Clinical trial results:
A Randomized, Double-blind, Placebo-controlled Phase 3 Efficacy Study of an Ad26.RSV.pre F-based Vaccine in the Prevention of Lower Respiratory Tract Disease Caused by RSV in Adults Aged 60 Years and Older

Summary

EudraCT number	2020-005458-97
Trial protocol	FI
Global end of trial date	21 July 2023

Results information

Result version number	v1 (current)
This version publication date	06 January 2024
First version publication date	06 January 2024

Trial information

Trial identification

Sponsor protocol code	VAC18193RSV3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04908683
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Vaccines & Prevention B.V.
Sponsor organisation address	Archimedesweg 4-6, Leiden, Netherlands, 2333 CN
Public contact	Clinical Registry Group, Janssen Vaccines & Prevention B.V., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Vaccines & Prevention B.V., ClinicalTrialsEU@its.jnj.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	21 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to demonstrate the efficacy of the active adenovirus serotype 26 respiratory syncytial virus pre-fusion conformation stabilised F protein (Ad26.RSV.preF) based study vaccine in the prevention of reverse transcriptase polymerase chain reaction (RT-PCR confirmed RSV-mediated lower respiratory tract disease (LRTD) when compared to placebo in adults aged 60 years and above.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 July 2021
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	Australia: 37
Country: Number of subjects enrolled	Brazil: 178
Country: Number of subjects enrolled	Canada: 824
Country: Number of subjects enrolled	Chile: 251
Country: Number of subjects enrolled	China: 1993
Country: Number of subjects enrolled	Estonia: 233
Country: Number of subjects enrolled	Finland: 56
Country: Number of subjects enrolled	United Kingdom: 1404
Country: Number of subjects enrolled	New Zealand: 673
Country: Number of subjects enrolled	Poland: 1573
Country: Number of subjects enrolled	Thailand: 311
Country: Number of subjects enrolled	Taiwan: 183
Country: Number of subjects enrolled	United States: 15448
Country: Number of subjects enrolled	South Africa: 1912
Worldwide total number of subjects	25076
EEA total number of subjects	1862

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)	2212
From 65 to 84 years	22587
85 years and over	277

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 25236 subjects were randomised, out of which 25076 were vaccinated.

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	Investigator, Carer, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Ad26.RSV.preF and RSV preF Protein

Arm description:

Subjects received a single intramuscular (IM) injection containing a mixture of Ad26.RSV.preF at a dose of 1*10^11 viral particles (vp) and RSV preF protein 150 micrograms (mcg) on Day 1.

Arm type	Experimental
Investigational medicinal product name	Ad26.RSV.preF and RSV preF protein
Investigational medicinal product code	
Other name	JNJ-64400141
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single IM injection of a mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

Arm title	Group 2: Placebo

Arm description:

Subjects received a single IM injection of matching placebo on Day 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received an IM injection of matching placebo on Day 1.

Number of subjects in period 1	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo
Started	16709	8367
Completed	124	59
Not completed	16585	8308
Adverse event, serious fatal	101	61
Subject met eligibility criteria but not needed	3	1
Physician decision	44	35
Initiated prohibited medication	3	-
Technical problems	12	9
- Unspecified	92	50
Withdrawal by legally authorised representative	1	-
Failure to meet continuation criteria	34	22
Withdrawal by subject	1188	570
Randomised by mistake	1	-
Adverse event, non-fatal	21	11
Sponsor Decision	14398	7205
Site Closure by Sponsor	6	3
Lost to follow-up	679	341
Protocol deviation	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: Ad26.RSV.preF and RSV preF Protein
Reporting group description:	
Subjects received a single intramuscular (IM) injection containing a mixture of Ad26.RSV.preF at a dose of 1*10^11 viral particles (vp) and RSV preF protein 150 micrograms (mcg) on Day 1.	
Reporting group title	Group 2: Placebo
Reporting group description:	
Subjects received a single IM injection of matching placebo on Day 1.	

Reporting group values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo	Total
Number of subjects	16709	8367	25076
Title for AgeCategorical			
Baseline characteristics data were analysed on Full analysis set (FAS) which included all subjects with a documented vaccine administration, regardless of the occurrence of protocol deviations.			
Units: subjects			
Adults (60-64 years)	1472	740	2212
From 65 to 84 years	15053	7534	22587
85 years and over	184	93	277
Title for AgeContinuous			
Units: years			
arithmetic mean	70.2	70.2	
standard deviation	± 5.24	± 5.23	-
Title for Gender			
Units: subjects			
Female	9063	4452	13515
Male	7645	3913	11558
Others	1	2	3
Race			
Units: Subjects			
American Indian or Alaska Native	58	17	75
Asian	1757	897	2654
Native Hawaiian or Other Pacific Islander	98	49	147
Black or African American	1820	935	2755
White	12649	6297	18946
More than one race	189	101	290
Unknown or Not Reported	138	71	209
Ethnicity			
Units: Subjects			
Hispanic or Latino	1555	741	2296
Not Hispanic or Latino	14903	7496	22399
Unknown or Not Reported	251	130	381

End points

End points reporting groups

Reporting group title	Group 1: Ad26.RSV.preF and RSV preF Protein
Reporting group description:	
Subjects received a single intramuscular (IM) injection containing a mixture of Ad26.RSV.preF at a dose of 1*10^11 viral particles (vp) and RSV preF protein 150 micrograms (mcg) on Day 1.	
Reporting group title	Group 2: Placebo
Reporting group description:	
Subjects received a single IM injection of matching placebo on Day 1.	

Primary: Number of Subjects With First Occurrence of Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)-Confirmed Respiratory Syncytial Virus (RSV) Mediated Lower Respiratory Tract Disease (LRTD)

End point title	Number of Subjects With First Occurrence of Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)-Confirmed Respiratory Syncytial Virus (RSV) Mediated Lower Respiratory Tract Disease (LRTD)[1]

End point description:

A subject was considered to have RT-PCR-confirmed RSV-mediated LRTD if following criteria were met: new onset/worsening from baseline of 3/more symptoms as captured on respiratory infection intensity and impact questionnaire (RiiQ, version 2) at same time point: cough, short of breath, coughing up phlegm (sputum) & wheezing and confirmation of RSV by RT-PCR in one/more of nasal swabs/sputum sample. RiiQ symptom scale: 13-items questionnaire, each symptom was rated on 4-point scale: 0 to 3 (0=None,1=Mild,2=Moderate,3=Severe). Higher scores=greater severity. Total LRTD symptom score: mean of 4 lower respiratory scores (cough, short of breath, coughing up phlegm [sputum] & wheezing). Per-protocol efficacy population: all randomised and vaccinated subjects, excluding those with major protocol deviations expecting to impact efficacy outcomes. Subjects with an RSV onset within 14 days after vaccination and who discontinued within 14 days after vaccination were excluded from PPE population.

End point type	Primary

End point timeframe:

From Baseline (Day 1) up to 12 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this endpoint.

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16263	8152		
Units: Subjects	44	63		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With First Occurrence of any RT-PCR-Confirmed

RSV-mediated Acute Respiratory Infection (ARI)

End point title	Number of Subjects With First Occurrence of any RT-PCR-Confirmed RSV-mediated Acute Respiratory Infection (ARI)

End point description:

A subject was considered to have RT-PCR-confirmed RSV-mediated ARI if the following were met: new symptoms or worsening from baseline of at least one of the symptoms as captured on the RiiQ at the same time point : sore throat, nasal congestion, cough, short of breath, coughing up phlegm (sputum), wheezing and confirmation of RSV by RT-PCR in one/more of the nasal swabs/ sputum sample. RiiQ symptom scale: 13-items questionnaire, each symptom was rated on 4-point scale: 0 to 3 (0=None, 1=Mild, 2=Moderate, and 3=Severe). Higher scores= greater severity. The total ARI symptom score: mean of the 4 lower respiratory scores (cough, short of breath, coughing up phlegm [sputum] & wheezing). PPE: all randomised and vaccinated subjects, excluding those with major protocol deviations expecting to impact efficacy outcomes. Subjects with an RSV onset within 14 days after vaccination and who discontinued within 14 days after vaccination were excluded from the PPE population.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) up to 12 months

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16263	8152		
Units: Subjects	77	101		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With First Occurrence of RT-PCR-Confirmed RSV Mediated LRTD During the Second Year

End point title	Number of Subjects With First Occurrence of RT-PCR-Confirmed RSV Mediated LRTD During the Second Year

End point description:

A subject was considered to have RT-PCR-confirmed RSV-mediated LRTD if following criteria met: new onset/worsening from baseline of 3/more symptoms as captured on respiratory infection intensity and impact questionnaire (RiiQ) at same time point:cough, short of breath, coughing up phlegm (sputum) & wheezing and confirmation RSV by RT-PCR in one/more of nasal swabs/sputum sample. RiiQ symptom scale: 13-items questionnaire, each symptom was rated on 4-point scale:0 to 3 (0=None,1=Mild,2=Moderate,3=Severe). Higher scores=greater severity. Total LRTD symptom score: mean of 4 lower respiratory scores (cough, short of breath, coughing up phlegm [sputum] & wheezing). PPE:all randomised and vaccinated subjects, except those with major protocol deviations expecting to impact efficacy outcomes.Subjects with RSV onset within 14 days after vaccination and who discontinued within 14 days after vaccination excluded from PPE population.'N' signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Month 12 up to Month 24

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10031	5011		
Units: Subjects	16	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With First Occurrence of Any RT-PCR-Confirmed RSV Mediated ARI During the Second Year

End point title	Number of Subjects With First Occurrence of Any RT-PCR-Confirmed RSV Mediated ARI During the Second Year

End point description:

A subject was considered to have RT-PCR-confirmed RSV-mediated ARI if following criteria met: new symptoms/worsening from baseline of at least one of symptoms as captured on respiratory infection intensity and impact questionnaire (RiiQ) at same time point: sore throat, nasal congestion, cough, short of breath, coughing up phlegm (sputum), wheezing and confirmation of RSV by RT-PCR in one/more of nasal swabs/sputum sample. RiiQ symptom scale:13-items questionnaire, each symptom was rated on 4-point scale:0 to 3 (0=None,1=Mild,2=Moderate,3=Severe). Higher scores= greater severity. Total ARI symptom score: mean of 4 lower respiratory scores (cough,short of breath, coughing up phlegm [sputum] & wheezing). PPE= all randomised and vaccinated subjects, excluding those with MPDs expecting to impact efficacy outcomes. Subjects with RSV onset within 14 days after vaccination and who discontinued within 14 days after vaccination were excluded.'N'=subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Month 12 up to Month 24

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10031	5011		
Units: Subjects	39	44		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with First Occurrence of Predefined Clinically Relevant Disease Associated With RT-PCR-Confirmed RSV-Mediated ARI Over the Whole Study

End point title	Number of Subjects with First Occurrence of Predefined Clinically Relevant Disease Associated With RT-PCR-Confirmed RSV-Mediated ARI Over the Whole Study

End point description:

A subject was considered to have clinically relevant disease with specific parameters associated with an RT-PCR-confirmed RSV-mediated ARI if the following criteria met: new symptoms/worsening from baseline of at least one of the symptoms as captured on RiiQ: sore throat, nasal congestion, cough, short of breath, coughing up phlegm (sputum), wheezing and confirmation of RSV by RT-PCR in one or more of the nasal swabs/sputum sample; any of the following associated with ARI: hspitalisation, emergency department visit, per clinical judgement of complications, decreased oxygen saturation, tachypnea, need of supplemental oxygen, hypotension, pulmonary function test and arterial blood gas result. PPE: all randomised and vaccinated subjects, excluding those with MPDs expecting to impact efficacy outcomes. Subjects with an RSV onset within 14 days after vaccination and who discontinued within 14 days after vaccination were excluded from the PPE population.

End point type	Secondary

End point timeframe:

Baseline (Day 1) up to 24 months

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16263	8152		
Units: Subjects	4	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Adverse Events (SAEs)

End point title	Number of Subjects With Serious Adverse Events (SAEs)

End point description:

Number of subjects with SAEs were reported. An adverse event (AE) is any untoward medical occurrence in a clinical study subject administered a pharmaceutical (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. An SAE is any untoward medical occurrence that at any dose may result in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, is a suspected transmission of any infectious agent via a medicinal product. Full Analysis Set (FAS): will include all participants with a documented vaccine administration, regardless of the occurrence of protocol deviations. Here, 'n' (number analysed)
represents number of subjects who were evaluable for specified timepoints.

End point type	Secondary

End point timeframe:

28 days post vaccination on Day 1 (Day 29); first year follow-up (from Day 29 up to 6 months, that is, up to Day 154

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16709	8367		
Units: Subjects				
28 days post vaccination on Day1 (n=16709,8367)	119	53		
First year follow-up (n=16532, 8275)	446	239		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potential Adverse Events of Special Interest (AESIs)

End point title	Number of Subjects With Potential Adverse Events of Special Interest (AESIs)

End point description:

Number of subjects with Potential AESIs were reported. AESIs were significant AEs that were judged to be of special interest because of clinical importance, known or suspected class effects, or based on nonclinical signals. AESIs were embolic and thrombotic events, hematopoietic thrombocytopenia, and cerebral hemorrhage. FAS included all subjects with a documented vaccine administration, regardless of the occurrence of protocol deviations. Here, 'n' (number analyzed) represents number of subjects who were evaluable for specified timepoints.

End point type	Secondary

End point timeframe:

28 days post vaccination on Day 1 (Day 29); first year follow-up (from Day 29 up to 6 months, that is, up to Day 154)

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16709	8367		
Units: Subjects				
28 days post vaccination on Day1 (n=16709,8367)	25	4		
First year follow-up (n=16532, 8275)	71	35		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Solicited Local Adverse Events (AEs) up to 7 Days After Vaccination

End point title	Number of Subjects With Solicited Local Adverse Events (AEs)

	up to 7 Days After Vaccination

End point description:

An AE was any untoward medical occurrence in a clinical study participant administered a medicinal (investigational/ non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Solicited local AEs were precisely defined events that subjects were specifically asked about and which were noted by subjects in the diary. Solicited local AEs: erythema, swelling, and pain/tenderness at the study vaccine injection site, were used to assess the reactogenicity of the study vaccine and were pre-defined local (injection site). All solicited AEs at the injection site (local) were considered related to the study vaccine administration. Safety subset included all subjects that consented to the collection of AEs (solicited AEs for up to 7 days after vaccination and unsolicited AEs for 28 days after vaccination). 'N' (Overall number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Up to Day 7 post vaccination on Day 1 (up to Day 8)

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2305	1155		
Units: Subjects	1076	169		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Solicited Systemic AEs up to 7 Days After Vaccination

End point title	Number of Subjects With Solicited Systemic AEs up to 7 Days After Vaccination

End point description:

Number of subjects with solicited systemic AEs 7 days post vaccination were reported. An AE was any untoward medical occurrence in a clinical study subject administered a medicinal(investigational/ non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Solicited systemic AEs included fatigue, headache, myalgia, nausea, pyrexia, for which subjects were specifically questioned and noted in their diary for 7 days post vaccination (day of vaccination and the subsequent 7 days). The safety subset included all subjects that consented to the collection of AEs (solicited AEs for up to 7 days after vaccination). Here, 'N' (Overall number of subjects analysed) signifies participants who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Up to Day 7 post vaccination on Day 1 (up to Day 8)

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2305	1155		
Units: Subjects	1018	236		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Unsolicited AEs up to 28 Days After Vaccination

End point title	Number of Subjects With Unsolicited AEs up to 28 Days After Vaccination

End point description:

Number of subjects with unsolicited AEs 28 days post vaccination were reported. An AE was any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Unsolicited adverse events included all adverse events for which the subject was not specifically questioned in the subject diary. The safety subset included all subjects that consented to the collection of AEs (unsolicited AEs for 28 days after vaccination).

End point type	Secondary

End point timeframe:

Up to 28 days post vaccination on Day 1 (up to Day 29)

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2330	1165		
Units: Subjects	554	206		

Statistical analyses

No statistical analyses for this end point

Secondary: Respiratory Syncytial Virus (RSV) A2 Strain Neutralization Antibody Titers at 14 Days Post Vaccination

End point title	Respiratory Syncytial Virus (RSV) A2 Strain Neutralization Antibody Titers at 14 Days Post Vaccination

End point description:

RSV A2 strain neutralizing antibody titers of the vaccine-induced immune response was assessed through virus neutralization assay. Per-protocol Immunogenicity (PPI) population included all randomised and vaccinated subjects who were part of the immuno subset (consisted of at least 360 participants, of whom ~50% were at increased risk for severe RSV disease and ~50% were 75 years or older) and for whom immunogenicity data were available. Here, 'N' (number of subjects analysed)

signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At 14 days post vaccination on Day 1 (Day 15)

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	108		
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline	7194 (6394 to 8093)	537 (455 to 634)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Prefusion F-protein (pre-F) Antibodies Immunoglobulin G (IgG) as Assessed by Enzyme-linked Immunosorbent Assay (ELISA) at 14 Days after Vaccination

End point title	Geometric Mean Titers (GMTs) of Prefusion F-protein (pre-F) Antibodies Immunoglobulin G (IgG) as Assessed by Enzyme-linked Immunosorbent Assay (ELISA) at 14 Days after Vaccination

End point description:

GMTs of preF antibodies IgG at 14 days after the administration of Ad26.RSV.preF-based vaccine as assessed by ELISA were reported. PPI population included all randomised and vaccinated subjects who were part of the immuno subset and for whom immunogenicity data were available. Here, 'N' (Overall number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

14 days post vaccination on Day 1 (Day 15)

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	108		
Units: Titers				
geometric mean (confidence interval 95%)	4932 (4477 to 5433)	410 (348 to 484)		

Statistical analyses

No statistical analyses for this end point

Secondary: T-cell Interferon (IFN) Gamma Responses to Respiratory Syncytial Virus (RSV) F Protein Peptides Analyzed by Enzyme-linked Immunospot Assay (ELISpot)

End point title	T-cell Interferon (IFN) Gamma Responses to Respiratory Syncytial Virus (RSV) F Protein Peptides Analyzed by Enzyme-linked Immunospot Assay (ELISpot)

End point description:

T-cell IFN gamma responses to RSV F protein specific peptides at 14 days after vaccination as measured by ELISpot assay were reported. RSV F specific T-cell IFN gamma ELISpot responses were measured as counts of spot forming cells per million peripheral blood mononuclear cells (SFC/10^6 PBMCs). PPI population included all randomized and vaccinated subjects who were part of the immuno subset and for whom immunogenicity data were available. "99999" indicated that median and lower limit of full range could not be estimated as it was below the lower limit of quantification (LLOQ). Median and lower limit of full range could not be estimated as it was below the lower limit of quantification (LLOQ: 68 SFC/10^6 PBMCs). Here, 'N' (Overall number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

14 days post vaccination on Day 1 (Day 15)

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	92		
Units: SFC/10^6 PBMCs				
median (full range (min-max))	533 (306 to 873)	-99999 (-99999 to 78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve (AUC) of the Change from Baseline in Respiratory Infection Intensity and Impact Questionnaire (RiiQ) Total Symptom Scale Score

End point title	Area Under the Curve (AUC) of the Change from Baseline in Respiratory Infection Intensity and Impact Questionnaire (RiiQ) Total Symptom Scale Score

End point description:

RiiQ symptom scale:13-items questionnaire, each symptom was rated on 4-point scale:0 to 3 (0=None, 1=Mild, 2=Moderate, and 3=Severe). Higher scores indicated greater severity. Respiratory symptoms

included 2 upper respiratory tract infection (RTI) symptoms (nasal congestion and sore throat), 4 lower RTI symptoms (cough, wheezing, short of breath, and coughing up phlegm/sputum) and 7 systemic symptoms (headache, feeling feverish, neck pain, body aches and pain, fatigue/tiredness, interrupted sleep, & loss of appetite). The AUC for the change from baseline for RiiQ total symptom score and RiiQ lower respiratory symptom score during the ARI was be calculated. PPE: all randomized and vaccinated subjects, excluding those with MPDs expecting to impact the efficacy outcomes. Subjects with an RSV onset within 14 days after vaccination and who discontinued within 14 days after vaccination were excluded from the PPE population. Here, 'N' signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) up to 24 months

End point values	Group 1: Ad26.RSV.preF and RSV preF Protein	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	143		
Units: Symptoms*Hours				
median (inter-quartile range (Q1-Q3))	82 (21 to 141)	107 (48 to 218)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 up to 24 months post-vaccination on Day 1 (Day 731).

Adverse event reporting additional description:

All-cause mortality and Serious AEs were analyzed on Full analysis set population. Other (not including serious) AEs as solicited and unsolicited AEs were collected and analyzed on a subset of FAS that is called safety subset. The safety subset included all participants that consented to the collection of AEs (solicited and unsolicited AEs).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Group 1: Ad26.RSV.preF and RSV preF Protein (Protein Mixture)

Reporting group description:

Subjects received a single intramuscular (IM) injection containing a mixture of Ad26.RSV.preF at a dose of 1*10^11 viral particles (vp) and RSV preF protein 150 micrograms (mcg) on Day 1.

Reporting group title	Group 2: Placebo (Placebo)

Reporting group description:

Subjects received a single IM injection of matching placebo on Day 1.

Serious adverse events	Group 1: Ad26.RSV.preF and RSV preF Protein (Protein Mixture)	Group 2: Placebo (Placebo)	
Total subjects affected by serious adverse events			
subjects affected / exposed	842 / 16709 (5.04%)	457 / 8367 (5.46%)	
number of deaths (all causes)	105	61	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign Renal Neoplasm			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Myeloid Leukaemia			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute Promyelocytic Leukaemia			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma of Colon			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-Cell Lymphoma			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal Cell Carcinoma			
subjects affected / exposed	1 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Cancer			
subjects affected / exposed	11 / 16709 (0.07%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 11	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brain Stem Glioma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cancer Pain			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral Haemangioma			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix Carcinoma			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cholangiocarcinoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Lymphocytic Leukaemia			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon Cancer			
subjects affected / exposed	3 / 16709 (0.02%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon Cancer Stage I			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal Cancer			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Desmoplastic Melanoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile Duct Cancer			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder Cancer			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder Squamous Cell Carcinoma Stage Iv			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bowen's Disease			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain Neoplasm			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Brain Neoplasm Malignant			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Cancer Stage Ii			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse Large B-Cell Lymphoma			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal Squamous Cell Carcinoma			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial Cancer			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial Cancer Stage I			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial Cancer Stage Ii			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Cancer			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Cancer			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic Cancer Stage Iv			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatocellular Carcinoma			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's Disease			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Metastasis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intraductal Proliferative Breast Lesion			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive Breast Carcinoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive Ductal Breast Carcinoma			
subjects affected / exposed	3 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive Lobular Breast Carcinoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratoacanthoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Benign Neoplasm			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial Adenocarcinoma			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Adenocarcinoma			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Carcinoma Cell Type Unspecified Stage I			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Carcinoma Cell Type Unspecified Stage Iii			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Neoplasm Malignant			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocytic Leukaemia			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Melanoma			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Melanoma Stage Iii			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Melanoma in Situ			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic Gastric Cancer			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic Malignant Melanoma			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic Renal Cell Carcinoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic Squamous Cell Carcinoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucinous Breast Carcinoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic Syndrome			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm Malignant			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Small Cell Lung Cancer Stage Iv			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal Carcinoma			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestine Adenocarcinoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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 Metastatic			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue Neoplasm Malignant Stage Unspecified			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic Carcinoma			
subjects affected / exposed	1 / 16709 (0.01%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pancreatic Carcinoma Metastatic			

subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatic Carcinoma Stage Iv			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pituitary Tumour Benign			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma Cell Myeloma			
subjects affected / exposed	0 / 16709 (0.00%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleomorphic Adenoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycythaemia Vera			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (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 / 16709 (0.11%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 18	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate Cancer Metastatic			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Adenocarcinoma			

subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal Cancer Stage Iv			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Cancer			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Cell Carcinoma			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Cancer			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous Cell Carcinoma of Lung			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsil Cancer			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine Cancer			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal Cancer			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral Cancer			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive Emergency			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive Crisis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	6 / 16709 (0.04%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extravasation Blood			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep Vein Thrombosis			

subjects affected / exposed	15 / 16709 (0.09%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	4 / 17	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriosclerosis			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial Occlusive Disease			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic Stenosis			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic Dissection			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic Aneurysm			
subjects affected / exposed	4 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Shock Haemorrhagic			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Shock			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peripheral Vascular Disorder			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Artery Thrombosis			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Artery Stenosis			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White Coat Hypertension			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Arterial Occlusive Disease			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic Hypotension			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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 / 16709 (0.03%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive Urgency			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous Thrombosis Limb			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Artery Aneurysm			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Drowning			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Death			
subjects affected / exposed	18 / 16709 (0.11%)	18 / 8367 (0.22%)	
occurrences causally related to treatment / all	0 / 18	0 / 18	
deaths causally related to treatment / all	0 / 18	0 / 18	
Accidental Death			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	

Asthenia			
subjects affected / exposed	0 / 16709 (0.00%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest Discomfort			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest Pain			
subjects affected / exposed	3 / 16709 (0.02%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication Associated with Device			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug Withdrawal Syndrome			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothermia			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malaise			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Organ Dysfunction Syndrome			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Non-Cardiac Chest Pain			

subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prosthetic Cardiac Valve Thrombosis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden Death			
subjects affected / exposed	2 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Vascular Stent Stenosis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Amyloidosis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic Reaction			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic Shock			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug Hypersensitivity			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Loss of Personal Independence in Daily Activities			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	3 / 16709 (0.02%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian Cyst			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine Prolapse			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterovaginal Prolapse			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Haemothorax			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Pulmonary Oedema			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute Respiratory Failure			
subjects affected / exposed	18 / 16709 (0.11%)	7 / 8367 (0.08%)	
occurrences causally related to treatment / all	0 / 19	0 / 7	
deaths causally related to treatment / all	0 / 6	0 / 3	
Asthma			
subjects affected / exposed	4 / 16709 (0.02%)	5 / 8367 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis Chronic			
subjects affected / exposed	3 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	4 / 16709 (0.02%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	

Dyspnoea			
subjects affected / exposed	6 / 16709 (0.04%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystic Lung Disease			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	31 / 16709 (0.19%)	14 / 8367 (0.17%)	
occurrences causally related to treatment / all	1 / 33	0 / 14	
deaths causally related to treatment / all	0 / 4	0 / 0	
Pulmonary Mass			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Thrombosis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	5 / 16709 (0.03%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
Sinus Disorder			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial Lung Disease			
subjects affected / exposed	1 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pharyngeal Mass			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural Effusion			
subjects affected / exposed	5 / 16709 (0.03%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic Pain			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumomediastinum			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	4 / 16709 (0.02%)	5 / 8367 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax Spontaneous			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	29 / 16709 (0.17%)	9 / 8367 (0.11%)	
occurrences causally related to treatment / all	5 / 29	0 / 9	
deaths causally related to treatment / all	0 / 2	0 / 1	
Pulmonary Haemorrhage			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary Hypertension			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Neurosis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Confusional State			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Drug Abuse			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major Depression			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental Status Changes			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal Ideation			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device Loosening			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device Malfunction			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device Pacing Issue			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device Dislocation			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis Chronic			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (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	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary Tract Disorder			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis Acute			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			

subjects affected / exposed	4 / 16709 (0.02%)	8 / 8367 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis Acute			
subjects affected / exposed	4 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	3 / 16709 (0.02%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Failure			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic Haemorrhage			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatorenal Syndrome			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic Cirrhosis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Body Temperature Increased			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Murmur			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Computerised Tomogram Thorax Abnormal			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram Abnormal			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart Rate Increased			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Human Metapneumovirus Test Positive			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sars-Cov-2 Test Positive			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Craniocerebral Injury			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Extradural Haematoma			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol Poisoning			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (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	1 / 16709 (0.01%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial Injury			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asbestosis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back Injury			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone Contusion			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical Vertebral Fracture			

subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle Fracture			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye Contusion			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face Injury			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Injury			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Dislocation			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Humerus Fracture			

subjects affected / exposed	4 / 16709 (0.02%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip Fracture			
subjects affected / exposed	6 / 16709 (0.04%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head Injury			
subjects affected / exposed	3 / 16709 (0.02%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand Fracture			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Foreign Body in Skin or Subcutaneous Tissue			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm Fracture			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot Fracture			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula Fracture			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur Fracture			
subjects affected / exposed	8 / 16709 (0.05%)	5 / 8367 (0.06%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral Neck Fracture			
subjects affected / exposed	1 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	5 / 16709 (0.03%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial Bones Fracture			
subjects affected / exposed	0 / 16709 (0.00%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament Rupture			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural Pain			
subjects affected / exposed	3 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Ileus			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post Vaccination Syndrome			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post Procedural Complication			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax Traumatic			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprosthetic Fracture			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprocedural Myocardial Infarction			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic Fracture			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella Fracture			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck Injury			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Fractures			

subjects affected / exposed	1 / 16709 (0.01%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus Injury			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (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 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Limb Fracture			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver Contusion			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb Injury			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural Complication			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia Fracture			

subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to Various Agents			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Traumatic Haematoma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic Haemothorax			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius Fracture			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib Fracture			
subjects affected / exposed	10 / 16709 (0.06%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road Traffic Accident			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Seroma			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Injury			

subjects affected / exposed	0 / 16709 (0.00%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Laceration			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Wound			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (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 / 16709 (0.00%)	1 / 8367 (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	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural Haematoma			
subjects affected / exposed	6 / 16709 (0.04%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural Haemorrhage			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon Rupture			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic Intracranial Haematoma			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Limb Fracture			
subjects affected / exposed	1 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound Dehiscence			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (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	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic Lung Injury			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (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			
Hypertrophic Cardiomyopathy			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitello-Intestinal Duct Remnant			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute Left Ventricular Failure			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute Coronary Syndrome			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Myocardial Infarction			
subjects affected / exposed	17 / 16709 (0.10%)	10 / 8367 (0.12%)	
occurrences causally related to treatment / all	0 / 17	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac Failure Chronic			
subjects affected / exposed	0 / 16709 (0.00%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina Unstable			
subjects affected / exposed	2 / 16709 (0.01%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic Valve Incompetence			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	0 / 16709 (0.00%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	2 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Arteriosclerosis Coronary Artery			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Fibrillation			

subjects affected / exposed	24 / 16709 (0.14%)	13 / 8367 (0.16%)	
occurrences causally related to treatment / all	0 / 24	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Flutter			
subjects affected / exposed	0 / 16709 (0.00%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Thrombosis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular Block Complete			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular Block Second Degree			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Arrest			
subjects affected / exposed	8 / 16709 (0.05%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 6	0 / 1	
Cardiac Failure			

subjects affected / exposed	7 / 16709 (0.04%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 1	
Angina Pectoris			
subjects affected / exposed	6 / 16709 (0.04%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Failure Congestive			
subjects affected / exposed	15 / 16709 (0.09%)	6 / 8367 (0.07%)	
occurrences causally related to treatment / all	0 / 16	0 / 7	
deaths causally related to treatment / all	0 / 3	0 / 0	
Ischaemic Cardiomyopathy			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Ventricular Thrombosis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-Respiratory Arrest			
subjects affected / exposed	3 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Cardiogenic Shock			
subjects affected / exposed	0 / 16709 (0.00%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiomyopathy			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Coronary Syndrome			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conduction Disorder			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive Cardiomyopathy			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cor Pulmonale			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cor Pulmonale Chronic			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary Artery Disease			
subjects affected / exposed	14 / 16709 (0.08%)	11 / 8367 (0.13%)	
occurrences causally related to treatment / all	0 / 14	0 / 12	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary Artery Occlusion			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary Artery Thrombosis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive Heart Disease			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interventricular Septum Rupture			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac Valve Disease			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral Valve Disease			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular Tachycardia			
subjects affected / exposed	3 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral Valve Stenosis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial Infarction			
subjects affected / exposed	23 / 16709 (0.14%)	12 / 8367 (0.14%)	
occurrences causally related to treatment / all	0 / 24	0 / 13	
deaths causally related to treatment / all	0 / 11	0 / 4	
Myocardial Ischaemia			
subjects affected / exposed	1 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial Effusion			

subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus Arrest			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus Bradycardia			
subjects affected / exposed	0 / 16709 (0.00%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus Tachycardia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress Cardiomyopathy			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular Tachycardia			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular Arrhythmia			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular Extrasystoles			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral Valve Incompetence			
subjects affected / exposed	3 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular Disorder			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance Disorder			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal Ganglia Haemorrhage			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bell's Palsy			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain Injury			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Carotid Artery Disease			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid Artery Stenosis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar Stroke			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	2 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cerebral Infarction			
subjects affected / exposed	9 / 16709 (0.05%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral Mass Effect			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral Venous Sinus Thrombosis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrospinal Fluid Leakage			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular Accident			
subjects affected / exposed	20 / 16709 (0.12%)	8 / 8367 (0.10%)	
occurrences causally related to treatment / all	0 / 20	1 / 8	
deaths causally related to treatment / all	0 / 3	0 / 2	
Cervical Radiculopathy			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar Radiculopathy			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic Neuropathy			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness Postural			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic Stroke			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epilepsy			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised Tonic-Clonic Seizure			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage Intracranial			
subjects affected / exposed	0 / 16709 (0.00%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Haemorrhagic Stroke			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Encephalopathy			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	0 / 16709 (0.00%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intracranial Mass			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic Stroke			

subjects affected / exposed	7 / 16709 (0.04%)	7 / 8367 (0.08%)	
occurrences causally related to treatment / all	1 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar Infarction			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar Stroke			
subjects affected / exposed	0 / 16709 (0.00%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of Consciousness			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbosacral Radiculopathy			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	7 / 16709 (0.04%)	7 / 8367 (0.08%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia Gravis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenic Syndrome			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (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 / 16709 (0.01%)	0 / 8367 (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	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic Migraine			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's Disease			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (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 / 16709 (0.01%)	0 / 8367 (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	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Progressive Supranuclear Palsy			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 16709 (0.01%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Claudication			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid Haemorrhage			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Monoplegia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo CNS Origin			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular Dementia			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal Neuralgia			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient Ischaemic Attack			
subjects affected / exposed	15 / 16709 (0.09%)	11 / 8367 (0.13%)	
occurrences causally related to treatment / all	1 / 15	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient Global Amnesia			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic Encephalopathy			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 16709 (0.03%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia Megaloblastic			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated Intravascular Coagulation			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Thrombocytopenia			

subjects affected / exposed	4 / 16709 (0.02%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy Mediastinal			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron Deficiency Anaemia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 16709 (0.01%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Angle Closure Glaucoma			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (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	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ocular Myasthenia			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pterygium			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision Blurred			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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 Hernia			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain			
subjects affected / exposed	5 / 16709 (0.03%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Abdominal Pain Upper			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Fissure			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			

subjects affected / exposed	3 / 16709 (0.02%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's Disease			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular Perforation			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum Intestinal Haemorrhagic			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal Perforation			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal Ulcer			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal Ulcer Haemorrhage			

subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Duodenitis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Polyps			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer Haemorrhage			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer Perforation			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Gastritis			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis Erosive			

subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Haemorrhage			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Gastrointestinal Perforation			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Ulcer			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus Hernia			
subjects affected / exposed	5 / 16709 (0.03%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal Hernia			

subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal Hernia Strangulated			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			
subjects affected / exposed	6 / 16709 (0.04%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Perforation			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Irritable Bowel Syndrome			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Perforation			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large Intestine Polyp			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric Panniculitis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal Haemorrhage			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal Rupture			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	1 / 16709 (0.01%)	0 / 8367 (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	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis Acute			
subjects affected / exposed	2 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic Ulcer Haemorrhage			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Obstruction			
subjects affected / exposed	8 / 16709 (0.05%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Perforation			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spigelian Hernia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue Dysplasia			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Gastrointestinal Haemorrhage			
subjects affected / exposed	3 / 16709 (0.02%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal Varices Haemorrhage			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Decubitus Ulcer			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	1 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkeratosis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (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			

Prerenal Failure			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	4 / 16709 (0.02%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritic Syndrome			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
End Stage Renal Disease			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic Kidney Disease			
subjects affected / exposed	2 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Kidney Injury			
subjects affected / exposed	7 / 16709 (0.04%)	5 / 8367 (0.06%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal Colic			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral Caruncle			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Injury			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Haemorrhage			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (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	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
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	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Disorder			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Retention			

subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Myxoedema			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary Cyst			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal Pain			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	1 / 16709 (0.01%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	3 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthropathy			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	4 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical Spinal Stenosis			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inclusion Body Myositis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intervertebral Disc Degeneration			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral Disc Protrusion			
subjects affected / exposed	4 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Effusion			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar Spinal Stenosis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			

subjects affected / exposed	16 / 16709 (0.10%)	13 / 8367 (0.16%)	
occurrences causally related to treatment / all	0 / 16	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic Fracture			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia Rheumatica			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid Arthritis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator Cuff Syndrome			
subjects affected / exposed	3 / 16709 (0.02%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scoliosis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft Tissue Necrosis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Osteoarthritis			
subjects affected / exposed	0 / 16709 (0.00%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Stenosis			

subjects affected / exposed	1 / 16709 (0.01%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral Foraminal Stenosis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis Perforated			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Abscess			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Jaw			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Limb			

subjects affected / exposed	3 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Abscess			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal Cellulitis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	2 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis Bacterial			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic Foot Infection			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial Infection			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Beta Haemolytic Streptococcal Infection			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchitis			

subjects affected / exposed	3 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis Viral			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbuncle			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	6 / 16709 (0.04%)	5 / 8367 (0.06%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis Staphylococcal			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium Colitis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium Difficile Infection			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic Abscess			
subjects affected / exposed	1 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus Infection			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus Pneumonia			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Covid-19			
subjects affected / exposed	29 / 16709 (0.17%)	12 / 8367 (0.14%)	
occurrences causally related to treatment / all	0 / 29	0 / 12	
deaths causally related to treatment / all	0 / 1	0 / 0	
Covid-19 Pneumonia			
subjects affected / exposed	6 / 16709 (0.04%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungaemia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia Sepsis			

subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottic Abscess			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis Infectious			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal Sepsis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis Intestinal Perforated			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	5 / 16709 (0.03%)	5 / 8367 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gangrene			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	5 / 16709 (0.03%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Salmonella			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Viral			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter Gastritis			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes Zoster			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected Bite			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected Skin Ulcer			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural Abscess			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningoencephalitis Herpetic			

subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Abscess			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Respiratory Tract Infection			
subjects affected / exposed	7 / 16709 (0.04%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Localised Infection			
subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver Abscess			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney Infection			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral Discitis			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 16709 (0.01%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infectious Pleural Effusion			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus Infection			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Legionella			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Influenzal			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Bacterial			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Aspiration			
subjects affected / exposed	5 / 16709 (0.03%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pneumonia			
subjects affected / exposed	46 / 16709 (0.28%)	26 / 8367 (0.31%)	
occurrences causally related to treatment / all	0 / 48	0 / 26	
deaths causally related to treatment / all	0 / 3	0 / 4	
Pharyngitis Streptococcal			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Perirectal Abscess			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	2 / 16709 (0.01%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Streptococcal			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Wound Infection			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Abscess			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (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	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus Infection			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	15 / 16709 (0.09%)	9 / 8367 (0.11%)	
occurrences causally related to treatment / all	0 / 15	0 / 10	
deaths causally related to treatment / all	0 / 2	0 / 3	
Wound Infection			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Labyrinthitis			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 16709 (0.00%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	7 / 16709 (0.04%)	4 / 8367 (0.05%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 16709 (0.02%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal Sepsis			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal Infection			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis Fungal			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic Shock			
subjects affected / exposed	4 / 16709 (0.02%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 2	
Postoperative Abscess			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Failure to Thrive			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased Appetite			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	5 / 16709 (0.03%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes Mellitus			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes Mellitus Inadequate Control			

subjects affected / exposed	3 / 16709 (0.02%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic Ketoacidosis			
subjects affected / exposed	4 / 16709 (0.02%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte Imbalance			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	1 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	2 / 16709 (0.01%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypokalaemia			
subjects affected / exposed	2 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	3 / 16709 (0.02%)	2 / 8367 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	0 / 16709 (0.00%)	1 / 8367 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic Acidosis			

subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 Diabetes Mellitus			
subjects affected / exposed	1 / 16709 (0.01%)	3 / 8367 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 16709 (0.01%)	0 / 8367 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Group 1: Ad26.RSV.preF and RSV preF Protein (Protein Mixture)	Group 2: Placebo (Placebo)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1477 / 16709 (8.84%)	408 / 8367 (4.88%)	
Investigations			
Blood Pressure Diastolic Increased			
subjects affected / exposed[1]	58 / 2330 (2.49%)	21 / 1165 (1.80%)	
occurrences (all)	58	21	
Blood Pressure Systolic Increased			
subjects affected / exposed[2]	150 / 2330 (6.44%)	60 / 1165 (5.15%)	
occurrences (all)	150	60	
Respiratory Rate Increased			
subjects affected / exposed[3]	89 / 2330 (3.82%)	49 / 1165 (4.21%)	
occurrences (all)	89	49	
Nervous system disorders			
Headache(Solicited)			
subjects affected / exposed[4]	597 / 2330 (25.62%)	128 / 1165 (10.99%)	
occurrences (all)	597	128	
General disorders and administration site conditions			

Fatigue(Solicited)			
subjects affected / exposed[5]	789 / 2330 (33.86%)	165 / 1165 (14.16%)	
occurrences (all)	789	165	
Pain			
subjects affected / exposed[6]	48 / 2330 (2.06%)	12 / 1165 (1.03%)	
occurrences (all)	61	18	
Pyrexia(Solicited)			
subjects affected / exposed[7]	171 / 2330 (7.34%)	5 / 1165 (0.43%)	
occurrences (all)	171	5	
Vaccination Site Erythema(Solicited)			
subjects affected / exposed[8]	63 / 2330 (2.70%)	5 / 1165 (0.43%)	
occurrences (all)	63	5	
Vaccination Site Pain(Solicited)			
subjects affected / exposed[9]	1065 / 2330 (45.71%)	168 / 1165 (14.42%)	
occurrences (all)	1065	168	
Vaccination Site Swelling(Solicited)			
subjects affected / exposed[10]	68 / 2330 (2.92%)	3 / 1165 (0.26%)	
occurrences (all)	68	3	
Gastrointestinal disorders			
Nausea(Solicited)			
subjects affected / exposed[11]	324 / 2330 (13.91%)	75 / 1165 (6.44%)	
occurrences (all)	324	75	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed[12]	68 / 2330 (2.92%)	25 / 1165 (2.15%)	
occurrences (all)	74	26	
Musculoskeletal and connective tissue disorders			
Myalgia(Solicited)			
subjects affected / exposed[13]	614 / 2330 (26.35%)	119 / 1165 (10.21%)	
occurrences (all)	614	119	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).
[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious AEs which included solicited and unsolicited AEs were collected and analyzed in a subset of FAS that is called safety subset. The safety subset included all subjects that consented to the collection of AEs (solicited and unsolicited AEs).

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 May 2021	The purpose of this amendment was to follow recommendations from regulatory authorities (eg, update of the primary hypothesis of vaccine efficacy against RT-PCR- confirmed RSV mediated lower respiratory tract disease (LRTD), stratification and minimization factors for the randomization, secondary endpoints testing strategy).
19 July 2021	The purpose of this amendment was to align the information and guidance for investigators on signs and symptoms and on medical management of thrombosis with thrombocytopenia syndrome (TTS) events across the VAC18193 program.
10 November 2021	The purpose of this amendment was to align the protocol following comments from CBER that all cases meeting the programmed case definition of RT-PCR confirmed RSV lower respiratory tract disease (LRTD) should be reviewed by the Clinical Event Adjudication Committee (CEC).
08 April 2022	The purpose of this amendment was to available immunogenicity data generated in ongoing clinical studies with the Ad26/protein preF RSV vaccine suggest that immune responses after a single vaccination are durable beyond one year, and that a revaccination at Month 12 is likely not necessary for efficacy. Therefore, the second dose at Month 12 has been removed from the protocol.
11 October 2022	The purpose of this amendment was to provide clarification around the timing of the end-of-study analyses and population included, to align risk language with the most recent safety data available, and to provide additional clarification around follow-up that is conducted via phone call versus onsite visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported