Clinical trial results:
Safety and Immunogenicity of a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adult and Elderly Subjects

Summary

EudraCT number	2011-001976-21
Trial protocol	DE
Global end of trial date	11 June 2012

Results information

Result version number	v1 (current)
This version publication date	05 February 2016
First version publication date	29 January 2015

Trial information

Trial identification

Sponsor protocol code	GQM01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1120-1486

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, F-69367 Lyon Cedex 07, France,
Public contact	Director, Clinical Development, Sanofi Pasteur, +33 (4) 37 37 58 50, Stephanie.Pepin@sanofipasteur.com
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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	27 September 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 June 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate non-inferiority of antibody responses induced by quadrivalent influenza vaccine (QIV) compared with the licensed 2011-2012 trivalent influenza vaccine (TIV; containing the B/Brisbane strain) and the investigational TIV (containing the B/Florida strain) as assessed in all subjects by geometric mean titer (GMT) for each strain

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. 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 was also available on site in case of any immediate allergic reactions.

Background therapy:

Not applicable

Evidence for comparator:

The licensed TIV for the 2011-2012 season containing the B/Brisbane strain (TIV1) was used as an active control.

Actual start date of recruitment	21 October 2011
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	France: 1088
Country: Number of subjects enrolled	Germany: 480
Worldwide total number of subjects	1568
EEA total number of subjects	1568

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)	1260
From 65 to 84 years	303
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 21 October 2011 to 10 November 2011 at 14 clinical sites in France and 4 in Germany.

Pre-assignment

Screening details:

A total of 1568 subjects who met all inclusion criteria and none of the exclusion criteria were enrolled and vaccinated.

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

Blinding implementation details:

This study was blinded to the Investigator and for all subjects in the QIV and TIV1 groups. After the 1st database lock, the code could be broken by the Investigator in the event of an SAE and if identification of the vaccine received could influence SAE treatment (Responsible Medical Officer was to be notified first) and by the GPV department for reporting to Health authorities in the case of an SAE as described in International Conference on Harmonisation (only for the subject in question).

Arms

Are arms mutually exclusive?	Yes
Arm title	QIV 18-60 years

Arm description:

Adults aged 18-60 years who received one dose of quadrivalent influenza vaccine (QIV).

Arm type	Experimental
Investigational medicinal product name	Quadrivalent influenza vaccine (split virion, inactivated) (QIV)
Investigational medicinal product code	481
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose, intramuscular to be injected into the deltoid muscle or deep subcutaneous (SC), one dose on Day 0.

Arm title	QIV >60 years

Arm description:

Elderly subjects aged >60 years who received one dose of quadrivalent influenza vaccine (QIV).

Arm type	Experimental
Investigational medicinal product name	Quadrivalent influenza vaccine (split virion, inactivated) (QIV)
Investigational medicinal product code	481
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose, intramuscular to be injected into the deltoid muscle or deep subcutaneous (SC), one dose on Day 0.

Arm title	Licensed TIV 18-60 years

Arm description:

Adults aged 18-60 years who received one dose of licensed trivalent influenza vaccine for the 2011-

2012 season that contained either the B strain from the Victoria lineage, the B/Brisbane strain (TIV1).

Arm type	Active comparator
Investigational medicinal product name	Sanofi Pasteur licensed TIV for the 2011-2012 season (TIV1)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose, intramuscular (IM) to be injected into the deltoid muscle or deep subcutaneous (SC), one dose on Day 0.

Arm title	Licensed TIV >60 years

Arm description:

Elderly subjects aged >60 years who received one dose of licensed trivalent influenza vaccine for the 2011-2012 season that contained either the B strain from the Victoria lineage, the B/Brisbane strain (TIV1).

Arm type	Active comparator
Investigational medicinal product name	Sanofi Pasteur licensed TIV for the 2011-2012 season (TIV1)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose, intramuscular (IM) to be injected into the deltoid muscle or deep subcutaneous (SC), one dose on Day 0.

Arm title	Investigational TIV 18-60 years

Arm description:

Adults aged 18-60 years who received one dose of investigational trivalent influenza vaccine containing the B strain from the Yamagata lineage, the B/Florida strain (TIV2).

Arm type	Active comparator
Investigational medicinal product name	Investigational TIV (split-virion, inactivated) (TIV2)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose, intramuscular (IM) to be injected into the deltoid muscle or deep subcutaneous (SC), one dose on Day 0.

Arm title	Investigational TIV >60 years

Arm description:

Elderly subjects aged >60 years who received one dose of investigational trivalent influenza vaccine containing the B strain from the Yamagata lineage, the B/Florida strain (TIV2).

Arm type	Active comparator
Investigational medicinal product name	Investigational TIV (split-virion, inactivated) (TIV2)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose, intramuscular (IM) to be injected into the deltoid muscle or deep subcutaneous (SC), one dose on Day 0.

Number of subjects in period 1	QIV 18-60 years	QIV >60 years	Licensed TIV 18-60 years
Started	559	558	113
Completed	557	557	113
Not completed	2	1	0
Consent withdrawn by subject	1	1	-
Adverse event, non-fatal	1	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	Licensed TIV >60 years	Investigational TIV 18-60 years	Investigational TIV >60 years
Started	113	111	114
Completed	113	110	113
Not completed	0	1	1
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Protocol deviation	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	QIV 18-60 years
Reporting group description:	
Adults aged 18-60 years who received one dose of quadrivalent influenza vaccine (QIV).	
Reporting group title	QIV >60 years
Reporting group description:	
Elderly subjects aged >60 years who received one dose of quadrivalent influenza vaccine (QIV).	
Reporting group title	Licensed TIV 18-60 years
Reporting group description:	
Adults aged 18-60 years who received one dose of licensed trivalent influenza vaccine for the 2011-2012 season that contained either the B strain from the Victoria lineage, the B/Brisbane strain (TIV1).	
Reporting group title	Licensed TIV >60 years
Reporting group description:	
Elderly subjects aged >60 years who received one dose of licensed trivalent influenza vaccine for the 2011-2012 season that contained either the B strain from the Victoria lineage, the B/Brisbane strain (TIV1).	
Reporting group title	Investigational TIV 18-60 years
Reporting group description:	
Adults aged 18-60 years who received one dose of investigational trivalent influenza vaccine containing the B strain from the Yamagata lineage, the B/Florida strain (TIV2).	
Reporting group title	Investigational TIV >60 years
Reporting group description:	
Elderly subjects aged >60 years who received one dose of investigational trivalent influenza vaccine containing the B strain from the Yamagata lineage, the B/Florida strain (TIV2).	

Reporting group values	QIV 18-60 years	QIV >60 years	Licensed TIV 18-60 years
Number of subjects	559	558	113
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)	559	410	113
From 65-84 years	0	148	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	41.6	68.7	41.3
standard deviation	± 12.7	± 5.89	± 12.4
Gender categorical Units: Subjects			
Female	355	303	62
Male	204	255	51

Reporting group values	Licensed TIV >60 years	Investigational TIV 18-60 years	Investigational TIV >60 years
Number of subjects	113	111	114
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)	33	111	34
From 65-84 years	77	0	78
85 years and over	3	0	2
Age continuous Units: years			
arithmetic mean	68.8	42.6	69.1
standard deviation	± 5.95	± 12.1	± 5.8
Gender categorical Units: Subjects			
Female	56	75	65
Male	57	36	49

Reporting group values	Total		
Number of subjects	1568		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	1260		
From 65-84 years	303		
85 years and over	5		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	916		
Male	652		

End points

End points reporting groups

Reporting group title	QIV 18-60 years
Reporting group description:	
Adults aged 18-60 years who received one dose of quadrivalent influenza vaccine (QIV).	
Reporting group title	QIV >60 years
Reporting group description:	
Elderly subjects aged >60 years who received one dose of quadrivalent influenza vaccine (QIV).	
Reporting group title	Licensed TIV 18-60 years
Reporting group description:	
Adults aged 18-60 years who received one dose of licensed trivalent influenza vaccine for the 2011-2012 season that contained either the B strain from the Victoria lineage, the B/Brisbane strain (TIV1).	
Reporting group title	Licensed TIV >60 years
Reporting group description:	
Elderly subjects aged >60 years who received one dose of licensed trivalent influenza vaccine for the 2011-2012 season that contained either the B strain from the Victoria lineage, the B/Brisbane strain (TIV1).	
Reporting group title	Investigational TIV 18-60 years
Reporting group description:	
Adults aged 18-60 years who received one dose of investigational trivalent influenza vaccine containing the B strain from the Yamagata lineage, the B/Florida strain (TIV2).	
Reporting group title	Investigational TIV >60 years
Reporting group description:	
Elderly subjects aged >60 years who received one dose of investigational trivalent influenza vaccine containing the B strain from the Yamagata lineage, the B/Florida strain (TIV2).	

Primary: Geometric Mean Titers (GMTs) of HAI Antibody Response to Quadrivalent Influenza Vaccine (QIV) Strains Before and After Vaccination with a QIV Administered via the Intramuscular Route in Adults and Elderly Subjects

End point title	Geometric Mean Titers (GMTs) of HAI Antibody Response to Quadrivalent Influenza Vaccine (QIV) Strains Before and After Vaccination with a QIV Administered via the Intramuscular Route in Adults and Elderly Subjects[1][2]
End point description:	
Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method.	
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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Immunogenicity data were presented based on vaccine and age group specified in the outcome title.

End point values	QIV 18-60 years	QIV >60 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	556	554		
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
A/California/7/2009 (H1N1); D0	38.5 (33 to 44.8)	29.7 (26 to 33.9)		
A/Victoria/210/2009 (H3N2); D0	28.5 (24.9 to 32.5)	43.1 (37.4 to 49.6)		
B/Brisbane/60/2008; D0	53.9 (47.2 to 61.5)	57.8 (51.1 to 65.4)		
B/Florida/04/2006; D0	117 (101 to 134)	93.5 (82.9 to 105)		
A/California/7/2009 (H1N1); D21	551 (495 to 614)	229 (204 to 258)		
A/Victoria/210/2009 (H3N2); D21	417 (374 to 465)	294 (262 to 331)		
B/Brisbane/60/2008; D21	657 (599 to 722)	278 (253 to 305)		
B/Florida/04/2006; D21	1536 (1397 to 1688)	673 (615 to 737)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroprotection Against Influenza Antigens Before and After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adults and Elderly Subjects

End point title	Percentage of Subjects With Seroprotection Against Influenza Antigens Before and After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adults and Elderly Subjects[3][4]

End point description:

Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method. Seroprotection was defined as subjects having titers ≥ 40 (1/dil) on Day 21.

End point type	Primary

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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Immunogenicity data were presented based on vaccine and age group specified in the outcome title.

End point values	QIV 18-60 years	QIV >60 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	556	554		
Units: Percentage of subjects				
number (not applicable)				
A/California/7/2009 (H1N1); D0	49.8	43.7		
A/Victoria/210/2009 (H3N2); D0	41.7	53.7		
B/Brisbane/60/2008; D0	58.1	65.1		
B/Florida/04/2006; D0	73.2	75.8		
A/California/7/2009 (H1N1); D21	96.4	90.1		
A/Victoria/210/2009 (H3N2); D21	97.1	93.7		
B/Brisbane/60/2008; D21	99.5	97.5		
B/Florida/04/2006; D21	99.6	99.8		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Achieving Seroconversion or Significant increase Against Influenza Antigens After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adults and Elderly Subjects

End point title	Percentage of Subjects Achieving Seroconversion or Significant increase Against Influenza Antigens After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adults and Elderly Subjects[5][6]

End point description:

Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method. Seroconversion was defined as for subjects with a pre-vaccination titer < 10 (1/dil): post-injection titer ≥ 40 (1/dil) on Day 21 or significant increase for subjects with a pre-vaccination titer ≥ 10 (1/dil): ≥ 4-fold increase from pre- to post-injection titer on Day 21.

End point type	Primary

End point timeframe:

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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Immunogenicity data were presented based on vaccine and age group specified in the outcome title.

End point values	QIV 18-60 years	QIV >60 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	556	554		
Units: Percentage of subjects				
number (not applicable)				
A/California/7/2009 (H1N1)	72.2	59.2		
A/Victoria/210/2009 (H3N2)	74.5	56.6		
B/Brisbane/60/2008	69.2	46.1		
B/Florida/04/2006	73.9	61.2		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of HAI antibody response to Trivalent Influenza Vaccine (TIV) strains Before and After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adults and Elderly Subjects

End point title	Geometric Mean Titers (GMTs) of HAI antibody response to Trivalent Influenza Vaccine (TIV) strains Before and After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adults and Elderly Subjects[7][8]

End point description:

Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 post-vaccination

Notes:

[7] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Immunogenicity data were presented based on vaccine and age group specified in the outcome title.

End point values	Licensed TIV 18-60 years	Licensed TIV >60 years	Investigational TIV 18-60 years	Investigational TIV >60 years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	113	110	111
Units: Titer (1/dil)				
geometric mean (confidence interval 95%)				
Licensed TIV B/Brisbane 60/2008; D0	69.7 (51.3 to 94.6)	51.3 (39.5 to 66.6)	0 (0 to 0)	0 (0 to 0)
Investigational TIV B/Florida/04/2006; D0	0 (0 to 0)	0 (0 to 0)	96.6 (69.4 to 135)	104 (80.2 to 136)
Licensed TIV B/Brisbane 60/2008; D21	841 (665 to 1062)	254 (201 to 321)	0 (0 to 0)	0 (0 to 0)
Investigational TIV B/Florida/04/2006; D21	0 (0 to 0)	0 (0 to 0)	1268 (1017 to 1580)	725 (591 to 890)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroprotection Against Trivalent Influenza Vaccine Antigens Before and After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adults and Elderly Subjects

End point title	Percentage of Subjects With Seroprotection Against Trivalent Influenza Vaccine Antigens Before and After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adults and Elderly Subjects[9][10]

End point description:

Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method. Seroprotection was defined as subjects having titers ≥ 40 (1/dil) on Day 21.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 post-vaccination

Notes:

[9] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Immunogenicity data were presented based on vaccine and age group specified in the outcome title.

End point values	Licensed TIV 18-60 years	Licensed TIV >60 years	Investigational TIV 18-60 years	Investigational TIV >60 years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	113	110	111
Units: Percentage of subjects				
number (not applicable)				
Licensed TIV B/Brisbane 60/2008; D0	62.8	60.2	0	0
Investigational TIV B/Florida/04/2006; D0	0	0	70	80.2
Licensed TIV B/Brisbane 60/2008; D21	99.1	96.5	0	0
Investigational TIV B/Florida/04/2006; D21	0	0	99.1	100

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Achieving Seroconversion or Significant increase Against Trivalent Influenza Vaccine Antigens After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adults and Elderly Subjects

End point title	Percentage of Subjects Achieving Seroconversion or Significant increase Against Trivalent Influenza Vaccine Antigens After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route in Adults and Elderly Subjects[11][12]

End point description:

Immunogenicity was evaluated using the hemagglutination inhibition (HAI) method. Seroconversion was defined as for subjects with a pre-vaccination titer < 10 (1/dil): post-injection titer ≥ 40 (1/dil) on Day 21 or significant increase for subjects with a pre-vaccination titer ≥ 10 (1/dil): ≥ 4-fold increase from pre- to post-injection titer on Day 21.

End point type	Primary

End point timeframe:

Day 21 post-vaccination

Notes:

[11] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.
[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Immunogenicity data were presented based on vaccine and age group specified in the outcome title.

End point values	Licensed TIV 18-60 years	Licensed TIV >60 years	Investigational TIV 18-60 years	Investigational TIV >60 years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	113	110	111
Units: Percentage of subjects				
number (not applicable)				
Licensed TIV B/Brisbane 60/2008	61.1	42.5	0	0
Investigational TIV B/Florida/04/2006	0	0	75.5	56.8

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route

End point title	Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction After Vaccination with a Quadrivalent Influenza Vaccine Administered via the Intramuscular Route[13]

End point description:

Solicited injection site: Pain, Erythema, Swelling, Induration and Ecchymosis. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Shivering. Grade 3 Solicited Injection site reactions: Pain – Significant, prevents daily activity; Erythema, Swelling, Induration, and Ecchymosis - >100 mm. Grade 3 Solicited systemic reactions: Fever - ≥39°C; Headache, Malaise, Myalgia, and Shivering – Significant, prevents daily activities.

End point type	Primary

End point timeframe:

Day 0 up to Day 7 post-vaccination

Notes:

[13] - 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	QIV 18-60 years	QIV >60 years	Licensed TIV 18-60 years	Licensed TIV >60 years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	558	558[14]	113	113[15]
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	59.4	29.9	48.7	27.4
Grade 3 Injection site Pain	0.5	0.2	0.9	0.9
Injection site Erythema	9.9	6.3	12.4	7.1
Grade 3 Injection site Erythema	0	0	0	0
Injection site Swelling	5.4	3.8	3.5	3.5
Grade 3 Injection site Swelling	0	0	0	0
Injection site Induration	6.1	3.6	3.5	1.8
Grade 3 Injection site Induration	0	0	0	0
Injection site Ecchymosis	0.7	0.4	1.8	0
Grade 3 Injection site Ecchymosis	0	0	0	0
Fever	2	0.7	1.8	0.9
Grade 3 Fever	0.4	0	1.8	0
Headache	31.8	16.1	31.9	12.4
Grade 3 Headache	2.3	0.4	4.4	0
Malaise	17.4	7.5	16.8	6.2
Grade 3 Malaise	1.3	0.2	1.8	0.9
Myalgia	30.3	15.4	29.2	12.4
Grade 3 Myalgia	1.4	0.4	1.8	0.9
Shivering	11.3	4.1	6.2	7.1
Grade 3 Shivering	1.1	0	1.8	0

Notes:

[14] - No vaccine outcome for this group.

[15] - No vaccine outcome for this group.

End point values	Investigational TIV 18-60 years	Investigational TIV >60 years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	113[16]		
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	54.5	23		
Grade 3 Injection site Pain	0	0		
Injection site Erythema	10	5.3		
Grade 3 Injection site Erythema	0.9	0		
Injection site Swelling	5.5	1.8		
Grade 3 Injection site Swelling	0.9	0		
Injection site Induration	7.3	1.8		
Grade 3 Injection site Induration	0	0		
Injection site Ecchymosis	0	0		
Grade 3 Injection site Ecchymosis	0	0		
Fever	0	1.8		
Grade 3 Fever	0	0		
Headache	30	14.2		
Grade 3 Headache	0.9	0.9		
Malaise	13.6	8.8		
Grade 3 Malaise	0	0		

Myalgia	23.6	8.8		
Grade 3 Myalgia	0	0		
Shivering	9.1	5.3		
Grade 3 Shivering	0.9	0		

Notes:

[16] - No vaccine outcome for this group.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse event data were collected from Day 0 (post-vaccination) up to Day 21 post-vaccination.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	QIV 18-60 years
Reporting group description:	
Adults aged 18-60 years who received one dose of quadrivalent influenza vaccine (QIV).	
Reporting group title	QIV >60 years
Reporting group description:	
Elderly subjects aged >60 years who received one dose of quadrivalent influenza vaccine (QIV).	
Reporting group title	Licensed TIV 18-60 years
Reporting group description:	
Adults aged 18-60 years who received one dose of licensed trivalent influenza vaccine for the 2011-2012 season that contained either the B strain from the Victoria lineage, the B/Brisbane strain (TIV1).	
Reporting group title	Licensed TIV >60 years
Reporting group description:	
Elderly subjects aged >60 years who received one dose of licensed trivalent influenza vaccine for the 2011-2012 season that contained either the B strain from the Victoria lineage, the B/Brisbane strain (TIV1).	
Reporting group title	Investigational TIV 18-60 years
Reporting group description:	
Adults aged 18-60 years who received one dose of investigational trivalent influenza vaccine containing the B strain from the Yamagata lineage, the B/Florida strain (TIV2).	
Reporting group title	Investigational TIV >60 years
Reporting group description:	
Elderly subjects aged >60 years who received one dose of investigational trivalent influenza vaccine containing the B strain from the Yamagata lineage, the B/Florida strain (TIV2).	

Serious adverse events	QIV 18-60 years	QIV >60 years	Licensed TIV 18-60 years
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 558 (0.18%)	2 / 558 (0.36%)	1 / 113 (0.88%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of the skin			
subjects affected / exposed	1 / 558 (0.18%)	0 / 558 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Breast cancer			
subjects affected / exposed	0 / 558 (0.00%)	1 / 558 (0.18%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholesteatoma			
subjects affected / exposed	0 / 558 (0.00%)	0 / 558 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cancer			
subjects affected / exposed	0 / 558 (0.00%)	1 / 558 (0.18%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 558 (0.18%)	0 / 558 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	1 / 558 (0.18%)	0 / 558 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 558 (0.00%)	1 / 558 (0.18%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 558 (0.00%)	0 / 558 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 558 (0.18%)	0 / 558 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 558 (0.00%)	1 / 558 (0.18%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 558 (0.00%)	0 / 558 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Gastric banding			
subjects affected / exposed	1 / 558 (0.18%)	0 / 558 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mammoplasty			
subjects affected / exposed	1 / 558 (0.18%)	0 / 558 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 558 (0.00%)	2 / 558 (0.36%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 558 (0.00%)	1 / 558 (0.18%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Inner ear disorder			
subjects affected / exposed	1 / 558 (0.18%)	0 / 558 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			

subjects affected / exposed	1 / 558 (0.18%)	0 / 558 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic haemorrhage			
subjects affected / exposed	0 / 558 (0.00%)	1 / 558 (0.18%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 558 (0.00%)	0 / 558 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	0 / 558 (0.00%)	1 / 558 (0.18%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Encephalitis herpes			
subjects affected / exposed	0 / 558 (0.00%)	0 / 558 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 558 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paronychia			
subjects affected / exposed	0 / 558 (0.00%)	1 / 558 (0.18%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 558 (0.00%)	0 / 558 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vestibular neuronitis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 558 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Licensed TIV >60 years	Investigational TIV 18-60 years	Investigational TIV >60 years
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 113 (0.88%)	1 / 110 (0.91%)	1 / 113 (0.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of the skin			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	1 / 113 (0.88%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholesteatoma			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cancer			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			

subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 113 (0.88%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 113 (0.88%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Gastric banding			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mammoplasty			

subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Inner ear disorder			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic haemorrhage			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Foot deformity			

subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Encephalitis herpes			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paronychia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	QIV 18-60 years	QIV >60 years	Licensed TIV 18-60 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	331 / 558 (59.32%)	167 / 558 (29.93%)	55 / 113 (48.67%)
Nervous system disorders			
Headache			
alternative assessment type: Systematic			

subjects affected / exposed[1]	177 / 557 (31.78%)	90 / 558 (16.13%)	36 / 113 (31.86%)
occurrences (all)	177	90	36
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed[2]	331 / 557 (59.43%)	167 / 558 (29.93%)	55 / 113 (48.67%)
occurrences (all)	331	167	55
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[3]	55 / 557 (9.87%)	35 / 558 (6.27%)	14 / 113 (12.39%)
occurrences (all)	55	35	14
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed[4]	30 / 557 (5.39%)	21 / 558 (3.76%)	4 / 113 (3.54%)
occurrences (all)	30	21	4
Injection site ecchymosis			
alternative assessment type: Systematic			
subjects affected / exposed[5]	4 / 557 (0.72%)	2 / 558 (0.36%)	2 / 113 (1.77%)
occurrences (all)	4	2	2
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed[6]	97 / 557 (17.41%)	42 / 558 (7.53%)	19 / 113 (16.81%)
occurrences (all)	97	42	19
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed[7]	63 / 557 (11.31%)	23 / 558 (4.12%)	7 / 113 (6.19%)
occurrences (all)	63	23	7
Skin and subcutaneous tissue disorders			
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed[8]	34 / 557 (6.10%)	20 / 558 (3.58%)	4 / 113 (3.54%)
occurrences (all)	34	20	4
Musculoskeletal and connective tissue disorders			

Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[9]	169 / 557 (30.34%)	86 / 558 (15.41%)	33 / 113 (29.20%)
occurrences (all)	169	86	33

Non-serious adverse events	Licensed TIV >60 years	Investigational TIV 18-60 years	Investigational TIV >60 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 113 (27.43%)	60 / 110 (54.55%)	26 / 113 (23.01%)
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[1]	14 / 113 (12.39%)	33 / 110 (30.00%)	16 / 113 (14.16%)
occurrences (all)	14	33	16
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed[2]	31 / 113 (27.43%)	60 / 110 (54.55%)	26 / 113 (23.01%)
occurrences (all)	31	60	26
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[3]	8 / 113 (7.08%)	11 / 110 (10.00%)	6 / 113 (5.31%)
occurrences (all)	8	11	6
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed[4]	4 / 113 (3.54%)	6 / 110 (5.45%)	2 / 113 (1.77%)
occurrences (all)	4	6	2
Injection site ecchymosis			
alternative assessment type: Systematic			
subjects affected / exposed[5]	0 / 113 (0.00%)	0 / 110 (0.00%)	0 / 113 (0.00%)
occurrences (all)	0	0	0
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed[6]	7 / 113 (6.19%)	15 / 110 (13.64%)	10 / 113 (8.85%)
occurrences (all)	7	15	10
Shivering			

alternative assessment type: Systematic			
subjects affected / exposed[7]	8 / 113 (7.08%)	10 / 110 (9.09%)	6 / 113 (5.31%)
occurrences (all)	8	10	6
Skin and subcutaneous tissue disorders			
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed[8]	2 / 113 (1.77%)	8 / 110 (7.27%)	2 / 113 (1.77%)
occurrences (all)	2	8	2
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[9]	14 / 113 (12.39%)	26 / 110 (23.64%)	10 / 113 (8.85%)
occurrences (all)	14	26	10

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects who returned the safety diary card and data were available for the event during the period.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects who returned the safety diary card and data were available for the event during the period.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects who returned the safety diary card and data were available for the event during the period.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects who returned the safety diary card and data were available for the event during the period.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects who returned the safety diary card and data were available for the event during the period.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects who returned the safety diary card and data were available for the event during the period.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects who returned the safety diary card and data were available for the event during the period.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects who returned the safety diary card and data were available for the event during the period.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects who returned the safety diary card and data were available for the event during the period.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2011	A statement was added that defined specific criteria for stopping the trial during the enrollment phase in case of post-vaccination safety concerns.
22 March 2012	The protocol was amended in regards to a site (Center 003) closing. For subjects included in Center 003, the 6-month safety follow-up would be conducted by Center 004 and subjects would be asked to sign an addendum to the ICF to consent to being contacted by Center 004. It also clarified how subjects from Center 003 would be handled in the clinical database if they refuse to be followed by Center 004 for the 6-month safety follow-up and where source documents of subjects included in Center 003 are archived.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported