Clinical trial results:
A Phase II, Observer-Blind, Parallel Groups, Single Center, Extension Study to Evaluate the Immunogenicity and Safety Following a Single Intramuscular Dose of Fluad® or Vaxigrip® Influenza Vaccines in Healthy Children who Received Either One or the Other Vaccine in the Previous V70P2 Study.

Summary

EudraCT number	2007-003339-22
Trial protocol	FI
Global end of trial date	11 June 2008

Results information

Result version number	v2 (current)
This version publication date	28 July 2016
First version publication date	07 December 2014
Version creation reason	• Correction of full data set Required for the re-QC project because of the EudraCT system glitch and possible updates to results may be required. Moreover, a change in system user for this study is necessary.

Trial information

Trial identification

Sponsor protocol code	V70P2E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00644540
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics S.r.l.
Sponsor organisation address	Via Fiorentina 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines, 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-000149-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	13 October 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 June 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To evaluate the immunogenicity of a single 0.25mL or 0.5mL IM injection of Fluad or Vaxigrip influenza vaccines in healthy children aged up to 48 months.
•To evaluate the safety and tolerability of a single 0.25mL or 0.5mL IM injection of Fluad or Vaxigrip influenza vaccines in healthy children aged up to 48 months.

Protection of trial subjects:

Study vaccines were not administered to individuals with known hypersensitivity to any component of the vaccines. An oral temperature ≥38.0°C (≥100.4°F) or serious active infection was a reason for delaying vaccination. Standard immunization practices were observed and care was taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate medical treatment and supervision was readily available in case of rare anaphylactic reactions following administration of the study vaccine. Epinephrine 1:1000 and diphenhydramine was available in case of any anaphylactic reactions. Care was taken to ensure that the vaccine is not injected into a blood vessel.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 November 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 89
Worldwide total number of subjects	89
EEA total number of subjects	89

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)	13
Children (2-11 years)	76
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 in one centre in Finland.

Pre-assignment

Screening details:

All children enrolled were included in the trial

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	aTIV <36

Arm description:

Each subject has received half a dose of a TIV.

Arm type	Experimental
Investigational medicinal product name	Adjuvunated trivalent influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of 0.25mL of vaccine is administered by IM injection into deltoid muscle of non-dominant arm.

Arm title	TIV <36

Arm description:

Each subject has received a half a dose of TIV.

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

Dosage and administration details:

Single dose of 0.25mL of vaccine is administered by IM injection into deltoid muscle of non-dominant arm.

Arm title	aTIV >36

Arm description:

Each subject has received a full dose of aTIV.

Arm type	Experimental

Investigational medicinal product name	Adjuvunated trivalent influenza virus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of 0.5mL of vaccine is administered by IM injection into deltoid muscle of non-dominant arm.

Arm title	TIV >36

Arm description:

Each subject has received a full dose of TIV.

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

Dosage and administration details:

Single dose of 0.5mL of vaccine is administered by IM injection into deltoid muscle of non-dominant arm.

Number of subjects in period 1	aTIV <36	TIV <36	aTIV >36
Started	25	23	18
Completed	24	23	16
Not completed	1	0	2
Withdrew Consent	-	-	-
Lost to follow-up	1	-	1
Inappropriate Enrollment	-	-	-
Protocol deviation	-	-	1

Number of subjects in period 1	TIV >36
Started	23
Completed	21
Not completed	2
Withdrew Consent	1
Lost to follow-up	-
Inappropriate Enrollment	1
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	aTIV <36
Reporting group description:	
Each subject has received half a dose of a TIV.	
Reporting group title	TIV <36
Reporting group description:	
Each subject has received a half a dose of TIV.	
Reporting group title	aTIV >36
Reporting group description:	
Each subject has received a full dose of aTIV.	
Reporting group title	TIV >36
Reporting group description:	
Each subject has received a full dose of TIV.	

Reporting group values	aTIV <36	TIV <36	aTIV >36
Number of subjects	25	23	18
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: days			
arithmetic mean	27.2	27.2	42.3
standard deviation	± 5.4	± 5.5	± 3
Gender categorical			
Units: Subjects			
Female	10	12	9
Male	15	11	9

Reporting group values	TIV >36	Total	
Number of subjects	23	89	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: days			
arithmetic mean	40.7		
standard deviation	± 3.3	-	
Gender categorical			
Units: Subjects			
Female	9	40	
Male	14	49	

End points

End points reporting groups

Reporting group title	aTIV <36
Reporting group description:	
Each subject has received half a dose of a TIV.	
Reporting group title	TIV <36
Reporting group description:	
Each subject has received a half a dose of TIV.	
Reporting group title	aTIV >36
Reporting group description:	
Each subject has received a full dose of aTIV.	
Reporting group title	TIV >36
Reporting group description:	
Each subject has received a full dose of TIV.	
Subject analysis set title	All enrolled population - TIV
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All children who have data in the DEMOG panel.	
Subject analysis set title	All enrolled population - aTIV
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All children who have data in the DEMOG panel.	
Subject analysis set title	Per Protocol Population - TIV
Subject analysis set type	Per protocol
Subject analysis set description:	
All enrolled subjects in the Full Analysis Set who received all the doses of vaccine correctly, provided evaluable serum samples at the relevant time points and had no major violations of inclusion/exclusion criteria.	
Subject analysis set title	Per Protocol Population - aTIV
Subject analysis set type	Per protocol
Subject analysis set description:	
All enrolled subjects in the Full Analysis Set who received all the doses of vaccine correctly, provided evaluable serum samples at the relevant time points and had no major violations of inclusion/exclusion criteria.	
Subject analysis set title	Safety Population - TIV
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the Exposed population who provided post-baseline safety data.	
Subject analysis set title	Safety Population - aTIV
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the Exposed population who provided post-baseline safety data.	

Primary: GMTs as measured by HI assay in the overall population and in the two age strata

End point title	GMTs as measured by HI assay in the overall population and in the two age strata
End point description:	
The immune response after a single IM injection of aTIV or TIV, in terms of post-vaccination GMTs is measured by hemagglutinin inhibition (HI) assay in the overall population and in the two age strata (<36 months and ≥36 months of age).	
End point type	Primary

End point timeframe:

Day 1 (baseline) and day 22

End point values	aTIV <36	TIV <36	aTIV >36	TIV >36
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	20	18	20
Units: GMT				
geometric mean (confidence interval 95%)				
A/H1N1 – Day 1	8.73 (5.94 to 13)	6.6 (3.69 to 12)	16 (6.12 to 40)	7.98 (4.36 to 15)
A/H1N1 – Day 22	1068 (671 to 1701)	283 (171 to 471)	978 (617 to 1549)	511 (297 to 879)
A/H3N2 – Day 1	84 (55 to 127)	32 (19 to 53)	60 (35 to 104)	32 (15 to 68)
A/H3N2 – Day 22	1401 (1020 to 1924)	251 (186 to 338)	1076 (765 to 1513)	608 (398 to 926)
B Day1	9.14 (6.84 to 12)	5 (5 to 5)	11 (6.92 to 18)	5.18 (4.81 to 5.57)
B Day 22	178 (137 to 231)	21 (14 to 32)	187 (130 to 269)	83 (56 to 121)

End point values	Per Protocol Population - TIV	Per Protocol Population - aTIV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40	41		
Units: GMT				
geometric mean (confidence interval 95%)				
A/H1N1 – Day 1	7.26 (4.86 to 11)	11 (7.18 to 18)		
A/H1N1 – Day 22	381 (264 to 549)	1027 (749 to 1409)		
A/H3N2 – Day 1	32 (21 to 49)	72 (52 to 100)		
A/H3N2 – Day 22	391 (294 to 519)	1248 (995 to 1564)		
B Day1	5.09 (4.91 to 5.27)	9.91 (7.72 to 13)		
B Day 22	41 (29 to 59)	182 (148 to 223)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Non inferiority a single aTIV vaccination respect to a single TIV vaccination against strain H1N1 is evaluated through the comparison of respective GMTs at day 22 as measured by the between groups ratios

Comparison groups	Per Protocol Population - TIV v Per Protocol Population - aTIV

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	ANOVA
Parameter estimate	Between Groups GMT Ratio
Point estimate	2.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.81
upper limit	3.99

Notes:

[1] - aTIV immune response is to be considered non inferior to TIV immune response if the lower limit of the 95% CI of the between groups ratios of GMTs at day 22 is greater than 0.5

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Non inferiority a single aTIV vaccination respect to a single TIV vaccination against strain H3N2 is evaluated through the comparison of respective GMTs at day 22 as measured by the between groups ratios

Comparison groups	Per Protocol Population - aTIV v Per Protocol Population - TIV
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Method	ANOVA
Parameter estimate	Between Groups GMT Ratio
Point estimate	3.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.38
upper limit	4.15

Notes:

[2] - aTIV immune response is to be considered non inferior to TIV immune response if the lower limit of the 95% CI of the between groups ratios of GMTs at day 22 is greater than 0.5

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Non inferiority a single aTIV vaccination respect to a single TIV vaccination against strain B is evaluated through the comparison of respective GMTs at day 22 as measured by the between groups ratios

Comparison groups	Per Protocol Population - aTIV v Per Protocol Population - TIV
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Method	ANOVA
Parameter estimate	Between Groups GMT Ratio
Point estimate	4.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	3.3
upper limit	5.86

Notes:

[3] - aTIV immune response is to be considered non inferior to TIV immune response if the lower limit of the 95% CI of the between groups ratios of GMTs at day 22 is greater than 0.5

Primary: Number of subjects who reported solicited local and systemic reactions from day 1 to day 7 after vaccination.

End point title	Number of subjects who reported solicited local and systemic reactions from day 1 to day 7 after vaccination.[4]

End point description:

Safety was assessed as the number of subjects who reported local and systemic reactions from day 1 to day 7 after vaccination with TIV and aTIV.

End point type	Primary

End point timeframe:

Days 1 to 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 inferential statistical analysis was done.

End point values	aTIV <36	TIV <36	aTIV >36	TIV >36
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	23	18	23
Units: Number of Subjects				
Local (Any)	15	10	15	11
Ecchymosis (Local)	2	3	1	4
Erythema (Local)	8	7	5	5
Induration (Local)	3	3	5	5
Swelling (Local)	3	4	3	0
Tenderness (Local)	8	7	0	0
Pain at Injection Site (Local)	0	0	12	6
Systemic (Any)	11	9	7	8
Change in eating habits (Systemic)	3	5	0	0
Sleepiness (Systemic)	1	4	0	0
Unusual crying (Systemic)	2	4	0	0
Irritability (Irritability)	9	5	0	0
Vomiting (Systemic)	0	1	0	0
Diarrhoea (Systemic)	6	3	0	0
Shivering (Systemic)	0	0	0	0
Other (Analgesic/Antipyretic Medication used) (Sy)	5	3	4	1
Chills (Systemic)	0	0	4	4
Malaise (Systemic)	0	0	2	4
Myalgia (Systemic)	0	0	2	1
Arthralgia (Systemic)	0	0	2	0
Headache (Systemic)	0	0	3	2
Fatigue (Systemic)	0	0	5	8

End point values	Safety Population - TIV	Safety Population - aTIV		

Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	43		
Units: Number of Subjects				
Local (Any)	21	30		
Ecchymosis (Local)	7	3		
Erythema (Local)	12	13		
Induration (Local)	8	8		
Swelling (Local)	4	6		
Tenderness (Local)	7	8		
Pain at Injection Site (Local)	6	12		
Systemic (Any)	17	18		
Change in eating habits (Systemic)	5	3		
Sleepiness (Systemic)	4	1		
Unusual crying (Systemic)	4	2		
Irritability (Irritability)	5	9		
Vomiting (Systemic)	1	0		
Diarrhoea (Systemic)	3	6		
Shivering (Systemic)	0	0		
Other (Analgesic/Antipyretic Medication used) (Sy)	4	9		
Chills (Systemic)	4	4		
Malaise (Systemic)	4	2		
Myalgia (Systemic)	1	2		
Arthralgia (Systemic)	0	2		
Headache (Systemic)	2	3		
Fatigue (Systemic)	8	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reported with unsolicited adverse events post vaccination

End point title	Number of subjects reported with unsolicited adverse events post vaccination[5]

End point description:

Safety was assessed as the number of subjects who reported Unsolicited AE’s during day 1 to day 181 after vaccination with TIV and aTIV.

End point type	Primary

End point timeframe:

Days 1 to day 181 (Study termination).

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 inferential statistical analysis was done.

End point values	aTIV <36	TIV <36	aTIV >36	TIV >36
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	23	18	23
Units: Number of Subjects				
Any Adverse Event	17	16	13	19
Serious Adverse Events	0	0	0	0
Medically attended AEs	15	9	9	12
AEs leading to discontinuation	0	0	0	0

End point values	Safety Population - TIV	Safety Population - aTIV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	43		
Units: Number of Subjects				
Any Adverse Event	35	30		
Serious Adverse Events	0	0		
Medically attended AEs	21	24		
AEs leading to discontinuation	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects Achieving Seroprotection and Seroconversion or Significant Increase in HI Titres, by Age Group

End point title	Percentages of Subjects Achieving Seroprotection and Seroconversion or Significant Increase in HI Titres, by Age Group

End point description:

The immune response after a single IM injection of aTIV or TIV is measured in terms of percentages of subjects achieving Seroprotection (SP) and Seroconversion (SC) in HI Titres.

End point type	Secondary

End point timeframe:

Day1(baseline) and day 22

End point values	aTIV <36	TIV <36	aTIV >36	TIV >36
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	20	18	20
Units: Percentages				
number (confidence interval 95%)				
A/H1N1 – Day 1 SP	9 (1 to 28)	5 (0 to 25)	22 (6 to 48)	5 (0 to 25)
A/H1N1 – Day 22 SP	100 (85 to 100)	100 (83 to 100)	100 (81 to 100)	100 (83 to 100)

A/H1N1 – Day 22 SC	100 (85 to 100)	95 (75 to 100)	89 (65 to 99)	95 (75 to 100)
A/H3N2 – Day 1 SP	96 (78 to 100)	50 (27 to 73)	78 (52 to 94)	30 (12 to 54)
A/H3N2 – Day 22 SP	100 (85 to 100)	100 (83 to 100)	100 (81 to 100)	100 (83 to 100)
A/H3N2 – Day 22 SC	100 (85 to 100)	85 (62 to 97)	94 (73 to 100)	85 (62 to 97)
B Day1 SP	4 (0 to 22)	0 (0 to 17)	17 (4 to 41)	0 (0 to 17)
B Day 22 SP	100 (85 to 100)	45 (23 to 68)	100 (81 to 100)	90 (68 to 99)
B Day 22 SC	96 (78 to 100)	45 (23 to 68)	100 (81 to 100)	90 (68 to 99)

End point values	Per Protocol Population - TIV	Per Protocol Population - aTIV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40	41		
Units: Percentages				
number (confidence interval 95%)				
A/H1N1 – Day 1 SP	5 (1 to 17)	15 (6 to 29)		
A/H1N1 – Day 22 SP	100 (91 to 100)	100 (91 to 100)		
A/H1N1 – Day 22 SC	95 (83 to 99)	95 (83 to 99)		
A/H3N2 – Day 1 SP	40 (25 to 57)	88 (74 to 96)		
A/H3N2 – Day 22 SP	100 (91 to 100)	100 (91 to 100)		
A/H3N2 – Day 22 SC	85 (70 to 94)	98 (87 to 100)		
B Day1 SP	0 (0 to 9)	10 (3 to 23)		
B Day 22 SP	68 (51 to 81)	100 (91 to 100)		
B Day 22 SC	68 (51 to 81)	98 (87 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean HI Titers against mismatched strains measured at day 1 and 22

End point title	Geometric Mean HI Titers against mismatched strains measured at day 1 and 22
End point description:	
Immunogenicity against mismatched strains was evaluated by measuring the post immunization geometric mean titers (GMTs), as measured by hemagglutinin inhibition (HI).	
End point type	Secondary
End point timeframe:	
Day1(baseline) and day 22	

End point values	aTIV <36	TIV <36	aTIV >36	TIV >36
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	20	18	20
Units: GMT				
geometric mean (confidence interval 95%)				
A/H1N1 – Day 1	18 (12 to 27)	9.66 (6.14 to 15)	23 (12 to 46)	10 (5.97 to 17)
A/H1N1 – Day 22	1037 (676 to 1590)	211 (127 to 351)	871 (586 to 1294)	485 (266 to 885)
A/H3N2 – Day 1	18 (11 to 31)	8.71 (4.91 to 15)	15 (8.31 to 26)	11 (5.2 to 25)
A/H3N2 – Day 22	378 (244 to 585)	87 (57 to 134)	308 (185 to 514)	181 (109 to 300)
B Day 1	5 (5 to 5)	5 (5 to 5)	5.2 (4.79 to 5.64)	5 (5 to 5)
B Day 22	24 (17 to 32)	6.16 (4.97 to 7.62)	22 (15 to 31)	10 (7.25 to 15)

End point values	Per Protocol Population - TIV	Per Protocol Population - aTIV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40	41		
Units: GMT				
geometric mean (confidence interval 95%)				
A/H1N1 – Day 1	9.83 (7.09 to 14)	20 (14 to 29)		
A/H1N1 – Day 22	320 (215 to 477)	960 (722 to 1277)		
A/H3N2 – Day 1	10 (6.26 to 16)	17 (11 to 24)		
A/H3N2 – Day 22	126 (90 to 176)	345 (251 to 475)		
B Day 1	5 (5 to 5)	5.09 (4.91 to 5.26)		
B Day 22	7.98 (6.44 to 9.9)	23 (18 to 29)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited adverse events (AEs) were collected from Day 1 through 7; Serious AEs were collected from day 1 to day 181 after vaccination.

Adverse event reporting additional description:

Solicited adverse events were collected by systematic assessment; Unsolicited adverse events were collected by non-systematic assessment;
analysis was performed as per the safety data set.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	aTIV <36

Reporting group description:

Each subject has received half a dose of a TIV.

Reporting group title	TIV <36

Reporting group description:

Each subject has received a half a dose of TIV.

Reporting group title	aTIV >36

Reporting group description:

Each subject has received a full dose of aTIV.

Reporting group title	TIV >36

Reporting group description:

Each subject has received a full dose of TIV.

Reporting group title	aTIV overall

Reporting group description:

Each subject received either half or full dose of aTIV.

Reporting group title	TIV overall

Reporting group description:

Each subject received either half or full dose of TIV.

Serious adverse events	aTIV <36	TIV <36	aTIV >36
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	TIV >36	aTIV overall	TIV overall
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	0 / 43 (0.00%)	0 / 46 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

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

Non-serious adverse events	aTIV <36	TIV <36	aTIV >36
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 25 (84.00%)	17 / 23 (73.91%)	17 / 18 (94.44%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 25 (4.00%)	4 / 23 (17.39%)	0 / 18 (0.00%)
occurrences (all)	1	5	0
Headache			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	3 / 18 (16.67%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	4 / 18 (22.22%)
occurrences (all)	0	0	4
Crying			
subjects affected / exposed	2 / 25 (8.00%)	5 / 23 (21.74%)	0 / 18 (0.00%)
occurrences (all)	2	5	0
Fatigue			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	5 / 18 (27.78%)
occurrences (all)	0	0	6
Injection Site Erythema			
subjects affected / exposed	8 / 25 (32.00%)	7 / 23 (30.43%)	5 / 18 (27.78%)
occurrences (all)	8	7	6
Injection Site Haemorrahage			
subjects affected / exposed	2 / 25 (8.00%)	3 / 23 (13.04%)	1 / 18 (5.56%)
occurrences (all)	2	3	1
Injection Site Induration			
subjects affected / exposed	3 / 25 (12.00%)	3 / 23 (13.04%)	5 / 18 (27.78%)
occurrences (all)	3	3	5
Injection Site Pain			

subjects affected / exposed	8 / 25 (32.00%)	7 / 23 (30.43%)	12 / 18 (66.67%)
occurrences (all)	9	7	13
Injection Site Swelling			
subjects affected / exposed	3 / 25 (12.00%)	4 / 23 (17.39%)	3 / 18 (16.67%)
occurrences (all)	3	4	3
Malaise			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	7 / 25 (28.00%)	4 / 23 (17.39%)	3 / 18 (16.67%)
occurrences (all)	7	4	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 25 (28.00%)	4 / 23 (17.39%)	0 / 18 (0.00%)
occurrences (all)	7	7	0
Lip dry			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Vomitting			
subjects affected / exposed	0 / 25 (0.00%)	1 / 23 (4.35%)	2 / 18 (11.11%)
occurrences (all)	0	1	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 25 (20.00%)	4 / 23 (17.39%)	4 / 18 (22.22%)
occurrences (all)	8	4	4
Asthma			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Psychiatric disorders			

Eating Disorder			
subjects affected / exposed	3 / 25 (12.00%)	5 / 23 (21.74%)	0 / 18 (0.00%)
occurrences (all)	3	5	0
Irritability			
subjects affected / exposed	9 / 25 (36.00%)	7 / 23 (30.43%)	0 / 18 (0.00%)
occurrences (all)	10	8	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	3
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 25 (8.00%)	2 / 23 (8.70%)	2 / 18 (11.11%)
occurrences (all)	2	2	2
Conjunctivitis			
subjects affected / exposed	0 / 25 (0.00%)	4 / 23 (17.39%)	2 / 18 (11.11%)
occurrences (all)	0	4	2
Ear Infection			
subjects affected / exposed	1 / 25 (4.00%)	2 / 23 (8.70%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Otitis media			
subjects affected / exposed	8 / 25 (32.00%)	7 / 23 (30.43%)	5 / 18 (27.78%)
occurrences (all)	10	11	9
Nasopharyngitis			
subjects affected / exposed	2 / 25 (8.00%)	1 / 23 (4.35%)	1 / 18 (5.56%)
occurrences (all)	2	1	1
Rhinitis			
subjects affected / exposed	4 / 25 (16.00%)	4 / 23 (17.39%)	2 / 18 (11.11%)
occurrences (all)	5	5	2
Sinusitis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 23 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Upper respiratory tract infection			

subjects affected / exposed	6 / 25 (24.00%)	3 / 23 (13.04%)	2 / 18 (11.11%)
occurrences (all)	7	3	2

Non-serious adverse events	TIV >36	aTIV overall	TIV overall
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 23 (82.61%)	38 / 43 (88.37%)	36 / 46 (78.26%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 23 (4.35%)	1 / 43 (2.33%)	5 / 46 (10.87%)
occurrences (all)	1	1	6
Headache			
subjects affected / exposed	3 / 23 (13.04%)	3 / 43 (6.98%)	3 / 46 (6.52%)
occurrences (all)	5	3	5
General disorders and administration site conditions			
Chills			
subjects affected / exposed	4 / 23 (17.39%)	4 / 43 (9.30%)	4 / 46 (8.70%)
occurrences (all)	4	4	4
Crying			
subjects affected / exposed	0 / 23 (0.00%)	2 / 43 (4.65%)	5 / 46 (10.87%)
occurrences (all)	0	2	5
Fatigue			
subjects affected / exposed	8 / 23 (34.78%)	5 / 43 (11.63%)	8 / 46 (17.39%)
occurrences (all)	8	6	8
Injection Site Erythema			
subjects affected / exposed	5 / 23 (21.74%)	13 / 43 (30.23%)	12 / 46 (26.09%)
occurrences (all)	5	14	12
Injection Site Haemorrahage			
subjects affected / exposed	4 / 23 (17.39%)	3 / 43 (6.98%)	7 / 46 (15.22%)
occurrences (all)	4	3	7
Injection Site Induration			
subjects affected / exposed	5 / 23 (21.74%)	8 / 43 (18.60%)	8 / 46 (17.39%)
occurrences (all)	5	8	8
Injection Site Pain			
subjects affected / exposed	6 / 23 (26.09%)	20 / 43 (46.51%)	13 / 46 (28.26%)
occurrences (all)	6	22	13
Injection Site Swelling			

subjects affected / exposed	0 / 23 (0.00%)	6 / 43 (13.95%)	4 / 46 (8.70%)
occurrences (all)	0	6	4
Malaise			
subjects affected / exposed	4 / 23 (17.39%)	2 / 43 (4.65%)	4 / 46 (8.70%)
occurrences (all)	4	2	4
Pyrexia			
subjects affected / exposed	5 / 23 (21.74%)	10 / 43 (23.26%)	9 / 46 (19.57%)
occurrences (all)	6	10	10
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 23 (4.35%)	7 / 43 (16.28%)	5 / 46 (10.87%)
occurrences (all)	1	7	8
Lip dry			
subjects affected / exposed	0 / 23 (0.00%)	1 / 43 (2.33%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Vomitting			
subjects affected / exposed	1 / 23 (4.35%)	2 / 43 (4.65%)	2 / 46 (4.35%)
occurrences (all)	1	2	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 23 (17.39%)	9 / 43 (20.93%)	8 / 46 (17.39%)
occurrences (all)	8	12	12
Asthma			
subjects affected / exposed	0 / 23 (0.00%)	1 / 43 (2.33%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 23 (0.00%)	1 / 43 (2.33%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 23 (0.00%)	1 / 43 (2.33%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Eating Disorder			
subjects affected / exposed	0 / 23 (0.00%)	3 / 43 (6.98%)	5 / 46 (10.87%)
occurrences (all)	0	3	5
Irritability			

subjects affected / exposed	0 / 23 (0.00%)	9 / 43 (20.93%)	7 / 46 (15.22%)
occurrences (all)	0	10	8
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 23 (0.00%)	2 / 43 (4.65%)	0 / 46 (0.00%)
occurrences (all)	0	2	0
Myalgia			
subjects affected / exposed	1 / 23 (4.35%)	2 / 43 (4.65%)	1 / 46 (2.17%)
occurrences (all)	1	3	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 23 (0.00%)	4 / 43 (9.30%)	2 / 46 (4.35%)
occurrences (all)	0	4	2
Conjunctivitis			
subjects affected / exposed	1 / 23 (4.35%)	2 / 43 (4.65%)	5 / 46 (10.87%)
occurrences (all)	1	2	5
Ear Infection			
subjects affected / exposed	1 / 23 (4.35%)	1 / 43 (2.33%)	3 / 46 (6.52%)
occurrences (all)	1	1	3
Otitis media			
subjects affected / exposed	7 / 23 (30.43%)	13 / 43 (30.23%)	14 / 46 (30.43%)
occurrences (all)	10	19	21
Nasopharyngitis			
subjects affected / exposed	1 / 23 (4.35%)	3 / 43 (6.98%)	2 / 46 (4.35%)
occurrences (all)	1	3	2
Rhinitis			
subjects affected / exposed	3 / 23 (13.04%)	6 / 43 (13.95%)	7 / 46 (15.22%)
occurrences (all)	3	7	8
Sinusitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 43 (2.33%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	5 / 23 (21.74%)	8 / 43 (18.60%)	8 / 46 (17.39%)
occurrences (all)	5	9	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 October 2007	• exclusion criteria have been amended • "Adherence to Treatment Allocation List" has been updated. • Flowchart for Serious Adverse Events reporting. • Outer label for both study vaccines was added and a typing error was amended.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported