Clinical trial results:
A Phase III, Observer-Blind, Randomized Multicenter Study to Evaluate the Safety of Trivalent Subunit Influenza Vaccines, Produced Either in Mammalian Cell Culture (TIVc) or in Embryonated Eggs (TIV), in Children and Adolescents 3 to <18 Years of Age at Risk for Influenza-Related Complications

Summary

EudraCT number	2013-002080-26
Trial protocol	IT ES
Global end of trial date	31 July 2014

Results information

Result version number	v1
This version publication date	29 June 2016
First version publication date	30 January 2015

Trial information

Trial identification

Sponsor protocol code	V58P15

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01998477
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics
Sponsor organisation address	Via Fiorentina, 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines and Diagnostics , RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics , RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000124-PIP01-07
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	23 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2014
Global end of trial reached?	Yes
Global end of trial date	31 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of 1 or 2 intramuscular doses (administered 4 weeks apart) of either the cell culture derived influenza vaccine TIVc or
the egg derived influenza vaccine TIV in children and adolescents, 3 to < 18 years of age, at risk for influenza related complications.

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with Good Clinical Practice (GCP), and the applicable regulatory requirement(s) for the country in which the trial was conducted according to International Conference on Harmonisation (ICH) guidelines, and applicable Standard Operating Procedures (SOPs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 October 2013
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	Spain: 327
Country: Number of subjects enrolled	Italy: 103
Worldwide total number of subjects	430
EEA total number of subjects	430

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)	214
Adolescents (12-17 years)	216
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 12 centers in Spain and 4 centers from Italy.

Pre-assignment

Screening details:

All enrolled subjects were included in the trial

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	TIVc

Arm description:

Vaccine naive and non-naïve subjects received one or two doses of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)

Arm type	Experimental
Investigational medicinal product name	Cell culture derived influenza vaccine
Investigational medicinal product code	V58
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

A 0.5 mL dose of Madin Darby Canine Kidney (MDCK) cell culture derived subunit influenza vaccine TIVc intramuscular (IM) injection.

Arm title	TIVe

Arm description:

Vaccine naive and non-naïve subjects received one or two doses of egg derived trivalent subunit influenza vaccine formulation (TIVe)

Arm type	Active comparator
Investigational medicinal product name	Egg derived subunit influenza vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

A 0.5 mL dose of a conventional egg derived subunit influenza vaccine (TIV) IM injection

Number of subjects in period 1	TIVc	TIVe
Started	282	148
Completed	272	143
Not completed	10	5
Consent withdrawn by subject	6	-
Lost to follow-up	4	5

Baseline characteristics

Reporting groups	
Reporting group title	TIVc
Reporting group description:	
Vaccine naive and non-naïve subjects received one or two doses of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)	
Reporting group title	TIVe
Reporting group description:	
Vaccine naive and non-naïve subjects received one or two doses of egg derived trivalent subunit influenza vaccine formulation (TIVe)	

Reporting group values	TIVc	TIVe	Total
Number of subjects	282	148	430
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)	140	74	214
Adolescents (12-17 years)	142	74	216
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	8.7	9	
standard deviation	± 4	± 3.9	-
Gender categorical Units: Subjects			
Female	121	63	184
Male	161	85	246

End points

End points reporting groups

Reporting group title	TIVc
Reporting group description:	
Vaccine naive and non-naïve subjects received one or two doses of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)	
Reporting group title	TIVe
Reporting group description:	
Vaccine naive and non-naïve subjects received one or two doses of egg derived trivalent subunit influenza vaccine formulation (TIVe)	
Subject analysis set title	TIVc _inj 1 (3 to <18 Years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Vaccine naïve and non-naive subjects received one or two doses of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)	
Subject analysis set title	TIVc_inj 2 (3 to <18 Years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Vaccine naïve and non-naive subjects received one or two doses of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)	
Subject analysis set title	TIV_inj 1 (3 to <18 Years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Vaccine naïve and non-naive subjects received one or two doses of egg derived trivalent subunit influenza vaccine formulation (TIV)	
Subject analysis set title	TIV_inj 2 (3 to <18 Years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Vaccine naïve and non-naive subjects received one or two doses of egg derived trivalent subunit influenza vaccine formulation (TIV)	
Subject analysis set title	TIVc_Non naive_inj 1 (3 to <6 years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Vaccine non-naïve subjects received one dose of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)	
Subject analysis set title	TIVc_naive_inj 1 (3 to <6 years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Vaccine naïve subjects received two doses of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)	
Subject analysis set title	TIVc_naive_inj 2 (3 to <6 years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Vaccine naïve subjects received two doses of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)	
Subject analysis set title	TIV_Non naive_inj 1 (3 to <6 years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Vaccine nonnaïve subjects received one dose of egg derived trivalent subunit influenza vaccine formulation (TIV)	
Subject analysis set title	TIV_naive_inj 1 (3 to <6 years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine naïve subjects received two doses of egg derived trivalent subunit influenza vaccine formulation (TIV)

Subject analysis set title	TIV_naive_inj 2 (3 to <6 years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine naïve subjects received two doses of egg derived trivalent subunit influenza vaccine formulation (TIV)

Subject analysis set title	TIVc_Non naive_Inj 1 (≥ 6 to < 9 years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine non-naïve subjects received one dose of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)

Subject analysis set title	TIVc_Naive_inj 1 (≥ 6 to < 9 years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine naïve subjects received two doses of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)

Subject analysis set title	TIVc_Naive_inj 2 (≥ 6 to < 9 years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine naïve subjects received two doses of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)

Subject analysis set title	TIV_Non Naive_inj 1 (≥ 6 to < 9 years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine non-naïve subjects received one dose of egg derived trivalent subunit influenza vaccine formulation (TIV)

Subject analysis set title	TIV_Naive_inj 1 (≥ 6 to < 9 years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine naïve subjects received two doses of egg derived trivalent subunit influenza vaccine formulation (TIV)

Subject analysis set title	TIV_Naive_inj 2 (≥ 6 to < 9 years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine naïve subjects received two doses of cell culture derived trivalent subunit influenza vaccine formulation (TIV)

Subject analysis set title	TIVc_Naive (3 to <9 Years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine naïve subjects received one dose of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)

Subject analysis set title	TIVc_Non naive (3 to <9 Years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine non naïve subjects received one dose of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)

Subject analysis set title	TIVc_Non naive (9 to <18 Years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine nonnaïve subjects received one dose of cell culture derived trivalent subunit influenza vaccine formulation (TIVc)

Subject analysis set title	TIV_Naive (3 to <9 Years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine naïve subjects received one dose of egg derived trivalent subunit influenza vaccine formulation

Subject analysis set title	TIV_Non naive (3 to <9 Years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine non naïve subjects received one dose of egg derived trivalent subunit influenza vaccine formulation (TIV)

Subject analysis set title	TIV_Non naive (9 to <18 Years)
Subject analysis set type	Safety analysis

Subject analysis set description:

Vaccine nonnaïve subjects received one dose of egg derived trivalent subunit influenza vaccine formulation (TIV)

Primary: 1.Number of subjects reporting solicited adverse events (AEs) following vaccination with either TIVc or TIV by overall age group

End point title	1.Number of subjects reporting solicited adverse events (AEs) following vaccination with either TIVc or TIV by overall age group[1]

End point description:

Safety was assessed in terms of number of the subjects (3 to < 18 years of age) who reported solicited local, systemic AEs as well as other solicited AEs after receiving one or two doses of either TIVc or TIV

End point type	Primary

End point timeframe:

Day 1 through Day 7 post injection 1 and Day 29 through Day 35 post injection 2

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: Statistical analysis not applicable for the outcome measure.

End point values	TIVc _inj 1 (3 to <18 Years)	TIVc_inj 2 (3 to <18 Years)	TIV_inj 1 (3 to <18 Years)	TIV_inj 2 (3 to <18 Years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	277	83	145	40
Units: Subjects				
Any Local	149	41	89	18
Injection Site Tenderness	25	20	17	6
Injection Site Pain	106	19	65	8
Injection site erythema < 6 years	8	3	4	4
Injection site induration < 6 years	7	5	4	3
Injection site ecchymosis <6 years	6	1	3	3
Injection site erythema >= 6 years	16	5	22	3
Injection site induration >= 6 years	22	3	23	3
Injection site ecchymosis >= 6 years	8	2	5	5
Any Systemic	117	29	55	8
Change in eating habits	12	6	7	2
Chills	32	6	9	0
Diarrhea	19	2	5	3
Irritability	14	5	7	2
Sleepiness	10	5	3	2
Vomiting	18	3	5	1
Arthralgia	24	0	9	0
Fatigue	28	4	16	0
Headache	35	8	24	1
Loss of appetite	30	5	16	2

Myalgia	35	5	14	0
Nausea	21	0	12	0
Body Temp. (>= 38C)	18	2	6	0
Treatment of pain and or Fever	28	7	11	1
Prevention of pain and or Fever	19	2	9	3

Statistical analyses

No statistical analyses for this end point

Primary: 2.Number of subjects reporting solicited adverse events (AEs), following vaccination with either TIVc or TIV by age sub-strata

End point title	2.Number of subjects reporting solicited adverse events (AEs), following vaccination with either TIVc or TIV by age sub-strata[2]

End point description:

Safety was assessed in terms of number of the subjects (3 to <6 years ,≥ 6 to < 9 years and 9 to <18 years of age) who reported solicited local,systemic AEs as well as other solicited AEs after receiving one or two doses of either TIVc or TIV

End point type	Primary

End point timeframe:

Day 1 through Day 7 after any vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis not applicable for the outcome measure.

End point values	TIVc_Non naive_inj 1 (3 to <6 years)	TIVc_naive_inj 1 (3 to <6 years)	TIVc_naive_inj 2 (3 to <6 years)	TIV_Non naive_inj 1 (3 to <6 years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	50	50	19
Units: Subjects				
Any Local	14	19	22	12
Tenderness(N=28,49,49,19,15,15,0,0,0,0,0,0,0,0)	10	15	20	11
Pain(N=0,0,0,0,0,0,26,32,31,16,22,22,0,0)	0	0	0	0
erythema27,50,50,18,15,15,26,34,32,16,23,23,131,61	7	1	3	4
Induration	2	5	5	2
Injection site ecchymosis	2	4	1	2
Any Systemic	10	22	14	9
Change in eating habits	5	7	6	3
Chills28,50,48,19,15,14,25,33,31,16,22,23,138,72	2	5	3	2
Diarrhea28,50,50,19,14,15,26,33,31,16,22,23,137,71	3	1	1	1
Irritability	6	8	5	5
Sleepiness(N=28,49,48,19,15,15,0,0,0,0,0,0,0,0)	4	6	5	3

Vomiting28,50,50,19,15,15,26,33,31,16,22,23,138,72	3	4	2	1
Arthralgia0,0,0,0,0,0,26,32,30,16,20,21,136,72	0	0	0	0
Fatigue0,0,0,0,0,0,26,32,30,16,20,21,137,72	0	0	0	0
Headache0,0,0,0,0,0,26,32,30,16,20,21,138,72	0	0	0	0
Loss appetite0,0,0,0,0,0,26,32,31,16,22,23,1	0	0	0	0
Myalgia0,0,0,0,0,0,26,32,30,16,20,21,138,72	0	0	0	0
Nausea0,0,0,0,0,0,26,32,30,16,20,21,137,72	0	0	0	0
Body Temp. (>= 38C)	4	8	2	3
Treatment of pain and or fever	6	9	3	3

End point values	TIV_naive_inj 1 (3 to <6 years)	TIV_naive_inj 2 (3 to <6 years)	TIVc_Non naive_Inj 1 (≥ 6 to < 9 years)	TIVc_Naive_inj 1 (≥ 6 to < 9 years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	15	15	26	35
Units: Subjects				
Any Local	7	7	16	19
Tenderness(N=28,49,49,19,15,15,0,0,0,0,0,0,0,0)	6	6	0	0
Pain(N=0,0,0,0,0,0,26,32,31,16,22,22,0,0)	0	0	15	18
erythema27,50,50,18,15,15,26,34,32,16,23,23,131,61	0	4	1	3
Induration	2	3	1	4
Injection site ecchymosis	1	3	2	3
Any Systemic	5	5	9	18
Change in eating habits	4	2	0	0
Chills28,50,48,19,15,14,25,33,31,16,22,23,138,72	0	0	3	3
Diarrhea28,50,50,19,14,15,26,33,31,16,22,23,137,71	0	2	1	3
Irritability	2	2	0	0
Sleepiness(N=28,49,48,19,15,15,0,0,0,0,0,0,0,0)	0	2	0	0
Vomiting28,50,50,19,15,15,26,33,31,16,22,23,138,72	0	1	0	3
Arthralgia0,0,0,0,0,0,26,32,30,16,20,21,136,72	0	0	2	4
Fatigue0,0,0,0,0,0,26,32,30,16,20,21,137,72	0	0	2	3
Headache0,0,0,0,0,0,26,32,30,16,20,21,138,72	0	0	1	5
Loss appetite0,0,0,0,0,0,26,32,31,16,22,23,1	0	0	2	8

Myalgia0,0,0,0,0,0,26,32,30,16,20,21,138,72	0	0	4	2
Nausea0,0,0,0,0,0,26,32,30,16,20,21,137,72	0	0	1	3
Body Temp. (>= 38C)	0	0	1	1
Treatment of pain and or fever	0	1	0	4

End point values	TIVc_Naive_inj 2 (≥ 6 to < 9 years)	TIV_Non Naive_inj 1 (≥ 6 to < 9 years)	TIV_Naive_inj 1 (≥ 6 to < 9 years)	TIV_Naive_inj 2 (≥ 6 to < 9 years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	16	23	24
Units: Subjects				
Any Local	19	8	13	11
Tenderness(N=28,49,49,19,15,15,0,0,0,0,0,0,0,0)	0	0	0	0
Pain(N=0,0,0,0,0,0,26,32,31,16,22,22,0,0)	19	8	10	8
erythema27,50,50,18,15,15,26,34,32,16,23,23,131,61	5	4	5	3
Induration	3	3	2	3
Injection site ecchymosis	2	0	3	5
Any Systemic	15	5	5	3
Change in eating habits	0	0	0	0
Chills28,50,48,19,15,14,25,33,31,16,22,23,138,72	3	1	0	0
Diarrhea28,50,50,19,14,15,26,33,31,16,22,23,137,71	1	0	0	1
Irritability	0	0	0	0
Sleepiness(N=28,49,48,19,15,15,0,0,0,0,0,0,0,0)	0	0	0	0
Vomiting28,50,50,19,15,15,26,33,31,16,22,23,138,72	1	1	0	0
Arthralgia0,0,0,0,0,0,26,32,30,16,20,21,136,72	0	1	1	0
Fatigue0,0,0,0,0,0,26,32,30,16,20,21,137,72	4	2	0	0
Headache0,0,0,0,0,0,26,32,30,16,20,21,138,72	8	3	2	1
Loss appetite0,0,0,0,0,0,26,32,31,16,22,23,1	5	2	2	2
Myalgia0,0,0,0,0,0,26,32,30,16,20,21,138,72	5	2	1	0
Nausea0,0,0,0,0,0,26,32,30,16,20,21,137,72	0	2	0	0
Body Temp. (>= 38C)	0	0	0	0
Treatment of pain and or fever	4	0	2	0

End point values	TIVc_Non	TIV_Non naive		

	naive (9 to <18 Years)	(9 to <18 Years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	138	72		
Units: Subjects				
Any Local	73	47		
Tenderness(N=28,49,49,19,15,15,0,0,0,0,0,0,0)	0	0		
Pain(N=0,0,0,0,0,0,26,32,31,16,22,22,0,0)	73	47		
erythema27,50,50,18,15,15,26,34,32,16,23,23,131,61	5	2		
Induration	6	7		
Injection site ecchymosis	0	0		
Any Systemic	58	31		
Change in eating habits	0	0		
Chills28,50,48,19,15,14,25,33,31,16,22,23,138,72	19	6		
Diarrhea28,50,50,19,14,15,26,33,31,16,22,23,137,71	11	4		
Irritability	0	0		
Sleepiness(N=28,49,48,19,15,15,0,0,0,0,0,0,0)	0	0		
Vomiting28,50,50,19,15,15,26,33,31,16,22,23,138,72	8	3		
Arthralgia0,0,0,0,0,0,0,26,32,30,16,20,21,136,72	18	7		
Fatigue0,0,0,0,0,0,0,26,32,30,16,20,21,137,72	23	14		
Headache0,0,0,0,0,0,0,26,32,30,16,20,21,138,72	29	19		
Loss appetite0,0,0,0,0,0,0,26,32,31,16,22,23,1	20	12		
Myalgia0,0,0,0,0,0,0,26,32,30,16,20,21,138,72	29	11		
Nausea0,0,0,0,0,0,0,26,32,30,16,20,21,137,72	17	10		
Body Temp. (>= 38C)	4	3		
Treatment of pain and or fever	9	6		

Statistical analyses

No statistical analyses for this end point

Primary: 3. Number of subjects reporting unsolicited adverse events following vaccination with either TIVc or TIV

End point title	3. Number of subjects reporting unsolicited adverse events following vaccination with either TIVc or TIV[3]

End point description:

Safety was assessed in terms of number of subjects who reported any unsolicited AEs (four weeks after 1st vaccination and up to three weeks after 2nd vaccination), serious adverse events (SAEs), new onset of chronic diseases (NOCD), medically attended AEs and AEs leading to vaccine/study withdrawal after

receiving one or two doses of either TIVc or TIV by overall age group (3 to <18 years) and age sub-strata (3 to <9 years and 9 to <18 years)

End point type	Primary

End point timeframe:

Day 1 –Day 181(one dose group) Day 1 –Day 209(two dose group)

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: Statistical analysis not applicable for the outcome measure.

End point values	TIVc	TIVe	TIVc_Naive (3 to <9 Years)	TIVc_Non naive (3 to <9 Years)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	278	148	85	54
Units: Subjects				
Any AEs	213	111	77	46
Any possibly related AEs	17	12	7	3
SAEs	12	4	4	2
Possibly or probably related SAE	0	0	0	0
AEs leading to NOCD	3	1	1	0
Medically Attended AEs	187	94	71	38
AEs leading to vaccine/study Withdrawal	0	0	0	0
Deaths	0	0	0	0

End point values	TIVc_Non naive (9 to <18 Years)	TIV_Naive (3 to <9 Years)	TIV_Non naive (3 to <9 Years)	TIV_Non naive (9 to <18 Years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	139	39	35	74
Units: Subjects				
Any AEs	90	32	29	50
Any possibly related AEs	7	5	3	4
SAEs	6	0	2	2
Possibly or probably related SAE	0	0	0	0
AEs leading to NOCD	2	0	1	0
Medically Attended AEs	78	28	24	42
AEs leading to vaccine/study Withdrawal	0	0	0	0
Deaths	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs Day 1 through end of study

Adverse event reporting additional description:

Solicited local,systemic AEs collected -day 1 through Day 7 post injection 1 and Day 29 through Day 35 post injection 2, unsolicited AEs -Day 1 through Day 29 post 1st vaccination and Day 29 to Day 57 post 2nd vaccination.Subjects 9 to <18 years of age were determined to be "previously vaccinated (vaccine non-naive)" by default

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	TIVc
Reporting group description: -	
Reporting group title	TIVe

Reporting group description:

Vaccine naive and non-naïve subjects received one or two doses of egg derived trivalent subunit influenza vaccine formulation (TIV)

Serious adverse events	TIVc	TIVe	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 278 (4.32%)	4 / 148 (2.70%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Post procedural complication			
subjects affected / exposed	0 / 278 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Sickle cell anaemia with crisis			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			

subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Complex partial seizures			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 278 (0.36%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	1 / 278 (0.36%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumopathy			

subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	0 / 278 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 278 (0.72%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	0 / 278 (0.00%)	1 / 148 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 278 (0.36%)	0 / 148 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	TIVc	TIVe	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	246 / 278 (88.49%)	126 / 148 (85.14%)	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	42 / 278 (15.11%)	26 / 148 (17.57%)	
occurrences (all)	56	35	
Somnolence			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 278 (5.04%)	5 / 148 (3.38%)	
occurrences (all)	17	6	
General disorders and administration site conditions			
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	36 / 278 (12.95%)	9 / 148 (6.08%)	
occurrences (all)	42	9	
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	31 / 278 (11.15%)	16 / 148 (10.81%)	
occurrences (all)	43	19	
Injection Site Erythema			
subjects affected / exposed	32 / 278 (11.51%)	32 / 148 (21.62%)	
occurrences (all)	35	36	

Injection Site Haemoorage			
subjects affected / exposed	17 / 278 (6.12%)	13 / 148 (8.78%)	
occurrences (all)	17	16	
Injection Site Induration			
subjects affected / exposed	35 / 278 (12.59%)	31 / 148 (20.95%)	
occurrences (all)	39	34	
Injection Site pain			
subjects affected / exposed	147 / 278 (52.88%)	86 / 148 (58.11%)	
occurrences (all)	178	97	
Pyrexia			
subjects affected / exposed	37 / 278 (13.31%)	21 / 148 (14.19%)	
occurrences (all)	45	25	
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 278 (9.35%)	8 / 148 (5.41%)	
occurrences (all)	30	9	
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 278 (8.27%)	13 / 148 (8.78%)	
occurrences (all)	26	13	
Vomitting			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 278 (9.71%)	16 / 148 (10.81%)	
occurrences (all)	33	16	
Respiratory, thoracic and mediastinal disorders			
Asthmatic Crisis			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 278 (6.47%)	12 / 148 (8.11%)	
occurrences (all)	32	20	
Bronchospasm			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 278 (4.68%)	8 / 148 (5.41%)	
occurrences (all)	19	10	
Cough			

alternative assessment type: Systematic			
subjects affected / exposed	26 / 278 (9.35%)	10 / 148 (6.76%)	
occurrences (all)	29	12	
Psychiatric disorders			
Decraesed Appetite			
alternative assessment type: Systematic			
subjects affected / exposed	33 / 278 (11.87%)	17 / 148 (11.49%)	
occurrences (all)	38	22	
Eating Disorder			
subjects affected / exposed	17 / 278 (6.12%)	7 / 148 (4.73%)	
occurrences (all)	19	9	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 278 (6.12%)	8 / 148 (5.41%)	
occurrences (all)	23	10	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 278 (9.71%)	11 / 148 (7.43%)	
occurrences (all)	29	11	
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	40 / 278 (14.39%)	14 / 148 (9.46%)	
occurrences (all)	47	15	
Infections and infestations			
Bronchitis			
subjects affected / exposed	21 / 278 (7.55%)	12 / 148 (8.11%)	
occurrences (all)	24	16	
Gastroenteritis			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 278 (6.83%)	10 / 148 (6.76%)	
occurrences (all)	21	14	
Nasopharyngitis			
subjects affected / exposed	35 / 278 (12.59%)	19 / 148 (12.84%)	
occurrences (all)	45	23	

Otitis Media Acute			
subjects affected / exposed	14 / 278 (5.04%)	3 / 148 (2.03%)	
occurrences (all)	14	3	
Pharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 278 (7.91%)	12 / 148 (8.11%)	
occurrences (all)	23	14	
Respiratory Tract Infection			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 278 (5.04%)	5 / 148 (3.38%)	
occurrences (all)	16	7	
Tonsilitis			
subjects affected / exposed	16 / 278 (5.76%)	6 / 148 (4.05%)	
occurrences (all)	20	6	
Viral infection			
subjects affected / exposed	16 / 278 (5.76%)	6 / 148 (4.05%)	
occurrences (all)	22	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported