Clinical trial results:
A Randomized, Observer-blind, Placebo-controlled, Multicenter, Phase 3 Study to Assess the Efficacy, Safety, and Immunogenicity of a Plant-Derived Quadrivalent VLP Influenza Vaccine in Adults 18-64 Years of Age

Summary

EudraCT number	2017-001239-38
Trial protocol	DE FI GB
Global end of trial date	09 May 2018

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-012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03301051
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medicago Inc.
Sponsor organisation address	1020 route de l'Église, bureau 600, Québec, Canada,
Public contact	Medical director, Medicago Inc, +1 418658-9393 x378, clinicaltrialenquiries@medicago.com
Scientific contact	Medical director, Medicago Inc, +1 418658-9393 x378, clinicaltrialenquiries@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	09 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy, relative to placebo, of a single dose of the Quadrivalent VLP Influenza Vaccine given at a dose of 30 µg / strain, against protocol-defined respiratory illness due to laboratory-confirmed influenza caused by vaccine matched strains.

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	31 August 2017
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	Canada: 1801
Country: Number of subjects enrolled	Philippines: 1134
Country: Number of subjects enrolled	Thailand: 1112
Country: Number of subjects enrolled	United States: 4229
Country: Number of subjects enrolled	United Kingdom: 436
Country: Number of subjects enrolled	Finland: 766
Country: Number of subjects enrolled	Germany: 682
Worldwide total number of subjects	10160
EEA total number of subjects	1448

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	10160
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were randomized in a 1:1 ratio to receive the Quadrivalent VLP Influenza Vaccine at a dose of 30 µg/strain or the placebo.

Pre-assignment

Screening details:

Participants were healthy adults 18 to 64 years of age assessed during the 2017-2018 influenza season.

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
Arm title	Quadrivalent VLP Vaccine

Arm description:

Participants received one intramuscular (IM) injection of 0.5 mililiter (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

Arm title	Placebo

Arm description:

Participants received one IM injection of 0.5 mL of placebo on Day 0.

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

Dosage and administration details:

Single dose of a placebo.

Number of subjects in period 1	Quadrivalent VLP Vaccine	Placebo
Started	5077	5083
Safety Analysis Set	5064	5072
Vaccinated	5065	5072
Completed	4731	4711
Not completed	346	372
Adverse event, serious fatal	1	1
Consent withdrawn by subject	59	65
Physician decision	1	3
Adverse event, non-fatal	-	4
Other	8	-
Miscellaneous	-	4
Lost to follow-up	263	282
Protocol deviation	1	3
Randomized, not vaccinated	13	10

Baseline characteristics

Reporting groups	
Reporting group title	Quadrivalent VLP Vaccine
Reporting group description:	
Participants received one intramuscular (IM) injection of 0.5 mililiter (mL) of 30 µg/ strain of the Quadrivalent VLP Influenza Vaccine on Day 0.	
Reporting group title	Placebo
Reporting group description:	
Participants received one IM injection of 0.5 mL of placebo on Day 0.	

Reporting group values	Quadrivalent VLP Vaccine	Placebo	Total
Number of subjects	5077	5083	10160
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5077	5083	10160
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	3059	3042	6101
Male	2018	2041	4059
Ethnicity (NIH/ OMB) Units: Subjects			
Hispanic or Latino	296	326	622
Not Hispanic or Latino	4779	4751	9530
Unknown or Not Reported	2	6	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	20	18	38
Asian	1195	1187	2382
Native Hawaiian or Other Pacific Islander	7	6	13
Black or African American	646	623	1269
White	3178	3220	6398
More than one race	23	23	46
Unknown or Not Reported	8	6	14

End points

End points reporting groups

Reporting group title	Quadrivalent VLP Vaccine
Reporting group description:	
Participants received one intramuscular (IM) injection of 0.5 mililiter (mL) of 30 µg/ strain of the Quadrivalent VLP Influenza Vaccine on Day 0.	
Reporting group title	Placebo
Reporting group description:	
Participants received one IM injection of 0.5 mL of placebo on Day 0.	

Primary: Number of Occurrences of Protocol-Defined Respiratory Illness Caused by Vaccine-Matched Influenza Strains

End point title	Number of Occurrences of Protocol-Defined Respiratory Illness Caused by Vaccine-Matched Influenza Strains

End point description:

Occurrences of protocol-defined respiratory illness caused by vaccine-matched influenza strains were assessed. The vaccine-matched strains included: H1N1 (A/Michigan/45/2015); H3N2 (A/Hong Kong/4801/2014); B/Brisbane (B/ Brisbane/60/2008); and B/Phuket (B/Phuket/3073/2013A). 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. Occurrences of all matched 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 ~8 months	

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4814	4812		
Units: number of cases	110	169		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Vaccine Efficacy (VE) of VLP vaccine versus placebo = (1 - attack rate in vaccinated participants [ARV]/attack rate in unvaccinated participants [ARU]) x 100%. The VE success criterion is defined as a >40% lower limit of the two-sided 95% confidence interval (CI).	
Comparison groups	Quadrivalent VLP Vaccine v Placebo

Number of subjects included in analysis	9626
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine Efficacy
Point estimate	34.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.6
upper limit	48.6

Secondary: Number of Occurrences of Protocol-Defined Respiratory Illness Cases Caused by Any Laboratory Confirmed Influenza Strain

End point title	Number of Occurrences of Protocol-Defined Respiratory Illness Cases Caused by Any Laboratory Confirmed Influenza Strain

End point description:

Occurrences of protocol-defined respiratory illness due to laboratory-confirmed influenza strain (matched, mismatched, and un-typed) were assessed. 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. PP set.

End point type	Secondary

End point timeframe:

Day 14 (post-vaccination) up to ~8 months

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4814	4812		
Units: number of cases	213	347		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

VE of VLP vaccine versus placebo = (1 - ARV/ARU) x 100%. The VE success criterion is defined as a >40% lower limit of the two-sided 95% CI.

Comparison groups	Quadrivalent VLP Vaccine v Placebo
Number of subjects included in analysis	9626
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine Efficacy
Point estimate	38.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	27.6
upper limit	48

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

End point description:

Occurrences of protocol-defined ILI due to laboratory-confirmed influenza caused by influenza viral types/subtypes that are matched (and/or antigenically similar) to the strains covered in the vaccine formulation were assessed. A participant is 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 (degree Farenheit), chills, tiredness, headache or myalgia. PP set.

End point type	Secondary

End point timeframe:

Day 14 (post-vaccination) up to ~8 months

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4814	4812		
Units: number of cases	98	148		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

VE of VLP vaccine versus placebo = (1 - ARV/ARU) x 100%.
The VE success criterion is defined as a >40% lower limit of the two-sided 95% CI.

Comparison groups	Quadrivalent VLP Vaccine v Placebo
Number of subjects included in analysis	9626
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine Efficacy
Point estimate	33.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.9
upper limit	48.5

Secondary: Number of Occurrences of Laboratory-Confirmed ILI Caused by Any Influenza Strain

End point title	Number of Occurrences of Laboratory-Confirmed ILI Caused by Any Influenza Strain

End point description:

Occurrences of laboratory-confirmed ILI caused by any influenza viral strains were assessed. A participant is 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. PP set.

End point type	Secondary

End point timeframe:

Day 14 (post-vaccination) up to ~8 months

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4814	4812		
Units: number of cases	178	285		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

VE of VLP vaccine versus placebo = (1 - ARV/ARU) x 100%.
The VE success criterion is defined as a > 40% lower limit of the two- sided 95% CI.

Comparison groups	Placebo v Quadrivalent VLP Vaccine
Number of subjects included in analysis	9626
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine Efficacy
Point estimate	37.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.1
upper limit	48

Secondary: Number of Occurrences of Protocol-Defined ILI Cases

End point title	Number of Occurrences of Protocol-Defined ILI Cases

End point description:

Occurrences of protocol-defined ILI cases (confirmed or not) were assessed. A participant is 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. PP set.

End point type	Secondary

End point timeframe:

Day 14 (post-vaccination) up to ~8 months

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4814	4812		
Units: number of cases	1576	1679		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

VE of VLP vaccine versus placebo = (1 - ARV/ARU) x 100%.
The VE success criterion is defined as a >40% lower limit of the two-sided 95% CI.

Comparison groups	Quadrivalent VLP Vaccine v Placebo
Number of subjects included in analysis	9626
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine Efficacy
Point estimate	6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	11.3

Secondary: Number of Participants With at Least One Immediate Complaint

End point title	Number of Participants With at Least One Immediate Complaint

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. The Safety Analysis Set (SAS) was defined as all participants who received either the Quadrivalent VLP Influenza Vaccine or the placebo.

End point type	Secondary

End point timeframe:

15 minutes post vaccination

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064	5072		
Units: participants	441	377		

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). Any solicited local or systemic immediate complaint was also included. SAS.

End point type	Secondary

End point timeframe:

Day 0 (post-vaccination) up to Day 7

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064	5072		
Units: participants	2776	1723		

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:

Participants monitored for solicited local reactions (erythema, swelling, and pain at injection site) and solicited systemic reactions (fever, headache, fatigue, muscle aches, joint aches, chills, a feeling of general discomfort, swelling in axilla and neck). Any solicited local or systemic immediate complaint also included. Intensity of solicited reactions: Mild (1)-easily tolerated and does not interfere with usual activity; moderate (2)-interferes with daily activity, but participant is still able to function; severe (3)-incapacitating and participant is unable to work or complete usual activity or potentially life threatening; (4)-likely to be life-threatening if not treated in timely manner, according to Food and Drug Administration (FDA) Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials. ≥ Severe events: severe and potentially life-threatening events. Any ≥severe solicited reactions reported.

End point type	Secondary

End point timeframe:

Day 0 (post-vaccination) up to Day 7

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064[1]	5072[2]		
Units: participants	75	85		

Notes:

[1] - SAS

[2] - SAS

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 Reactions

End point description:

Participants were monitored for 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 according to the FDA Toxicity Grading Scale: mild (1), moderate (2), severe (3) or potentially life threatening (4). The causal relationship with the study vaccine was assessed as "definitely not related" (clearly not related), "probably not related" (no medical evidence), "possibly related" (reasonable possibility of cause and effect), "probably related" (plausible biologic mechanism and temporal relationship) or "definitely related" (direct cause and effect relationship). The ≥ severe events included "severe" and "potentially life-threatening" and the related category included "possibly related", "probably related" and "definitely related".SAS

End point type	Secondary

End point timeframe:

Day 0 (post-vaccination) up to Day 7

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064	5072		
Units: participants	56	62		

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)

End point description:

Participants were monitored for unsolicited TEAEs (e.g., nasopharyngitis, upper respiratory tract infection, headache, and oropharyngeal pain). An adverse event (AE) or adverse experience was defined as any untoward medical occurrence in a participant or clinical investigation participant who was administered a pharmaceutical product, 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. An AE was considered treatment-emergent if it began on or after the date and time of Study Day 0 vaccination. SAS.

End point type	Secondary

End point timeframe:

Day 0 (post-vaccination) up to Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064	5072		
Units: participants	661	639		

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

End point description:

The intensity of the unsolicited TEAEs 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: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials. The ≥ Severe events included severe and potentially life-threatening events. AE and TEAEs are defined in the outcome measure :Number of Participants With Unsolicited Treatment-Emergent Adverse Events (TEAEs).SAS.

End point type	Secondary

End point timeframe:

Day 0 (post-vaccination) up to Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064	5072		
Units: participants	13	25		

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

End point description:

The intensity of the solicited local and systemic reactions was graded as: mild (1), moderate (2), severe (3) or potentially life threatening (4). The causal relationship with the study vaccine was assessed as "definitely not related" (clearly not related), "probably not related" (no medical evidence), "possibly related" (reasonable possibility of cause and effect), "probably related" (plausible biologic mechanism and temporal relationship) or "definitely related" (direct cause and effect relationship). The ≥ severe events included "severe" and "potentially life-threatening" and the related category included "possibly related", "probably related", and "definitely related." AE and TEAEs are defined in outcome measure: Number of Participants With Unsolicited Treatment-Emergent Adverse Events (TEAEs). SAS.

End point type	Secondary

End point timeframe:

Day 0 (post-vaccination) up to Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064	5072		
Units: participants	4	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With an Occurrence of Death

End point title	Number of Participants With an Occurrence of Death

End point description:

The number of participants in each treatment group with an occurrence of death was assessed. SAS.

End point type	Secondary

End point timeframe:

Day 0 up to ~8 months

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064	5072		
Units: participants	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With at Least One Serious TEAE

End point title	Number of Participants With at Least One Serious TEAE

End point description:

A serious adverse event (SAE) is an AE that results in death, is life threatening, results in a persistent or significant disability or incapacity, results in or prolongs an existing hospitalization, is a congenital anomaly or birth defect, or is another important medical event. An SAE was considered treatment-emergent if it was aggravated in severity or frequency following the administration of the study vaccine, up to and including the last visit of the study. AE is defined in outcome measure : 'Number of Participants With Unsolicited Treatment-Emergent Adverse Events (TEAEs)'. SAS.

End point type	Secondary

End point timeframe:

Day 0 up to ~8 months

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064	5072		
Units: participants	55	51		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With at Least One AE Leading to Withdrawal

End point title	Number of Participants With at Least One AE Leading to Withdrawal

End point description:

An AE or adverse experience was defined as any untoward medical occurrence in a participant or clinical investigation participant who was administered a pharmaceutical product, 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. The number of participants with at least one adverse event leading to withdrawal was assessed. SAS.

End point type	Secondary

End point timeframe:

Day 0 up to ~8 months

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064	5072		
Units: participants	0	5		

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)

End point description:

All NOCDs that may plausibly have an allergic, autoimmune or inflammatory component were assessed and reported. Plausibility should be interpreted broadly; the only clear exceptions are 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. SAS.

End point type	Secondary

End point timeframe:

Day 0 up to ~8 months

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5064	5072		
Units: participants	54	41		

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 Strain

End point title	Geometric Mean Titers (GMTs) of Hemagglutination Inhibition (HI) Antibody Response for Each Homologous and Heterologous Influenza Strain

End point description:

The GMTs in each treatment group were measured using a HI assay for the homologous strains: H1 A/ Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008, B/Phuket/3073/2013, and the heterologous strains: A/Brisbane/59/2007 (IVR-148) (HIN1), A/Uruguay/716/2007 (H3N2), B/Florida/4/2006, B/ Malaysia/2506/2004. Immunogenicity Per Protocol (IPP) Set consisted of a subset of participants who participated in the immunogenicity portion of the study, who had a Day 21 immunogenicity sample collection.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination), Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: titers				
geometric mean (confidence interval 95%)				
Homologous (H1N1): Day 0	24.2 (20.7 to 28.3)	30.0 (22.9 to 39.3)		
Homologous (H1N1): Day 21	84.8 (71.4 to 100.8)	27.8 (21.6 to 35.9)		
Homologous (H3N2): Day 0	26.2 (21.8 to 31.4)	29.0 (21.9 to 38.4)		
Homologous (H3N2): Day 21	144.9 (121.9 to 172.4)	28.0 (20.9 to 37.4)		
Homologous (B/Brisbane/60/2008): Day 0	12.8 (11.3 to 14.4)	12.9 (10.6 to 15.7)		
Homologous (B/Brisbane/60/2008): Day 21	28.1 (24.8 to 31.9)	12.1 (10.0 to 14.8)		
Homologous (B/Phuket/3073/2013): Day 0	28.8 (24.5 to 33.9)	28.1 (21.7 to 36.5)		
Homologous (B/Phuket/3073/2013): Day 21	87.8 (74.3 to 103.9)	26.4 (20.4 to 34.1)		
Heterologous (H1N1): Day 0	14.5 (12.7 to 16.6)	14.5 (12.0 to 17.5)		
Heterologous (H1N1): Day 21	16.4 (16.4 to 18.8)	14.4 (11.8 to 17.6)		
Heterologous (H3N2): Day 0	17.2 (14.7 to 20.2)	19.7 (15.4 to 25.3)		
Heterologous (H3N2): Day 21	44.1 (37.1 to 52.3)	17.7 (13.9 to 22.6)		
Heterologous (B/Florida/4/2006): Day 0	26.8 (22.8 to 31.6)	31.5 (24.2 to 41.1)		
Heterologous (B/Florida/4/2006): Day 21	65.3 (55.8 to 76.5)	26.0 (20.1 to 33.7)		
Heterologous (B/Malaysia/2506/2004): Day 0	11.5 (10.2 to 12.9)	10.7 (8.8 to 13.0)		
Heterologous (B/Malaysia/2506/2004): Day 21	24.6 (21.6 to 27.9)	10.6 (8.7 to 12.9)		

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

End point description:

Seroconversion rate: the percentage of participants in a given treatment group with either a ≥ 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 ≥ 40 on Day 21 was measured using an HI assay for the

homologous strains: H1 A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008, B/Phuket/3073/2013, and the heterologous strains: A/ Brisbane/59/2007 (IVR-148) (HIN1), A/Uruguay/716/2007 (H3N2), B/Florida/4/2006, B/Malaysia/2506/2004. IPP set.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) up to Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: percentage of participants				
number (confidence interval 95%)				
Homologous (HIN1)	37.1 (31.4 to 43.0)	0 (0 to 0)		
Homologous (H3N2)	46.4 (40.4 to 52.5)	0 (0 to 0)		
Homologous (B/Brisbane/60/2008)	17.6 (13.3 to 22.6)	0 (0 to 0)		
Homologous (B/Phuket/3073/2013)	31.7 (26.2 to 37.5)	0 (0 to 0)		
Heterologous (HIN1)	2.5 (1.0 to 5.1)	0 (0 to 0)		
Heterologous (H3N2)	23.0 (18.2 to 28.4)	0 (0 to 0)		
Heterologous (B/Florida/4/2006)	27.0 (21.9 to 32.6)	0 (0 to 0)		
Heterologous (B/Malaysia/2506/2004)	18.3 (14.0 to 23.4)	0 (0 to 0)		

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

End point description:

Seroprotection rate: the percentage of participants in a given treatment group attaining a reciprocal HI titer of ≥ 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 the homologous strains: H1 A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008, B/Phuket/3073/2013, and the heterologous strains: A/Brisbane/59/2007 (IVR-148) (HIN1), A/ Uruguay/716/2007 (H3N2), B/Florida/4/2006, B/Malaysia/2506/2004. IPP set.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) up to Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: percentage of participants				
number (confidence interval 95%)				
Homologous (HIN1): Day 0	40.6 (34.8 to 46.7)	47.4 (37.2 to 57.8)		
Homologous (HIN1): Day 21	74.8 (69.3 to 79.8)	39.2 (29.4 to 49.6)		
Homologous (H3N2): Day 0	46.4 (40.4 to 52.5)	46.4 (36.2 to 56.8)		
Homologous (H3N2): Day 21	85.3 (80.5 to 89.2)	48.5 (38.2 to 58.8)		
Homologous (B/Brisbane/60/2008): Day 0	19.4 (14.9 to 24.6)	20.6 (13.1 to 30.0)		
Homologous (B/Brisbane/60/2008: Day 21	41.0 (35.2 to 47.0)	15.5 (8.9 to 24.2)		
Homologous (B/Phuket/3073/2013): Day 0	47.5 (41.5 to 53.5)	46.4 (36.2 to 56.8)		
Homologous (B/Phuket/3073/2013): Day 21	76.3 (70.8 to 81.1)	43.3 (33.3 to 53.7)		
Heterologous (HIN1): Day 0	23.4 (18.5 to 28.8)	16.5 (9.7 to 25.4)		
Heterologous (HIN1): Day 21	27.0 (21.9 to 32.6)	16.5 (9.7 to 25.4)		
Heterologous (H3N2): Day 0	31.3 (25.9 to 37.1)	34.0 (24.7 to 44.3)		
Heterologous (H3N2): Day 21	58.6 (52.6 to 64.5)	29.9 (21.0 to 40.0)		
Heterologous (B/Florida/4/2006): Day 0	46.8 (40.8 to 52.8)	48.5 (38.2 to 58.8)		
Heterologous (B/Florida/4/2006): Day 21	70.9 (65.1 to 76.1)	46.4 (36.2 to 56.8)		
Heterologous (B/Malaysia/2506/2004): Day 0	20.1 (15.6 to 25.3)	15.5 (8.9 to 24.2)		
Heterologous (B/Malaysia/2506/2004): Day 21	43.2 (37.3 to 49.2)	13.4 (7.3 to 21.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Ratio (GMFR) of HI Antibody Response for Each Homologous and Heterologous Strain

End point title	Geometric Mean Fold Ratio (GMFR) of HI Antibody Response for Each Homologous and Heterologous Strain

End point description:

GMFR, the geometric mean of the ratio of GMTs (Day 21/Day 0) in each treatment group was measured using an HI assay for the homologous strains: H1 A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), B/ Brisbane/60/2008, B/Phuket/3073/2013, and the heterologous strains: A/Brisbane/59/2007 (IVR-148) (HIN1), A/ Uruguay/716/2007 (H3N2), B/Florida/4/2006, B/Malaysia/2506/2004. IPP Set.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination), Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: ratio				
geometric mean (confidence interval 95%)				
Homologous (HIN1)	3.4 (3.0 to 3.9)	1.0 (0.8 to 1.2)		
Homologous (H3N2)	5.5 (4.7 to 6.3)	1.0 (0.8 to 1.3)		
Homologous (B/Brisbane/60/2008)	2.2 (2.0 to 2.4)	0.9 (0.8 to 1.1)		
Homologous (B/Phuket/3073/2013)	3.1 (2.7 to 3.4)	0.9 (0.8 to 1.1)		
Heterologous (HIN1)	1.1 (1.1 to 1.2)	1.0 (0.9 to 1.1)		
Heterologous (H3N2)	2.5 (2.3 to 2.9)	0.9 (0.8 to 1.1)		
Heterologous (B/Florida/4/2006)	2.4 (2.2 to 2.7)	0.9 (0.7 to 1.0)		
Heterologous (B/Malaysia/2506/2004)	2.2 (2.0 to 2.4)	1.0 (0.8 to 1.1)		

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

End point description:

The GMTs in each treatment group were measured using an MN assay for homologous strains: H1 A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008, B/Phuket/3073/2013. IPP Set.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination), Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: titers				
geometric mean (confidence interval 95%)				
Homologous (HIN1): Day 0	88.1 (76.7 to 101.1)	112.3 (91.1 to 138.6)		
Homologous (HIN1): Day 21	366.1 (316.1 to 424.1)	135.7 (110.4 to 166.9)		
Homologous (H3N2): Day 0	46.7 (41.9 to 52.1)	62.1 (53.1 to 72.6)		

Homologous (H3N2): Day 21	120.3 (108.9 to 132.9)	67.2 (57.0 to 79.1)		
Homologous (B/Brisbane/60/2008): Day 0	15.2 (13.8 to 16.7)	14.9 (12.9 to 17.3)		
Homologous (B/Brisbane/60/2008): Day 21	38.2 (34.3 to 42.7)	16.0 (13.7 to 18.6)		
Homologous (B/Phuket/3073/2013): Day 0	18.2 (16.3 to 20.4)	18.9 (16.0 to 22.3)		
Homologous (B/Phuket/3073/2013): Day 21	52.0 (46.1 to 58.6)	21.3 (18.0 to 25.2)		

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

End point description:

Seroconversion rate: the percentage of participants in a given treatment group with either a ≥ 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 ≥ 28.3 at Day 21 post-vaccination were measured using an MN assay for homologous strains: H1 A/ Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008, B/Phuket/3073/2013. IPP set.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) up to Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: percentage of participants				
number (confidence interval 95%)				
Homologous (HIN1)	41.7 (35.9 to 47.8)	2.1 (0.3 to 7.3)		
Homologous (H3N2)	28.1 (22.9 to 33.7)	0 (0 to 0)		
Homologous (B/Brisbane/60/2008)	30.6 (25.2 to 36.4)	0 (0 to 0)		
Homologous (B/Phuket/3073/2013)	31.3 (25.9 to 37.1)	1.0 (0.0 to 5.6)		

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 in each treatment group using an MN assay for the homologous strains: H1 A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), B/ Brisbane/60/2008, and B/Phuket/3073/2013. IPP set.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination), Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: ratio				
geometric mean (confidence interval 95%)				
Homologous (HIN1)	4.0 (3.6 to 4.6)	1.3 (1.1 to 1.6)		
Homologous (H3N2)	2.5 (2.2 to 2.7)	1.2 (1.1 to 1.5)		
Homologous (B/Brisbane/60/2008)	2.5 (2.3 to 2.8)	1.1 (0.9 to 1.2)		
Homologous (B/Phuket/3073/2013)	2.8 (2.6 to 3.1)	1.1 (1.0 to 1.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Area (GMA) of Single Radial Hemolysis (SRH) Antibody Response for Each Homologous Strain

End point title	Geometric Mean Area (GMA) of Single Radial Hemolysis (SRH) Antibody Response for Each Homologous Strain

End point description:

The GMA in each treatment group were measured using an SRH assay for homologous strains: H1 A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008, B/Phuket/3073/2013. The GMA calculations were performed by taking the anti-log of the mean of the log titer transformations. IPP set

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination), Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: mm^2				
geometric mean (confidence interval 95%)				
Homologous (HIN1): Day 0	10.3 (8.7 to 12.1)	15.4 (12.0 to 19.8)		

Homologous (HIN1): Day 21	31.4 (27.6 to 35.7)	20.9 (16.4 to 26.6)		
Homologous (H3N2): Day 0	15.6 (12.9 to 18.8)	19.3 (14.2 to 26.1)		
Homologous (H3N2): Day 21	56.0 (50.2 to 62.5)	28.4 (21.2 to 38.1)		
Homologous (B/Brisbane/60/2008): Day 0	8.2 (6.9 to 9.9)	6.8 (5.0 to 9.3)		
Homologous (B/Brisbane/60/2008): Day 21	31.9 (27.4 to 37.1)	9.3 (6.7 to 12.9)		
Homologous (B/Phuket/3073/2013): Day 0	11.4 (9.5 to 13.7)	11.7 (8.8 to 15.7)		
Homologous (B/Phuket/3073/2013): Day 21	36.7 (31.9 to 42.1)	15.5 (11.5 to 20.8)		

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

End point description:

Seroconversion rate: the percentage of participants in a given treatment group showing at least 50 % increase in GMA between Days 0 and 21 were measured using a SRH assay for homologous strains: H1 A/Michigan/45/2015 (H1N1), A/ Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008, B/Phuket/3073/2013. IPP set.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) up to Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: Percentage of Participants				
number (confidence interval 95%)				
Homologous (HIN1)	53.6 (47.5 to 59.6)	14.4 (8.1 to 23.0)		
Homologous (H3N2)	48.2 (42.2 to 54.2)	14.4 (8.1 to 23.0)		
Homologous (B/Brisbane/60/2008)	45.7 (39.7 to 51.7)	9.3 (4.3 to 16.9)		
Homologous (B/Phuket/3073/2013)	47.1 (41.1 to 53.2)	12.4 (6.6 to 20.6)		

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:

Seroprotection rate: the percentage of participants in a given treatment group attaining an area ≥ 25 mm^2 following vaccination (Day 21) were measured using an SRH assay for homologous strains: H1 A/Michigan/45/2015 (H1N1), A/ Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008, B/Phuket/3073/2013. IPP set.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) up to Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: Percentage of Participants				
number (confidence interval 95%)				
Homologous (HIN1): Day 0	36.3 (30.7 to 42.3)	42.3 (32.3 to 52.7)		
Homologous (HIN1): Day 21	75.9 (70.4 to 80.8)	57.7 (47.3 to 67.7)		
Homologous (H3N2): Day 0	54.7 (48.6 to 60.6)	57.7 (47.3 to 67.7)		
Homologous (H3N2): Day 21	92.1 (88.3 to 95.0)	74.2 (64.3 to 82.6)		
Homologous (B/Brisbane/60/2008): Day 0	40.3 (34.5 to 46.3)	37.1 (27.5 to 47.5)		
Homologous (B/Brisbane/60/2008): Day 21	81.3 (76.2 to 85.7)	45.4 (35.2 to 55.8)		
Homologous (B/Phuket/3073/2013): Day 0	47.5 (41.5 to 53.5)	44.3 (34.2 to 54.8)		
Homologous (B/Phuket/3073/2013): Day 21	81.7 (76.6 to 86.0)	54.6 (44.2 to 64.8)		

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 in each treatment group using an SRH assay for the homologous strains: H1 A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008, and B/Phuket/3073/2013.IPP set.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination), Day 21

End point values	Quadrivalent VLP Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	97		
Units: Ratio				
geometric mean (confidence interval 95%)				
Homologous (HIN1)	2.9 (2.6 to 3.2)	1.6 (1.3 to 1.9)		
Homologous (H3N2)	3.5 (3.1 to 3.9)	1.6 (1.4 to 2.0)		
Homologous (B/Brisbane/60/2008)	4.0 (3.5 to 4.5)	1.3 (1.0 to 1.6)		
Homologous (B/Phuket/3073/2013)	3.2 (2.9 to 3.6)	1.3 (1.1 to 1.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 0 (post-vaccination) up to ~8 months	
Adverse event reporting additional description:	
SAS. The unsolicited serious adverse events (SAEs), unsolicited non-serious adverse events (NSAEs), and all deaths were reported.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Quadrivalent VLP Vaccine
Reporting group description:	
Participants received one IM injection of 0.5 mL of 30 µg/strain of the Quadrivalent VLP Influenza Vaccine or placebo on Day 0.	
Reporting group title	Placebo
Reporting group description:	
Participants received one IM injection of 0.5 mL of placebo on Day 0.	

Serious adverse events	Quadrivalent VLP Vaccine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	55 / 5064 (1.09%)	51 / 5072 (1.01%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer metastatic			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal stromal cancer			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant pleural effusion			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral venous disease			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pre-eclampsia			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature delivery			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (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	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication associated with device			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (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 / 5064 (0.00%)	1 / 5072 (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			
Dyspnoea			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Borderline personality disorder			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Drug abuse			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood potassium decreased			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (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			
Abdominal wound dehiscence			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Comminuted fracture			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (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	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin abrasion			

subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Snake bite			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extrasystoles			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoesthesia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischemic attack			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Haemorrhagic anaemia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Meniere’s disease			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Colitis			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (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	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus			

subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
End stage renal disease			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stag horn calculus			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (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	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal infection			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 5064 (0.04%)	2 / 5072 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelitis			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis streptococcal			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 5064 (0.06%)	3 / 5072 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Quadrivalent VLP Vaccine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	930 / 5064 (18.36%)	918 / 5072 (18.10%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Large intestine benign neoplasm			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Uterine leiomyoma			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Flushing			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Haematoma			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Hot flush			

subjects affected / exposed	3 / 5064 (0.06%)	1 / 5072 (0.02%)	
occurrences (all)	3	1	
Hypertension			
subjects affected / exposed	18 / 5064 (0.36%)	16 / 5072 (0.32%)	
occurrences (all)	18	16	
Hypertensive crisis			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Hypotension			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Lymphoedema			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Peripheral coldness			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Peripheral venous disease			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Thrombophlebitis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Vasculitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	82 / 5064 (1.62%)	87 / 5072 (1.72%)	
occurrences (all)	102	122	
Asthenia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Axillary pain			

subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Chest discomfort			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	2 / 5064 (0.04%)	5 / 5072 (0.10%)	
occurrences (all)	2	5	
Chills			
subjects affected / exposed	19 / 5064 (0.38%)	13 / 5072 (0.26%)	
occurrences (all)	19	13	
Cyst			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Discomfort			
subjects affected / exposed	2 / 5064 (0.04%)	2 / 5072 (0.04%)	
occurrences (all)	2	2	
Drug withdrawal syndrome			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Facial pain			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	28 / 5064 (0.55%)	29 / 5072 (0.57%)	
occurrences (all)	32	29	
Feeling hot			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Hangover			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Inflammation			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Injection site bruising			

subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Injection site erythema			
subjects affected / exposed	3 / 5064 (0.06%)	2 / 5072 (0.04%)	
occurrences (all)	3	2	
Injection site haematoma			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Injection site hypersensitivity			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Injection site hypoaesthesia			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Injection site inflammation			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Injection site oedema			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Injection site pain			
subjects affected / exposed	29 / 5064 (0.57%)	8 / 5072 (0.16%)	
occurrences (all)	29	8	
Injection site pruritus			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Injection site reaction			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Injection site swelling			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Injection site warmth			
subjects affected / exposed	3 / 5064 (0.06%)	0 / 5072 (0.00%)	
occurrences (all)	3	0	
Injury associated with device			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	5 / 5064 (0.10%)	5 / 5072 (0.10%)	
occurrences (all)	5	5	
Oedema peripheral			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Pain			
subjects affected / exposed	4 / 5064 (0.08%)	3 / 5072 (0.06%)	
occurrences (all)	4	3	
Peripheral swelling			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	11 / 5064 (0.22%)	13 / 5072 (0.26%)	
occurrences (all)	11	14	
Swelling			
subjects affected / exposed	3 / 5064 (0.06%)	7 / 5072 (0.14%)	
occurrences (all)	3	7	
Vaccination site haematoma			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Immune system disorders			
Allergy to animal			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Allergy to arthropod bite			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Allergy to arthropod sting			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Drug hypersensitivity			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	

Food allergy			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Hypersensitivity			
subjects affected / exposed	2 / 5064 (0.04%)	3 / 5072 (0.06%)	
occurrences (all)	2	3	
Seasonal allergy			
subjects affected / exposed	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences (all)	1	2	
Social circumstances			
Sexual abuse			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Bartholin's cyst			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Dysmenorrhoea			
subjects affected / exposed	3 / 5064 (0.06%)	4 / 5072 (0.08%)	
occurrences (all)	3	4	
Genital rash			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Menopausal symptoms			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Menorrhagia			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	2	
Metrorrhagia			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Nipple pain			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Ovarian cyst			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Prostatitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Testicular torsion			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Vaginal haemorrhage			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Allergic cough			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Allergic sinusitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Asthma			
subjects affected / exposed	3 / 5064 (0.06%)	4 / 5072 (0.08%)	
occurrences (all)	3	4	
Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 5064 (0.06%)	2 / 5072 (0.04%)	
occurrences (all)	3	2	
Cough			
subjects affected / exposed	39 / 5064 (0.77%)	41 / 5072 (0.81%)	
occurrences (all)	39	43	
Dry throat			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Dysphonia			

subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	8 / 5064 (0.16%)	4 / 5072 (0.08%)	
occurrences (all)	8	4	
Dyspnoea exertional			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	4 / 5064 (0.08%)	4 / 5072 (0.08%)	
occurrences (all)	4	6	
Increased upper airway secretion			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	49 / 5064 (0.97%)	28 / 5072 (0.55%)	
occurrences (all)	51	29	
Nasal discomfort			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Nasal pruritus			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Nasal septum deviation			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Organising pneumonia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal discomfort			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Oropharyngeal pain			
subjects affected / exposed	54 / 5064 (1.07%)	57 / 5072 (1.12%)	
occurrences (all)	56	61	
Painful respiration			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Paranasal sinus discomfort			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Pharyngeal erythema			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Pharyngeal paraesthesia			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Pharyngeal ulceration			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Pleurisy			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	9 / 5064 (0.18%)	7 / 5072 (0.14%)	
occurrences (all)	10	7	
Rales			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Respiratory disorder			
subjects affected / exposed	24 / 5064 (0.47%)	28 / 5072 (0.55%)	
occurrences (all)	25	28	
Respiratory distress			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Respiratory symptom			
subjects affected / exposed	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences (all)	1	2	
Respiratory tract congestion			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Rhinitis allergic			

subjects affected / exposed	10 / 5064 (0.20%)	5 / 5072 (0.10%)	
occurrences (all)	10	5	
Rhinorrhoea			
subjects affected / exposed	40 / 5064 (0.79%)	39 / 5072 (0.77%)	
occurrences (all)	42	40	
Sinus congestion			
subjects affected / exposed	1 / 5064 (0.02%)	4 / 5072 (0.08%)	
occurrences (all)	1	4	
Sinus pain			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Sneezing			
subjects affected / exposed	26 / 5064 (0.51%)	18 / 5072 (0.35%)	
occurrences (all)	27	18	
Sputum discoloured			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Sputum increased			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Throat irritation			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Tonsillar disorder			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract congestion			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Wheezing			
subjects affected / exposed	2 / 5064 (0.04%)	4 / 5072 (0.08%)	
occurrences (all)	2	4	
Psychiatric disorders			
Affect lability			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	

Anxiety			
subjects affected / exposed	3 / 5064 (0.06%)	7 / 5072 (0.14%)	
occurrences (all)	3	7	
Attention deficit/hyperactivity disorder			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Bipolar disorder			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Depression			
subjects affected / exposed	3 / 5064 (0.06%)	5 / 5072 (0.10%)	
occurrences (all)	3	5	
Insomnia			
subjects affected / exposed	8 / 5064 (0.16%)	5 / 5072 (0.10%)	
occurrences (all)	8	5	
Major depression			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Panic attack			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Investigations			
Blood cholesterol increased			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Blood iron decreased			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Blood magnesium decreased			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Blood oestrogen decreased			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Blood pressure decreased			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Blood pressure diastolic increased			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Blood pressure increased			
subjects affected / exposed	5 / 5064 (0.10%)	0 / 5072 (0.00%)	
occurrences (all)	5	0	
Body temperature increased			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Cardiac murmur			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Influenza B virus test positive			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Progesterone decreased			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Respiratory rate increased			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Vitamin B12 decreased			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Vitamin D decreased			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 5064 (0.02%)	4 / 5072 (0.08%)	
occurrences (all)	1	4	
Animal scratch			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Arthropod bite			
subjects affected / exposed	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences (all)	1	2	
Arthropod sting			
subjects affected / exposed	3 / 5064 (0.06%)	1 / 5072 (0.02%)	
occurrences (all)	3	1	
Back injury			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Burns second degree			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Concussion			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	5 / 5064 (0.10%)	3 / 5072 (0.06%)	
occurrences (all)	7	3	
Craniocerebral injury			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Eye injury			

subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Foot fracture			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Foreign body in eye			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Hand fracture			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Jaw fracture			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Joint dislocation			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Laceration			
subjects affected / exposed	3 / 5064 (0.06%)	1 / 5072 (0.02%)	
occurrences (all)	3	1	
Ligament sprain			
subjects affected / exposed	4 / 5064 (0.08%)	7 / 5072 (0.14%)	
occurrences (all)	4	7	
Limb injury			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Mucosal excoriation			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Multiple injuries			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Muscle strain			

subjects affected / exposed	5 / 5064 (0.10%)	5 / 5072 (0.10%)	
occurrences (all)	6	5	
Periorbital haematoma			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Post procedural swelling			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Post-traumatic pain			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Postoperative fever			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Procedural nausea			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	5 / 5064 (0.10%)	10 / 5072 (0.20%)	
occurrences (all)	5	10	
Radius fracture			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Rib fracture			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Road traffic accident			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Skin abrasion			
subjects affected / exposed	2 / 5064 (0.04%)	2 / 5072 (0.04%)	
occurrences (all)	2	2	
Soft tissue injury			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Superficial injury of eye			

subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Thermal burn			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Tooth fracture			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Wrist fracture			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Wound			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	3	
Atrial fibrillation			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Cardiac failure			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Cardiac flutter			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Myocardial ischaemia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	2 / 5064 (0.04%)	2 / 5072 (0.04%)	
occurrences (all)	2	2	
Nervous system disorders			
Amnesia			

subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Aphonia			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Burning sensation			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Carotid artery stenosis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Dizziness			
subjects affected / exposed	11 / 5064 (0.22%)	9 / 5072 (0.18%)	
occurrences (all)	11	9	
Facial paralysis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	113 / 5064 (2.23%)	111 / 5072 (2.19%)	
occurrences (all)	132	127	
Hyperaesthesia			
subjects affected / exposed	3 / 5064 (0.06%)	0 / 5072 (0.00%)	
occurrences (all)	3	0	
Hypoaesthesia			
subjects affected / exposed	2 / 5064 (0.04%)	2 / 5072 (0.04%)	
occurrences (all)	2	2	
Intercostal neuralgia			
subjects affected / exposed	2 / 5064 (0.04%)	2 / 5072 (0.04%)	
occurrences (all)	2	2	
Loss of consciousness			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Migraine			

subjects affected / exposed	5 / 5064 (0.10%)	6 / 5072 (0.12%)	
occurrences (all)	5	6	
Muscle contractions involuntary			
subjects affected / exposed	1 / 5064 (0.02%)	3 / 5072 (0.06%)	
occurrences (all)	1	3	
Neuropathy peripheral			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Paraesthesia			
subjects affected / exposed	3 / 5064 (0.06%)	1 / 5072 (0.02%)	
occurrences (all)	3	1	
Presyncope			
subjects affected / exposed	3 / 5064 (0.06%)	1 / 5072 (0.02%)	
occurrences (all)	3	1	
Retinal migraine			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	1 / 5064 (0.02%)	4 / 5072 (0.08%)	
occurrences (all)	1	4	
Sensory loss			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Tension headache			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Lymph node pain			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	

Lymphadenitis			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Lymphadenopathy			
subjects affected / exposed	2 / 5064 (0.04%)	5 / 5072 (0.10%)	
occurrences (all)	2	5	
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Ear pain			
subjects affected / exposed	4 / 5064 (0.08%)	5 / 5072 (0.10%)	
occurrences (all)	4	8	
Excessive cerumen production			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
External ear inflammation			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Hypoacusis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Tympanic membrane perforation			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Vertigo			
subjects affected / exposed	4 / 5064 (0.08%)	4 / 5072 (0.08%)	
occurrences (all)	4	4	
Vertigo positional			
subjects affected / exposed	2 / 5064 (0.04%)	3 / 5072 (0.06%)	
occurrences (all)	2	3	
Eye disorders			

Cataract			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Conjunctival haemorrhage			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Corneal opacity			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Eye discharge			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Eye irritation			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Eye paraesthesia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Eye pruritus			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Eye swelling			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Glaucoma			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Keratitis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	0 / 5064 (0.00%)	3 / 5072 (0.06%)	
occurrences (all)	0	3	

Ocular hyperaemia			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Photokeratitis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Retinal detachment			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Visual impairment			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	10 / 5064 (0.20%)	4 / 5072 (0.08%)	
occurrences (all)	10	4	
Abdominal pain upper			
subjects affected / exposed	3 / 5064 (0.06%)	2 / 5072 (0.04%)	
occurrences (all)	3	2	
Acid peptic disease			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Barrett's oesophagus			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Coeliac disease			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Colitis			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 5064 (0.02%)	3 / 5072 (0.06%)	
occurrences (all)	1	3	
Dental caries			
subjects affected / exposed	3 / 5064 (0.06%)	1 / 5072 (0.02%)	
occurrences (all)	3	1	
Diarrhoea			
subjects affected / exposed	14 / 5064 (0.28%)	20 / 5072 (0.39%)	
occurrences (all)	14	22	
Dyspepsia			
subjects affected / exposed	1 / 5064 (0.02%)	4 / 5072 (0.08%)	
occurrences (all)	1	4	
Enteritis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	3 / 5064 (0.06%)	0 / 5072 (0.00%)	
occurrences (all)	3	0	
Food poisoning			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Gastric ulcer			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Gastric ulcer perforation			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Gastrointestinal disorder			
subjects affected / exposed	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences (all)	1	2	
Gastrointestinal inflammation			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 5064 (0.06%)	5 / 5072 (0.10%)	
occurrences (all)	3	5	
Gingival swelling			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Glossodynia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Hypoaesthesia oral			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Inguinal hernia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	21 / 5064 (0.41%)	10 / 5072 (0.20%)	
occurrences (all)	21	10	
Noninfective gingivitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Odynophagia			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Paraesthesia oral			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Proctalgia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Rectal haemorrhage			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	0 / 5064 (0.00%)	3 / 5072 (0.06%)	
occurrences (all)	0	3	
Tooth impacted			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	5 / 5064 (0.10%)	4 / 5072 (0.08%)	
occurrences (all)	5	4	
Umbilical hernia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Uvulitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	13 / 5064 (0.26%)	9 / 5072 (0.18%)	
occurrences (all)	13	9	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			

subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Actinic keratosis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Cold urticaria			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Dermal cyst			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Dermatitis allergic			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Dry skin			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Eczema			
subjects affected / exposed	0 / 5064 (0.00%)	4 / 5072 (0.08%)	
occurrences (all)	0	4	
Erythema			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Guttate psoriasis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Hidradenitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	2 / 5064 (0.04%)	2 / 5072 (0.04%)	
occurrences (all)	2	2	
Ingrown hair			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Night sweats			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	2	
Pityriasis rosea			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	2 / 5064 (0.04%)	5 / 5072 (0.10%)	
occurrences (all)	2	5	
Pruritus generalised			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Psoriasis			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	6 / 5064 (0.12%)	6 / 5072 (0.12%)	
occurrences (all)	6	7	
Rash generalised			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Rash macular			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Rash pruritic			
subjects affected / exposed	1 / 5064 (0.02%)	4 / 5072 (0.08%)	
occurrences (all)	1	4	
Skin exfoliation			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Skin lesion			

subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Swelling face			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	3 / 5064 (0.06%)	4 / 5072 (0.08%)	
occurrences (all)	3	4	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Hypertonic bladder			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Nephrolithiasis			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Renal cyst			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Urinary retention			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Hypogonadism			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Hypothyroidism			
subjects affected / exposed	3 / 5064 (0.06%)	2 / 5072 (0.04%)	
occurrences (all)	3	2	
Thyroid cyst			

subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 5064 (0.34%)	17 / 5072 (0.34%)	
occurrences (all)	19	17	
Arthritis			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Back pain			
subjects affected / exposed	22 / 5064 (0.43%)	18 / 5072 (0.35%)	
occurrences (all)	23	18	
Bursa disorder			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Costochondritis			
subjects affected / exposed	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences (all)	1	2	
Fibromyalgia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Flank pain			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Gouty arthritis			
subjects affected / exposed	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences (all)	1	2	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Joint instability			

subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	2	
Limb mass			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Muscle disorder			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 5064 (0.02%)	3 / 5072 (0.06%)	
occurrences (all)	1	3	
Muscular weakness			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	3	
Musculoskeletal discomfort			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Musculoskeletal pain			
subjects affected / exposed	9 / 5064 (0.18%)	3 / 5072 (0.06%)	
occurrences (all)	9	3	
Musculoskeletal stiffness			
subjects affected / exposed	2 / 5064 (0.04%)	3 / 5072 (0.06%)	
occurrences (all)	2	3	
Myalgia			
subjects affected / exposed	28 / 5064 (0.55%)	28 / 5072 (0.55%)	
occurrences (all)	28	28	
Myalgia intercostal			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Myofascial pain syndrome			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Neck pain			

subjects affected / exposed	7 / 5064 (0.14%)	3 / 5072 (0.06%)	
occurrences (all)	7	3	
Osteoarthritis			
subjects affected / exposed	0 / 5064 (0.00%)	3 / 5072 (0.06%)	
occurrences (all)	0	3	
Osteoporosis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	13 / 5064 (0.26%)	6 / 5072 (0.12%)	
occurrences (all)	15	6	
Pain in jaw			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Periarthritis			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Plantar fasciitis			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Psoriatic arthropathy			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Rotator cuff syndrome			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Spinal osteoarthritis			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Spinal pain			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Synovial cyst			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Tendon disorder			

subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	3 / 5064 (0.06%)	0 / 5072 (0.00%)	
occurrences (all)	3	0	
Torticollis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	126 / 5064 (2.49%)	117 / 5072 (2.31%)	
occurrences (all)	139	126	
Abscess limb			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Abscess of eyelid			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Acarodermatitis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Acute sinusitis			
subjects affected / exposed	1 / 5064 (0.02%)	3 / 5072 (0.06%)	
occurrences (all)	1	3	
Atypical pneumonia			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Bacterial infection			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Bacterial vaginosis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Bacterial vulvovaginitis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	

Balanitis candida			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	13 / 5064 (0.26%)	25 / 5072 (0.49%)	
occurrences (all)	13	25	
Bullous impetigo			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Carbuncle			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Cellulitis			
subjects affected / exposed	4 / 5064 (0.08%)	1 / 5072 (0.02%)	
occurrences (all)	4	1	
Chronic sinusitis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Clostridium difficile infection			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	4 / 5064 (0.08%)	7 / 5072 (0.14%)	
occurrences (all)	4	7	
Conjunctivitis bacterial			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	6 / 5064 (0.12%)	2 / 5072 (0.04%)	
occurrences (all)	6	2	
Diarrhoea infectious			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Diverticulitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	

Ear infection			
subjects affected / exposed	3 / 5064 (0.06%)	4 / 5072 (0.08%)	
occurrences (all)	3	5	
Epididymitis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Eye infection			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Fungal skin infection			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Furuncle			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Gastroenteritis			
subjects affected / exposed	10 / 5064 (0.20%)	20 / 5072 (0.39%)	
occurrences (all)	10	21	
Gastroenteritis viral			
subjects affected / exposed	3 / 5064 (0.06%)	2 / 5072 (0.04%)	
occurrences (all)	3	2	
Gastrointestinal infection			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Gastrointestinal viral infection			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Gingivitis			
subjects affected / exposed	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences (all)	1	2	
Gonorrhoea			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	

Hepatitis infectious mononucleosis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Herpes simplex			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	2 / 5064 (0.04%)	2 / 5072 (0.04%)	
occurrences (all)	2	2	
Hordeolum			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Impetigo			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Infectious mononucleosis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	8 / 5064 (0.16%)	5 / 5072 (0.10%)	
occurrences (all)	8	5	
Kidney infection			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Labyrinthitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	
Localised infection			
subjects affected / exposed	1 / 5064 (0.02%)	3 / 5072 (0.06%)	
occurrences (all)	1	3	
Lower respiratory tract infection			
subjects affected / exposed	3 / 5064 (0.06%)	4 / 5072 (0.08%)	
occurrences (all)	4	4	

Mastitis			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Measles			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	56 / 5064 (1.11%)	55 / 5072 (1.08%)	
occurrences (all)	57	57	
Oral herpes			
subjects affected / exposed	6 / 5064 (0.12%)	2 / 5072 (0.04%)	
occurrences (all)	7	2	
Oral infection			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Osteomyelitis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Otitis externa			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Otitis media			
subjects affected / exposed	6 / 5064 (0.12%)	3 / 5072 (0.06%)	
occurrences (all)	6	3	
Paronychia			
subjects affected / exposed	3 / 5064 (0.06%)	0 / 5072 (0.00%)	
occurrences (all)	3	0	
Pelvic inflammatory disease			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Pericoronitis			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	

Periodontitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Peritonitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	10 / 5064 (0.20%)	11 / 5072 (0.22%)	
occurrences (all)	10	12	
Pharyngitis streptococcal			
subjects affected / exposed	11 / 5064 (0.22%)	7 / 5072 (0.14%)	
occurrences (all)	12	7	
Pharyngotonsillitis			
subjects affected / exposed	2 / 5064 (0.04%)	2 / 5072 (0.04%)	
occurrences (all)	2	2	
Pilonidal cyst			
subjects affected / exposed	1 / 5064 (0.02%)	1 / 5072 (0.02%)	
occurrences (all)	1	1	
Pneumonia			
subjects affected / exposed	8 / 5064 (0.16%)	11 / 5072 (0.22%)	
occurrences (all)	8	12	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Rash pustular			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	8 / 5064 (0.16%)	2 / 5072 (0.04%)	
occurrences (all)	8	2	
Respiratory tract infection viral			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	31 / 5064 (0.61%)	27 / 5072 (0.53%)	
occurrences (all)	38	32	

Sinusitis			
subjects affected / exposed	24 / 5064 (0.47%)	18 / 5072 (0.35%)	
occurrences (all)	26	18	
Skin candida			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Skin infection			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Staphylococcal infection			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Systemic viral infection			
subjects affected / exposed	1 / 5064 (0.02%)	3 / 5072 (0.06%)	
occurrences (all)	1	3	
Tonsillitis			
subjects affected / exposed	8 / 5064 (0.16%)	5 / 5072 (0.10%)	
occurrences (all)	8	5	
Tooth abscess			
subjects affected / exposed	0 / 5064 (0.00%)	7 / 5072 (0.14%)	
occurrences (all)	0	7	
Tooth infection			
subjects affected / exposed	4 / 5064 (0.08%)	3 / 5072 (0.06%)	
occurrences (all)	4	3	
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	12 / 5064 (0.24%)	12 / 5072 (0.24%)	
occurrences (all)	14	12	
Urosepsis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Vaginal infection			

subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Varicella zoster virus infection			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Viral infection			
subjects affected / exposed	1 / 5064 (0.02%)	2 / 5072 (0.04%)	
occurrences (all)	1	2	
Viral pharyngitis			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Viral sinusitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Viral tonsilitis			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 5064 (0.00%)	5 / 5072 (0.10%)	
occurrences (all)	0	5	
Vulvovaginal mycotic infection			
subjects affected / exposed	3 / 5064 (0.06%)	0 / 5072 (0.00%)	
occurrences (all)	3	0	
Wound infection			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 5064 (0.06%)	0 / 5072 (0.00%)	
occurrences (all)	3	0	
Dehydration			
subjects affected / exposed	0 / 5064 (0.00%)	1 / 5072 (0.02%)	
occurrences (all)	0	1	
Diabetes mellitus inadequate control			
subjects affected / exposed	2 / 5064 (0.04%)	0 / 5072 (0.00%)	
occurrences (all)	2	0	

Gout			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Hypercholesterolaemia			
subjects affected / exposed	2 / 5064 (0.04%)	3 / 5072 (0.06%)	
occurrences (all)	2	3	
Hyperlipidaemia			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Hyperuricaemia			
subjects affected / exposed	0 / 5064 (0.00%)	2 / 5072 (0.04%)	
occurrences (all)	0	2	
Hypoglycaemia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Malnutrition			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Obesity			
subjects affected / exposed	1 / 5064 (0.02%)	0 / 5072 (0.00%)	
occurrences (all)	1	0	
Type 2 diabetes mellitus			
subjects affected / exposed	3 / 5064 (0.06%)	3 / 5072 (0.06%)	
occurrences (all)	3	3	
Vitamin D deficiency			
subjects affected / exposed	2 / 5064 (0.04%)	1 / 5072 (0.02%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2017	Major changes in the conduct of the study are described as follows: • The inclusion criteria no. 7 (acceptable contraceptive methods) was generalized to support the use of different regional acceptable methods of contraception in a single protocol and details of these regional acceptable contraceptive methods were presented in a new appendix in the protocol. • Clarification regarding the needle length to use to administer the study treatments to subjects based on their BMI was included in the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33065035