



Clinical trial results:

A phase 3, Observed-Blind, Randomized, Multi-center Study to Evaluate Safety and Immunogenicity of an Adjuvanted Trivalent Influenza Vaccine in Children 6 to <72 Months of Age in Mexico.

Summary

EudraCT number	2014-004248-36
Trial protocol	Outside EU/EEA
Global end of trial date	16 July 2015

Results information

Result version number	v1 (current)
This version publication date	21 February 2016
First version publication date	21 February 2016

Trial information

Trial identification

Sponsor protocol code	V70_50
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02255279
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma Services AG
Sponsor organisation address	Lichtstrasse 35, Basel, Switzerland, 4056
Public contact	Clinical Trial Information Desk, Novartis Pharma Services AG, RegistryContactVaccinesUS@novartis.com
Scientific contact	Clinical Trial Information Desk, Novartis Pharma Services AG, RegistryContactVaccinesUS@novartis.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 January 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To assess the safety of aTIV and TIV vaccines administered to healthy subjects 6 to <72 months of age, from day 1 to day 50 (naïve subjects) and from day 1 to day 22 (non-naïve subjects).
2. To demonstrate non-inferiority of aTIV to TIV as measured by geometric mean titers (GMTs) in all three homologous virus strains, 21 days after last immunization, in subjects 6 to <72 months of age.

Protection of trial subjects:

This clinical study was designed and shall be implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice, with applicable local regulations including Norma Oficial Mexicana NOM-012-SSA3-2012, Novartis codes on protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki (European Council 2001, US Code of Federal Regulations, ICH 1997).

Child's personal information will not be revealed and is protected under the "Federal Law of Protection of Personal Information in Possession of Individuals" published in "El Diario Oficial de la Federacion (Official Journal of the Federation)" the 5th July of 2010, in Mexico.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 October 2014
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	Mexico: 287
Worldwide total number of subjects	287
EEA total number of subjects	0

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)	125
Children (2-11 years)	162
Adolescents (12-17 years)	0

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled from 3 study centers in Mexico.

Pre-assignment

Screening details:

All enrolled subjects were included in study.

Period 1

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

Blinding implementation details:

The trial is designed as an observer-blind study. Unblinded designated qualified health care personnel were responsible for administering the study vaccines to subjects. They were instructed not to reveal the identity of vaccines either to the subject and/or parent(s)/legal guardian(s) or the investigative site personnel involved in the trial monitoring, processing samples and performing immunogenicity assays etc, except in an emergency up until completion of the trial and final data review.

Arms

Are arms mutually exclusive?	Yes
Arm title	aTIV (6 Months to < 72 Months)

Arm description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of aTIV to be administered.

Arm type	Experimental
Investigational medicinal product name	Fluad
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

6 to <36 months: 0.25 mL
≥36 to <72 months: 0.5mL

Arm title	TIV (6 Months to < 72 Months)
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Arm description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of TIV to be administered.

Arm type	Active comparator
Investigational medicinal product name	Fluzone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

6 to <36 months: 0.25 mL
≥36 to <72 months: 0.5mL

Number of subjects in period 1	aTIV (6 Months to < 72 Months)	TIV (6 Months to < 72 Months)
Started	144	143
Completed	139	134
Not completed	5	9
Consent withdrawn by subject	3	6
Lost to follow-up	2	2
Protocol deviation	-	1

Baseline characteristics

Reporting groups

Reporting group title	aTIV (6 Months to < 72 Months)
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Reporting group description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of aTIV to be administered.

Reporting group title	TIV (6 Months to < 72 Months)
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Reporting group description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of TIV to be administered.

Reporting group values	aTIV (6 Months to < 72 Months)	TIV (6 Months to < 72 Months)	Total
Number of subjects	144	143	287
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)	63	62	125
Children (2-11 years)	81	81	162
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: months			
arithmetic mean	29.5	30.1	
standard deviation	± 18.2	± 19.1	-
Gender categorical			
Units: Subjects			
Female	68	72	140
Male	76	71	147

End points

End points reporting groups

Reporting group title	aTIV (6 Months to < 72 Months)
Reporting group description: A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of aTIV to be administered.	
Reporting group title	TIV (6 Months to < 72 Months)
Reporting group description: A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of TIV to be administered.	
Subject analysis set title	All Enrolled Set
Subject analysis set type	Intention-to-treat
Subject analysis set description: All screened subjects who provide informed consent and provide demographic and/or baseline screening assessments, regardless of the subject's randomization and treatment status in the study and received a Subject ID.	
Subject analysis set title	Solicited Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects in the Exposed Set with any solicited adverse event data and/or indicators of solicited adverse events.	
Subject analysis set title	Unsolicited Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects in the Exposed Set with any unsolicited adverse event data.	
Subject analysis set title	Per Protocol Set (PPS)
Subject analysis set type	Per protocol
Subject analysis set description: All subjects in the Enrolled Set who: - receive a study vaccination and provide immunogenicity data on day 1 and day 22 (non-naïve subjects)/50 (naïve subjects); - are not excluded due to reasons defined prior to unblinding or analysis, such as protocol deviations, early termination, withdrawal of informed consent, etc.	
Subject analysis set title	Naïve_aTIV (6 Months to <36 Months)
Subject analysis set type	Safety analysis
Subject analysis set description: A 0.25 mL (for children 6 to <36 months old) dose of aTIV to be administered.	
Subject analysis set title	Naïve_aTIV (≥ 36 Months to < 72 Months)
Subject analysis set type	Safety analysis
Subject analysis set description: A 0.5 mL (for children ≥36 months to < 72 months old) dose of aTIV to be administered.	
Subject analysis set title	Naïve_TIV (6 Months to < 36 Months)
Subject analysis set type	Safety analysis
Subject analysis set description: A 0.25 mL (for children 6 to <36 months old) dose of TIV to be administered.	
Subject analysis set title	Naïve_TIV (≥ 36 Months to < 72 Months)
Subject analysis set type	Safety analysis
Subject analysis set description: A 0.5 mL (for children ≥ 36 months to < 72 months old) dose of TIV to be administered.	
Subject analysis set title	Non-naïve_aTIV (6 Months to <36 Months)
Subject analysis set type	Safety analysis

Subject analysis set description:

A 0.25 mL (for children 6 months to < 36 months old) dose of aTIV to be administered.

Subject analysis set title	Non-naïve_aTIV (≥ 36 Months to < 72 Months)
Subject analysis set type	Safety analysis

Subject analysis set description:

A 0.5 mL (for children ≥ 36 months to < 72 months old) dose of aTIV to be administered.

Subject analysis set title	Non-naïve_TIV (6 Months to <36 Months)
Subject analysis set type	Safety analysis

Subject analysis set description:

A 0.25 mL (for children 6 to < 36 months old) dose of TIV to be administered.

Subject analysis set title	Non-naïve_TIV (≥ 36 Months to < 72 Months)
Subject analysis set type	Safety analysis

Subject analysis set description:

A 0.5 mL (for children ≥ 36 months to < 72 months old) dose of TIV to be administered.

Subject analysis set title	Naïve_aTIV (6 Months to < 72 Months)
Subject analysis set type	Safety analysis

Subject analysis set description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of aTIV to be administered.

Subject analysis set title	Naïve_TIV (6 Months to < 72 Months)
Subject analysis set type	Safety analysis

Subject analysis set description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of TIV to be administered.

Subject analysis set title	Non-naïve_aTIV (6 Months to < 72 Months)
Subject analysis set type	Safety analysis

Subject analysis set description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of aTIV to be administered.

Subject analysis set title	Non-naïve_TIV (6 Months to < 72 Months)
Subject analysis set type	Safety analysis

Subject analysis set description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of TIV to be administered.

Primary: 1. Number of Naïve Subjects 6 to < 36 Months Old Reporting Solicited Local and Systemic Adverse Events (AEs) From Day 1 to Day 7 Following Each Vaccination.

End point title	1. Number of Naïve Subjects 6 to < 36 Months Old Reporting Solicited Local and Systemic Adverse Events (AEs) From Day 1 to Day 7 Following Each Vaccination. ^[1]
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End point description:

Number of naïve subjects 6 to < 36 months old reporting solicited local and systemic AEs from Day 1 to Day 7 after first vaccination and from Day 29 to Day 35 after second vaccination.

Analysis performed on the Solicited Safety Set.

End point type	Primary
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End point timeframe:

From Day 1 to Day 7 by 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: No statistical analyses for this end point.

End point values	Naïve_aTIV (6 Months to <36 Months)	Naïve_TIV (6 Months to < 36 Months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	69		
Units: Participants				
Any Local (Vac-1)	35	20		
Any Local (Vac-2, N= 67,67)	21	15		
Injection site ecchymosis (Vac-1, N= 65,69)	2	2		
Injection site ecchymosis (Vac-2, N= 66,67)	1	1		
Injection site induration (Vac-1, N= 66,69)	5	6		
Injection site induration (Vac-2, N= 66,67)	3	4		
Injection site swelling (Vac-1, N= 65,69)	8	2		
Injection site swelling (Vac-2, N= 66,67)	2	2		
Injection site erythema (Vac-1, N= 64,69)	9	8		
Injection site erythema (Vac-2, N= 66,67)	7	4		
Injection site tenderness (Vac-1, N= 66,69)	26	16		
Injection site tenderness (Vac-1, N= 66,66)	17	13		
Any Systemic (Vac-1)	34	27		
Any Systemic (Vac-2, N= 67,67)	27	22		
Body Temperature ($\geq 40^{\circ}$ C) (Vac-1, N= 67,68)	0	0		
Body Temperature ($\geq 40^{\circ}$ C) (Vac-2, N= 67,67)	0	0		
Fever (Vac-1)	7	5		
Fever (Vac-2, N= 67,67)	7	2		
Change in eating habits (Vac-1, N= 67,69)	14	4		
Change in eating habits (Vac-2, N= 66,67)	11	7		
Diarrhea (Vac-1, N= 67,69)	15	15		
Diarrhea (Vac-2, N= 66,67)	11	11		
Irritability (Vac-1, N= 67,69)	18	13		
Irritability (Vac-2, N= 66,67)	17	9		
Persistent Crying (Vac-1, N= 67,69)	15	11		
Persistent Crying (Vac-2, N= 66,67)	11	9		
Sleepiness (Vac-1, N= 67,68)	10	11		
Sleepiness (Vac-2, N= 65,67)	8	9		
Vomiting (Vac-1, N= 67,68)	5	4		
Vomiting (Vac-2, N= 65,67)	2	2		
Prevention of Pain and/or Fever (Vac-1, N= 67,67)	2	2		
Prevention of Pain and/or Fever (Vac-2, N= 64,67)	3	2		
Treatment of Pain and/or Fever (Vac-1, N= 67,67)	9	7		
Treatment of Pain and/or Fever (Vac-2, N= 66,67)	10	2		

Statistical analyses

No statistical analyses for this end point

Primary: 2. Number of Non-naïve Subjects 6 to < 36 Months Old Reporting Solicited Local and Systemic AEs From Day 1 to Day 7 After Vaccination.

End point title	2. Number of Non-naïve Subjects 6 to < 36 Months Old Reporting Solicited Local and Systemic AEs From Day 1 to Day 7 After Vaccination. ^[2]
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End point description:

Number of non-naïve subjects 6 to <36 months old reporting solicited local and systemic adverse events (AEs) from Day 1 to Day 7 after vaccination.

Analysis performed on the Solicited Safety Set.

End point type	Primary
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End point timeframe:

From Day 1 to Day 7.

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: No statistical analyses for this end point.

End point values	Non-naïve_aTIV (6 Months to <36 Months)	Non-naïve_TIV (6 Months to <36 Months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	22		
Units: Participants				
Any Local	10	7		
Injection site ecchymosis	0	1		
Injection site induration	2	0		
Injection site swelling	1	1		
Injection site erythema	2	4		
Injection site tenderness (N= 22,21)	9	4		
Any Systemic	9	7		
Body Temperature ($\geq 40.0^{\circ}\text{C}$)	0	0		
Fever	6	1		
Change in eating habits	4	3		
Diarrhea	3	6		
Irritability	4	3		
Persistent Crying	1	1		
Sleepiness	2	0		
Vomiting (N= 21,21)	1	1		
Prevention of Pain and/or Fever (N= 21,22)	0	0		
Treatment of Pain and/or Fever (N= 21,22)	2	1		

Statistical analyses

No statistical analyses for this end point

Primary: 3. Number of Naïve Subjects ≥ 36 Months to < 72 Months Old Reporting Solicited Local and Systemic AEs From Day 1 to Day 7 Following Each Vaccination.

End point title	3. Number of Naïve Subjects ≥ 36 Months to < 72 Months Old Reporting Solicited Local and Systemic AEs From Day 1 to Day 7 Following Each Vaccination. ^[3]
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End point description:

Number of naïve subjects ≥36 months to < 72 months old reporting solicited local and systemic AEs from Day 1 to Day 7 after first vaccination and from Day 29 to Day 35 after second vaccination. Analysis performed on the Solicited Safety Set.

End point type	Primary
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End point timeframe:

From Day 1 to Day 7 by 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: No statistical analyses for this end point.

End point values	Naïve_aTIV (≥ 36 Months to < 72 Months)	Naïve_TIV (≥ 36 Months to < 72 Months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	4		
Units: Participants				
Any Local (Vac-1)	5	2		
Any Local (Vac-2, N= 6,3)	4	2		
Injection site ecchymosis (Vac-1)	0	0		
Injection site ecchymosis (Vac-2, N= 6,3)	0	0		
Injection site induration (Vac-1)	2	1		
Injection site induration (Vac-2, N= 6,3)	2	0		
Injection site swelling (Vac-1)	2	0		
Injection site swelling (Vac-2, N= 6,3)	0	0		
Injection site erythema (Vac-1)	1	0		
Injection site erythema (Vac-2, N= 6,3)	0	0		
Injection site pain (Vac-1)	3	2		
Injection site pain (Vac-2, N= 6,3)	3	2		
Any Systemic (Vac-1)	3	1		
Any Systemic (Vac-2, N= 6,3)	2	0		
Fatigue (Vac-1)	1	1		
Fatigue (Vac-2, N= 6,3)	2	0		
Myalgia (Vac-1)	2	0		
Myalgia (Vac-2, N= 6,3)	1	0		
Arthralgia (Vac-1)	0	0		

Arthralgia (Vac-2, N= 6,2)	0	0		
Headache (Vac-1)	1	1		
Headache (Vac-2, N= 6,2)	1	0		
Body Temperature ($\geq 40.0^{\circ}\text{C}$) (Vac-1)	0	0		
Body Temperature ($\geq 40.0^{\circ}\text{C}$) (Vac-2, N= 6,3)	0	0		
Fever (Vac-1)	2	0		
Fever (Vac-2, N= 6,3)	1	0		
Chills (Vac-1)	0	0		
Chills (Vac-2, N= 6,3)	0	0		
Change in Eating Habits (Vac-1, N= 5,4)	2	0		
Change in Eating Habits (Vac-2, N= 6,3)	0	0		
Diarrhea (Vac-1)	0	0		
Diarrhea (Vac-2, N= 6,3)	0	0		
Vomiting (Vac-1)	0	0		
Vomiting (Vac-2, N= 6,3)	0	0		
Prevention of Pain and/or Fever (Vac-1, N= 6,2)	1	0		
Prevention of Pain and/or Fever (Vac-2, N= 4,2)	0	0		
Treatment of Pain and/or Fever (Vac-1, N= 6,2)	0	0		
Treatment of Pain and/or Fever (Vac-2, N= 5,2)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: 4. Number of Non-naïve Subjects ≥ 36 Months to < 72 Months Old Reporting Solicited Local and Systemic AEs From Day 1 to Day 7 Following Each Vaccination.

End point title	4. Number of Non-naïve Subjects ≥ 36 Months to < 72 Months Old Reporting Solicited Local and Systemic AEs From Day 1 to Day 7 Following Each Vaccination. ^[4]
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End point description:

Number of non-naïve subjects ≥ 36 months to < 72 months old reporting solicited local and systemic AEs from Day 1 to Day 7 after vaccination.
Analysis performed on the Solicited Safety Set.

End point type	Primary
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End point timeframe:

From Day 1 to Day 7.

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: No statistical analyses for this end point.

End point values	Non-naïve_aTIV (≥ 36 Months to < 72 Months)	Non-naïve_TIV (≥ 36 Months to < 72 Months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	41		
Units: Numbers				
Any Local	17	20		
Injection site ecchymosis	2	1		
Injection site induration	6	3		
Injection site swelling	4	3		
Injection site erythema (N= 43,40)	6	7		
Injection site pain (N= 44,40)	14	16		
Injection site tenderness	0	0		
Any Systemic	15	7		
Fatigue (N= 44,40)	6	2		
Myalgia (N= 44, 40)	7	0		
Arthralgia (N= 44, 40)	4	0		
Headache (N= 44, 40)	3	2		
Body Temperature (≥ 40.0°C) (N= 44, 40)	0	0		
Fever	2	1		
Chills (N= 44, 40)	2	0		
Change in eating habits (N= 44, 39)	8	3		
Diarrhea (N= 44, 39)	4	3		
Vomiting (N= 44, 40)	2	1		
Prevention of Pain and/or Fever (N= 42, 40)	0	0		
Treatment of Pain and/or Fever (N=42, 40)	5	0		

Statistical analyses

No statistical analyses for this end point

Primary: 5. Number of Naïve Subjects Aged 6 to < 72 Months Reporting All Unsolicited AEs From Day 1 to Day 50.

End point title	5. Number of Naïve Subjects Aged 6 to < 72 Months Reporting All Unsolicited AEs From Day 1 to Day 50. ^[5]
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End point description:

Number of naïve subjects aged 6 to < 72 months reporting all unsolicited AEs, medically attended AEs, AE leading to study withdrawal and serious AEs (SAEs) from Day 1 to Day 50.
Analysis performed on the Unsolicited Safety Set.

End point type	Primary
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End point timeframe:

From Day 1 to Day 50.

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: No statistical analyses for this end point.

End point values	Naïve_aTIV (6 Months to < 72 Months)	Naïve_TIV (6 Months to < 72 Months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	74	73		
Units: Numbers				
Any AE	33	28		
At least Possibly related AE	4	4		
SAE	0	0		
At least possibly related SAE	0	0		
AE leading to study withdrawal	0	0		
Medically attended AE	26	25		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: 6. Number of Non-naïve Subjects Aged 6 to < 72 Months Reporting All Unsolicited AEs From Day 1 to Day 22.

End point title	6. Number of Non-naïve Subjects Aged 6 to < 72 Months Reporting All Unsolicited AEs From Day 1 to Day 22. ^[6]
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End point description:

Number of non-naïve subjects aged 6 to < 72 months reporting all unsolicited AEs, medically attended AEs, AE leading to study withdrawal and serious AEs (SAEs) from Day 1 to Day 22.
Analysis performed on the Unsolicited Safety Set.

End point type	Primary
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End point timeframe:

From Day 1 to Day 22.

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: No statistical analyses for this end point.

End point values	Non-naïve_aTIV (6 Months to < 72 Months)	Non-naïve_TIV (6 Months to < 72 Months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	66	64		
Units: Numbers				
Any AE	9	6		
At least Possibly related AE	2	0		
SAE	0	0		
At least possibly related SAE	0	0		
AE leading to study withdrawal	0	0		
Medically attended AE	3	4		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Geometric Mean Titers (GMTs), in All Three Homologous Virus Strains in Subjects 6 to < 72 Months of Age.

End point title	7. Geometric Mean Titers (GMTs), in All Three Homologous Virus Strains in Subjects 6 to < 72 Months of Age.
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End point description:

Antibody response was assessed in terms of geometric mean titers (GMTs) in all three homologous virus strains, 21 days after last immunization, in subjects 6 to <72 months of age.

The study is considered a success if the 21 days after last immunization GMT ratios of aTIV relative to TIV demonstrate as non-inferior with the lower limit of the two sided 95% CI above 0.67 (-0.176 on log10 scale) for each vaccine strain (Center for Biologics Evaluation and Research, CBER Guideline on Seasonal Vaccines May 2007).

Analysis performed on the Per Protocol Set.

End point type	Secondary
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End point timeframe:

Day 1 and Day 22 (vaccine non-naïve subjects) or Day 50 (vaccine naïve subjects) post vaccination

End point values	aTIV (6 Months to < 72 Months)	TIV (6 Months to < 72 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	112		
Units: Titers				
geometric mean (confidence interval 95%)				
A/H1N1 (Day 1) (N= 113,112)	14 (11 to 19)	15 (11 to 20)		
A/H1N1 (Day 22 or Day 50)	675 (536 to 849)	166 (132 to 208)		
A/H3N2 (Day 1)	59 (40 to 86)	55 (38 to 81)		
A/H3N2 (Day 22 or Day 50)	1280 (1077 to 1521)	495 (417 to 588)		
B (Day 1)	7.47 (6.41 to 8.71)	6.92 (5.95 to 8.06)		
B (Day 22 or Day 50)	76 (61 to 93)	16 (13 to 20)		

Statistical analyses

Statistical analysis title	aTIV (6 to < 72 Months), TIV (6 to < 72 Months)
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Statistical analysis description:

Geometric mean titers (GMTs), in H1N1 strain of all the three strains in Subjects 6 to < 72 months of Age.

Comparison groups	aTIV (6 Months to < 72 Months) v TIV (6 Months to < 72 Months)
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Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[7]
Method	ANCOVA
Parameter estimate	Ratio of GMTs
Point estimate	4.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	5.51

Notes:

[7] - Hypothesis: Demonstrate non-inferiority (NI) of aTIV to TIV:

$H_0 : \mu_{Ai} - \mu_{Bi} \leq -0.176$ (Null) $H_1 : \mu_{Ai} - \mu_{Bi} \geq -0.176$ (alternative) (i= H1N1, H3N2, B) μ_A and μ_B are means of log10-transformed titers 21 days after last vaccination of the aTIV & TIV vaccine groups respectively. NI is claimed if LL of 95% CI for GMT ratios is >0.67 .

Significance level is $\alpha = 2.5\%$ (1-sided), which needs no further adjustment for multiplicity as to reach NI, above hypothesis needs to be rejected for all 3 strains.

Statistical analysis title	aTIV (6 to < 72 Months), TIV (6 to < 72 Months)
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Statistical analysis description:

Geometric mean titers (GMTs), in H3N2 strain of all the three strains in Subjects 6 to < 72 months of Age.

Comparison groups	aTIV (6 Months to < 72 Months) v TIV (6 Months to < 72 Months)
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[8]
Method	ANCOVA
Parameter estimate	Ratio of GMTs
Point estimate	2.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.05
upper limit	3.25

Notes:

[8] - Hypothesis: Demonstrate non-inferiority (NI) of aTIV to TIV:

$H_0 : \mu_{Ai} - \mu_{Bi} \leq -0.176$ (Null) $H_1 : \mu_{Ai} - \mu_{Bi} \geq -0.176$ (alternative) (i= H1N1, H3N2, B) μ_A and μ_B are means of log10-transformed titers 21 days after last vaccination of the aTIV & TIV vaccine groups respectively. NI is claimed if LL of 95% CI for GMT ratios is >0.67 .

Significance level is $\alpha = 2.5\%$ (1-sided), which needs no further adjustment for multiplicity as to reach NI, above hypothesis needs to be rejected for all 3 strains.

Statistical analysis title	aTIV (6 to < 72 Months), TIV (6 to < 72 Months)
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Statistical analysis description:

Geometric mean titers (GMTs), in B strain of all the three strains in Subjects 6 to < 72 months of Age.

Comparison groups	aTIV (6 Months to < 72 Months) v TIV (6 Months to < 72 Months)
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[9]
Method	ANCOVA
Parameter estimate	Ratio of GMTs
Point estimate	4.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.52
upper limit	6.2

Notes:

[9] - Hypothesis: Demonstrate non-inferiority (NI) of aTIV to TIV:

$H_0 : \mu_{Ai} - \mu_{Bi} \leq -0.176$ (Null) $H_1 : \mu_{Ai} - \mu_{Bi} \geq -0.176$ (alternative) (i= H1N1, H3N2, B) μ_A and μ_B are means of log10-transformed titers 21 days after last vaccination of the aTIV & TIV vaccine groups respectively. NI is claimed if LL of 95% CI for GMT ratios is >0.67 .

Significance level is $\alpha = 2.5\%$ (1-sided), which needs no further adjustment for multiplicity as to reach NI, above hypothesis needs to be rejected for all 3 strains.

Secondary: 8. Percentages of Subjects Achieving Seroconversion in HI Titers and Vaccine Group Differences at Day 1 and 21 Days After Last Vaccination with aTIV or TIV in Naïve and Non-naïve Subjects.

End point title	8. Percentages of Subjects Achieving Seroconversion in HI Titers and Vaccine Group Differences at Day 1 and 21 Days After Last Vaccination with aTIV or TIV in Naïve and Non-naïve Subjects.
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End point description:

Percentages of subjects with seroconversion in all three homologous virus strains, 21 days after last immunization, in subjects 6 to <72 months of age, defined as: HI ≥ 40 subject with a pre-vaccination HI titer <10 ; a minimum 4-fold increase HI titer for subjects with a prevaccination HI titer ≥ 10 , on Day 22 (non-naïve subjects) or Day 50 (naïve subjects), as applicable.

Analysis performed on the Per Protocol Set.

End point type	Secondary
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End point timeframe:

Day 1 and Day 22 (vaccine non-naïve subjects) or Day 50 (vaccine naïve subjects) post vaccination.

End point values	aTIV (6 Months to <72 Months)	TIV (6 Months to <72 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	112		
Units: Percentages of subjects				
number (confidence interval 95%)				
H1N1 strain (N= 113,112)	90 (83.2 to 95)	75 (65.9 to 82.7)		
H3N2 strain	77 (68.4 to 84.5)	67 (57.4 to 75.6)		
B strain	78 (69.4 to 85.3)	22 (15 to 31.2)		

Statistical analyses

Statistical analysis title	aTIV (6 to <72 Months), TIV (6 to <72 Months)
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Statistical analysis description:

Percentage of subjects achieving seroconversion in H1N1 strain after last vaccination with aTIV or TIV in naïve and non-naïve subjects.

Comparison groups	aTIV (6 Months to <72 Months) v TIV (6 Months to <72 Months)
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Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[10]
Method	Loglinear model
Parameter estimate	Vaccine Group Differences
Point estimate	17
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.1
upper limit	26.3

Notes:

[10] - The following hypotheses should be tested to demonstrate non-inferiority of aTIV to TIV:
 $H_{0i}: \pi_{i1} > \pi_{i2} - 0.1$ vs. $H_{1i}: \pi_{i1} > \pi_{i2} - 0.1$ where H_{0i} and H_{1i} represent the null and the alternative hypothesis (respectively) of the non-inferiority objective and π_{i1} and π_{i2} represent the seroresponse rates 21 days after last immunization of the aTIV and TIV vaccine groups respectively in the i-th strain (H1N1, H3N2, B). The non-inferiority criterion is -0.1 (i.e., -10%).

Statistical analysis title	aTIV (6 to < 72 Months), TIV (6 to < 72 Months)
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Statistical analysis description:

Percentage of subjects achieving seroconversion in H3N2 strain after last vaccination with aTIV or TIV in naïve and non-naïve subjects.

Comparison groups	aTIV (6 Months to < 72 Months) v TIV (6 Months to < 72 Months)
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[11]
Method	Loglinear model
Parameter estimate	Vaccine Group Differences
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	21

Notes:

[11] - The following hypotheses should be tested to demonstrate non-inferiority of aTIV to TIV:
 $H_{0i}: \pi_{i1} > \pi_{i2} - 0.1$ vs. $H_{1i}: \pi_{i1} > \pi_{i2} - 0.1$ where H_{0i} and H_{1i} represent the null and the alternative hypothesis (respectively) of the non-inferiority objective and π_{i1} and π_{i2} represent the seroresponse rates 21 days after last immunization of the aTIV and TIV vaccine groups respectively in the i-th strain (H1N1, H3N2, B). The non-inferiority criterion is -0.1 (i.e., -10%).

Statistical analysis title	aTIV (6 to < 72 Months), TIV (6 to < 72 Months)
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Statistical analysis description:

Percentage of subjects achieving seroconversion in B strains after last vaccination with aTIV or TIV in naïve and non naïve subjects.

Comparison groups	aTIV (6 Months to < 72 Months) v TIV (6 Months to < 72 Months)
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[12]
Method	Loglinear model
Parameter estimate	Vaccine Group Differences
Point estimate	58

Confidence interval	
level	95 %
sides	2-sided
lower limit	47.5
upper limit	68.5

Notes:

[12] - The following hypotheses should be tested to demonstrate non-inferiority of aTIV to TIV:
 $H_{0i}: \mu_{i1} > \mu_{i2} - 0.1$ vs. $H_{1i}: \mu_{i1} > \mu_{i2} - 0.1$ where H_{0i} and H_{1i} represent the null and the alternative hypothesis (respectively) of the non-inferiority objective and μ_{i1} and μ_{i2} represent the seroresponse rates 21 days after last immunization of the aTIV and TIV vaccine groups respectively in the i-th strain (H1N1, H3N2, B). The non-inferiority criterion is -0.1 (i.e., -10%).

Secondary: 9. Geometric Mean Ratios (GMRs) of HI and Vaccine Group Differences at Day 1 and 21 Days After Last Vaccination With aTIV or TIV in Naïve and Non-naïve Subjects.

End point title	9. Geometric Mean Ratios (GMRs) of HI and Vaccine Group Differences at Day 1 and 21 Days After Last Vaccination With aTIV or TIV in Naïve and Non-naïve Subjects.
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End point description:

GMRs of HI, day 22/day 1 (non-naïve subjects) or day 50/day 1 (naïve subjects) in all three homologous virus strains, 21 days after last immunization, in subjects 6 to <72 months of age. Being non-inferiority of aTIV to TIV established, GMT ratio of aTIV relative to TIV in all three homologous virus strains, 21 days after last immunization in subjects 6 to <72 months of age was evaluated using margins greater than the non-inferiority cut-off of 0.67.

Analysis performed on the Per Protocol Set.

End point type	Secondary
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End point timeframe:

Day 1 and Day 22 (vaccine non-naïve subjects) or Day 50 (vaccine naïve subjects) post vaccination.

End point values	aTIV (6 Months to < 72 Months)	TIV (6 Months to < 72 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	112		
Units: Ratios				
number (confidence interval 95%)				
H1N1 strain (N= 113, 112)	46 (34 to 62)	11 (8.12 to 15)		
H3N2 strain	21 (16 to 28)	8.39 (6.26 to 11)		
B strain	10 (8.25 to 13)	2.3 (1.84 to 2.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Percentages of Subjects With a HI Titer ≥ 40 , ≥ 110 and ≥ 330 and Vaccine Group Differences at Day 1 and 21 Days After Last Vaccination With aTIV or TIV in Naïve and Non-naïve Subjects.

End point title	10. Percentages of Subjects With a HI Titer ≥ 40 , ≥ 110 and ≥ 330 and Vaccine Group Differences at Day 1 and 21 Days After
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End point description:

Percentage of subjects with a HI titer ≥ 40 , ≥ 110 and ≥ 330 on Day 1, Day 22 (non naïve subjects) or Day 50 (naïve subjects), in all three homologous virus strains, 21 days after last immunization, in subjects 6 to <72 months of age.

End point type

Secondary

End point timeframe:

Day 1 and Day 22 (vaccine non-naïve subjects) or Day 50 (vaccine naïve subjects) post vaccination.

End point values	aTIV (6 Months to < 72 Months)	TIV (6 Months to < 72 Months)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	112		
Units: Percentages of subjects				
number (confidence interval 95%)				
H1N1 strain (HI titer ≥ 40 , Day 1) (N= 113, 112)	32 (23.4 to 41.3)	33 (24.4 to 42.6)		
H1N1 strain (HI titer ≥ 40 , Day 22 or Day 50)	99 (95.2 to 99.98)	88 (81 to 93.7)		
H1N1 strain (HI titer ≥ 110 , Day 1) (N= 113, 112)	19 (11.9 to 27)	20 (12.7 to 28.2)		
H1N1 strain (HI titer ≥ 110 , Day 22 or Day 50)	96 (90.1 to 98.6)	68 (58.4 to 76.4)		
H1N1 strain (HI titer ≥ 330 , Day 1)	4 (1.5 to 10)	7 (3.1 to 13.6)		
H1N1 strain (HI titer ≥ 330 , Day 22 or Day 50)	78 (69.4 to 85.3)	37 (27.7 to 46.2)		
H3N2 strain (HI titer ≥ 40 , Day 1)	56 (46.5 to 65.4)	58 (48.3 to 67.3)		
H3N2 strain (HI titer ≥ 40 , Day 22 or Day 50)	100 (96.8 to 100)	97 (92.4 to 99.4)		
H3N2 strain (HI titer ≥ 110 , Day 1)	44 (34.6 to 53.5)	44 (34.4 to 53.4)		
H3N2 strain (HI titer ≥ 110 , Day 22 or Day 50)	99 (95.2 to 99.98)	84 (75.8 to 90.2)		
H3N2 strain (HI titer ≥ 330 , Day 1)	33 (24.8 to 42.8)	30 (22 to 39.8)		
H3N2 strain (HI titer ≥ 330 , Day 22 or Day 50)	86 (78.2 to 91.8)	61 (51 to 69.8)		
B strain (HI titer ≥ 40 , Day 1)	9 (4.3 to 15.5)	9 (4.4 to 15.8)		
B strain (HI titer ≥ 40 , Day 22 or Day 50)	84 (76.2 to 90.4)	32 (23.6 to 41.6)		
B strain (HI titer ≥ 110 , Day 1)	2 (0.21 to 6.2)	1 (0.02 to 4.9)		
B strain (HI titer ≥ 110 , Day 22 or Day 50)	43 (33.7 to 52.6)	6 (2.5 to 12.5)		
B strain (HI titer ≥ 330 , Day 1)	0 (0 to 3.2)	0 (0 to 3.2)		
B strain (HI titer ≥ 330 , Day 22 or Day 50)	8 (3.7 to 14.5)	0 (0 to 3.2)		

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study; Day 1 - Day 50 (naïve subjects) and Day 1 - Day 22 (non-naïve subjects).

Adverse event reporting additional description:

Solicited adverse events were collected daily by the subject parent(s)/legal guardian(s) for 7 consecutive days starting from the day of vaccination/s (day 1 and day 29 for naïve subjects; day 1 for non-naïve subjects).

Unsolicited adverse events were collected from day 1 to day 50 for naïve subjects, from day 1 to day 22 for non-naïve subjects.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19
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Reporting groups

Reporting group title	Naïve_aTIV (6 Months to < 72 Months)
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Reporting group description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of aTIV to be administered.

Reporting group title	Naïve_TIV (6 Months to < 72 Months)
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Reporting group description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of TIV to be administered.

Reporting group title	Non-naïve_aTIV (6 Months to < 72 Months)
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Reporting group description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of aTIV to be administered.

Reporting group title	Non-naïve_TIV (6 Months to < 72 Months)
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Reporting group description:

A 0.25 mL (for children 6 to <36 months old) and 0.5 mL (for children ≥36 months to < 72 months old) dose of TIV to be administered.

Serious adverse events	Naïve_aTIV (6 Months to < 72 Months)	Naïve_TIV (6 Months to < 72 Months)	Non-naïve_aTIV (6 Months to < 72 Months)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 77 (0.00%)	0 / 78 (0.00%)	0 / 67 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Non-naïve_TIV (6 Months to < 72 Months)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 64 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from	0		

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

Non-serious adverse events	Naïve_aTIV (6 Months to < 72 Months)	Naïve_TIV (6 Months to < 72 Months)	Non-naïve_aTIV (6 Months to < 72 Months)
Total subjects affected by non-serious adverse events subjects affected / exposed	58 / 77 (75.32%)	52 / 78 (66.67%)	35 / 67 (52.24%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	16 / 77 (20.78%)	14 / 78 (17.95%)	2 / 67 (2.99%)
occurrences (all)	24	21	0
General disorders and administration site conditions			
Crying			
subjects affected / exposed	20 / 77 (25.97%)	15 / 78 (19.23%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	3 / 77 (3.90%)	1 / 78 (1.28%)	6 / 67 (8.96%)
occurrences (all)	1	3	3
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 77 (16.88%)	11 / 78 (14.10%)	8 / 67 (11.94%)
occurrences (all)	14	18	11
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 77 (12.99%)	10 / 78 (12.82%)	8 / 67 (11.94%)
occurrences (all)	12	12	3
Injection site pain			
subjects affected / exposed	33 / 77 (42.86%)	25 / 78 (32.05%)	23 / 67 (34.33%)
occurrences (all)	34	50	20
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 77 (15.58%)	2 / 78 (2.56%)	5 / 67 (7.46%)
occurrences (all)	6	12	4

Pyrexia subjects affected / exposed occurrences (all)	16 / 77 (20.78%) 12	11 / 78 (14.10%) 22	9 / 67 (13.43%) 2
Gastrointestinal disorders Diarrhoea alternative assessment type: Systematic subjects affected / exposed occurrences (all) Vomiting alternative assessment type: Systematic subjects affected / exposed occurrences (all)	22 / 77 (28.57%) 35 7 / 77 (9.09%) 6	21 / 78 (26.92%) 36 6 / 78 (7.69%) 11	7 / 67 (10.45%) 10 4 / 67 (5.97%) 2
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	6 / 77 (7.79%) 9 2 / 77 (2.60%) 4	8 / 78 (10.26%) 6 4 / 78 (5.13%) 2	2 / 67 (2.99%) 0 0 / 67 (0.00%) 1
Psychiatric disorders Eating disorder subjects affected / exposed occurrences (all) Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all)	20 / 77 (25.97%) 12 25 / 77 (32.47%) 25	9 / 78 (11.54%) 33 17 / 78 (21.79%) 42	12 / 67 (17.91%) 6 4 / 67 (5.97%) 3
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	0 / 77 (0.00%) 0 2 / 77 (2.60%) 0	0 / 78 (0.00%) 0 0 / 78 (0.00%) 3	4 / 67 (5.97%) 0 7 / 67 (10.45%) 0
Infections and infestations			

Conjunctivitis			
subjects affected / exposed	0 / 77 (0.00%)	4 / 78 (5.13%)	0 / 67 (0.00%)
occurrences (all)	4	0	0
Gastroenteritis			
subjects affected / exposed	4 / 77 (5.19%)	3 / 78 (3.85%)	0 / 67 (0.00%)
occurrences (all)	3	4	0
Nasopharyngitis			
subjects affected / exposed	16 / 77 (20.78%)	8 / 78 (10.26%)	2 / 67 (2.99%)
occurrences (all)	9	18	2
Pharyngitis			
subjects affected / exposed	6 / 77 (7.79%)	10 / 78 (12.82%)	0 / 67 (0.00%)
occurrences (all)	10	7	0

Non-serious adverse events	Non-naïve_TIV (6 Months to < 72 Months)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 64 (48.44%)		
Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
Crying			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	6		
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 64 (17.19%)		
occurrences (all)	8		
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 64 (4.69%)		
occurrences (all)	8		
Injection site pain			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>20 / 64 (31.25%)</p> <p>23</p>			
<p>Injection site swelling</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>4 / 64 (6.25%)</p> <p>5</p>			
<p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 64 (3.13%)</p> <p>11</p>			
<p>Gastrointestinal disorders</p> <p>Diarrhoea</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>9 / 64 (14.06%)</p> <p>7</p> <p>Vomiting</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 64 (3.13%)</p> <p>4</p>			
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 64 (0.00%)</p> <p>2</p> <p>Rhinorrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 64 (1.56%)</p> <p>0</p>			
<p>Psychiatric disorders</p> <p>Eating disorder</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>6 / 64 (9.38%)</p> <p>13</p> <p>Irritability</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>3 / 64 (4.69%)</p> <p>4</p>			
<p>Musculoskeletal and connective tissue disorders</p>			

Arthralgia			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	4		
Myalgia			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	7		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	2 / 64 (3.13%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 February 2014	In V70_50 protocol version 1 the sponsor is defined as "Novartis Vaccines and Diagnostics AG", the protocol is amended to introduce the correct sponsor name: "Novartis Vaccines and Diagnostics".
03 April 2014	Adult and pediatric presentations of Fluzone (0.5 and 0.25 prefilled syringes, respectively) were planned to be used for the study. However, for the required season Sanofi did not produce the Fluzone TIV pediatric presentation (0.25 prefilled syringe) which should have been used for vaccinating subjects 6 to <36 months of age. The study was therefore conducted using Fluzone 5 mL multidose vials for all subjects. Graduated syringes were provided to the sites to aspirate the appropriate volume for vaccination (0.25 mL for subjects 6 to <36 months of age, 0.5 mL for subjects >36 to <72 months of age). The protocol was amended to reflect this change in the comparator vaccine presentation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported