-022/006 Pooled GSK1437173A >=70 YOA Group	Zoster-022/006 Pooled Placebo >=70 YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2258	2263		
Units: Subjects				
Any Pain, Dose 1 (N=2246;2255)	1336	128		
Grade 3 Pain, Dose 1 (N=2246;2255)	42	1		
Any Redness, Dose 1 (N=2246;2255)	606	17		
Grade 3 Redness, Dose 1 (N=2246;2255)	43	0		
Any Swelling, Dose 1 (N=2246;2255)	355	17		
Grade 3 Swelling, Dose 1 (N=2246;2255)	17	0		
Any Pain, Dose 2 (N=2160;2169)	1241	107		
Grade 3 Pain, Dose 2 (N=2160;2169)	60	3		
Any Redness, Dose 2 (N=2160;2169)	582	14		
Grade 3 Redness, Dose 2 (N=2160;2169)	39	0		
Any Swelling, Dose 2 (N=2160;2169)	344	10		
Grade 3 Swelling, Dose 2 (N=2160;2169)	15	0		
Any Pain, Across Doses (N=2258;2263)	1562	199		
Grade 3 Pain, Across Doses (N=2258;2263)	90	4		
Any Redness, Across Doses (N=2258;2263)	851	27		
Grade 3 Redness, Across Doses (N=2258;2263)	70	0		
Any Swelling, Across Doses (N=2258;2263)	519	25		
Grade 3 Swelling, Across Doses (N=2258;2263)	30	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any, Grade 3 and related solicited general symptoms

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any, Grade 3 and related solicited general symptoms

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal symptoms, headache, myalgia, shivering and fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.0 °C. Related = symptom assessed by the investigator as related to the vaccination. The analysis was performed on the total vaccinated cohort – Diary Card, which was a subset of subjects from the total vaccinated cohort, who completed diary cards with any solicited symptoms during the 7 days (Day 0 to Day 6) post vaccination period.

End point type	Secondary

End point timeframe:

Within the 7-day (Days 0-6) post-vaccination period following each dose and across doses

End point values	Zoster-022/006 Pooled GSK1437173A >=70 YOA Group	Zoster-022/006 Pooled Placebo >=70 YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2252	2264		
Units: Subjects				
Any Fatigue, Dose 1 (N=2237;2256)	545	231		
Grade 3 Fatigue, Dose 1 (N=2237;2256)	31	13		
Related Fatigue, Dose 1 (N=2237;2256)	441	147		
Any Gastrointestinal, Dose 1 (N=2237;2256)	170	123		
Grade 3 Gastrointestinal, Dose 1 (N=2237;2256)	15	6		
Related Gastrointestinal, Dose 1 (N=2237;2256)	101	67		
Any Headache, Dose 1 (N=2237;2256)	380	189		
Grade 3 Headache, Dose 1 (N=2237;2256)	7	8		
Related Headache, Dose 1 (N=2237;2256)	293	132		
Any Myalgia, Dose 1 (N=2237;2256)	530	159		
Grade 3 Myalgia, Dose 1 (N=2237;2256)	26	7		
Related Myalgia, Dose 1 (N=2237;2256)	445	101		
Any Shivering, Dose 1 (N=2237;2256)	206	73		
Grade 3 Shivering, Dose 1 (N=2237;2256)	15	3		
Related Shivering, Dose 1 (N=2237;2256)	173	50		
Any Temperature, Dose 1 (N=2237;2256)	142	34		
Grade 3 Temperature, Dose 1 (N=2237;2256)	1	2		

Related Temperature, Dose 1 (N=2237;2256)	111	16		
Any Fatigue, Dose 2 (N=2159;2166)	579	169		
Grade 3 Fatigue, Dose 2 (N=2159;2166)	53	4		
Related Fatigue, Dose 2 (N=2159;2166)	495	116		
Any Gastrointestinal, Dose 2 (N=2159;2166)	188	75		
Grade 3 Gastrointestinal, Dose 2 (N=2159;2166)	14	5		
Related Gastrointestinal, Dose 2 (N=2159;2166)	142	35		
Any Headache, Dose 2 (N=2159;2166)	455	133		
Grade 3 Headache, Dose 2 (N=2159;2166)	30	2		
Related Headache, Dose 2 (N=2159;2166)	386	86		
Any Myalgia, Dose 2 (N=2159;2166)	560	112		
Grade 3 Myalgia, Dose 2 (N=2159;2166)	42	4		
Related Myalgia, Dose 2 (N=2159;2166)	484	75		
Any Shivering, Dose 2 (N=2159;2166)	334	55		
Grade 3 Shivering, Dose 2 (N=2159;2166)	36	4		
Related Shivering, Dose 2 (N=2159;2166)	292	34		
Any Temperature, Dose 2 (N=2159;2166)	224	30		
Grade 3 Temperature, Dose 2 (N=2159;2166)	2	3		
Related Temperature, Dose 2 (N=2159;2166)	189	14		
Any Fatigue, Across Doses (N=2252;2264)	825	326		
Grade 3 Fatigue, Across Doses (N=2252;2264)	79	17		
Related Fatigue, Across Doses (N=2252;2264)	699	220		
Any Gastrointestinal, Across Doses (N=2252;2264)	304	172		
Grade 3 Gastrointestinal,Across Doses(N=2252;2264)	26	10		
Related Gastrointestinal,Across Doses(N=2252;2264)	210	91		
Any Headache, Across Doses (N=2252;2264)	653	268		
Grade 3 Headache, Across Doses (N=2252;2264)	34	10		
Related Headache, Across Doses (N=2252;2264)	547	185		
Any Myalgia, Across Doses (N=2252;2264)	790	225		
Grade 3 Myalgia, Across Doses (N=2252;2264)	62	10		
Related Myalgia, Across Doses (N=2252;2264)	689	157		
Any Shivering, Across Doses (N=2252;2264)	439	110		
Grade 3 Shivering, Across Doses (N=2252;2264)	49	6		

Related Shivering, Across Doses (N=2252;2264)	380	75		
Any Temperature, Across Doses (N=2252;2264)	323	61		
Grade 3 Temperature, Across Doses (N=2252;2264)	3	3		
Related Temperature, Across Doses (N=2252;2264)	265	30		

Statistical analyses

No statistical analyses for this end point

Secondary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any, grade 3 and related unsolicited AEs in subjects ≥ 70 YOA

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any, grade 3 and related unsolicited AEs in subjects ≥ 70 YOA

End point description:

Occurrence, intensity and relationship to vaccination of unsolicited AEs during 30 days (Days 0-29) after each vaccination, according to the MedDRA classification, in subjects ≥ 70 YOA.An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

Within 30 days (Days 0 - 29) after each vaccination

End point values	Zoster-022/006 Pooled GSK1437173A >=70 YOA Group	Zoster-022/006 Pooled Placebo >=70 YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8758	8773		
Units: Subjects				
Any AE(s)	4366	2732		
Grade 3 AE(s)	553	335		
Related AE(s)	2961	578		

Statistical analyses

No statistical analyses for this end point

Secondary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any and related SAE

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any and related SAE

End point description:

Occurrence and relationship to vaccination of all SAEs from Month 0 to Month 14 in subjects ≥ 70 YOA. Related SAEs also included any SAEs related to study participation or concurrent GSK medication/vaccine.

End point type	Secondary

End point timeframe:

From Month 0 to Month 14

End point values	Zoster-022/006 Pooled GSK1437173A >=70 YOA Group	Zoster-022/006 Pooled Placebo >=70 YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8758	8773		
Units: Subjects				
Any SAEs up to Mont 14	1117	1171		
Related SAEs up to Month 14	12	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any and related pIMDs

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any and related pIMDs

End point description:

Occurrence and relationship to vaccination of any pIMDs during the entire study period in subjects ≥ 70 YOA. The analysis was based on the total vaccinated cohort, which included all vaccinated subjects with study vaccine or placebo administered.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022/006 Pooled GSK1437173A >=70 YOA Group	Zoster-022/006 Pooled Placebo >=70 YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8758	8773		
Units: Subjects				
Any pIMD(s)	110	118		
Related pIMD(s)	8	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any and related medically attended visits

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with any and related medically attended visits

End point description:

Occurrence and relationship to vaccination of medically attended visits (defined as hospitalizations, emergency room visits or visits to or from medical personnel), other than routine health care visits, from Month 0 to Month 8 in subjects ≥ 70 YOA.

End point type	Secondary

End point timeframe:

From Month 0 to Month 8 post-vaccination

End point values	Zoster-022/006 Pooled GSK1437173A >=70 YOA Group	Zoster-022/006 Pooled Placebo >=70 YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8758	8773		
Units: Subjects				
Any MAE(s)	3593	3648		
Related MAE(s)	180	80		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with fatal serious adverse events (SAEs)

End point title	Number of subjects with fatal serious adverse events (SAEs)

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity. This analysis was based on the the total vaccinated cohort, which included all subjects with at least one dose of study vaccine or placebo administered.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022 GSK1437173A Group	Zoster-022 Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6950	6950		
Units: Participants				
Fatal SAE(s)	426	459		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAEs related to study participation or concomitant GSK medication

End point title	Number of subjects with SAEs related to study participation or concomitant GSK medication

End point description:

The number of subjects with SAEs related to study participation or concomitant GSK medication were tabulated. The analysis was based on the total vaccinated cohort, which included all subjects with at least one dose of study vaccine or placebo administered.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following day 0)

End point values	Zoster-022 GSK1437173A Group	Zoster-022 Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6950	6950		
Units: Participants	57	84		

Statistical analyses

No statistical analyses for this end point

Secondary: Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with fatal SAEs

End point title	Outcome measure for the pooled analysis of combined data from studies Zoster-006 (NCT01165177) and Zoster-022 (NCT01165229): Number of subjects with fatal SAEs

End point description:

Fatal SAEs during the entire study period in subjects ≥ 70 YOA. The analysis was based on the total vaccinated cohort, which included all vaccinated subjects with study vaccine or placebo administered.

End point type	Secondary

End point timeframe:

During the entire study period (3 to 5 year period following Day 0)

End point values	Zoster-022/006 Pooled GSK1437173A >=70 YOA Group	Zoster-022/006 Pooled Placebo >=70 YOA Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8758	8773		
Units: Subjects	128	144		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: Within 7 (Days 0-6) days after vaccination; Unsolicited adverse events: within 30 days (Days 0-29) after vaccination; Serious adverse events: during the entire study period (3 to 5 year period following Day 0)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Zoster-022 Placebo Group

Reporting group description:

Subjects receiving saline solution (NaCl solution) as control according to a 0, 2-month schedule.

Reporting group title	Zoster-022 GSK1437173A Group

Reporting group description:

Subjects receiving herpes zoster subunit vaccine (gE/AS01B vaccine) according to a 0, 2-month schedule.

Serious adverse events	Zoster-022 Placebo Group	Zoster-022 GSK1437173A Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1214 / 6950 (17.47%)	1153 / 6950 (16.59%)	
number of deaths (all causes)	459	426	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acral lentiginous melanoma			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute monocytic leukaemia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	

Adenocarcinoma			
subjects affected / exposed	3 / 6950 (0.04%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	1 / 6950 (0.01%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Adenocarcinoma of colon			
subjects affected / exposed	4 / 6950 (0.06%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Adrenal adenoma			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal gland cancer			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaplastic astrocytoma			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Anaplastic thyroid cancer			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
B precursor type acute leukaemia			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
B-cell lymphoma			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	3 / 6950 (0.04%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of thyroid gland			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign ovarian tumour			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct cancer			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Bladder cancer			
subjects affected / exposed	13 / 6950 (0.19%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 13	0 / 6	
deaths causally related to treatment / all	0 / 2	0 / 1	
Bladder cancer recurrent			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			

subjects affected / exposed	4 / 6950 (0.06%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bladder papilloma			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma recurrent			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bone cancer			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bowen’s disease			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm benign			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	4 / 6950 (0.06%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Breast cancer metastatic			

subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Carcinoid tumour pulmonary			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Central nervous system neoplasm			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Cholesteatoma			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colon adenoma			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	6 / 6950 (0.09%)	9 / 6950 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 9	
deaths causally related to treatment / all	0 / 4	0 / 3	
Colon cancer metastatic			
subjects affected / exposed	3 / 6950 (0.04%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 3	0 / 3	
Colon neoplasm			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large B-cell lymphoma stage IV			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Endometrial adenocarcinoma			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Fallopian tube cancer			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Follicular thyroid cancer			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder cancer			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastric cancer			
subjects affected / exposed	3 / 6950 (0.04%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 3	0 / 4	
Gastrointestinal carcinoma			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Gastrointestinal stromal tumour			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal tract adenoma			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Glioblastoma multiforme			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic cancer			

subjects affected / exposed	6 / 6950 (0.09%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 5	0 / 2	
Hepatic cancer metastatic			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic neoplasm			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Hypergammaglobulinaemia benign monoclonal			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive papillary breast carcinoma			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large cell lung cancer			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Large intestine benign neoplasm			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung adenocarcinoma			
subjects affected / exposed	6 / 6950 (0.09%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 4	0 / 0	
Lung adenocarcinoma metastatic			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Lung adenocarcinoma stage III			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	4 / 6950 (0.06%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 4	0 / 6	
Lung neoplasm			

subjects affected / exposed	3 / 6950 (0.04%)	1 / 6950 (0.01%)		
occurrences causally related to treatment / all	0 / 3	0 / 1		
deaths causally related to treatment / all	0 / 3	0 / 0		
Lung neoplasm malignant				
subjects affected / exposed	13 / 6950 (0.19%)	22 / 6950 (0.32%)		
occurrences causally related to treatment / all	0 / 13	0 / 22		
deaths causally related to treatment / all	0 / 10	0 / 18		
Lymphoma				
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)		
occurrences causally related to treatment / all	0 / 3	0 / 2		
deaths causally related to treatment / all	0 / 2	0 / 1		
Malignant fibrous histiocytoma of bone				
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 1		
Malignant lymphoma unclassifiable high grade				
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Malignant mast cell neoplasm				
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 1	0 / 0		
Malignant melanoma				
subjects affected / exposed	4 / 6950 (0.06%)	3 / 6950 (0.04%)		
occurrences causally related to treatment / all	0 / 4	0 / 3		
deaths causally related to treatment / all	0 / 1	0 / 2		
Malignant melanoma in situ				
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Malignant neoplasm of ampulla of Vater				

subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 2		
Malignant palate neoplasm				
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Meningioma				
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)		
occurrences causally related to treatment / all	0 / 2	0 / 0		
deaths causally related to treatment / all	0 / 1	0 / 0		
Mesothelioma				
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)		
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	0 / 6950 (0.00%)	1 / 6950 (0.01%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 1		
Metastases to bone				
subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)		
occurrences causally related to treatment / all	0 / 4	0 / 2		
deaths causally related to treatment / all	0 / 3	0 / 2		
Metastases to central nervous system				
subjects affected / exposed	2 / 6950 (0.03%)	4 / 6950 (0.06%)		
occurrences causally related to treatment / all	0 / 2	0 / 4		
deaths causally related to treatment / all	0 / 1	0 / 4		
Metastases to gastrointestinal tract				
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 1	0 / 0		
Metastases to liver				

subjects affected / exposed	5 / 6950 (0.07%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 5	0 / 4	
Metastases to lung			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to lymph nodes			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to peritoneum			
subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Metastases to stomach			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastasis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic carcinoma of the bladder			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Metastatic gastric cancer			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Metastatic malignant melanoma			

subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Metastatic neoplasm			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Metastatic renal cell carcinoma			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic squamous cell carcinoma			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neoplasm malignant			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Neoplasm prostate			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-Hodgkin’s lymphoma			
subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Non-small cell lung cancer			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Non-small cell lung cancer stage IV			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal adenocarcinoma metastatic			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal cancer metastatic			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Oesophageal carcinoma			
subjects affected / exposed	1 / 6950 (0.01%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 5	
Oesophageal squamous cell carcinoma			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Ovarian cancer			
subjects affected / exposed	0 / 6950 (0.00%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 4	
Ovarian cancer recurrent			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ovarian epithelial cancer			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian germ cell teratoma benign			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	10 / 6950 (0.14%)	7 / 6950 (0.10%)	
occurrences causally related to treatment / all	0 / 10	0 / 7	
deaths causally related to treatment / all	0 / 10	0 / 7	
Pancreatic carcinoma metastatic			
subjects affected / exposed	2 / 6950 (0.03%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 3	
Pancreatic neoplasm			
subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pancreatic neuroendocrine tumour			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraganglion neoplasm			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroid tumour benign			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour benign			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	18 / 6950 (0.26%)	19 / 6950 (0.27%)	
occurrences causally related to treatment / all	0 / 18	0 / 19	
deaths causally related to treatment / all	0 / 5	0 / 3	
Prostate cancer metastatic			
subjects affected / exposed	2 / 6950 (0.03%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Prostate cancer recurrent			
subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prostate cancer stage IV			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Prostatic adenoma			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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	1 / 6950 (0.01%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 3	
Rectal adenoma			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal cancer recurrent			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal cancer metastatic			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	4 / 6950 (0.06%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Renal cell carcinoma recurrent			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal oncocytoma			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland cancer			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sarcoma			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Small cell lung cancer metastatic			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Small intestine adenocarcinoma			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma			

subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma of skin			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sweat gland tumour			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-cell lymphoma			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Throat cancer			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Thyroid cancer			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue neoplasm malignant stage unspecified			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Transitional cell carcinoma			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma metastatic			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urethral neoplasm			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aneurysm			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aneurysm ruptured			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aortic aneurysm			
subjects affected / exposed	2 / 6950 (0.03%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 2	
Aortic aneurysm rupture			

subjects affected / exposed	4 / 6950 (0.06%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 3	0 / 4	
Aortic arteriosclerosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Aortic occlusion			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aortic rupture			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aortic stenosis			
subjects affected / exposed	8 / 6950 (0.12%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 8	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Arteriosclerosis			
subjects affected / exposed	5 / 6950 (0.07%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Arteriovenous fistula			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	3 / 6950 (0.04%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 3	0 / 4	
Deep vein thrombosis			
subjects affected / exposed	9 / 6950 (0.13%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 9	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Embolism			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Femoral artery aneurysm			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery occlusion			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	6 / 6950 (0.09%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemorrhage			
subjects affected / exposed	3 / 6950 (0.04%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Hypertension			

subjects affected / exposed	25 / 6950 (0.36%)	22 / 6950 (0.32%)	
occurrences causally related to treatment / all	0 / 25	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 3	
Hypertensive crisis			
subjects affected / exposed	6 / 6950 (0.09%)	7 / 6950 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	5 / 6950 (0.07%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Inferior vena caval occlusion			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Internal haemorrhage			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Labile hypertension			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microscopic polyangiitis			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis ischaemic			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	6 / 6950 (0.09%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peripheral artery aneurysm			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Temporal arteritis			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboangiitis obliterans			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Venous thrombosis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polypectomy			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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			
Accidental death			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Administration site erythema			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Administration site pain			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adverse drug reaction			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	

Cardiac death			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chest discomfort			
subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	19 / 6950 (0.27%)	20 / 6950 (0.29%)	
occurrences causally related to treatment / all	0 / 19	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	29 / 6950 (0.42%)	17 / 6950 (0.24%)	
occurrences causally related to treatment / all	0 / 29	0 / 17	
deaths causally related to treatment / all	0 / 29	0 / 17	
Device battery issue			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device deposit issue			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			

subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device leakage			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drowning			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fatigue			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Generalised oedema			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ill-defined disorder			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	12 / 6950 (0.17%)	9 / 6950 (0.13%)	
occurrences causally related to treatment / all	0 / 12	0 / 9	
deaths causally related to treatment / all	0 / 11	0 / 9	
Non-cardiac chest pain			
subjects affected / exposed	4 / 6950 (0.06%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organ failure			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Peripheral swelling			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 2	
Sudden death			
subjects affected / exposed	4 / 6950 (0.06%)	13 / 6950 (0.19%)	
occurrences causally related to treatment / all	0 / 4	0 / 13	
deaths causally related to treatment / all	0 / 4	0 / 13	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thrombosis in device			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic granulomatous angiitis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amyloidosis			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			

subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Atrophic vulvovaginitis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign prostatic hyperplasia			
subjects affected / exposed	7 / 6950 (0.10%)	9 / 6950 (0.13%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast dysplasia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic obstruction			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatomegaly			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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	4 / 6950 (0.06%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal prolapse			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal ulceration			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
Acute respiratory failure			
subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 4	0 / 2	
Aspiration			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthma			
subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	18 / 6950 (0.26%)	21 / 6950 (0.30%)	
occurrences causally related to treatment / all	0 / 18	0 / 21	
deaths causally related to treatment / all	0 / 7	0 / 8	
Diaphragmatic disorder			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Epistaxis			
subjects affected / exposed	3 / 6950 (0.04%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Lung disorder			

subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nasal septum deviation			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	8 / 6950 (0.12%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pleurisy			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	3 / 6950 (0.04%)	10 / 6950 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 10	
deaths causally related to treatment / all	0 / 3	0 / 7	
Pneumothorax			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary cavitation			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	21 / 6950 (0.30%)	15 / 6950 (0.22%)	
occurrences causally related to treatment / all	0 / 21	0 / 15	
deaths causally related to treatment / all	0 / 9	0 / 3	
Pulmonary fibrosis			
subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Pulmonary mass			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
Respiratory arrest			
subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Respiratory distress			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Respiratory failure			
subjects affected / exposed	15 / 6950 (0.22%)	15 / 6950 (0.22%)	
occurrences causally related to treatment / all	0 / 15	0 / 15	
deaths causally related to treatment / all	0 / 11	0 / 11	
Psychiatric disorders			
Abnormal behaviour			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute psychosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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 / 6950 (0.00%)	1 / 6950 (0.01%)	
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	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Confusional state			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			

subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Depressed mood			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	3 / 6950 (0.04%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder due to a general medical condition			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			

subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic attack			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic disorder			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizoaffective disorder bipolar type			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatoform disorder			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatine phosphokinase increased			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose fluctuation			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart rate decreased			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight increased			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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			
Accident			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Accidental overdose			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	5 / 6950 (0.07%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back injury			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone fissure			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cervical vertebral fracture			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chest injury			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compression fracture			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	3 / 6950 (0.04%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	5 / 6950 (0.07%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery reocclusion			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery restenosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis postoperative			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye penetration			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fall			
subjects affected / exposed	5 / 6950 (0.07%)	8 / 6950 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 2	
Femoral neck fracture			
subjects affected / exposed	6 / 6950 (0.09%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Femur fracture			
subjects affected / exposed	15 / 6950 (0.22%)	10 / 6950 (0.14%)	
occurrences causally related to treatment / all	0 / 15	0 / 10	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun shot wound			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	4 / 6950 (0.06%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hip fracture			
subjects affected / exposed	2 / 6950 (0.03%)	7 / 6950 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 2	
Humerus fracture			
subjects affected / exposed	6 / 6950 (0.09%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Jaw fracture			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney contusion			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb crushing injury			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	2 / 6950 (0.03%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Muscle rupture			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			

subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	1 / 6950 (0.01%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax traumatic			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural pulmonary embolism			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound complication			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural intestinal perforation			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Procedural pain				
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Pubis fracture				
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)		
occurrences causally related to treatment / all	0 / 3	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Radius fracture				
subjects affected / exposed	5 / 6950 (0.07%)	5 / 6950 (0.07%)		
occurrences causally related to treatment / all	0 / 5	0 / 5		
deaths causally related to treatment / all	0 / 0	0 / 0		
Respiratory fume inhalation disorder				
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 1	0 / 0		
Rib fracture				
subjects affected / exposed	7 / 6950 (0.10%)	6 / 6950 (0.09%)		
occurrences causally related to treatment / all	0 / 7	0 / 6		
deaths causally related to treatment / all	0 / 0	0 / 0		
Road traffic accident				
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Skin wound				
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Skull fracture				

subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Spinal compression fracture			
subjects affected / exposed	1 / 6950 (0.01%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury cervical			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	6 / 6950 (0.09%)	9 / 6950 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 9	
deaths causally related to treatment / all	0 / 1	0 / 4	
Subdural haemorrhage			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Synovial rupture			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	4 / 6950 (0.06%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	2 / 6950 (0.03%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Ulna fracture			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	4 / 6950 (0.06%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Wound haemorrhage			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			

subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Congenital cystic kidney disease			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyloric stenosis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal dysplasia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	4 / 6950 (0.06%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute left ventricular failure			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	28 / 6950 (0.40%)	21 / 6950 (0.30%)	
occurrences causally related to treatment / all	0 / 28	1 / 21	
deaths causally related to treatment / all	0 / 14	0 / 10	

Angina pectoris			
subjects affected / exposed	6 / 6950 (0.09%)	13 / 6950 (0.19%)	
occurrences causally related to treatment / all	0 / 6	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	7 / 6950 (0.10%)	7 / 6950 (0.10%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aortic valve incompetence			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	3 / 6950 (0.04%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Arrhythmia			
subjects affected / exposed	9 / 6950 (0.13%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 3	
Arrhythmia supraventricular			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	3 / 6950 (0.04%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 0	
Atrial fibrillation			

subjects affected / exposed	54 / 6950 (0.78%)	40 / 6950 (0.58%)	
occurrences causally related to treatment / all	0 / 54	0 / 40	
deaths causally related to treatment / all	0 / 0	0 / 5	
Atrial flutter			
subjects affected / exposed	5 / 6950 (0.07%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	4 / 6950 (0.06%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	2 / 6950 (0.03%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block first degree			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	3 / 6950 (0.04%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	8 / 6950 (0.12%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	17 / 6950 (0.24%)	23 / 6950 (0.33%)	
occurrences causally related to treatment / all	0 / 17	0 / 23	
deaths causally related to treatment / all	0 / 17	0 / 22	
Cardiac disorder			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	57 / 6950 (0.82%)	51 / 6950 (0.73%)	
occurrences causally related to treatment / all	0 / 57	0 / 51	
deaths causally related to treatment / all	0 / 38	0 / 31	
Cardiac failure acute			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	6 / 6950 (0.09%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 4	0 / 2	
Cardiac failure congestive			
subjects affected / exposed	33 / 6950 (0.47%)	23 / 6950 (0.33%)	
occurrences causally related to treatment / all	0 / 33	0 / 23	
deaths causally related to treatment / all	0 / 12	0 / 9	
Cardiac tamponade			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac valve disease			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			

subjects affected / exposed	5 / 6950 (0.07%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 3	0 / 3	
Cardiogenic shock			
subjects affected / exposed	2 / 6950 (0.03%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomegaly			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronotropic incompetence			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cor pulmonale			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			

subjects affected / exposed	25 / 6950 (0.36%)	28 / 6950 (0.40%)	
occurrences causally related to treatment / all	0 / 25	0 / 28	
deaths causally related to treatment / all	0 / 2	0 / 4	
Coronary artery insufficiency			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Coronary artery occlusion			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	6 / 6950 (0.09%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diastolic dysfunction			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extrasystoles			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart valve incompetence			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			

subjects affected / exposed	4 / 6950 (0.06%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Left ventricular failure			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular hypertrophy			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mitral valve incompetence			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	45 / 6950 (0.65%)	41 / 6950 (0.59%)	
occurrences causally related to treatment / all	0 / 45	0 / 41	
deaths causally related to treatment / all	0 / 26	0 / 24	
Myocardial ischaemia			
subjects affected / exposed	16 / 6950 (0.23%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 16	0 / 5	
deaths causally related to treatment / all	0 / 5	0 / 1	
Palpitations			
subjects affected / exposed	3 / 6950 (0.04%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Right ventricular failure			

subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Sinus arrest			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	6 / 6950 (0.09%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	2 / 6950 (0.03%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tricuspid valve incompetence			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Ventricular tachycardia			
subjects affected / exposed	6 / 6950 (0.09%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ataxia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance disorder			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal ganglia haemorrhage			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Basilar artery thrombosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brain stem infarction			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem syndrome			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid sinus syndrome			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system lesion			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar haemorrhage			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebellar ischaemia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral artery embolism			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral artery thrombosis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral atrophy			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	7 / 6950 (0.10%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 6	0 / 5	
Cerebral infarction			

subjects affected / exposed	17 / 6950 (0.24%)	16 / 6950 (0.23%)	
occurrences causally related to treatment / all	1 / 17	0 / 16	
deaths causally related to treatment / all	0 / 6	0 / 5	
Cerebral ischaemia			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Cerebrospinal fluid leakage			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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	31 / 6950 (0.45%)	34 / 6950 (0.49%)	
occurrences causally related to treatment / all	1 / 31	0 / 34	
deaths causally related to treatment / all	0 / 17	0 / 11	
Cerebrovascular disorder			
subjects affected / exposed	1 / 6950 (0.01%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cervical myelopathy			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dementia			

subjects affected / exposed	2 / 6950 (0.03%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 2	
Dementia Alzheimer’s type			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia with Lewy bodies			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic coma			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dizziness			
subjects affected / exposed	5 / 6950 (0.07%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drop attacks			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dural arteriovenous fistula			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspraxia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epilepsy			

subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Haemorrhagic stroke			
subjects affected / exposed	4 / 6950 (0.06%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Headache			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertonia			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraventricular haemorrhage			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ischaemic stroke			
subjects affected / exposed	6 / 6950 (0.09%)	7 / 6950 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 4	
Lacunar infarction			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lumbar radiculopathy			

subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Miller Fisher syndrome			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mixed dementia			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myasthenia gravis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myoclonus			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve compression			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paralysis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinsonism			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson’s disease			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post herpetic neuralgia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Progressive supranuclear palsy			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Radiculopathy			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restless legs syndrome			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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	4 / 6950 (0.06%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Senile dementia			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Somnolence			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitic myelopathy			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	7 / 6950 (0.10%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 5	
Syncope			
subjects affected / exposed	20 / 6950 (0.29%)	11 / 6950 (0.16%)	
occurrences causally related to treatment / all	1 / 20	0 / 11	
deaths causally related to treatment / all	0 / 1	0 / 0	
Thalamic infarction			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamus haemorrhage			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thrombotic cerebral infarction			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Transient global amnesia			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	14 / 6950 (0.20%)	20 / 6950 (0.29%)	
occurrences causally related to treatment / all	0 / 14	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIIth nerve lesion			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular dementia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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	13 / 6950 (0.19%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 13	0 / 6	
deaths causally related to treatment / all	0 / 2	0 / 0	
Anaemia vitamin B12 deficiency			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhagic anaemia			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersplenism			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	4 / 6950 (0.06%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrogenic anaemia			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pernicious anaemia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	4 / 6950 (0.06%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			

subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amaurosis fugax			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	7 / 6950 (0.10%)	7 / 6950 (0.10%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choroidal effusion			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iridocele			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iritis			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ocular hypertension			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ocular vascular disorder			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal degeneration			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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	4 / 6950 (0.06%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Abdominal discomfort			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	7 / 6950 (0.10%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal strangulated hernia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal prolapse			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Autoimmune pancreatitis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Barrett’s oesophagus			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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 / 6950 (0.01%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	2 / 6950 (0.03%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn’s disease			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic hernia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic hernia, obstructive			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	4 / 6950 (0.06%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	3 / 6950 (0.04%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Duodenal ulcer perforation			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Enteritis			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecal incontinence			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric perforation			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	6 / 6950 (0.09%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastric ulcer haemorrhage			
subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer perforation			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastritis			

subjects affected / exposed	6 / 6950 (0.09%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal angiodysplasia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	4 / 6950 (0.06%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 6950 (0.03%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	7 / 6950 (0.10%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	10 / 6950 (0.14%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 10	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia strangulated			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal infarction			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Intestinal obstruction			

subjects affected / exposed	6 / 6950 (0.09%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 3	0 / 1	
Intestinal perforation			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Large intestine perforation			
subjects affected / exposed	2 / 6950 (0.03%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Large intestine polyp			
subjects affected / exposed	4 / 6950 (0.06%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mallory-Weiss syndrome			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery embolism			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Mesenteric artery thrombosis			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mesenteritis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth ulceration			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal spasm			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer haemorrhage			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic disorder			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	8 / 6950 (0.12%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatitis acute			
subjects affected / exposed	4 / 6950 (0.06%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 4	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peptic ulcer haemorrhage			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngo-oesophageal diverticulum			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal perforation			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal prolapse			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland calculus			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	4 / 6950 (0.06%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subileus			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis mesenteric vessel			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Umbilical hernia			

subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bile duct obstruction			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	3 / 6950 (0.04%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary dilatation			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			

subjects affected / exposed	5 / 6950 (0.07%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cholangitis acute			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cholecystitis			
subjects affected / exposed	15 / 6950 (0.22%)	7 / 6950 (0.10%)	
occurrences causally related to treatment / all	0 / 15	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cholecystitis acute			
subjects affected / exposed	4 / 6950 (0.06%)	7 / 6950 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cholecystitis chronic			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	14 / 6950 (0.20%)	14 / 6950 (0.20%)	
occurrences causally related to treatment / all	0 / 14	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cholestasis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic hepatic failure			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cirrhosis alcoholic			

subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Drug-induced liver injury			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gallbladder perforation			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hepatic failure			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Hepatic function abnormal			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis alcoholic			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyperbilirubinaemia			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Dermal cyst			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis contact			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatomyositis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	5 / 6950 (0.07%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Drug eruption			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lichen planus			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stasis dermatitis			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	19 / 6950 (0.27%)	18 / 6950 (0.26%)	
occurrences causally related to treatment / all	0 / 19	0 / 18	
deaths causally related to treatment / all	0 / 7	0 / 8	
Acute prerenal failure			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
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 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder perforation			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder prolapse			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus ureteric			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			

subjects affected / exposed	11 / 6950 (0.16%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 11	0 / 4	
deaths causally related to treatment / all	0 / 3	0 / 0	
Cystitis haemorrhagic			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cystitis interstitial			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysuria			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	2 / 6950 (0.03%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephroangiosclerosis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			

subjects affected / exposed	2 / 6950 (0.03%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurogenic bladder			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal disorder			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	11 / 6950 (0.16%)	11 / 6950 (0.16%)	
occurrences causally related to treatment / all	0 / 11	0 / 11	
deaths causally related to treatment / all	0 / 3	0 / 7	
Renal hypertension			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal mass			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	4 / 6950 (0.06%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral haemorrhage			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urethral meatus stenosis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
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	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary retention			
subjects affected / exposed	3 / 6950 (0.04%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract disorder			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Autoimmune thyroiditis			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cushingoid			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperparathyroidism primary			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Acquired claw toe			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthrofibrosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	5 / 6950 (0.07%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondropathy			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	4 / 6950 (0.06%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscal degeneration			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mixed connective tissue disease			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	17 / 6950 (0.24%)	26 / 6950 (0.37%)	
occurrences causally related to treatment / all	0 / 17	0 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondritis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	4 / 6950 (0.06%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	1 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyositis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pseudarthrosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (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	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	2 / 6950 (0.03%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sjogren’s syndrome			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			

subjects affected / exposed	6 / 6950 (0.09%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	5 / 6950 (0.07%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondyloarthropathy			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
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 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Still’s disease adult onset			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			

subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigger finger			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acarodermatitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcaligenes infection			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula infection			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal cellulitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendiceal abscess			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	5 / 6950 (0.07%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerotic gangrene			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bacteraemia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Biliary tract infection			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	7 / 6950 (0.10%)	8 / 6950 (0.12%)	
occurrences causally related to treatment / all	0 / 7	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 2	
Bronchitis bacterial			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	4 / 6950 (0.06%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Candida infection			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida sepsis			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cavernous sinus thrombosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	14 / 6950 (0.20%)	8 / 6950 (0.12%)	
occurrences causally related to treatment / all	0 / 14	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cholecystitis infective			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium bacteraemia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	5 / 6950 (0.07%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Clostridium difficile infection			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Colonic abscess			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cystitis			

subjects affected / exposed	0 / 6950 (0.00%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis klebsiella			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Device related infection			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	11 / 6950 (0.16%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 11	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis viral			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Endocarditis			

subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Enterocolitis viral			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	7 / 6950 (0.10%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 7	1 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Escherichia infection			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastroenteritis			

subjects affected / exposed	8 / 6950 (0.12%)	8 / 6950 (0.12%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastroenteritis clostridial			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter infection			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	3 / 6950 (0.04%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster disseminated			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster meningitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster oticus			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site infection			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infectious colitis			

subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Intestinal gangrene			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Labyrinthitis			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			

subjects affected / exposed	1 / 6950 (0.01%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	8 / 6950 (0.12%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 3	0 / 0	
Localised infection			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Medical device site infection			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Necrotising fasciitis streptococcal			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neuroborreliosis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Oesophageal candidiasis			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal candidiasis			

subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ovarian abscess			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic abscess			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	4 / 6950 (0.06%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 4	
Peritonitis bacterial			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	81 / 6950 (1.17%)	70 / 6950 (1.01%)	
occurrences causally related to treatment / all	0 / 81	0 / 70	
deaths causally related to treatment / all	0 / 38	0 / 24	
Pneumonia bacterial			

subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia influenzal			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pneumonia klebsiella			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia streptococcal			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Postoperative abscess			
subjects affected / exposed	0 / 6950 (0.00%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			

subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pseudomonas infection			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psittacosis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psoas abscess			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Purulence			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	4 / 6950 (0.06%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	0 / 6950 (0.00%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory moniliasis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	3 / 6950 (0.04%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	17 / 6950 (0.24%)	26 / 6950 (0.37%)	
occurrences causally related to treatment / all	0 / 17	0 / 26	
deaths causally related to treatment / all	0 / 11	0 / 16	
Septic shock			
subjects affected / exposed	14 / 6950 (0.20%)	11 / 6950 (0.16%)	
occurrences causally related to treatment / all	0 / 14	0 / 11	
deaths causally related to treatment / all	0 / 12	0 / 10	
Sinusitis			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			

subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 6950 (0.01%)	4 / 6950 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Staphylococcal osteomyelitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	24 / 6950 (0.35%)	28 / 6950 (0.40%)	
occurrences causally related to treatment / all	0 / 24	0 / 28	
deaths causally related to treatment / all	0 / 6	0 / 2	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	9 / 6950 (0.13%)	7 / 6950 (0.10%)	
occurrences causally related to treatment / all	0 / 9	0 / 7	
deaths causally related to treatment / all	0 / 3	0 / 1	
Vestibular neuronitis			
subjects affected / exposed	3 / 6950 (0.04%)	0 / 6950 (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	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vulvitis			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	2 / 6950 (0.03%)	3 / 6950 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			

subjects affected / exposed	2 / 6950 (0.03%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Decreased appetite			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	8 / 6950 (0.12%)	8 / 6950 (0.12%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diabetes mellitus			
subjects affected / exposed	3 / 6950 (0.04%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Gout			

subjects affected / exposed	0 / 6950 (0.00%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercholesterolaemia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	2 / 6950 (0.03%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hyperlipidaemia			
subjects affected / exposed	1 / 6950 (0.01%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	4 / 6950 (0.06%)	6 / 6950 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	2 / 6950 (0.03%)	7 / 6950 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			

subjects affected / exposed	5 / 6950 (0.07%)	2 / 6950 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			
subjects affected / exposed	0 / 6950 (0.00%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lactic acidosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	2 / 6950 (0.03%)	1 / 6950 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Marasmus			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	6 / 6950 (0.09%)	5 / 6950 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uraemic acidosis			
subjects affected / exposed	1 / 6950 (0.01%)	0 / 6950 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Zoster-022 Placebo Group	Zoster-022 GSK1437173A Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	610 / 6950 (8.78%)	3067 / 6950 (44.13%)	
Nervous system disorders			
Headache			
subjects affected / exposed	243 / 6950 (3.50%)	586 / 6950 (8.43%)	
occurrences (all)	307	717	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	39 / 6950 (0.56%)	353 / 6950 (5.08%)	
occurrences (all)	46	415	
Fatigue			
subjects affected / exposed	169 / 6950 (2.43%)	474 / 6950 (6.82%)	
occurrences (all)	192	592	
Injection site erythema			
subjects affected / exposed	27 / 6950 (0.39%)	864 / 6950 (12.43%)	
occurrences (all)	29	1150	
Injection site pain			
subjects affected / exposed	148 / 6950 (2.13%)	1975 / 6950 (28.42%)	
occurrences (all)	165	2762	
Injection site swelling			
subjects affected / exposed	16 / 6950 (0.23%)	613 / 6950 (8.82%)	
occurrences (all)	18	773	
Pain			
subjects affected / exposed	60 / 6950 (0.86%)	428 / 6950 (6.16%)	
occurrences (all)	67	669	
Pyrexia			
subjects affected / exposed	52 / 6950 (0.75%)	535 / 6950 (7.70%)	
occurrences (all)	56	633	
Musculoskeletal and connective tissue disorders			

Myalgia subjects affected / exposed occurrences (all)	99 / 6950 (1.42%) 113	378 / 6950 (5.44%) 472	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported