



## Clinical trial results:

### A Randomized, Observer-blind, Active Comparator-controlled, Multicenter, Phase 3 Study to Assess the Efficacy, Safety, and Immunogenicity of a Plant-derived Quadrivalent VLP Influenza Vaccine in Adults 65 Years of Age and Older

#### Summary

EudraCT number	2018-001894-26
Trial protocol	DE FI
Global end of trial date	16 July 2019

#### Results information

Result version number	v1 (current)
This version publication date	29 September 2023
First version publication date	29 September 2023

#### Trial information

##### Trial identification

Sponsor protocol code	CP-PRO-QVLP-014
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03739112
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Medicago
Sponsor organisation address	1020 route de l'Église, bureau 600, Québec, Canada,
Public contact	Medical Director, Medicago, +1 418658-9393, clinicaltrialinquiries@medicago.com
Scientific contact	Medical Director, Medicago, +1 418658-9393, clinicaltrialinquiries@medicago.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	16 July 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 July 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

- To evaluate the efficacy, relative to an active comparator, of a single 30 microgram ( $\mu\text{g}$ )/strain dose of the Quadrivalent Virus-like Particle (VLP) Influenza Vaccine, against protocol-defined influenza-like illness (ILI) caused by any influenza viral type/subtype (reverse transcription polymerase chain reaction [RT-PCR]).

Protection of trial subjects:

This study was conducted in accordance with the current International Council for Harmonisation (ICH) guidance, Good Clinical Practice (GCP) as established by the ICH (ICH E6 GCP), the European Union Clinical Trials Directive 2001 / 20 / EC, United States (US) 21 Code of Federal Regulations dealing with clinical studies, applicable federal, state, and/or local laws and regulations in the countries where the clinical study was conducted, clinical study contractual obligations, and the principles enunciated in the World Medical Association Declaration of Helsinki.

The Investigator or designee fully informed the subject of the risks and requirements of the study and, during the study, subjects were given any new information that could have affected their decision to continue participation. Subjects were told that their consent to participate in the study was voluntary and that it could be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only subjects who were fully able to understand the risks, benefits, and potential adverse events (AEs) of the study, and who provided their consent voluntarily were enrolled. The Investigator or designee answered all questions prior to requesting the subject's signature on the informed consent form (ICF). Subjects had sufficient time to consider the risks and benefits associated with participation in the study prior to signing the ICF. Each subject signed the ICF containing appropriate study and study drug information and was provided a copy of the ICF.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 1329
Country: Number of subjects enrolled	Germany: 2683
Country: Number of subjects enrolled	Thailand: 537
Country: Number of subjects enrolled	Canada: 2517
Country: Number of subjects enrolled	United States: 5728
Worldwide total number of subjects	12794
EEA total number of subjects	4012

Notes:

<b>Subjects enrolled per age group</b>	
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)	0
From 65 to 84 years	12419
85 years and over	375

## Subject disposition

### Recruitment

Recruitment details:

Participants were randomized in a 1:1 ratio to receive the Quadrivalent virus-like particle (VLP) Influenza Vaccine at a dose of 30 µg/strain or the active comparator.

### Pre-assignment

Screening details:

Participants aged 65 years or older with no acute or evolving medical problems were assessed.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Quadrivalent (30 µg) VLP Vaccine
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Arm description:

Participants received one intramuscular (IM) injection of 0.5 mL of 30 µg/strain of the Quadrivalent VLP Influenza Vaccine on Day 0.

Arm type	Experimental
Investigational medicinal product name	Quadrivalent VLP Influenza Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of a 30 µg/strain of Quadrivalent VLP Vaccine.

<b>Arm title</b>	Active Comparator (Fluarix)
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Arm description:

Participants received one IM injection of 0.5 milliliter (mL) of 15 µg/strain of the Fluarix Quadrivalent® comparator vaccine on Day 0.

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

Dosage and administration details:

Single dose of a 15 µg/strain of Fluarix Quadrivalent® Comparator Vaccine.

<b>Number of subjects in period 1</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)
Started	6396	6398
Completed	6196	6222
Not completed	200	176
Adverse event, serious fatal	12	16
Consent withdrawn by subject	38	19
Physician decision	1	-
Site went on hold	65	67
Adverse event, non-fatal	2	2
Randomized but not vaccinated	31	25
Other than specified	8	5
Lost to follow-up	31	33
Protocol deviation	12	9

## Baseline characteristics

### Reporting groups

Reporting group title	Quadrivalent (30 µg) VLP Vaccine
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Reporting group description:

Participants received one intramuscular (IM) injection of 0.5 mL of 30 µg/strain of the Quadrivalent VLP Influenza Vaccine on Day 0.

Reporting group title	Active Comparator (Fluarix)
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Reporting group description:

Participants received one IM injection of 0.5 milliliter (mL) of 15 µg/strain of the Fluarix Quadrivalent® comparator vaccine on Day 0.

Reporting group values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)	Total
Number of subjects	6396	6398	12794
Age categorical			
Units: Subjects			

Age continuous			
Baseline characteristics are summarized for the SAS.			
Units: years			
arithmetic mean	72.2	72.2	-
standard deviation	± 5.67	± 5.7	
Gender categorical			
Units: Subjects			
Female	3577	3575	7152
Male	2819	2823	5642
Ethnicity			
Units: Subjects			
Hispanic or Latino	202	198	400
Not Hispanic or Latino	6179	6190	12369
Unknown or Not Reported	15	10	25
Race			
Units: Subjects			
American Indian or Alaska Native	19	13	32
Asian	308	300	608
Native Hawaiian or Other Pacific Islander	5	5	10
Black or African American	251	266	517
White	5805	5803	11608
More than one race	6	10	16
Unknown or Not Reported	2	1	3

## End points

### End points reporting groups

Reporting group title	Quadrivalent (30 µg) VLP Vaccine
Reporting group description: Participants received one intramuscular (IM) injection of 0.5 mL of 30 µg/strain of the Quadrivalent VLP Influenza Vaccine on Day 0.	
Reporting group title	Active Comparator (Fluarix)
Reporting group description: Participants received one IM injection of 0.5 milliliter (mL) of 15 µg/strain of the Fluarix Quadrivalent® comparator vaccine on Day 0.	

### Primary: Number of occurrences of protocol-defined Influenza-like Illness (ILI) due to any laboratory-confirmed Influenza strains

End point title	Number of occurrences of protocol-defined Influenza-like Illness (ILI) due to any laboratory-confirmed Influenza strains
End point description: Occurrences of laboratory-confirmed ILI caused by any influenza viral strains was measured by reverse transcriptase polymerase chain reaction (RT-PCR). A participant was considered to have protocol-defined ILI if the participant met at least one of the following pre-defined respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing and at least one of the following systemic symptoms: fever (defined as a temperature > 37.2 °C or > 99.0 °F), chills, tiredness, headache, or myalgia. The number of laboratory-confirmed ILI cases caused by any influenza strains are reported. The Per protocol (PP) set consisted of the participants who participated in the study until at least the end of the peak period or for at least five months or until the end of the surveillance period.	
End point type	Primary
End point timeframe: Day 14 (post vaccination) up to 9 months	

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5996	6026		
Units: Number of cases				
number (not applicable)	118	130		

### Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Vaccine efficacy (VE) of VLP vaccine versus Fluarix = $(1 - ARVv/ARVc) \times 100\%$ where ARVv = attack rate in participants vaccinated with the Quadrivalent VLP Influenza vaccine and ARVc = attack rate in participants vaccinated with an active Fluarix.	
Comparison groups	Quadrivalent (30 µg) VLP Vaccine v Active Comparator (Fluarix)

Number of subjects included in analysis	12022
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[1]</sup>
Parameter estimate	percent VE
Point estimate	8.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.7
upper limit	28.7

Notes:

[1] - Non-inferiority was concluded if the lower limit of the two-sided 95% confidence interval (CI) for relative VE was > -20%.

### **Secondary: Number of occurrences of laboratory confirmed protocol-defined Influenza-like Illness (ILI) caused by vaccine-matched Influenza strains**

End point title	Number of occurrences of laboratory confirmed protocol-defined Influenza-like Illness (ILI) caused by vaccine-matched Influenza strains
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End point description:

Occurrences of protocol-defined ILI due to laboratory-confirmed influenza caused by influenza viral types/subtypes that were matched (and/or antigenically similar) to the strains covered in the vaccine formulation was measured by sequential RT-PCR & serotyping. The vaccine-matched strains included: homologous A/Michigan/45/2015 [H1N1], homologous A/Singapore/INFIMH-16-0019/2016 [H3N2], homologous B/Colorado/06/2017 and homologous B/Phuket/3073/2013) covered in the vaccine formulation. A participant was considered to have protocol-defined ILI if the participant met at least one of the following pre-defined respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing and at least one of the following systemic symptoms: fever (defined as a temperature > 37.2 °C or > 99.0 °F), chills, tiredness, headache, or myalgia. The number of laboratory-confirmed ILI cases caused by vaccine-matched influenza strains (all matched strains) are reported. PP set.

End point type	Secondary
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End point timeframe:

Day 14 (post vaccination) up to 9 months

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5996	6026		
Units: Number of cases				
number (not applicable)	42	46		

### **Statistical analyses**

No statistical analyses for this end point

### **Secondary: Number of occurrences of protocol-defined respiratory illness due to any laboratory confirmed Influenza strains**

End point title	Number of occurrences of protocol-defined respiratory illness due to any laboratory confirmed Influenza strains
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End point description:

Occurrences of protocol-defined respiratory illness due to laboratory-confirmed influenza strain (matched, mismatched, and un-typed) was measured by sequential RT-PCR. A protocol-defined respiratory illness was determined by the occurrence of at least 1 of the following respiratory symptoms: sneezing, stuffy nose, sore throat, cough, sputum production, wheezing, or difficulty breathing. The number of protocol-defined respiratory illness cases caused by any laboratory-confirmed influenza strain (matched, mismatched, and un-typed) are reported. PP set.

End point type Secondary

End point timeframe:

Day 14 (post vaccination) up to 9 months

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5996	6026		
Units: Number of cases				
number (not applicable)	148	167		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of occurrences of protocol-defined respiratory illness vaccine caused by vaccine-matched Influenza strains

End point title Number of occurrences of protocol-defined respiratory illness vaccine caused by vaccine-matched Influenza strains

End point description:

Occurrences of protocol-defined respiratory illness vaccine caused by vaccine-matched influenza strains was measured by sequential RT-PCR & serotyping. The vaccine-matched strains included: homologous A/Michigan/45/2015 [H1N1], homologous A/Singapore/INFIMH-16-0019/2016 [H3N2], homologous B/Colorado/06/2017 and homologous B/Phuket/3073/2013. The protocol-defined respiratory illness was determined by the occurrence of at least 1 of the following respiratory symptoms: sneezing, stuffy nose, sore throat, cough, sputum production, wheezing, or difficulty breathing. The number of protocol-defined respiratory illness cases caused by one or more vaccine-matched strains are reported. PP set.

End point type Secondary

End point timeframe:

Day 14 (post vaccination) up to 9 months

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5996	6026		
Units: Number of cases				
number (not applicable)	50	55		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of occurrences of protocol-defined ILI

End point title	Number of occurrences of protocol-defined ILI
End point description: Occurrences of protocol-defined ILI that were confirmed or not by laboratory testing were assessed. A participant was considered to have protocol-defined ILI if the participant met at least one of the following pre-defined respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing and at least one of the following systemic symptoms: fever (defined as a temperature > 37.2 °C or > 99.0 °F), chills, tiredness, headache or myalgia. The number of protocol-defined ILI cases (confirmed or not) are reported. PP set.	
End point type	Secondary
End point timeframe: Day 14 (post vaccination) up to 9 months	

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5996	6026		
Units: Number of cases				
number (not applicable)	1249	1243		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with at least one immediate complaints

End point title	Number of participants with at least one immediate complaints
End point description: Immediate complaints were defined as any solicited local or systemic reactions. Solicited local reactions included: erythema, swelling, and pain at the injection site) and solicited systemic reactions included: fever, headache, fatigue, muscle aches, joint aches, chills, a feeling of general discomfort, swelling in the axilla, and swelling in the neck. Safety Analysis Set (SAS) was defined as all participants who received either the Quadrivalent VLP Influenza Vaccine or the active comparator. Participants that were non-compliant to protocol/Good Clinical Practice (GCP), as per investigator, were excluded from analysis.	
End point type	Secondary
End point timeframe: 15 minutes post vaccination	

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352	6366		
Units: Participants				
number (not applicable)	272	184		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with ≥ Severe solicited local and systemic reactions

End point title	Number of participants with ≥ Severe solicited local and systemic reactions
End point description:	
<p>Participants were monitored for both solicited local reactions (erythema, swelling, and pain at the injection site) and solicited systemic reactions (fever, headache, fatigue, muscle aches, joint aches, chills, a feeling of general discomfort, swelling in the axilla, and swelling in the neck). The intensity of the solicited reactions was graded as mild (1)-easily tolerated and does not interfere with usual activity; moderate (2)-interferes with daily activity, but the participant is still able to function; severe (3)-incapacitating and the participant is unable to work or complete usual activity or potentially life threatening; (4)-likely to be life-threatening if not treated in a timely manner, according to the Food and Drug Administration (FDA) Guidance for Industry. ≥ Severe events included severe and potentially life-threatening events. Any ≥severe solicited reactions are reported.</p>	
End point type	Secondary
End point timeframe:	
Day 0 (post-vaccination) to Day 7	

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352 <sup>[2]</sup>	6366 <sup>[3]</sup>		
Units: Participants				
number (not applicable)	47	62		

Notes:

[2] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

[3] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with ≥ Severe related solicited reactions

End point title	Number of participants with ≥ Severe related solicited
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## End point description:

Participants were monitored for both solicited local reactions (erythema, swelling, & pain at the injection site) & solicited systemic reactions (fever, headache, fatigue, muscle aches, joint aches, chills, a feeling of general discomfort, swelling in axilla, & swelling in neck). The intensity of solicited reactions was graded as mild (1)-easily tolerated and does not interfere with usual activity; moderate (2)-interferes with daily activity, but the participant is still able to function; severe (3)-incapacitating and the participant is unable to work or complete usual activity or potentially life threatening; (4)-likely to be life-threatening if not treated in a timely manner, according to the FDA Guidance for Industry.  $\geq$  Severe events included severe and potentially life-threatening events. Any  $\geq$ severe related (possibly related, probably related, and definitely related to the study treatments [as defined by investigator]) solicited events are reported.

End point type	Secondary
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## End point timeframe:

Day 0 (post-vaccination) to Day 7

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352 <sup>[4]</sup>	6366 <sup>[5]</sup>		
Units: Participants				
number (not applicable)	28	51		

## Notes:

[4] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

[5] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of participants with unsolicited Treatment-Emergent Adverse Events (TEAEs)**

End point title	Number of participants with unsolicited Treatment-Emergent Adverse Events (TEAEs)
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## End point description:

Participants were monitored for unsolicited TEAEs (e.g., nasopharyngitis, upper respiratory tract infection, headache, and pain). An adverse event (AE) or adverse experience was defined as any untoward medical occurrence in a participant or clinical investigation participant who received study drug, with or without a causal relationship with the treatment. An AE was considered treatment-emergent if it began on or after the date and time of Study Day 0 vaccination. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

End point type	Secondary
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## End point timeframe:

Day 0 (post-vaccination) to Day 21

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352	6366		
Units: Participants				
number (not applicable)	849	824		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with ≥ Severe unsolicited TEAEs

End point title	Number of participants with ≥ Severe unsolicited TEAEs
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End point description:

Participants were monitored for unsolicited TEAEs (e.g., nasopharyngitis, upper respiratory tract infection, headache, and pain). AE: any untoward medical occurrence in a participant or clinical investigation participant who received study drug, with or without a causal relationship with the treatment. An AE was considered treatment-emergent if it began on or after the date and time of Study Day 0 vaccination. The intensity of the solicited reactions was graded as mild (1)-easily tolerated and does not interfere with usual activity; moderate (2)-interferes with daily activity, but the participant is still able to function; severe (3)-incapacitating and the participant is unable to work or complete usual activity or potentially life threatening; (4)-likely to be life-threatening if not treated in a timely manner, according to the FDA Guidance for Industry. ≥ severe events included severe and potentially life-threatening events. Any ≥ severe unsolicited reactions are reported.

End point type	Secondary
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End point timeframe:

Day 0 (post-vaccination) to Day 21

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352 <sup>[6]</sup>	6366 <sup>[7]</sup>		
Units: Participants				
number (not applicable)	33	34		

Notes:

[6] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

[7] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with ≥ Severe related unsolicited reactions

End point title	Number of participants with ≥ Severe related unsolicited reactions
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End point description:

Participants were monitored for unsolicited TEAEs (e.g., nasopharyngitis, upper respiratory tract infection, headache, & pain). AE: any untoward medical occurrence in a participant who received study drug, with or without a causal relationship with treatment. An AE was considered treatment-emergent if

it began on or after date & time of Study Day 0 vaccination. Intensity of solicited reactions was graded as mild (1) easily tolerated & not interfere with usual activity; moderate (2) interferes with daily activity, but participant still able to function; severe (3) incapacitating & participant unable to work/complete usual activity/ potentially life threatening; (4) likely to be life-threatening if not treated in a timely manner, according to FDA Guidance for Industry. ≥ severe events included severe & potentially life-threatening events. Any ≥severe related (possibly, probably, & definitely related to study treatments [as defined by investigator]) unsolicited events are reported.

End point type	Secondary
End point timeframe:	
Day 0 (post-vaccination) to Day 21	

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352 <sup>[8]</sup>	6366 <sup>[9]</sup>		
Units: Participants				
number (not applicable)	1	3		

Notes:

[8] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

[9] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with at least one Serious Adverse Event (SAE)

End point title	Number of participants with at least one Serious Adverse Event (SAE)
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End point description:

An AE was any untoward medical occurrence in a participant who received study drug, with or without a causal relationship with treatment. An SAE was an AE that resulted in death, was life threatening, resulted in a persistent or significant disability or incapacity, resulted in or prolonged an existing hospitalization, was a congenital anomaly or birth defect, or was another important medical event. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

End point type	Secondary
End point timeframe:	
Day 0 to 9 months	

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352	6366		
Units: Participants				
number (not applicable)	263	266		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of occurrences of death

End point title | Number of occurrences of death

End point description:

The number of participants who died during the study was assessed. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

End point type | Secondary

End point timeframe:

Day 0 up to 9 months

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352	6366		
Units: Participants				
number (not applicable)	12	17		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants who withdrew due to an AE

End point title | Number of participants who withdrew due to an AE

End point description:

An AE or adverse experience was defined as any untoward medical occurrence in a participant or clinical investigation participant who received study drug, with or without a causal relationship with the treatment. An AE can be any favorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to a medicinal product. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

End point type | Secondary

End point timeframe:

Day 0 up to 9 months

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352	6366		
Units: Participants				
number (not applicable)	15	20		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with at least one New Onset Chronic Diseases (NOCDs)

End point title	Number of participants with at least one New Onset Chronic Diseases (NOCDs)
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End point description:

All NOCDs that may plausibly have an allergic, autoimmune or inflammatory component were reported. Plausibility should be interpreted broadly; however, the only clear exceptions were degenerative conditions such as osteoarthritis, age-related physiologic changes and life-style diseases. In this context, most cancers, cardiac conditions and kidney diseases should be reported. NOCDs were collected from vaccination on Day 0 to the end of the surveillance period. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

End point type	Secondary
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End point timeframe:

Day 0 up to 9 months

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352	6366		
Units: Participants				
number (not applicable)	36	23		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric mean titers (GMTs) of Hemagglutination Inhibition (HI) antibody response for each homologous and heterologous Influenza strains

End point title	Geometric mean titers (GMTs) of Hemagglutination Inhibition (HI) antibody response for each homologous and heterologous Influenza strains
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End point description:

GMTs were measured using a HI assay for the homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013, and the heterologous strains: H1N1 = A/Brisbane/59/2007; H3N2 = A/Uruguay/716/2007; B/Malaysia = B/Malaysia/2506/2004; B/Florida = B/Florida/4/2006. The Immunogenicity Per Protocol (IPP) set consisted of a subset of participants who participated in the immunogenicity portion of the study and who had a Day 21 immunogenicity sample collection.

End point type	Secondary
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End point timeframe:  
Baseline (Day 0), Day 21

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: Titers				
geometric mean (confidence interval 95%)				
Homologous Strain (H1N1): Day 0	43.8 (36.3 to 52.7)	36.3 (30.0 to 43.9)		
Homologous Strain (H1N1): Day 21	88.9 (73.7 to 107.2)	146.8 (121.4 to 177.7)		
Homologous Strain (H3N2): Day 0	31.1 (25.5 to 37.8)	30.9 (25.3 to 37.8)		
Homologous Strain (H3N2): Day 21	79.5 (65.2 to 97.1)	90.2 (73.7 to 110.5)		
Homologous Strain (B/Colorado): Day 0	15.5 (13.3 to 18.1)	13.2 (11.3 to 15.5)		
Homologous Strain (B/Colorado): Day 21	23.0 (19.3 to 27.4)	51.7 (43.3 to 61.8)		
Homologous Strain (B/Phuket): Day 0	24.4 (20.8 to 28.7)	22.6 (19.2 to 26.6)		
Homologous Strain (B/Phuket): Day 21	45.0 (37.8 to 53.5)	75.5 (63.3 to 90.1)		
Heterologous Strain (H1N1): Day 0	15.5 (13.6 to 17.6)	13.5 (11.8 to 15.4)		
Heterologous Strain (H1N1): Day 21	16.6 (14.3 to 19.2)	32.4 (28.0 to 37.6)		
Heterologous Strain (H3N2): Day 0	19.5 (16.4 to 23.3)	22.6 (18.9 to 27.1)		
Heterologous Strain (H3N2): Day 21	32.4 (27.1 to 38.6)	46.6 (38.9 to 55.8)		
Heterologous Strain (B/Malaysia): Day 0	12.6 (11.0 to 14.5)	11.4 (10.0 to 13.1)		
Heterologous Strain (B/Malaysia): Day 21	15.9 (13.6 to 18.7)	34.8 (29.5 to 41.0)		
Heterologous Strain (B/Florida): Day 0	22.5 (19.2 to 26.4)	20.6 (17.5 to 24.2)		
Heterologous Strain (B/Florida): Day 21	38.0 (32.2 to 44.8)	72.1 (61.0 to 85.2)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with seroconversion measured by HI antibody response for each homologous and heterologous strain

End point title	Percentage of participants with seroconversion measured by HI antibody response for each homologous and heterologous strain
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**End point description:**

The percentage of participants in a given treatment group with either a  $\geq 4$ -fold increase in reciprocal HI titers between Day 0 and Day 21 or a rise of undetectable HI titer (i.e.  $< 10$ ) pre-vaccination (Day 0) to an HI titer of  $\geq 40$  on Day 21 was measured using an HI assay for the homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013, and the heterologous strains: H1N1 = A/Brisbane/59/2007; H3N2 = A/Uruguay/716/2007; B/Malaysia = B/Malaysia/2506/2004; B/Florida = B/Florida/4/2006. IPP set.

End point type	Secondary
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**End point timeframe:**

Day 0 (pre-vaccination) to Day 21

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: Percentage of participants				
number (confidence interval 95%)				
Homologous Strain (H1N1)	15.5 (10.9 to 21.2)	40.7 (33.8 to 47.9)		
Homologous Strain (H3N2)	25.2 (19.5 to 31.7)	28.1 (22.0 to 34.9)		
Homologous Strain (B/Colorado)	10.2 (6.4 to 15.2)	38.2 (31.4 to 45.3)		
Homologous Strain (B/Phuket)	16.5 (11.7 to 22.3)	34.7 (28.1 to 41.7)		
Heterologous Strain (H1N1)	0.5 (0.0 to 2.7)	24.1 (18.4 to 30.7)		
Heterologous Strain (H3N2)	10.7 (6.8 to 15.7)	14.6 (10.0 to 20.3)		
Heterologous Strain (B/Malaysia)	5.3 (2.7 to 9.4)	30.7 (24.3 to 37.6)		
Heterologous Strain (B/Florida)	12.1 (8.0 to 17.4)	37.7 (30.9 to 44.8)		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of participants with seroprotection measured by HI antibody response for each homologous and heterologous strain**

End point title	Percentage of participants with seroprotection measured by HI antibody response for each homologous and heterologous strain
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**End point description:**

The percentage of participants in a given treatment group attaining a reciprocal HI titer of  $\geq 40$  on Day 21 (the percentage of vaccine recipients with a serum HI titer of at least 1:40 following vaccination) was measured using an HI assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013, and the heterologous strains: H1N1 = A/Brisbane/59/2007; H3N2 = A/Uruguay/716/2007; B/Malaysia = B/Malaysia/2506/2004; B/Florida = B/Florida/4/2006. IPP set.

End point type	Secondary
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End point timeframe:  
Baseline (Day 0), Day 21

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: Percentage of participants				
number (confidence interval 95%)				
Homologous Strain (H1N1): Day 0	57.3 (50.2 to 64.1)	52.8 (45.6 to 59.9)		
Homologous Strain (H1N1): Day 21	77.2 (70.8 to 82.7)	87.9 (82.6 to 92.1)		
Homologous Strain (H3N2): Day 0	48.5 (41.5 to 55.6)	52.8 (45.6 to 59.9)		
Homologous Strain (H3N2): Day 21	72.3 (65.7 to 78.3)	78.4 (72.0 to 83.9)		
Homologous Strain (B/Colorado): Day 0	28.6 (22.6 to 35.3)	22.1 (16.5 to 28.5)		
Homologous Strain (B/Colorado): Day 21	40.3 (33.5 to 47.3)	62.3 (55.2 to 69.1)		
Homologous Strain (B/Phuket): Day 0	46.6 (39.6 to 53.7)	38.7 (31.9 to 45.8)		
Homologous Strain (B/Phuket): Day 21	64.1 (57.1 to 70.6)	79.4 (73.1 to 84.8)		
Heterologous Strain (H1N1): Day 0	21.8 (16.4 to 28.1)	18.1 (13.0 to 24.2)		
Heterologous Strain (H1N1): Day 21	22.8 (17.3 to 29.2)	49.2 (42.1 to 56.4)		
Heterologous Strain (H3N2): Day 0	35.4 (28.9 to 42.4)	40.2 (33.3 to 47.4)		
Heterologous Strain (H3N2): Day 21	50.0 (43.0 to 57.0)	63.8 (56.7 to 70.5)		
Heterologous Strain (B/Malaysia): Day 0	22.8 (17.3 to 29.2)	17.6 (12.6 to 23.6)		
Heterologous Strain (B/Malaysia): Day 21	30.1 (23.9 to 36.9)	53.8 (46.6 to 60.8)		
Heterologous Strain (B/Florida): Day 0	37.4 (30.8 to 44.4)	31.2 (24.8 to 38.1)		
Heterologous Strain (B/Florida): Day 21	58.7 (51.7 to 65.5)	76.9 (70.4 to 82.6)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric mean fold rise (GMFR) of HI antibody response for each homologous and heterologous strain

End point title	Geometric mean fold rise (GMFR) of HI antibody response for each homologous and heterologous strain
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End point description:

GMFR, the geometric mean of the ratio of GMTs (Day 21/Day 0), was measured using an HI assay

homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013, and the heterologous strains: H1N1 = A/Brisbane/59/2007; H3N2 = A/Uruguay/716/2007; B/Malaysia = B/Malaysia/2506/2004; B/Florida = B/Florida/4/2006. IPP set.

End point type	Secondary
End point timeframe:	
Baseline (Day 0), Day 21	

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: Ratio				
geometric mean (confidence interval 95%)				
Homologous Strain (H1N1)	2.1 (1.8 to 2.4)	3.9 (3.4 to 4.5)		
Homologous Strain (H3N2)	2.6 (2.2 to 3.0)	2.9 (2.5 to 3.4)		
Homologous Strain (B/Colorado)	1.5 (1.3 to 1.8)	3.8 (3.3 to 4.4)		
Homologous Strain (B/Phuket)	1.9 (1.6 to 2.1)	3.3 (2.9 to 3.8)		
Heterologous Strain (H1N1)	1.1 (1.0 to 1.2)	2.4 (2.2 to 2.6)		
Heterologous Strain (H3N2)	1.6 (1.5 to 1.8)	2.1 (1.9 to 2.3)		
Heterologous Strain (B/Malaysia)	1.3 (1.1 to 1.4)	3.0 (2.7 to 3.4)		
Heterologous Strain (B/Florida)	1.7 (1.5 to 1.9)	3.4 (3.0 to 3.9)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: GMTs of Microneutralization (MN) antibody response for each homologous strain

End point title	GMTs of Microneutralization (MN) antibody response for each homologous strain
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End point description:

GMTs were measured using an MN assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set.

End point type	Secondary
End point timeframe:	
Baseline (Day 0), Day 21	

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: Titers				
geometric mean (confidence interval 95%)				
H1N1: Day 0	501.4 (420.6 to 597.8)	511.2 (427.5 to 611.3)		
H1N1: Day 21	1120.7 (926.3 to 1355.9)	1807.0 (1488.6 to 2193.6)		
H3N2: Day 0	227.4 (194.9 to 265.3)	240.1 (205.3 to 280.8)		
H3N2: Day 21	558.5 (461.2 to 676.3)	437.0 (359.7 to 531.0)		
B/Colorado: Day 0	62.7 (54.1 to 72.6)	55.1 (47.5 to 64.0)		
B/Colorado: Day 21	124.1 (105.4 to 146.2)	193.1 (163.5 to 228.1)		
B/Phuket: Day 0	50.5 (44.4 to 57.6)	45.8 (40.1 to 52.3)		
B/Phuket: Day 21	98.2 (85.7 to 112.6)	143.4 (143.4 to 164.7)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with seroconversion measured by MN antibody response for each homologous strain

End point title	Percentage of participants with seroconversion measured by MN antibody response for each homologous strain
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End point description:

The percentage of participants in a given treatment group with either a  $\geq 4$ -fold increase in reciprocal MN titers between Day 0 and Day 21 or a rise of undetectable MN titer (i.e. 7.1) pre-vaccination (Day 0) to an MN titer of  $\geq 28.3$  at Day 21 post-vaccination were measured using an MN assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set.

End point type	Secondary
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End point timeframe:

Day 0 (pre-vaccination) to Day 21

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: Percentage of participants				
number (confidence interval 95%)				
H1N1	25.7 (19.9 to 32.3)	43.2 (36.2 to 50.4)		

H3N2	36.4 (29.8 to 43.4)	26.6 (20.6 to 33.3)		
B/Colorado	19.9 (14.7 to 26.0)	43.7 (36.7 to 50.9)		
B/Phuket	19.4 (14.2 to 25.5)	41.2 (34.3 to 48.4)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: GMFR of MN antibody response for each homologous strain

End point title	GMFR of MN antibody response for each homologous strain
End point description: GMFR, the geometric mean of the ratio of GMTs (Day 21/Day 0), was measured using an MN assay for H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set.	
End point type	Secondary
End point timeframe: Baseline (Day 0), Day 21	

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: Ratio				
geometric mean (confidence interval 95%)				
H1N1	2.2 (1.9 to 2.6)	3.5 (3.0 to 4.1)		
H3N2	2.4 (2.1 to 2.8)	1.8 (1.6 to 2.1)		
B/Colorado	2.0 (1.8 to 2.3)	3.4 (3.0 to 3.9)		
B/Phuket	2.0 (1.8 to 2.2)	3.1 (2.8 to 3.4)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Areas (GMA) of Single Radial Hemolysis (SRH) antibody response for each homologous strain

End point title	Geometric Mean Areas (GMA) of Single Radial Hemolysis (SRH) antibody response for each homologous strain
End point description: GMA was measured using an SRH assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set.	
End point type	Secondary

End point timeframe:  
Baseline (Day 0), Day 21

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: mm <sup>2</sup>				
geometric mean (confidence interval 95%)				
H1N1: Day 0	23.8 (20.4 to 27.7)	20.7 (17.7 to 24.2)		
H1N1: Day 21	38.7 (34.7 to 43.1)	48.9 (43.8 to 54.6)		
H3N2: Day 0	6.3 (5.1 to 7.9)	5.1 (4.1 to 6.3)		
H3N2: Day 21	21.9 (17.2 to 28.0)	13.2 (10.3 to 17.0)		
B/Colorado: Day 0	33.7 (28.1 to 40.3)	29.2 (24.3 to 35.1)		
B/Colorado: Day 21	54.1 (47.3 to 61.8)	61.0 (53.3 to 69.9)		
B/Phuket: Day 0	21.5 (17.7 to 26.0)	20.4 (16.8 to 24.8)		
B/Phuket: Day 21	38.8 (33.5 to 44.9)	50.2 (43.3 to 58.3)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with seroconversion measured by SRH antibody response for each homologous strain

End point title	Percentage of participants with seroconversion measured by SRH antibody response for each homologous strain
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End point description:

The percentage of participants in a given treatment group showing at least 50 % increase in GMA between Days 0 and 21 were measured using an SRH assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set.

End point type	Secondary
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End point timeframe:

Day 0 (pre-vaccination) to Day 21

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: Percentage of participants				
number (confidence interval 95%)				
H1N1	34.0 (27.5 to 40.9)	55.3 (48.1 to 62.3)		
H3N2	45.1 (38.2 to 52.2)	34.7 (28.1 to 41.7)		
B/Colorado	32.0 (25.7 to 38.9)	49.7 (42.6 to 56.9)		
B/Phuket	35.9 (29.4 to 42.9)	52.3 (45.1 to 59.4)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with seroprotection measured by SRH antibody response for each homologous strain

End point title	Percentage of participants with seroprotection measured by SRH antibody response for each homologous strain
End point description:	The percentage of participants in a given treatment group attaining an area $\geq 25 \text{ mm}^2$ following vaccination (Day 21) were measured using an SRH assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set.
End point type	Secondary
End point timeframe:	Baseline (Day 0), Day 21

<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: Percentage of participants				
number (confidence interval 95%)				
H1N1: Day 0	56.8 (49.7 to 63.7)	51.8 (44.6 to 58.9)		
H1N1: Day 21	77.7 (71.4 to 83.2)	89.4 (84.3 to 93.3)		
H3N2: Day 0	27.7 (21.7 to 34.3)	23.6 (17.9 to 30.1)		
H3N2: Day 21	63.6 (56.6 to 70.2)	51.8 (44.6 to 58.9)		
B/Colorado: Day 0	71.8 (65.2 to 77.9)	69.8 (63.0 to 76.1)		
B/Colorado: Day 21	87.9 (82.6 to 92.0)	89.4 (84.3 to 93.3)		

B/Phuket: Day 0	63.6 (56.6 to 70.2)	60.8 (53.7 to 67.6)		
B/Phuket: Day 21	76.2 (69.8 to 81.9)	87.9 (82.6 to 92.1)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: GMFR of SRH antibody response for each homologous strain

End point title	GMFR of SRH antibody response for each homologous strain
End point description:	GMFR, the geometric mean of the ratio of GMTs (Day 21/Day 0), was measured using an SRH assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set.
End point type	Secondary
End point timeframe:	Baseline (Day 0), Day 21

End point values	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	199		
Units: Ratio				
geometric mean (confidence interval 95%)				
H1N1	1.7 (1.6 to 1.8)	2.3 (2.1 to 2.5)		
H3N2	3.6 (2.9 to 4.4)	2.5 (2.0 to 3.1)		
B/Colorado	1.7 (1.5 to 1.9)	2.0 (1.8 to 2.2)		
B/Phuket	1.8 (1.6 to 2.1)	2.4 (2.2 to 2.7)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with at least one solicited local and systemic reactions

End point title	Number of participants with at least one solicited local and systemic reactions
End point description:	Participants were monitored for both solicited local reactions (erythema, swelling, and pain at the injection site) and solicited systemic reactions (fever, headache, fatigue, muscle aches, joint aches, chills, a feeling of general discomfort, swelling in the axilla, and swelling in the neck) from the time of vaccination through Day 7. Any solicited local or systemic immediate complaint was also included. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.
End point type	Secondary

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End point timeframe:

Day 0 (post-vaccination) to Day 7

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<b>End point values</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6352	6366		
Units: Participants				
number (not applicable)				
Solicited Local Reactions	1954	1460		
Solicited Systemic Reactions	1682	1497		

### **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 0 (post-vaccination) up to ~9 months

Adverse event reporting additional description:

SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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### Reporting groups

Reporting group title	Quadrivalent (30 µg) VLP Vaccine
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Reporting group description:

Participants received one IM injection of 0.5 mL of 30 µg/strain of the Quadrivalent VLP Influenza Vaccine on Day 0.

Reporting group title	Active Comparator (Fluarix)
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Reporting group description:

Participants received one IM injection of 0.5 mL of 15 µg/strain of the Fluarix Quadrivalent® comparator vaccine on Day 0.

<b>Serious adverse events</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)	
Total subjects affected by serious adverse events			
subjects affected / exposed	263 / 6352 (4.14%)	266 / 6366 (4.18%)	
number of deaths (all causes)	12	17	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acral lentiginous melanoma			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Basal cell carcinoma			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
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	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of bladder			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary neoplasm			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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 / 6352 (0.02%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 6352 (0.02%)	5 / 6366 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial neoplasm			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			

subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Endometrial cancer stage I		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Female reproductive neoplasm		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic cancer metastatic		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
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	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Intraductal papillary mucinous neoplasm		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Invasive ductal breast carcinoma		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Laryngeal cancer		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lung adenocarcinoma		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
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	4 / 6352 (0.06%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lung squamous cell carcinoma stage III		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lymphoplasmacytoid lymphoma/immunocytoma recurrent		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Malignant melanoma		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Malignant melanoma stage II		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Mesothelioma		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Metastatic malignant melanoma		

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Neoplasm malignant		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophageal adenocarcinoma		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatic carcinoma		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Papillary thyroid cancer		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Parathyroid tumour benign		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Plasma cell myeloma		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Prostate cancer		
subjects affected / exposed	3 / 6352 (0.05%)	6 / 6366 (0.09%)
occurrences causally related to treatment / all	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0
Prostate cancer metastatic		

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal cancer		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Renal neoplasm		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Squamous cell carcinoma		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Throat cancer		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Thyroid cancer recurrent		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Tonsil cancer		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Triple negative breast cancer			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Waldenstrom's macroglobulinaemia			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiodysplasia			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Extremity necrosis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypertension		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Hypertensive crisis		
subjects affected / exposed	3 / 6352 (0.05%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypertensive emergency		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypotension		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Orthostatic hypotension		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Atrial appendage closure			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	3 / 6352 (0.05%)	4 / 6366 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Incarcerated hernia			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-cardiac chest pain			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical failure			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent stenosis			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endometriosis			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal prolapse			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicocele			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Acute pulmonary oedema			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	5 / 6352 (0.08%)	6 / 6366 (0.09%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			

subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Haemoptysis</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pneumothorax</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pulmonary embolism</b>			
subjects affected / exposed	4 / 6352 (0.06%)	6 / 6366 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pulmonary fibrosis</b>			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pulmonary oedema</b>			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Respiratory failure</b>			
subjects affected / exposed	0 / 6352 (0.00%)	3 / 6366 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
<b>Psychiatric disorders</b>			
<b>Anxiety</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Chronic idiopathic pain syndrome</b>			

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Confusional state			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
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 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mood disorder due to a general medical condition			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hepatobiliary disorders</b>			
<b>Bile duct stenosis</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Bile duct stone</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cholecystitis</b>			
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cholecystitis acute</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cholecystitis chronic</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cholelithiasis</b>			
subjects affected / exposed	2 / 6352 (0.03%)	3 / 6366 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cholestasis</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hepatic cirrhosis</b>			

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sphincter of Oddi dysfunction			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Fibrin D dimer increased			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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			
Acetabulum fracture			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal attack			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
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	2 / 6352 (0.03%)	4 / 6366 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Concussion			
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Contusion			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 6352 (0.02%)	3 / 6366 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fascial rupture			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	4 / 6352 (0.06%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body aspiration			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured coccyx			

subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Fractured sacrum		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Head injury		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hip fracture		
subjects affected / exposed	3 / 6352 (0.05%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Lacrimal structure injury		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Limb injury		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
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 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Meniscus injury		
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pelvic fracture		

subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Postoperative ileus		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Procedural pain		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pubis fracture		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Radius fracture		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Rib fracture		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Road traffic accident		
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Spinal compression fracture		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Spinal fracture		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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 / 6352 (0.02%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)	
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	1 / 6352 (0.02%)	3 / 6366 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention postoperative			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (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			
Arteriovenous malformation			

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hamartoma</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Syringomyelia</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cardiac disorders</b>			
<b>Acute coronary syndrome</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Acute myocardial infarction</b>			
subjects affected / exposed	6 / 6352 (0.09%)	8 / 6366 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
<b>Angina pectoris</b>			
subjects affected / exposed	3 / 6352 (0.05%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Angina unstable</b>			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Arrhythmia</b>			
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
<b>Arteriosclerosis coronary artery</b>			

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Atrial fibrillation		
subjects affected / exposed	11 / 6352 (0.17%)	12 / 6366 (0.19%)
occurrences causally related to treatment / all	0 / 12	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 0
Atrial flutter		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Bradycardia		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac arrest		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Cardiac failure		
subjects affected / exposed	0 / 6352 (0.00%)	3 / 6366 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac failure chronic		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Cardiac failure congestive		
subjects affected / exposed	5 / 6352 (0.08%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1
Cardio-respiratory arrest		

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Coronary artery disease		
subjects affected / exposed	5 / 6352 (0.08%)	3 / 6366 (0.05%)
occurrences causally related to treatment / all	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Coronary artery occlusion		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Coronary artery stenosis		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Myocardial infarction		
subjects affected / exposed	5 / 6352 (0.08%)	3 / 6366 (0.05%)
occurrences causally related to treatment / all	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 2	0 / 0
Pericardial effusion		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pericarditis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pulseless electrical activity		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Sinus arrest		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Sinus bradycardia</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Sinus node dysfunction</b>			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Tachyarrhythmia</b>			
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Nervous system disorders</b>			
<b>Carotid artery stenosis</b>			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cerebellar stroke</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cerebral haemorrhage</b>			
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cerebral infarction</b>			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Cerebrovascular accident</b>			

subjects affected / exposed	7 / 6352 (0.11%)	9 / 6366 (0.14%)
occurrences causally related to treatment / all	0 / 7	0 / 9
deaths causally related to treatment / all	0 / 1	0 / 2
Chronic inflammatory demyelinating polyradiculoneuropathy		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dementia		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Dementia Alzheimer's type		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Diabetic neuropathy		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dizziness		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic encephalopathy		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hydrocephalus		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
IVth nerve paralysis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Loss of consciousness		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Neuropathy peripheral		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Parkinsonism		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Parkinson's disease		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Sciatica		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Seizure		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Spondylitic myelopathy</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Syncope</b>			
subjects affected / exposed	2 / 6352 (0.03%)	5 / 6366 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Transient global amnesia</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Transient ischaemic attack</b>			
subjects affected / exposed	6 / 6352 (0.09%)	3 / 6366 (0.05%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Vertebrobasilar insufficiency</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Blood and lymphatic system disorders</b>			
<b>Anaemia</b>			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Febrile neutropenia</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Haemorrhagic anaemia</b>			

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Iron deficiency anaemia</b>			
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Microcytic anaemia</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Splenic haematoma</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Ear and labyrinth disorders</b>			
<b>Deafness</b>			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Vertigo</b>			
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Vertigo positional</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Vestibular disorder</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Eye disorders</b>			

Amaurosis fugax			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal degeneration			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dacryostenosis acquired			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric ulcer perforation		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal haemorrhage		
subjects affected / exposed	3 / 6352 (0.05%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Gastrointestinal inflammation		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrooesophageal reflux disease		
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hiatus hernia		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ileus		
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Incarcerated inguinal hernia		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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 / 6352 (0.05%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Intestinal obstruction		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Mesenteric arterial occlusion		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatitis acute		
subjects affected / exposed	0 / 6352 (0.00%)	3 / 6366 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Portal hypertensive gastropathy		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Proctitis ulcerative		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Reactive gastropathy		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Rectal haemorrhage</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Small intestinal obstruction</b>			
subjects affected / exposed	4 / 6352 (0.06%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Subileus</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Skin and subcutaneous tissue disorders</b>			
<b>Angioedema</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Renal and urinary disorders</b>			
<b>Acute kidney injury</b>			
subjects affected / exposed	1 / 6352 (0.02%)	3 / 6366 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Bladder prolapse</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Glomerulonephritis</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Haematuria</b>			

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Nephrolithiasis</b>			
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Renal colic</b>			
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Renal failure</b>			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Ureterolithiasis</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Urinary incontinence</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Endocrine disorders</b>			
<b>Goitre</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Musculoskeletal and connective tissue disorders</b>			
<b>Arthralgia</b>			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Camptocormia			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exostosis			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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	2 / 6352 (0.03%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lateral patellar compression syndrome			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Musculoskeletal pain</b>		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Osteitis</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Osteoarthritis</b>		
subjects affected / exposed	9 / 6352 (0.14%)	9 / 6366 (0.14%)
occurrences causally related to treatment / all	0 / 9	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pain in extremity</b>		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pathological fracture</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Polymyalgia rheumatica</b>		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Spinal column stenosis</b>		
subjects affected / exposed	1 / 6352 (0.02%)	3 / 6366 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Spinal osteoarthritis</b>		

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Spondylolisthesis</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Synovial cyst</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Systemic scleroderma</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
<b>Abscess</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Appendicitis</b>			
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Appendicitis perforated</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Bronchitis</b>			
subjects affected / exposed	1 / 6352 (0.02%)	4 / 6366 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Bursitis infective</b>			

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cellulitis		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Diverticulitis		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Empyema		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Endocarditis		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0
Erysipelas		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis		
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)
occurrences causally related to treatment / all	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis Escherichia coli		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis viral		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
H1N1 influenza		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Herpes zoster		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Influenza		
subjects affected / exposed	3 / 6352 (0.05%)	4 / 6366 (0.06%)
occurrences causally related to treatment / all	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Localised infection		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Necrotising fasciitis staphylococcal		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Orchitis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Osteomyelitis		

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Osteomyelitis bacterial</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pharyngeal abscess</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pneumonia</b>		
subjects affected / exposed	20 / 6352 (0.31%)	11 / 6366 (0.17%)
occurrences causally related to treatment / all	0 / 20	0 / 12
deaths causally related to treatment / all	0 / 1	0 / 1
<b>Pneumonia legionella</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pneumonia viral</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Postoperative wound infection</b>		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pseudomonal sepsis</b>		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Pyelonephritis</b>		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Respiratory syncytial virus infection</b>		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Sepsis</b>		
subjects affected / exposed	4 / 6352 (0.06%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Sialoadenitis</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Sinusitis</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Staphylococcal infection</b>		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Streptococcal bacteraemia</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Urinary tract infection</b>		
subjects affected / exposed	3 / 6352 (0.05%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
<b>Urosepsis</b>		

subjects affected / exposed	3 / 6352 (0.05%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
<b>Metabolism and nutrition disorders</b>			
<b>Dehydration</b>			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Diabetes mellitus</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gout</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hyperkalaemia</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hypoglycaemia</b>			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hypokalaemia</b>			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hyponatraemia</b>			
subjects affected / exposed	1 / 6352 (0.02%)	3 / 6366 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hypovolaemia</b>			

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (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 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	Quadrivalent (30 µg) VLP Vaccine	Active Comparator (Fluarix)
Total subjects affected by non-serious adverse events		
subjects affected / exposed	88 / 6352 (1.39%)	138 / 6366 (2.17%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Adenocarcinoma of colon		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Basal cell carcinoma		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Benign neoplasm of thyroid gland		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Breast cancer stage I		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Chronic lymphocytic leukaemia		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Eye naevus		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Haemangioma of liver		

subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Malignant melanoma subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Squamous cell carcinoma subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 5	0 / 6366 (0.00%) 0
Squamous cell carcinoma of skin subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
<b>Vascular disorders</b>		
Aneurysm subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Aortic arteriosclerosis subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	3 / 6366 (0.05%) 3
Aortic dilatation subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Aortic disorder subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Aortic stenosis subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	0 / 6366 (0.00%) 0
Deep vein thrombosis subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Flushing subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	3 / 6366 (0.05%) 4
Haematoma subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2

Hot flush			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences (all)	2	0	
Hypertension			
subjects affected / exposed	35 / 6352 (0.55%)	27 / 6366 (0.42%)	
occurrences (all)	35	27	
Hypertensive crisis			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)	
occurrences (all)	0	2	
Microangiopathy			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences (all)	0	1	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences (all)	0	1	
Peripheral coldness			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences (all)	1	1	
Peripheral vascular disorder			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences (all)	1	1	
Thrombosis			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences (all)	1	0	
Varicose vein			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 6352 (0.06%)	0 / 6366 (0.00%)	
occurrences (all)	4	0	
Axillary pain			

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Chest discomfort		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Chest pain		
subjects affected / exposed	3 / 6352 (0.05%)	5 / 6366 (0.08%)
occurrences (all)	3	5
Chills		
subjects affected / exposed	15 / 6352 (0.24%)	15 / 6366 (0.24%)
occurrences (all)	15	15
Discomfort		
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)
occurrences (all)	2	2
Face oedema		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Facial pain		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Fatigue		
subjects affected / exposed	26 / 6352 (0.41%)	32 / 6366 (0.50%)
occurrences (all)	27	35
Feeling hot		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Gait disturbance		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences (all)	0	2
General physical health deterioration		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Hypothermia		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Induration		

subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Inflammation subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2
Influenza like illness subjects affected / exposed occurrences (all)	8 / 6352 (0.13%) 8	11 / 6366 (0.17%) 11
Injected limb mobility decreased subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Injection site bruising subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	4 / 6366 (0.06%) 4
Injection site erythema subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	3 / 6366 (0.05%) 3
Injection site haematoma subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1
Injection site induration subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	0 / 6366 (0.00%) 0
Injection site pain subjects affected / exposed occurrences (all)	12 / 6352 (0.19%) 12	7 / 6366 (0.11%) 7
Injection site pruritus subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	4 / 6366 (0.06%) 4
Injection site reaction subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Injection site swelling subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	5 / 6366 (0.08%) 5
Injection site warmth		

subjects affected / exposed occurrences (all)	4 / 6352 (0.06%) 4	2 / 6366 (0.03%) 2
Malaise		
subjects affected / exposed occurrences (all)	11 / 6352 (0.17%) 11	6 / 6366 (0.09%) 6
Mass		
subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Oedema peripheral		
subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	3 / 6366 (0.05%) 3
Pain		
subjects affected / exposed occurrences (all)	4 / 6352 (0.06%) 4	2 / 6366 (0.03%) 2
Peripheral swelling		
subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1
Pyrexia		
subjects affected / exposed occurrences (all)	9 / 6352 (0.14%) 9	15 / 6366 (0.24%) 16
Swelling		
subjects affected / exposed occurrences (all)	5 / 6352 (0.08%) 5	6 / 6366 (0.09%) 6
Tenderness		
subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Vaccination site haematoma		
subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Vaccination site hypoaesthesia		
subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Vaccination site induration		
subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Vaccination site pain		

subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	
Vaccination site pruritus subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Seasonal allergy subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	3 / 6366 (0.05%) 3	
Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	4 / 6352 (0.06%) 4	7 / 6366 (0.11%) 7	
Erectile dysfunction subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	
Ovarian cyst subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Prostatomegaly subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Vulvovaginal pruritus subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Respiratory, thoracic and mediastinal disorders Allergic cough subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Asthma subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	0 / 6366 (0.00%) 0	
Atelectasis			

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Chronic obstructive pulmonary disease		
subjects affected / exposed	8 / 6352 (0.13%)	5 / 6366 (0.08%)
occurrences (all)	8	5
Cough		
subjects affected / exposed	42 / 6352 (0.66%)	46 / 6366 (0.72%)
occurrences (all)	42	47
Dry throat		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Dysphonia		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Dyspnoea		
subjects affected / exposed	4 / 6352 (0.06%)	7 / 6366 (0.11%)
occurrences (all)	4	7
Dyspnoea exertional		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Emphysema		
subjects affected / exposed	3 / 6352 (0.05%)	2 / 6366 (0.03%)
occurrences (all)	3	2
Epistaxis		
subjects affected / exposed	4 / 6352 (0.06%)	1 / 6366 (0.02%)
occurrences (all)	4	1
Nasal congestion		
subjects affected / exposed	29 / 6352 (0.46%)	30 / 6366 (0.47%)
occurrences (all)	31	32
Nasal discomfort		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Oropharyngeal pain		
subjects affected / exposed	47 / 6352 (0.74%)	41 / 6366 (0.64%)
occurrences (all)	47	42

Pharyngeal oedema		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Pharyngeal paraesthesia		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Productive cough		
subjects affected / exposed	10 / 6352 (0.16%)	21 / 6366 (0.33%)
occurrences (all)	10	22
Pulmonary hypertension		
subjects affected / exposed	2 / 6352 (0.03%)	3 / 6366 (0.05%)
occurrences (all)	2	3
Pulmonary mass		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Pulmonary oedema		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Respiratory disorder		
subjects affected / exposed	16 / 6352 (0.25%)	17 / 6366 (0.27%)
occurrences (all)	16	17
Respiratory symptom		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences (all)	0	2
Respiratory tract congestion		
subjects affected / exposed	4 / 6352 (0.06%)	0 / 6366 (0.00%)
occurrences (all)	4	0
Rhinitis allergic		
subjects affected / exposed	0 / 6352 (0.00%)	3 / 6366 (0.05%)
occurrences (all)	0	3
Rhinorrhoea		
subjects affected / exposed	41 / 6352 (0.65%)	56 / 6366 (0.88%)
occurrences (all)	42	56
Sinus congestion		
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences (all)	2	1

Sinus pain			
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)	
occurrences (all)	1	2	
Sleep apnoea syndrome			
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)	
occurrences (all)	2	1	
Sneezing			
subjects affected / exposed	31 / 6352 (0.49%)	25 / 6366 (0.39%)	
occurrences (all)	33	27	
Throat irritation			
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)	
occurrences (all)	2	2	
Throat tightness			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences (all)	1	0	
Tonsillar cyst			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences (all)	1	0	
Tonsillar hypertrophy			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences (all)	0	1	
Upper respiratory tract congestion			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences (all)	1	0	
Upper-airway cough syndrome			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences (all)	1	1	
Wheezing			
subjects affected / exposed	4 / 6352 (0.06%)	1 / 6366 (0.02%)	
occurrences (all)	4	1	
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences (all)	1	0	
Aggression			

subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Anxiety subjects affected / exposed occurrences (all)	5 / 6352 (0.08%) 5	1 / 6366 (0.02%) 1
Confusional state subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1
Fear subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Initial insomnia subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	4 / 6352 (0.06%) 4	2 / 6366 (0.03%) 2
Listless subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Nervousness subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1
Restlessness subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 2
Sleep disorder subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 3	0 / 6366 (0.00%) 0
Investigations Blood cholesterol increased subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	3 / 6366 (0.05%) 3

Blood pressure increased subjects affected / exposed occurrences (all)	13 / 6352 (0.20%) 13	9 / 6366 (0.14%) 9	
Blood thyroid stimulating hormone increased subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Body temperature increased subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2	
Cardiac imaging procedure abnormal subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Thyroid hormones decreased subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Injury, poisoning and procedural complications			
Anaemia postoperative subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Animal bite subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Arthropod bite subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	4 / 6366 (0.06%) 4	
Arthropod sting subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	
Back injury subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Chest injury			

subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Contusion subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	2 / 6366 (0.03%) 3
Epicondylitis subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Eye injury subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Face injury subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Facial bones fracture subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	7 / 6366 (0.11%) 7
Head injury subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Joint injury subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Laceration subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	4 / 6366 (0.06%) 4
Ligament sprain subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	0 / 6366 (0.00%) 0
Limb injury subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	0 / 6366 (0.00%) 0
Meniscus injury		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Muscle contusion		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Muscle rupture		
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences (all)	2	0
Muscle strain		
subjects affected / exposed	5 / 6352 (0.08%)	3 / 6366 (0.05%)
occurrences (all)	5	3
Post-traumatic pain		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Procedural pain		
subjects affected / exposed	3 / 6352 (0.05%)	5 / 6366 (0.08%)
occurrences (all)	3	6
Pubis fracture		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Rib fracture		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Scratch		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Skin abrasion		
subjects affected / exposed	0 / 6352 (0.00%)	3 / 6366 (0.05%)
occurrences (all)	0	3
Spinal compression fracture		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Sunburn		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Synovial rupture		

subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Tendon rupture subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 3	0 / 6366 (0.00%) 0	
Tibia fracture subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Tongue injury subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Toxicity to various agents subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Wound subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	
Wound complication subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Wrist fracture subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Bone contusion subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Cardiac disorders			
Acute left ventricular failure subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	
Angina pectoris subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Aortic valve incompetence subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	

Aortic valve stenosis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Arrhythmia		
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)
occurrences (all)	2	2
Arteriosclerosis coronary artery		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Atrial fibrillation		
subjects affected / exposed	11 / 6352 (0.17%)	11 / 6366 (0.17%)
occurrences (all)	11	11
Atrial flutter		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Bradycardia		
subjects affected / exposed	3 / 6352 (0.05%)	0 / 6366 (0.00%)
occurrences (all)	3	0
Bundle branch block bilateral		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Cardiac dysfunction		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Cardiac failure congestive		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Cardiomegaly		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Cardiomyopathy		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences (all)	0	2
Cardiovascular disorder		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1

Coronary artery disease subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	5 / 6366 (0.08%) 5
Coronary artery stenosis subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Dilatation atrial subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2
Extrasystoles subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Hypertensive heart disease subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Left atrial dilatation subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2
Left ventricular dysfunction subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2
Left ventricular hypertrophy subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	5 / 6366 (0.08%) 5
Mitral valve calcification subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Mitral valve incompetence subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	4 / 6366 (0.06%) 4
Palpitations subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2
Pulmonary valve incompetence subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2

Right atrial dilatation subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Sinus node dysfunction subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Tachycardia subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	
Tricuspid valve incompetence subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	5 / 6366 (0.08%) 5	
Nervous system disorders			
Carotid artery stenosis subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	1 / 6366 (0.02%) 1	
Carpal tunnel syndrome subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	
Cerebral atrophy subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	3 / 6366 (0.05%) 3	
Cerebral microangiopathy subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Complex regional pain syndrome subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Dementia subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Dementia Alzheimer's type subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	
Dizziness			

subjects affected / exposed	19 / 6352 (0.30%)	24 / 6366 (0.38%)
occurrences (all)	20	25
Dysgeusia		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Facial paralysis		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Head discomfort		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Headache		
subjects affected / exposed	61 / 6352 (0.96%)	66 / 6366 (1.04%)
occurrences (all)	73	71
Hypoaesthesia		
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences (all)	2	1
Hypogeusia		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Memory impairment		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Migraine		
subjects affected / exposed	2 / 6352 (0.03%)	3 / 6366 (0.05%)
occurrences (all)	2	3
Movement disorder		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Myasthenia gravis		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Neuralgia		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Neuropathy peripheral		

subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences (all)	0	3
Paraesthesia		
subjects affected / exposed	3 / 6352 (0.05%)	0 / 6366 (0.00%)
occurrences (all)	3	0
Parkinson's disease		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Polyneuropathy		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Posterior cortical atrophy		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Presyncope		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Radiculopathy		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Restless legs syndrome		
subjects affected / exposed	2 / 6352 (0.03%)	3 / 6366 (0.05%)
occurrences (all)	2	3
Sciatica		
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)
occurrences (all)	2	2
Sinus headache		
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)
occurrences (all)	2	2
Somnolence		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Syncope		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Tension headache		

subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	0 / 6366 (0.00%) 0	
Trigeminal neuralgia subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Vlith nerve paralysis subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Visual field defect subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 3	
White matter lesion subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
<b>Blood and lymphatic system disorders</b>			
Anaemia subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	2 / 6366 (0.03%) 2	
Increased tendency to bruise subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Iron deficiency anemia subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Lymph node pain subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	0 / 6366 (0.00%) 0	
Lymphadenopathy subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	1 / 6366 (0.02%) 1	
<b>Ear and labyrinth disorders</b>			
Cerumen impaction subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	0 / 6366 (0.00%) 0	
Ear discomfort			

subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	
Ear pain subjects affected / exposed occurrences (all)	7 / 6352 (0.11%) 7	7 / 6366 (0.11%) 7	
Tinnitus subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Vertigo subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	4 / 6366 (0.06%) 4	
Vertigo positional subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Eye disorders			
Astigmatism subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2	
Binocular eye movement disorder subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Blepharitis subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Blepharochalasis subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Blindness transient subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Cataract subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Chalazion subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	

Conjunctival haemorrhage		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Corneal warpage		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Dry age-related macular degeneration		
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences (all)	2	0
Dry eye		
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences (all)	2	1
Eye discharge		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Eye haemorrhage		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Eye inflammation		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Eye irritation		
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences (all)	2	0
Eye pain		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Eye pruritus		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences (all)	0	2
Eye swelling		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences (all)	0	2
Eyelid irritation		

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
<b>Eyelid margin crusting</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
<b>Eyelid oedema</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
<b>Eyelid pain</b>		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
<b>Glaucoma</b>		
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences (all)	2	1
<b>Hyalosis asteroid</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
<b>Keratitis</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
<b>Lacrimation increased</b>		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
<b>Macular degeneration</b>		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
<b>Macular fibrosis</b>		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
<b>Neovascular age-related macular degeneration</b>		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
<b>Ocular hyperaemia</b>		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1

Ocular rosacea			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences (all)	1	1	
Visual impairment			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences (all)	0	1	
Vitreous haemorrhage			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	3 / 6352 (0.05%)	0 / 6366 (0.00%)	
occurrences (all)	3	0	
Abdominal distension			
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)	
occurrences (all)	2	1	
Abdominal hernia			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	8 / 6352 (0.13%)	7 / 6366 (0.11%)	
occurrences (all)	8	7	
Abdominal pain lower			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	2 / 6352 (0.03%)	8 / 6366 (0.13%)	
occurrences (all)	2	10	
Anal incontinence			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences (all)	0	1	
Aphthous ulcer			

subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Barrett's oesophagus		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Cheilitis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Chronic gastritis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Constipation		
subjects affected / exposed	4 / 6352 (0.06%)	6 / 6366 (0.09%)
occurrences (all)	4	6
Diarrhoea		
subjects affected / exposed	50 / 6352 (0.79%)	53 / 6366 (0.83%)
occurrences (all)	53	56
Diverticulum		
subjects affected / exposed	1 / 6352 (0.02%)	3 / 6366 (0.05%)
occurrences (all)	1	3
Diverticulum intestinal		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Dry mouth		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Dyspepsia		
subjects affected / exposed	2 / 6352 (0.03%)	3 / 6366 (0.05%)
occurrences (all)	2	3
Dysphagia		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Enlarged uvula		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Faeces soft		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Flatulence		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Food poisoning		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Gastric ulcer		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Gastritis		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Gastroesophageal reflux disease		
subjects affected / exposed	3 / 6352 (0.05%)	5 / 6366 (0.08%)
occurrences (all)	3	5
Haemorrhoidal haemorrhage		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Haemorrhoids		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Hiatus hernia		
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)
occurrences (all)	2	2
Irritable bowel syndrome		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences (all)	0	2
Large intestine polyp		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Lip erythema		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	2
Lip pruritus		

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	2
Lip swelling		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Lip ulceration		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Malocclusion		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Nausea		
subjects affected / exposed	27 / 6352 (0.43%)	30 / 6366 (0.47%)
occurrences (all)	27	32
Oesophageal food impaction		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Oesophageal motility disorder		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Oesophagitis		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Oral pruritus		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Palatal oedema		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Rectal haemorrhage		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Salivary gland calculus		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Swollen tongue		

subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Tongue blistering subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Tooth impacted subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Tooth loss subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	0 / 6366 (0.00%) 0	
Toothache subjects affected / exposed occurrences (all)	8 / 6352 (0.13%) 8	6 / 6366 (0.09%) 6	
Vomiting subjects affected / exposed occurrences (all)	13 / 6352 (0.20%) 13	13 / 6366 (0.20%) 14	
Hepatobiliary disorders			
Biliary colic subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	0 / 6366 (0.00%) 0	
Cholangitis subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Cholangitis acute subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Cholecystitis acute subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Hepatic cirrhosis subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2	

Portal vein thrombosis			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences (all)	0	1	
Steatohepatitis			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences (all)	0	1	
<b>Skin and subcutaneous tissue disorders</b>			
Acne			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences (all)	1	0	
Blood blister			
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)	
occurrences (all)	0	1	
Dermatitis allergic			
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)	
occurrences (all)	1	2	
Dermatitis contact			
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)	
occurrences (all)	2	2	
Diabetic foot			
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)	
occurrences (all)	2	0	
Eczema			
subjects affected / exposed	3 / 6352 (0.05%)	3 / 6366 (0.05%)	
occurrences (all)	3	3	
Erythema			
subjects affected / exposed	1 / 6352 (0.02%)	5 / 6366 (0.08%)	
occurrences (all)	1	5	
Hyperhidrosis			
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)	
occurrences (all)	1	1	
Ingrowing nail			

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Ingrown hair		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Nail bed disorder		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Night sweats		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Pruritus		
subjects affected / exposed	9 / 6352 (0.14%)	8 / 6366 (0.13%)
occurrences (all)	10	9
Pruritus generalised		
subjects affected / exposed	3 / 6352 (0.05%)	3 / 6366 (0.05%)
occurrences (all)	3	4
Rash		
subjects affected / exposed	12 / 6352 (0.19%)	8 / 6366 (0.13%)
occurrences (all)	12	8
Rash generalised		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Skin discolouration		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Skin ulcer		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Stasis dermatitis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Urticaria		
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)
occurrences (all)	2	2
Renal and urinary disorders		

Acute kidney injury		
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences (all)	2	0
Bladder discomfort		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Calculus urinary		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Chronic kidney disease		
subjects affected / exposed	3 / 6352 (0.05%)	4 / 6366 (0.06%)
occurrences (all)	3	4
Hypertensive nephropathy		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Hypertonic bladder		
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences (all)	2	0
Micturition urgency		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Nephrolithiasis		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Nephrotic syndrome		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Pollakiuria		
subjects affected / exposed	0 / 6352 (0.00%)	3 / 6366 (0.05%)
occurrences (all)	0	3
Renal cyst		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Renal disorder		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1

Urinary incontinence subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Urinary tract obstruction subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Lower urinary tract symptoms subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Endocrine disorders			
Goitre subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	2 / 6366 (0.03%) 2	
Hyperthyroidism subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	1 / 6366 (0.02%) 1	
Hypothyroidism subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	4 / 6366 (0.06%) 4	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	25 / 6352 (0.39%) 25	30 / 6366 (0.47%) 30	
Arthritis subjects affected / exposed occurrences (all)	4 / 6352 (0.06%) 4	1 / 6366 (0.02%) 1	
Back pain subjects affected / exposed occurrences (all)	20 / 6352 (0.31%) 21	26 / 6366 (0.41%) 27	
Bone pain subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Bursitis subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	3 / 6366 (0.05%) 3	
Coccydynia			

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Dupuytren's contracture		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Facet joint syndrome		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences (all)	0	2
Flank pain		
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences (all)	2	0
Groin pain		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Intervertebral disc degeneration		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Intervertebral disc protrusion		
subjects affected / exposed	3 / 6352 (0.05%)	0 / 6366 (0.00%)
occurrences (all)	3	0
Joint swelling		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Limb discomfort		
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences (all)	2	1
Lumbar spinal stenosis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Muscle spasms		
subjects affected / exposed	9 / 6352 (0.14%)	3 / 6366 (0.05%)
occurrences (all)	9	3
Muscle tightness		
subjects affected / exposed	3 / 6352 (0.05%)	1 / 6366 (0.02%)
occurrences (all)	3	1
Muscular weakness		

subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences (all)	2	0
Musculoskeletal chest pain		
subjects affected / exposed	1 / 6352 (0.02%)	3 / 6366 (0.05%)
occurrences (all)	1	3
Musculoskeletal pain		
subjects affected / exposed	11 / 6352 (0.17%)	12 / 6366 (0.19%)
occurrences (all)	11	12
Musculoskeletal stiffness		
subjects affected / exposed	1 / 6352 (0.02%)	5 / 6366 (0.08%)
occurrences (all)	1	5
Myalgia		
subjects affected / exposed	32 / 6352 (0.50%)	35 / 6366 (0.55%)
occurrences (all)	34	35
Myosclerosis		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Neck mass		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Neck pain		
subjects affected / exposed	10 / 6352 (0.16%)	10 / 6366 (0.16%)
occurrences (all)	11	10
Nuchal rigidity		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Osteoarthritis		
subjects affected / exposed	7 / 6352 (0.11%)	12 / 6366 (0.19%)
occurrences (all)	7	12
Osteopenia		
subjects affected / exposed	2 / 6352 (0.03%)	2 / 6366 (0.03%)
occurrences (all)	2	2
Osteoporosis		
subjects affected / exposed	6 / 6352 (0.09%)	4 / 6366 (0.06%)
occurrences (all)	6	4
Osteosclerosis		

subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Pain in extremity		
subjects affected / exposed	14 / 6352 (0.22%)	11 / 6366 (0.17%)
occurrences (all)	14	11
Periarthritis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Plantar fasciitis		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Polyarthritis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Polymyalgia rheumatica		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Rheumatoid arthritis		
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences (all)	2	1
Rotator cuff syndrome		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences (all)	0	2
Spinal column stenosis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Spinal osteoarthritis		
subjects affected / exposed	3 / 6352 (0.05%)	1 / 6366 (0.02%)
occurrences (all)	3	1
Spondylitis		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Spondylolisthesis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Synovial cyst		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Temporomandibular joint syndrome		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Tendonitis		
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences (all)	2	0
Torticollis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Vertebral foraminal stenosis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Infections and infestations		
Acute sinusitis		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Adenovirus infection		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Borrelia infection		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Bronchitis		
subjects affected / exposed	12 / 6352 (0.19%)	8 / 6366 (0.13%)
occurrences (all)	12	8
Cellulitis		
subjects affected / exposed	1 / 6352 (0.02%)	3 / 6366 (0.05%)
occurrences (all)	1	3
Conjunctivitis		
subjects affected / exposed	2 / 6352 (0.03%)	3 / 6366 (0.05%)
occurrences (all)	2	3
Cystitis		
subjects affected / exposed	2 / 6352 (0.03%)	6 / 6366 (0.09%)
occurrences (all)	2	6

Cystitis escherichia		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Diverticulitis		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Ear infection		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Erysipelas		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Eye infection		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Eye infection bacterial		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Folliculitis		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Gastroenteritis		
subjects affected / exposed	6 / 6352 (0.09%)	8 / 6366 (0.13%)
occurrences (all)	6	8
Gastroenteritis viral		
subjects affected / exposed	3 / 6352 (0.05%)	1 / 6366 (0.02%)
occurrences (all)	3	1
Gastrointestinal infection		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Gastrointestinal viral infection		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Genital infection fungal		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0

Gingivitis		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Haemorrhagic fever with renal syndrome		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Helicobacter infection		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Hepatitis C		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Herpes simplex		
subjects affected / exposed	1 / 6352 (0.02%)	3 / 6366 (0.05%)
occurrences (all)	1	3
Herpes zoster		
subjects affected / exposed	5 / 6352 (0.08%)	5 / 6366 (0.08%)
occurrences (all)	5	5
Hordeolum		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Infected bite		
subjects affected / exposed	0 / 6352 (0.00%)	2 / 6366 (0.03%)
occurrences (all)	0	2
Infection		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Influenza		
subjects affected / exposed	3 / 6352 (0.05%)	13 / 6366 (0.20%)
occurrences (all)	3	14
Laryngitis		
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences (all)	2	0
Localised infection		

subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Lower respiratory tract infection		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Nasal herpes		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Nasopharyngitis		
subjects affected / exposed	88 / 6352 (1.39%)	76 / 6366 (1.19%)
occurrences (all)	88	77
Onychomycosis		
subjects affected / exposed	1 / 6352 (0.02%)	2 / 6366 (0.03%)
occurrences (all)	1	2
Oral candidiasis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Oral herpes		
subjects affected / exposed	5 / 6352 (0.08%)	3 / 6366 (0.05%)
occurrences (all)	5	3
Otitis media		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Periodontitis		
subjects affected / exposed	2 / 6352 (0.03%)	1 / 6366 (0.02%)
occurrences (all)	2	1
Pertussis		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Pharyngitis		
subjects affected / exposed	4 / 6352 (0.06%)	0 / 6366 (0.00%)
occurrences (all)	4	0
Pilonidal cyst		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Pneumonia		

subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	4 / 6366 (0.06%) 4
Respiratory tract infection subjects affected / exposed occurrences (all)	8 / 6352 (0.13%) 8	5 / 6366 (0.08%) 5
Respiratory tract infection viral subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	0 / 6366 (0.00%) 0
Rhinitis subjects affected / exposed occurrences (all)	9 / 6352 (0.14%) 9	6 / 6366 (0.09%) 6
Root canal infection subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1
Sinusitis subjects affected / exposed occurrences (all)	13 / 6352 (0.20%) 13	9 / 6366 (0.14%) 9
Sinusitis bacterial subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Streptococcal infection subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Tinea infection subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0
Tooth abscess subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1
Tooth infection subjects affected / exposed occurrences (all)	2 / 6352 (0.03%) 2	1 / 6366 (0.02%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	52 / 6352 (0.82%) 53	47 / 6366 (0.74%) 48
Urinary tract infection		

subjects affected / exposed occurrences (all)	15 / 6352 (0.24%) 15	13 / 6366 (0.20%) 13	
Vaginal infection subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Varicella zoster virus infection subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Viral infection subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	0 / 6366 (0.00%) 0	
Wound infection subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
<b>Metabolism and nutrition disorders</b>			
Dehydration subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	0 / 6366 (0.00%) 0	
Dyslipidaemia subjects affected / exposed occurrences (all)	3 / 6352 (0.05%) 3	2 / 6366 (0.03%) 2	
Glucose tolerance impaired subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	
Gout subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	5 / 6366 (0.08%) 5	
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 6352 (0.00%) 0	1 / 6366 (0.02%) 1	
Hypercholesterolaemia subjects affected / exposed occurrences (all)	8 / 6352 (0.13%) 8	5 / 6366 (0.08%) 5	
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 6352 (0.02%) 1	1 / 6366 (0.02%) 1	

Hyperlipidaemia		
subjects affected / exposed	5 / 6352 (0.08%)	2 / 6366 (0.03%)
occurrences (all)	5	2
Hypoglycaemia		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	3
Hypokalaemia		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Iron deficiency		
subjects affected / exposed	2 / 6352 (0.03%)	0 / 6366 (0.00%)
occurrences (all)	2	0
Ketoacidosis		
subjects affected / exposed	1 / 6352 (0.02%)	0 / 6366 (0.00%)
occurrences (all)	1	0
Lactose intolerance		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Lipid metabolism disorder		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1
Type 2 diabetes mellitus		
subjects affected / exposed	4 / 6352 (0.06%)	8 / 6366 (0.13%)
occurrences (all)	4	8
Vitamin B12 deficiency		
subjects affected / exposed	0 / 6352 (0.00%)	1 / 6366 (0.02%)
occurrences (all)	0	1
Vitamin D deficiency		
subjects affected / exposed	1 / 6352 (0.02%)	1 / 6366 (0.02%)
occurrences (all)	1	1

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2018	The purpose of Amendment No. 01 was to add precision to Protocol version 1.1 around key elements of the protocol: <ul style="list-style-type: none"><li>• Clarification of the testing to be applied for primary, secondary, and exploratory outcomes;</li><li>• Clarification of the rationale for comparator vaccine choice;</li><li>• Clarification of the statistical analysis plan;</li><li>• Specification of the needle length required for obese subjects (body mass index greater than 30 kg/m<sup>2</sup>).</li></ul>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported