



Clinical trial results: Immunogenicity and Safety of Quadrivalent Influenza Vaccine (VaxigripTetra™) in Pregnant Women

Summary

EudraCT number	2016-004763-40
Trial protocol	FI
Global end of trial date	14 June 2018

Results information

Result version number	v1 (current)
This version publication date	26 May 2019
First version publication date	26 May 2019

Trial information

Trial identification

Sponsor protocol code	GQM14
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1183-5650

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur
Sponsor organisation address	14 Espace Henry Vallée, Lyon, France, 69007
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.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	23 November 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	14 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity:

To describe the immune response of VaxigripTetra and Vaxigrip, 21 days after vaccination in pregnant women.

Safety:

To describe the safety profile of one dose of VaxigripTetra or Vaxigrip, 21 days after vaccination in pregnant women.

Protection of trial subjects:

Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 September 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	Finland: 346
Worldwide total number of subjects	346
EEA total number of subjects	346

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)	346
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 10 centers in Finland from 15 September 2017 to 26 January 2018.

Pre-assignment

Screening details:

A total of 346 subjects who met all of the inclusion criteria and none of the exclusion criteria were enrolled and randomized in the study.

Period 1

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

Blinding implementation details:

The study was conducted in a blind observer manner. Neither the Investigator responsible for safety assessment, nor the subject knew which vaccine was administered.

Arms

Are arms mutually exclusive?	Yes
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Arm title	Quadrivalent Influenza Vaccine (VaxigripTetra)
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Arm description:

Pregnant women aged ≥ 18 years and who were in the late second/third trimester of pregnancy received a single dose of VaxigripTetra vaccine.

Arm type	Experimental
Investigational medicinal product name	Sanofi Pasteur licensed quadrivalent influenza vaccine (split-virion, inactivated)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use, Subcutaneous use

Dosage and administration details:

0.5 mL, intramuscular (IM) or deep subcutaneous (SC) injection, single dose on Day 0.

Arm title	Trivalent Influenza Vaccine (Vaxigrip)
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Arm description:

Pregnant women aged ≥ 18 years and who were in the late second/third trimester of pregnancy received a single dose of Vaxigrip vaccine.

Arm type	Active comparator
Investigational medicinal product name	Sanofi Pasteur licensed trivalent influenza vaccine (split-virion, inactivated)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use, Subcutaneous use

Dosage and administration details:

0.5 mL, intramuscular (IM) or deep subcutaneous (SC) injection, single dose on Day 0.

Number of subjects in period 1	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)
Started	230	116
Completed	228	115
Not completed	2	1
Consent withdrawn by subject	1	-
Lost to follow-up	-	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Quadrivalent Influenza Vaccine (VaxigripTetra)
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Reporting group description:

Pregnant women aged ≥ 18 years and who were in the late second/third trimester of pregnancy received a single dose of VaxigripTetra vaccine.

Reporting group title	Trivalent Influenza Vaccine (Vaxigrip)
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Reporting group description:

Pregnant women aged ≥ 18 years and who were in the late second/third trimester of pregnancy received a single dose of Vaxigrip vaccine.

Reporting group values	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)	Total
Number of subjects	230	116	346
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	32.0 ± 4.39	31.4 ± 4.76	-
Gender categorical Units: Subjects			
Female	230	116	346
Male	0	0	0

End points

End points reporting groups

Reporting group title	Quadrivalent Influenza Vaccine (VaxigripTetra)
Reporting group description: Pregnant women aged ≥ 18 years and who were in the late second/third trimester of pregnancy received a single dose of VaxigripTetra vaccine.	
Reporting group title	Trivalent Influenza Vaccine (Vaxigrip)
Reporting group description: Pregnant women aged ≥ 18 years and who were in the late second/third trimester of pregnancy received a single dose of Vaxigrip vaccine.	
Subject analysis set title	Quadrivalent Influenza Vaccine (VaxigripTetra)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Babies born to pregnant women aged ≥ 18 years, who were in the late second/third trimester of pregnancy received a single dose of VaxigripTetra vaccine.	
Subject analysis set title	Trivalent Influenza Vaccine (Vaxigrip)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Babies born to pregnant women aged ≥ 18 years, who were in the late second/third trimester of pregnancy received a single dose of Vaxigrip vaccine.	

Primary: Hemagglutination Inhibition (HAI) Antibody Titers After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip)

End point title	Hemagglutination Inhibition (HAI) Antibody Titers After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip) ^[1]
End point description: Serum antibody titers for the strains A/H1N1, A/H3N2, B1 and B2 were assessed by HAI assay. Antibody titers were expressed as geometric mean titers (GMTs). Analysis was performed on Per-Protocol Analysis set which included subjects who received one dose of any of the study vaccines and had no protocol deviations.	
End point type	Primary
End point timeframe: Day 0 (Pre-vaccination) and Day 21 (Post-vaccination)	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Only descriptive data was planned to be reported for this endpoint.	

End point values	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	216	109		
Units: Titer (1/dilution)				
geometric mean (confidence interval 95%)				
A/H1N1: Pre vaccination	138 (114 to 166)	121 (88.4 to 166)		
A/H1N1: Post vaccination	525 (466 to 592)	638 (529 to 769)		
A/H3N2: Pre vaccination	39.6 (32.2 to 48.6)	40.0 (29.4 to 54.5)		

A/H3N2: Post vaccination	341 (286 to 407)	369 (283 to 483)		
B1: Pre vaccination	67.1 (55.2 to 81.4)	72.5 (54.7 to 96.1)		
B1: Post vaccination	568 (496 to 651)	697 (569 to 855)		
B2: Pre vaccination	159 (131 to 193)	155 (120 to 202)		
B2: Post vaccination	993 (870 to 1134)	529 (415 to 674)		

Statistical analyses

No statistical analyses for this end point

Primary: Individual Antibody Titer Ratio After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip)

End point title	Individual Antibody Titer Ratio After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip) ^[2]
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End point description:

Individual antibody titer ratio for the strains A/H1N1, A/H3N2, B1 and B2 were assessed by HAI assay. Antibody titer ratio were expressed as Day 21/Day 0. Analysis was performed on Per-Protocol Analysis set.

End point type	Primary
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End point timeframe:

Day 0 (Pre-vaccination) and Day 21 (Post-vaccination)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

End point values	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	216	109		
Units: titer ratio				
geometric mean (confidence interval 95%)				
A/H1N1	3.81 (3.11 to 4.66)	5.26 (3.66 to 7.55)		
A/H3N2	8.63 (6.85 to 10.9)	9.23 (6.56 to 13.0)		
B1	8.48 (6.81 to 10.6)	9.62 (6.89 to 13.4)		
B2	6.26 (5.12 to 7.65)	3.40 (2.68 to 4.32)		

Statistical analyses

Primary: Percentage of Subjects With Detectable Antibody Titer After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip)

End point title	Percentage of Subjects With Detectable Antibody Titer After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip) ^[3]
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End point description:

Detectable antibody titers for the strains A/H1N1, A/H3N2, B1 and B2 were assessed by HAI assay. Detectable antibody titer value was ≥ 10 (1/dilution [1/dil]). Analysis was performed on Per-Protocol Analysis set.

End point type	Primary
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End point timeframe:

Day 0 (Pre-vaccination) and Day 21 (Post-vaccination)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

End point values	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	216	109		
Units: Percentage of Subjects				
number (not applicable)				
A/H1N1: Pre vaccination	94.9	89.0		
A/H1N1: Post vaccination	100	100		
A/H3N2: Pre vaccination	77.8	75.2		
A/H3N2: Post vaccination	99.1	100		
B1: Pre vaccination	89.8	90.8		
B1: Post vaccination	100	100		
B2: Pre vaccination	94.9	99.1		
B2: Post vaccination	100	100		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Antibody Titer ≥ 40 (1/Dilution) After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip)

End point title	Percentage of Subjects With Antibody Titer ≥ 40 (1/Dilution) After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip) ^[4]
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End point description:

Antibody titer ≥ 40 (1/dilution) for the strains A/H1N1, A/H3N2, B1 and B2 were assessed by HAI assay. Analysis was performed on Per-Protocol Analysis set.

End point type	Primary
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End point timeframe:

Day 0 (Pre-vaccination) and Day 21 (Post-vaccination)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

End point values	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	216	109		
Units: Percentage of Subjects				
number (not applicable)				
A/H1N1: Pre vaccination	86.1	78.0		
A/H1N1: Post vaccination	99.5	100		
A/H3N2: Pre vaccination	55.1	53.2		
A/H3N2: Post vaccination	95.8	94.5		
B1: Pre vaccination	69.4	65.1		
B1: Post vaccination	100	99.1		
B2: Pre vaccination	85.2	83.5		
B2: Post vaccination	100	97.2		

Statistical analyses

No statistical analyses for this end point

Primary: Seroconversion or Significant Increase of Antibody Titers After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip)

End point title	Seroconversion or Significant Increase of Antibody Titers After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip) ^[5]
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End point description:

Seroconversion was defined as the pre-vaccination titer < 10 (1/dil) on Day 0 and post-vaccination titer \geq 40 (1/dil) on Day 21, or significant increase was defined as the pre vaccination titer \geq 10 (1/dil) and \geq 4-fold increase of post-injection titer on Day 21. Analysis was performed on Per-Protocol Analysis set.

End point type	Primary
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End point timeframe:

Day 0 (Pre-vaccination) and Day 21 (Post-vaccination)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

End point values	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	216	109		
Units: percentage of subjects				
number (not applicable)				

A/H1N1	38.0	41.3		
A/H3N2	59.3	62.4		
B1	61.1	60.6		
B2	59.7	38.5		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Solicited Injection Site or Systemic Reactions After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip)

End point title	Percentage of Subjects Reporting Solicited Injection Site or Systemic Reactions After Vaccination With Quadrivalent Influenza Vaccine (VaxigripTetra) or Trivalent Influenza Vaccine (Vaxigrip) ^[6]
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End point description:

Percentage of subjects experiencing at least 1 solicited injection site reaction (pain, erythema, swelling, induration and ecchymosis) and at least 1 systemic reaction (fever, headache, malaise, myalgia, and shivering) were reported. Analysis was performed on safety analysis set which included all subjects who had received at least 1 dose of the study or control vaccine; all subjects had their safety analyzed according to the vaccine actually received.

End point type	Primary
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End point timeframe:

Day 0 to Day 7 (Post-vaccination)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be reported for this endpoint.

End point values	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	115		
Units: Percentage of Subjects				
number (not applicable)				
Injection site pain	88.7	76.5		
Injection site erythema	10.4	13.9		
Injection site swelling	5.7	5.2		
Injection site induration	3.5	4.3		
Injection site ecchymosis	0.9	1.7		
Fever	0	1.7		
Headache	41.7	47.8		
Malaise	29.1	27.8		
Myalgia	37.0	25.2		
Shivering	26.5	26.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Ratio of the Hemagglutination-Inhibition Titers in Infants and Mothers at the Time of Delivery

End point title	Geometric Mean Ratio of the Hemagglutination-Inhibition Titers in Infants and Mothers at the Time of Delivery
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End point description:

Geometric mean ratio of the Hemagglutination-Inhibition titers in infants and mothers for each strain at the time of delivery was reported. Analysis was performed on Other Immunogenicity Analysis Set which included subjects who received one dose of any of the study vaccines, delivered at least 2 weeks after injection and with available cord blood sample (BL) and mother BL at the time of delivery or at Visit 2 (Day 21) if delivery occurred during the time window of Visit 2 (Day 21).

End point type	Secondary
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End point timeframe:

At the time of Delivery (on average 103 day after vaccination)

End point values	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	178	89		
Units: geometric mean ratio				
geometric mean (confidence interval 95%)				
A/H1N1	1.89 (1.72 to 2.08)	1.83 (1.64 to 2.04)		
A/H3N2	1.71 (1.56 to 1.87)	1.75 (1.55 to 1.97)		
B1	1.53 (1.37 to 1.71)	1.64 (1.46 to 1.85)		
B2	1.69 (1.54 to 1.85)	1.47 (1.28 to 1.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Birth Outcomes

End point title	Birth Outcomes
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End point description:

Number of babies with different birth outcomes assessed by methods used in routine at the hospital. Analysis was performed on the Babies other Safety analysis set which included babies of the subjects from the other Safety analysis set (defined as the subset of subjects who received one dose of the study or control vaccine and delivered at least 2 weeks after vaccination).

End point type	Secondary
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End point timeframe:

At the time of Delivery (on average 103 day after vaccination)

End point values	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	231	119		
Units: babies				
Live Birth	231	119		
Spontaneous Abortion (< 20 week gestation)	0	0		
Early Fetal Death (20-27 weeks gestation)	0	0		
Late Fetal Death (at least 28 weeks gestation)	0	0		
Elective Abortion	0	0		
Maternal Death Resulting in Fetal Death	0	0		
Ectopic Pregnancy	0	0		
Congenital Abnormalities	6	5		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event (AE) data collected from Day 0 (pre-vaccination) up to date of delivery (on an average 103 day after vaccination)

Adverse event reporting additional description:

Solicited adverse reaction (SAR): An AE, i.e. prelisted in electronic case report form (eCRF) and considered related to vaccination. SAR is an adverse drug reaction observed, reported under the conditions (nature and onset) prelisted (i.e. solicited) in eCRF. Unsolicited AE: an observed AE that does not fulfill conditions prelisted in eCRF. Safety set

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Quadrivalent Influenza Vaccine (VaxigripTetra)
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Reporting group description:

Pregnant women aged ≥ 18 years and in late second/third trimester of pregnancy received a single dose of VaxigripTetra vaccine.

Reporting group title	Trivalent Influenza Vaccine (Vaxigrip)
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Reporting group description:

Pregnant women aged ≥ 18 years and in late second/third trimester of pregnancy received a single dose of Vaxigrip vaccine.

Serious adverse events	Quadrivalent Influenza Vaccine (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)	
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 230 (11.30%)	18 / 116 (15.52%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Perineal Injury			
subjects affected / exposed	1 / 230 (0.43%)	0 / 116 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine Rupture			
subjects affected / exposed	0 / 230 (0.00%)	1 / 116 (0.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			

subjects affected / exposed	2 / 230 (0.87%)	0 / 116 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 230 (0.43%)	0 / 116 (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			
Gestational Hypertension			
subjects affected / exposed	1 / 230 (0.43%)	1 / 116 (0.86%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intrapartum Haemorrhage			
subjects affected / exposed	2 / 230 (0.87%)	0 / 116 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructed Labour			
subjects affected / exposed	0 / 230 (0.00%)	1 / 116 (0.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripartum Haemorrhage			
subjects affected / exposed	0 / 230 (0.00%)	1 / 116 (0.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpartum Haemorrhage			
subjects affected / exposed	16 / 230 (6.96%)	13 / 116 (11.21%)	
occurrences causally related to treatment / all	0 / 16	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pre-Eclampsia			
subjects affected / exposed	2 / 230 (0.87%)	0 / 116 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Premature Labour			
subjects affected / exposed	1 / 230 (0.43%)	0 / 116 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Preterm Premature Rupture Of Membranes			
subjects affected / exposed	1 / 230 (0.43%)	0 / 116 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholestasis Of Pregnancy			
subjects affected / exposed	1 / 230 (0.43%)	0 / 116 (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			
Amniotic Cavity Infection			
subjects affected / exposed	0 / 230 (0.00%)	1 / 116 (0.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 230 (0.00%)	1 / 116 (0.86%)	
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 / 230 (0.43%)	0 / 116 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post Procedural Infection			
subjects affected / exposed	1 / 230 (0.43%)	0 / 116 (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 (VaxigripTetra)	Trivalent Influenza Vaccine (Vaxigrip)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	216 / 230 (93.91%)	107 / 116 (92.24%)	
Nervous system disorders			
Headache			
subjects affected / exposed	102 / 230 (44.35%)	58 / 116 (50.00%)	
occurrences (all)	112	62	
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	24 / 230 (10.43%)	16 / 116 (13.79%)	
occurrences (all)	24	16	
Injection Site Pain			
subjects affected / exposed	204 / 230 (88.70%)	88 / 116 (75.86%)	
occurrences (all)	204	88	
Injection Site Swelling			
subjects affected / exposed	13 / 230 (5.65%)	6 / 116 (5.17%)	
occurrences (all)	13	6	
Malaise			
subjects affected / exposed	67 / 230 (29.13%)	33 / 116 (28.45%)	
occurrences (all)	67	33	
Shivering			
subjects affected / exposed	61 / 230 (26.52%)	30 / 116 (25.86%)	
occurrences (all)	61	30	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	16 / 230 (6.96%)	4 / 116 (3.45%)	
occurrences (all)	16	4	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	8 / 230 (3.48%)	7 / 116 (6.03%)	
occurrences (all)	9	8	
Myalgia			
subjects affected / exposed	86 / 230 (37.39%)	29 / 116 (25.00%)	
occurrences (all)	86	29	
Infections and infestations			

Rhinitis			
subjects affected / exposed	11 / 230 (4.78%)	6 / 116 (5.17%)	
occurrences (all)	12	6	
Upper Respiratory Tract Infection			
subjects affected / exposed	26 / 230 (11.30%)	14 / 116 (12.07%)	
occurrences (all)	28	14	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 February 2018	Corrections made to the following sections of the protocol: the objectives, endpoints, statistical methods and sample size. Recently available information regarding vaccine development and strains content was also added to background of IP. One additional month was allotted to the enrollment period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported