Clinical trial results:
Randomized, Double-Blind, Active-Controlled Study in Adults to Assess the Safety and Immunogenicity of Abbott's Candidate Quadrivalent Influenza Vaccine and its Non-Inferiority to Trivalent Influenza Vaccine.

Summary

EudraCT number	2014-001042-24
Trial protocol	DE LV HU LT BE
Global end of trial date	06 January 2016

Results information

Result version number	v1 (current)
This version publication date	09 December 2016
First version publication date	09 December 2016

Trial information

Trial identification

Sponsor protocol code	INFQ3001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Abbott Biologicals B.V.
Sponsor organisation address	C.J. van Houtenlaan 36, Weesp, Netherlands, NL-1381 CP
Public contact	Global Clinical Director, Abbott Healthcare Products B.V., serge.vandewitte@abbott.com
Scientific contact	Global Clinical Director, Abbott Healthcare Products B.V., serge.vandewitte@abbott.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	07 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 January 2016
Global end of trial reached?	Yes
Global end of trial date	06 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate in subjects ≥ 18 years of age the non-inferiority of QIV with respect to post-vaccination geometric mean hemagglutinin inhibition (HI) antibody titers against the shared strains compared with the trivalent influenza vaccines (TIV) with either the B-strain of the Victoria (TIV(Vic)) or the B-strain of the Yamagata lineage (TIV(Yam)).

Protection of trial subjects:

This study has been conducted in accordance with the ICH Guidelines on Good Clinical Practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 May 2015
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	Belgium: 216
Country: Number of subjects enrolled	Germany: 478
Country: Number of subjects enrolled	Hungary: 518
Country: Number of subjects enrolled	Latvia: 429
Country: Number of subjects enrolled	Lithuania: 339
Worldwide total number of subjects	1980
EEA total number of subjects	1980

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)	1207

From 65 to 84 years	749
85 years and over	24

Subject disposition

Recruitment

Recruitment details:

Twenty study centres in five countries (Belgium, Germany, Hungary, Latvia, and Lithuania) screened and enrolled subjects. The first subject entered the study on 28 May 2015 and the last subject completed the last visit on 06 Jan 2016.

Pre-assignment

Screening details:

A total of 2,011 subjects provided informed consent and were screened for eligibility. Of these, 31 subjects failed screening and 1,980 subjects were randomly assigned to receive a study vaccine.

Period 1

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

Blinding implementation details:

All of the syringes were identical in appearance and packaged in the proper proportion to ensure that the desired dosages were used and that blinding was maintained.

Arms

Are arms mutually exclusive?	Yes
Arm title	Quadrivalent influenza vaccine

Arm description:

A single 0.5 mL dose of quadrivalent influenza subunit vaccine containing approximately 15 µg HA antigen per virus strain, given intramuscularly in the deltoid muscle of the upper arm.

Arm type	Experimental
Investigational medicinal product name	Quadrivalent Influenza Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of 0.5 mL of quadrivalent influenza vaccine administered by intramuscular injection on Day 1 (Visit 1).

Arm title	Trivalent influenza vaccine (Vic)

Arm description:

A single 0.5 mL dose of trivalent influenza subunit vaccine (Victoria) containing approximately 15 µg HA antigen per virus strain, given intramuscularly in the deltoid muscle of the upper arm.

Arm type	Active comparator
Investigational medicinal product name	Trivalent Influenza Vaccine (Vic)
Investigational medicinal product code	
Other name	Influvac
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of 0.5 mL of trivalent influenza vaccine (Vic) administered by intramuscular injection on Day 1 (Visit 1).

Arm title	Trivalent influenza vaccine (Yam)

Arm description:

A single 0.5 mL dose of trivalent influenza subunit vaccine (Yamagata) containing approximately 15 µg HA antigen per virus strain, given intramuscularly in the deltoid muscle of the upper arm.

Arm type	Active comparator
Investigational medicinal product name	Trivalent Influenza Vaccine (Yam)
Investigational medicinal product code	
Other name	Influvac
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of 0.5 mL of influenza vaccine (Yam) administered by intramuscular injection on Day 1 (Visit 1).

Number of subjects in period 1	Quadrivalent influenza vaccine	Trivalent influenza vaccine (Vic)	Trivalent influenza vaccine (Yam)
Started	1538	221	221
Completed	1530	220	219
Not completed	8	1	2
Consent withdrawn by subject	2	1	1
Administrative	1	-	-
Adverse event, non-fatal	3	-	-
Lost to follow-up	2	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	1980	1980	
Age categorical Units: Subjects			
Adults (18-64 years)	1207	1207	
From 65-84 years	749	749	
85 years and over	24	24	
Gender categorical Units: Subjects			
Male	859	859	
Female	1121	1121	

End points

End points reporting groups

Reporting group title	Quadrivalent influenza vaccine
Reporting group description:	
A single 0.5 mL dose of quadrivalent influenza subunit vaccine containing approximately 15 µg HA antigen per virus strain, given intramuscularly in the deltoid muscle of the upper arm.	
Reporting group title	Trivalent influenza vaccine (Vic)
Reporting group description:	
A single 0.5 mL dose of trivalent influenza subunit vaccine (Victoria) containing approximately 15 µg HA antigen per virus strain, given intramuscularly in the deltoid muscle of the upper arm.	
Reporting group title	Trivalent influenza vaccine (Yam)
Reporting group description:	
A single 0.5 mL dose of trivalent influenza subunit vaccine (Yamagata) containing approximately 15 µg HA antigen per virus strain, given intramuscularly in the deltoid muscle of the upper arm.	
Subject analysis set title	Primary Efficacy Analysis
Subject analysis set type	Per protocol
Subject analysis set description:	
The per-protocol (PP) sample was defined through blind data review and consisted of all subjects who were included in the Full Analysis subject sample and did not present any major protocol violations.	
Subject analysis set title	Secondary Efficacy Analysis
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis (FA) subject sample consisted of all subjects who were in the safety sample and had at least one post-vaccination efficacy observation.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety-subject sample consisted of all subjects who were in the all-subjects-vaccinated sample and had at least one post-vaccination safety observation. The safety data from the subjects vaccinated with a trivalent formulation were pooled.	

Primary: Postvaccination geometric HI antibody titers against A-H1N1 strain

End point title	Postvaccination geometric HI antibody titers against A-H1N1 strain
End point description:	
End point type	Primary
End point timeframe:	
Geometric means of the HI titers were measured on Day 22 (Visit 2) post-vaccination.	

End point values	Quadrivalent influenza vaccine	Trivalent influenza vaccine (Vic)	Trivalent influenza vaccine (Yam)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1528	217	219	
Units: titre				
geometric mean (standard deviation)	186.1 (± 4.2)	234.8 (± 3.9)	207.9 (± 4.3)	

Statistical analyses

Statistical analysis title	Non-inferiority analysis

Statistical analysis description:

95% Confidence Interval was obtained from an ANOVA model with vaccine, country and site as a covariate.

Comparison groups	Quadrivalent influenza vaccine v Trivalent influenza vaccine (Vic) v Trivalent influenza vaccine (Yam)
Number of subjects included in analysis	1964
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANOVA
Parameter estimate	Geometric mean ratio
Confidence interval	
level	95 %
sides	2-sided

Primary: Postvaccination geometric HI antibody titers against A-H3N2 strain

End point title	Postvaccination geometric HI antibody titers against A-H3N2 strain

End point description:

End point type	Primary

End point timeframe:

Geometric means of the HI titers were measured on Day 22 (Visit 2) post-vaccination.

End point values	Quadrivalent influenza vaccine	Trivalent influenza vaccine (Vic)	Trivalent influenza vaccine (Yam)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1528	217	219	
Units: titre				
geometric mean (standard deviation)	339.1 (± 3.5)	386.1 (± 3.6)	442.6 (± 3.8)	

Statistical analyses

Statistical analysis title	Non-inferiority analysis
Comparison groups	Quadrivalent influenza vaccine v Trivalent influenza vaccine (Vic) v Trivalent influenza vaccine (Yam)
Number of subjects included in analysis	1964
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANOVA
Parameter estimate	Geometric mean ratio
Confidence interval	
level	95 %
sides	2-sided

Primary: Postvaccination geometric HI antibody titers against B Victoria strain

End point title	Postvaccination geometric HI antibody titers against B Victoria strain

End point description:

End point type	Primary

End point timeframe:

Geometric means of the HI titers were measured on Day 22 (Visit 2) post-vaccination.

End point values	Quadrivalent influenza vaccine	Trivalent influenza vaccine (Vic)	Trivalent influenza vaccine (Yam)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1528	217	219	
Units: titre				
geometric mean (standard deviation)	152.9 (± 4.3)	142 (± 4.7)	64.2 (± 5.4)	

Statistical analyses

Statistical analysis title	Non-inferiority analysis

Statistical analysis description:

95% Confidence Interval was obtained from an ANOVA model with vaccine, country and site as a covariate.

Comparison groups	Quadrivalent influenza vaccine v Trivalent influenza vaccine (Vic) v Trivalent influenza vaccine (Yam)
Number of subjects included in analysis	1964
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANOVA
Parameter estimate	Geometric mean ratio

Confidence interval	
level	95 %
sides	2-sided

Primary: Postvaccination geometric HI antibody titers against B Yamagata strain

End point title	Postvaccination geometric HI antibody titers against B Yamagata strain

End point description:

End point type	Primary

End point timeframe:

Geometric means of the HI titers were measured on Day 22 (Visit 2) post-vaccination.

End point values	Quadrivalent influenza vaccine	Trivalent influenza vaccine (Vic)	Trivalent influenza vaccine (Yam)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1528	217	219	
Units: titre				
geometric mean (standard deviation)	102.1 (± 4.3)	47.5 (± 5)	86.1 (± 4.2)	

Statistical analyses

Statistical analysis title	Non-inferiority analysis

Statistical analysis description:

95% Confidence Interval was obtained from an ANOVA model with vaccine, country and site as a covariate.

Comparison groups	Quadrivalent influenza vaccine v Trivalent influenza vaccine (Vic) v Trivalent influenza vaccine (Yam)
Number of subjects included in analysis	1964
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANOVA
Confidence interval	
level	95 %
sides	2-sided

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events (AEs) have been reported separately for the period up to the Day 22 visit (all AEs) and between the Day 22 visit and Phone Contact 2 (Day 183) period (only new serious AEs and new chronic illnesses).

Adverse event reporting additional description:

The safety data from the subjects vaccinated with QIV or TIV were be done by age group. To assess safety and reactogenicity, the following assessments were made: solicited local and systemic reactions (reactogenicity, reported 7 days post vaccination), overall inconvenience, and unsolicited AEs. Data of the subjects vaccinated with TIV were pooled.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Quadrivalent influenza vaccine

Reporting group description:

A single 0.5 mL dose of quadrivalent influenza subunit vaccine containing approximately 15 µg HA antigen per virus strain, given intramuscularly in the deltoid muscle of the upper arm.

Reporting group title	Trivalent influenza vaccine

Reporting group description:

A single 0.5 mL dose of trivalent influenza subunit vaccine containing approximately 15 µg HA antigen per virus strain, given intramuscularly in the deltoid muscle of the upper arm.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: None of the non-serious adverse events met the threshold of up to 5% for reporting.

Serious adverse events	Quadrivalent influenza vaccine	Trivalent influenza vaccine	
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 1535 (3.00%)	14 / 441 (3.17%)	
number of deaths (all causes)	5	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma stage II			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			

subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (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 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism arterial			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	2 / 1535 (0.13%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Selective abortion			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous incomplete			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
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			
Device malfunction			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			

subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 1535 (0.07%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Cartilage injury			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			

subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 1535 (0.07%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 1535 (0.13%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			

subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	2 / 1535 (0.13%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			

subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraventricular haemorrhage			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine with aura			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculitis lumbosacral			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reversible ischaemic neurological deficit			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular encephalopathy			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			

subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancreatitis acute			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin and subcutaneous tissue disorders			
Hyperkeratosis			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (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 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 1535 (0.07%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amniotic cavity infection			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder abscess			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infectious colitis			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subacute endocarditis			
subjects affected / exposed	0 / 1535 (0.00%)	1 / 441 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 1535 (0.07%)	0 / 441 (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: 5 %

Non-serious adverse events	Quadrivalent influenza vaccine	Trivalent influenza vaccine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1535 (0.00%)	0 / 441 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 April 2015	Changes in conduct or management of the trial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported