Clinical trial results:
A Phase II, Observer-Blind, Randomized, Multi-center Study to Evaluate the Safety and Immunogenicity of Two 0.25 mL or 0.5 mL Doses of Fluad® and Fluzone® Influenza Vaccines in Healthy Children Aged 6 to <60 Months.

Summary

EudraCT number	2014-004543-12
Trial protocol	Outside EU/EEA
Global end of trial date	15 October 2008

Results information

Result version number	v2 (current)
This version publication date	28 July 2016
First version publication date	07 January 2015
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	V70P6

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00649883
WHO universal trial number (UTN)	-
Other trial identifiers	Sample data: Sample data

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines
Sponsor organisation address	Via Fiorentina, 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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 June 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 October 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunogenicity of two 0.25 mL IM doses of Fluad or Fluzone influenza vaccines in terms of post-vaccination geometric mean titers (GMTs), seroprotection rates and seroconversion rates, as measured by HI assay.

To evaluate the immunogenicity induced by two 0.25 mL IM doses of Fluad or Fluzone influenza vaccines against influenza virus strains different from those included in the study vaccines formulations (Northern Hemisphere 2007/2008), in terms of postvaccination GMTs, seroconversion rates and seroprotection rates, as measured by HI
assay

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	28 January 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Guatemala: 360
Worldwide total number of subjects	360
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)	166
Children (2-11 years)	194
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:

Participants were enrolled from one country sites in Guatemala

Pre-assignment

Screening details:

All subjects 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

Arms

Are arms mutually exclusive?	Yes
Arm title	aTIV (≥6to ≤36 months)

Arm description:

Children 6 to <36 months of age received two 0.25 mL doses of MF59 adjuvanted trivalent influenza vaccine(aTIV), administered four weeks apart

Arm type	Experimental
Investigational medicinal product name	Adjuvanted trivalent influenza virus vaccine (surface antigen, inactivated, adjuvanted with MF59C.1, egg-derived)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Children 6 to <36 months received two 0.25mL doses of MF59- aTIV. Administered by IM injection (four weeks apart) into the deltoid muscle preferably of the non-dominant arm

Arm title	TIV (≥6 to ≤36 months)

Arm description:

Children 6 to <36 months of age received two 0.25 mL doses of non-adjuvanted split influenza vaccine (TIV), administered four weeks apart

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

Dosage and administration details:

Children 6 to <36 months received two 0.25mL doses of TIV. Administered by IM injection (four weeks apart) into the deltoid muscle preferably of the non-dominant arm

Arm title	aTIV (≥36 to ≤60 months)

Arm description:

Children 36 to <60 months of age received two 0.5 mL doses of aTIV, administered four weeks apart

Arm type	Experimental

Investigational medicinal product name	Adjuvanted trivalent influenza virus vaccine (surface antigen, inactivated, adjuvanted with MF59C.1, egg-derived)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Children 36 to <60months received two 0.5mL doses of MF59- aTIV administered by IM injection (four weeks apart) into the deltoid muscle preferably of the non-dominant arm

Arm title	TIV (≥36 to ≤60 months)

Arm description:

Children 36 to <60 months of age received two 0.5 mL doses of either TIV, administered four weeks apart.

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

Dosage and administration details:

Children 36 to <60months received two 0.5mL doses of TIV administered by IM injection (four weeks apart) into the deltoid muscle preferably of the non-dominant arm

Number of subjects in period 1	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)
Started	136	132	44
Completed	123	118	42
Not completed	13	14	2
Consent withdrawn by subject	4	6	1
Adverse Event	-	-	1
Death	-	1	-
Lost to follow-up	9	7	-

Number of subjects in period 1	TIV (≥36 to ≤60 months)
Started	48
Completed	44
Not completed	4
Consent withdrawn by subject	1
Adverse Event	1
Death	-
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	aTIV (≥6to ≤36 months)
Reporting group description:	
Children 6 to <36 months of age received two 0.25 mL doses of MF59 adjuvanted trivalent influenza vaccine(aTIV), administered four weeks apart	
Reporting group title	TIV (≥6 to ≤36 months)
Reporting group description:	
Children 6 to <36 months of age received two 0.25 mL doses of non-adjuvanted split influenza vaccine (TIV), administered four weeks apart	
Reporting group title	aTIV (≥36 to ≤60 months)
Reporting group description:	
Children 36 to <60 months of age received two 0.5 mL doses of aTIV, administered four weeks apart	
Reporting group title	TIV (≥36 to ≤60 months)
Reporting group description:	
Children 36 to <60 months of age received two 0.5 mL doses of either TIV, administered four weeks apart.	

Reporting group values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)
Number of subjects	136	132	44
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: months			
arithmetic mean	1.2	1.2	3.4
standard deviation	± 0.7	± 0.7	± 0.5
Gender categorical			
Units: Subjects			
Female	64	63	16
Male	72	69	28

Reporting group values	TIV (≥36 to ≤60 months)	Total	
Number of subjects	48	360	
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: months			
arithmetic mean	3.5		
standard deviation	± 0.5	-	
Gender categorical			
Units: Subjects			
Female	23	166	
Male	25	194	

End points

End points reporting groups

Reporting group title	aTIV (≥6to ≤36 months)
Reporting group description:	
Children 6 to <36 months of age received two 0.25 mL doses of MF59 adjuvanted trivalent influenza vaccine(aTIV), administered four weeks apart	
Reporting group title	TIV (≥6 to ≤36 months)
Reporting group description:	
Children 6 to <36 months of age received two 0.25 mL doses of non-adjuvanted split influenza vaccine (TIV), administered four weeks apart	
Reporting group title	aTIV (≥36 to ≤60 months)
Reporting group description:	
Children 36 to <60 months of age received two 0.5 mL doses of aTIV, administered four weeks apart	
Reporting group title	TIV (≥36 to ≤60 months)
Reporting group description:	
Children 36 to <60 months of age received two 0.5 mL doses of either TIV, administered four weeks apart.	
Subject analysis set title	aTIV (≥6to ≤60 months)
Subject analysis set type	Per protocol
Subject analysis set description:	
all subjects in the Full Analysis Set who: 1) received all the relevant doses of vaccine correctly, and 2) provided evaluable serum samples at the relevant time points, and 3) had no major protocol violation as defined prior to unblinding	
Subject analysis set title	aTIV (≥6to ≤60 months)-Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
all subjects enrolled who: 1) had received study vaccination 2) provided post-baseline safety data	
Subject analysis set title	TIV (≥6 to ≤60 months)
Subject analysis set type	Per protocol
Subject analysis set description:	
all subjects in the Full Analysis Set who: 1) received all the relevant doses of vaccine correctly, and 2) provided evaluable serum samples at the relevant time points, and 3) had no major protocol violation as defined prior to unblinding	
Subject analysis set title	TIV (≥6 to ≤60 months)-Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
all subjects enrolled who: 1) had received study vaccination 2) provided post-baseline safety data	
Subject analysis set title	Enrolled
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
all subjects who: 1) had been screened and entered the study	

Primary: Comparison of Antibody Responses of aTIV With TIV in Terms of Geometric Mean Titers (GMTs) Against Homologous Strains

End point title	Comparison of Antibody Responses of aTIV With TIV in Terms of Geometric Mean Titers (GMTs) Against Homologous Strains[1]

End point description:

The Hemagglutination Inhibition (HI) antibody responses of aTIV compared to TIV assessed in terms of post vaccination GMTs at three weeks after last vaccination against the three homologous vaccine strains.

End point type	Primary

End point timeframe:

Day 1, Day 29 and Day 50

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: There were no statistical analysis done.

End point values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)	TIV (≥36 to ≤60 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	102	23	20
Units: Titers				
geometric mean (confidence interval 95%)				
A/H1N1 Day 1	14 (9.85 to 20)	14 (10 to 20)	26 (12 to 57)	30 (13 to 70)
A/H1N1 Day 29	588 (416 to 833)	409 (292 to 574)	969 (458 to 2052)	687 (302 to 1560)
A/H1N1 Day 50	1612 (1304 to 1992)	1379 (1122 to 1696)	1821 (1328 to 2497)	1539 (1090 to 2173)
A/H3N2 Day 1	34 (22 to 53)	31 (20 to 47)	69 (31 to 152)	110 (46 to 261)
A/H3N2 Day 29	904 (648 to 1261)	342 (247 to 472)	1442 (764 to 2723)	1762 (879 to 3530)
A/H3N2 Day 50	2370 (1957 to 2869)	928 (770 to 1118)	1702 (1091 to 2655)	2114 (1300 to 3436)
B Strain Day 1	5.81 (5.38 to 6.28)	5.82 (5.4 to 6.27)	5.85 (4.44 to 7.73)	6.98 (5.16 to 9.46)
B Strain Day 29	23 (18 to 30)	12 (8.95 to 15)	50 (23 to 111)	30 (13 to 72)
B Strain Day 50	200 (161 to 248)	57 (46 to 71)	171 (99 to 295)	152 (84 to 275)

End point values	aTIV (≥6to ≤60 months)	TIV (≥6 to ≤60 months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	120	122		
Units: Titers				
geometric mean (confidence interval 95%)				
A/H1N1 Day 1	15 (11 to 21)	15 (11 to 21)		
A/H1N1 Day 29	624 (450 to 866)	434 (313 to 601)		
A/H1N1 Day 50	1639 (1361 to 1975)	1397 (1161 to 1682)		
A/H3N2 Day 1	37 (25 to 55)	36 (24 to 53)		
A/H3N2 Day 29	913 (669 to 1247)	416 (305 to 567)		
A/H3N2 Day 50	2134 (1773 to 2568)	1029 (856 to 1238)		
B Strain Day 1	5.88 (5.39 to 6.4)	6.01 (5.52 to 6.55)		

B Strain Day 29	27 (20 to 36)	13 (10 to 18)		
B Strain Day 50	198 (159 to 248)	67 (54 to 84)		

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of Antibody Responses of aTIV With TIV in Terms of Geometric Mean Ratio (GMRs) Against Homologous Strains

End point title	Comparison of Antibody Responses of aTIV With TIV in Terms of Geometric Mean Ratio (GMRs) Against Homologous Strains[2]

End point description:

The GMR of post-vaccination versus pre-vaccination HI titers against homologous strains, three weeks (day 29/day 1; day 50/day 1

End point type	Primary

End point timeframe:

Day 29 and Day 50

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: There were no statistical analysis done.

End point values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)	TIV (≥36 to ≤60 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	102	23	20
Units: Ratio				
geometric mean (confidence interval 95%)				
A/H1N1 Day 29/Day 1	41 (33 to 52)	29 (23 to 36)	37 (23 to 59)	23 (14 to 39)
A/H1N1 Day 50/Day 1	113 (84 to 153)	97 (72 to 129)	69 (33 to 142)	51 (23 to 113)
A/H3N2 Day 29/Day 1	26 (20 to 35)	11 (8.43 to 15)	21 (12 to 37)	16 (8.52 to 30)
A/H3N2 Day 50/Day 1	69 (47 to 100)	30 (21 to 44)	25 (13 to 46)	19 (9.81 to 38)
B Strain Day 29/Day 1	3.97 (3.16 to 4.97)	2 (1.61 to 2.5)	8.61 (4.34 to 17)	4.33 (2.05 to 9.16)
B Strain Day 50/Day 1	34 (28 to 42)	9.86 (8.07 to 12)	29 (17 to 51)	22 (12 to 40)

End point values	aTIV (≥6to ≤60 months)	TIV (≥6 to ≤60 months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	120	122		
Units: Ratio				
geometric mean (confidence interval 95%)				
A/H1N1 Day 29/Day 1	41 (33 to 51)	28 (23 to 35)		
A/H1N1 Day 50/Day 1	108 (82 to 144)	91 (69 to 121)		

A/H3N2 Day 29/Day 1	24 (19 to 32)	12 (8.97 to 15)		
A/H3N2 Day 50/Day 1	57 (41 to 80)	29 (21 to 41)		
B Strain Day 29/Day 1	4.59 (3.62 to 5.82)	2.23 (1.76 to 2.82)		
B Strain Day 50/Day 1	34 (27 to 42)	11 (9.11 to 14)		

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of Antibody Responses of aTIV With TIV in Terms of Percentage of Subjects Achieving Seroconversion or 4-fold Increase in HI Titers Against Homologous Strains

End point title	Comparison of Antibody Responses of aTIV With TIV in Terms of Percentage of Subjects Achieving Seroconversion or 4-fold Increase in HI Titers Against Homologous Strains[3]

End point description:

Seroconversion rate is defined as either pre-vaccination HI titer <10 and a post-vaccination HI titer ≥40 or a prevaccination HI titer ≥10 and a minimum four-fold rise in post-vaccination HI antibody titer

End point type	Primary

End point timeframe:

Day 1, Day 29 and Day 50

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: There were no statistical analysis done.

End point values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)	TIV (≥36 to ≤60 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	102	23	20
Units: Percentages of subjects				
number (confidence interval 95%)				
A/H1N1 Day 29	97 (91 to 99)	97 (92 to 99)	100 (85 to 100)	95 (75 to 100)
A/H1N1 Day 50	99 (94 to 100)	98 (93 to 100)	96 (78 to 100)	95 (75 to 100)
A/H3N2 Day 29	95 (88 to 98)	85 (77 to 92)	91 (72 to 99)	90 (68 to 99)
A/H3N2 Day 50	98 (93 to 100)	89 (82 to 94)	91 (72 to 99)	95 (75 to 100)
B Strain Day 29	32 (23 to 42)	9 (4 to 16)	61 (39 to 80)	30 (12 to 54)
B Strain Day 50	95 (88 to 98)	75 (65 to 83)	96 (78 to 100)	80 (56 to 94)

End point values	aTIV (≥6to ≤60 months)	TIV (≥6 to ≤60 months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	120	122		
Units: Percentages of subjects				
number (confidence interval 95%)				
A/H1N1 Day 29	98 (93 to 99)	97 (92 to 99)		
A/H1N1 Day 50	98 (94 to 100)	98 (93 to 99)		
A/H3N2 Day 29	94 (88 to 98)	86 (79 to 92)		

A/H3N2 Day 50	97 (92 to 99)	90 (83 to 95)		
B Strain Day 29	38 (29 to 47)	12 (7 to 19)		
B Strain Day 50	95 (89 to 98)	75 (67 to 83)		

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of Antibody Responses of aTIV With TIV in Terms of Percentage of Subjects Achieving Seroprotection as measured by HI Titers Against Homologous Strains

End point title	Comparison of Antibody Responses of aTIV With TIV in Terms of Percentage of Subjects Achieving Seroprotection as measured by HI Titers Against Homologous Strains[4]

End point description:

Immunogenicity was assessed in terms of percentage of subjects achieving seroconversion as measured by HI assay. Seroprotection is defined as an HI titer ≥ 40

End point type	Primary

End point timeframe:

Day 1, Day 29 and Day 50

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: There were no statistical analysis done.

End point values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)	TIV (≥36 to ≤60 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	102	23	20
Units: Percentages of subjects				
number (confidence interval 95%)				
A/H1N1 Day 1	29 (20 to 39)	30 (22 to 40)	52 (31 to 73)	60 (36 to 81)
A/H1N1 Day 29	100 (96 to 100)	99 (95 to 100)	100 (85 to 100)	95 (75 to 100)
A/H1N1 Day 50	100 (96 to 100)	100 (96 to 100)	100 (83 to 100)	100 (83 to 100)
A/H3N2 Day 1	41 (31 to 52)	37 (28 to 47)	52 (31 to 73)	70 (46 to 88)
A/H3N2 Day 29	100 (96 to 100)	99 (95 to 100)	100 (85 to 100)	95 (75 to 100)
A/H3N2 Day 50	100 (96 to 100)	100 (96 to 100)	100 (85 to 100)	100 (83 to 100)
B Strain Day 1	1 (0.026 to 6)	0 (0 to 4)	4 (0 to 22)	5 (0 to 25)
B Strain Day 29	33 (24 to 43)	9 (4 to 16)	61 (39 to 80)	30 (12 to 54)
B Strain Day 50	95 (88 to 98)	75 (65 to 83)	96 (78 to 100)	80 (56 to 94)

End point values	aTIV (≥6to ≤60 months)	TIV (≥6 to ≤60 months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	120	122		

Units: Percentages of subjects				
number (confidence interval 95%)				
A/H1N1 Day 1	33 (25 to 43)	35 (27 to 44)		
A/H1N1 Day 29	100 (97 to 100)	98 (94 to 100)		
A/H1N1 Day 50	100 (97 to 100)	100 (97 to 100)		
A/H3N2 Day 1	43 (34 to 53)	43 (34 to 52)		
A/H3N2 Day 29	100 (97 to 100)	98 (94 to 100)		
A/H3N2 Day 50	100 (97 to 100)	100 (97 to 100)		
B Strain Day 1	2 (0 to 6)	1 (0.021 to 4)		
B Strain Day 29	38 (30 to 48)	12 (7 to 19)		
B Strain Day 50	95 (89 to 98)	75 (67 to 83)		

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of Antibody Responses of aTIV With TIV in Terms of Geometric Mean Ratio (GMRs) Against mismatched Strains (Drifted Strains)

End point title	Comparison of Antibody Responses of aTIV With TIV in Terms of Geometric Mean Ratio (GMRs) Against mismatched Strains (Drifted Strains)[5]

End point description:

The GMR of post-vaccination versus pre-vaccination HI titers against homologous strains, three weeks (day 29/day 1; day 50/day 1)

End point type	Primary

End point timeframe:

Day 29 and 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: There were no statistical analysis done.

End point values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)	TIV (≥36 to ≤60 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	102	23	20
Units: Ratios				
geometric mean (confidence interval 95%)				
A/H1N1 Day 29/Day 1	4.78 (3.5 to 6.52)	3.49 (2.58 to 4.73)	11 (5.38 to 22)	6.27 (2.88 to 14)
A/H1N1 Day 50/Day 1	9.09 (7.06 to 12)	6.24 (4.88 to 7.97)	12 (6.7 to 20)	7.01 (3.83 to 13)
A/H3N2 Day 29/Day 1	8.85 (6.5 to 12)	3.49 (2.58 to 4.71)	9.76 (5.76 to 17)	13 (7.22 to 23)
A/H3N2 Day 50/Day 1	25 (19 to 33)	8.71 (6.64 to 11)	16 (8.97 to 27)	16 (8.59 to 29)
B Strain Day 29/Day 1	1.69 (1.41 to 2.03)	1.31 (1.1 to 1.57)	3.58 (2.38 to 5.39)	1.49 (0.96 to 2.33)
B Strain Day 50/Day 1	3.73 (3.06 to 4.54)	1.77 (1.46 to 2.15)	4.58 (2.92 to 7.2)	2.24 (1.37 to 3.66)

End point values	aTIV (≥6to ≤60 months)	TIV (≥6 to ≤60 months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	120	122		
Units: Ratios				
geometric mean (confidence interval 95%)				
A/H1N1 Day 29/Day 1	5.29 (3.93 to 7.13)	3.67 (2.73 to 4.94)		
A/H1N1 Day 50/Day 1	9.36 (7.4 to 12)	6.26 (4.96 to 7.91)		
A/H3N2 Day 29/Day 1	8.73 (6.55 to 12)	4.2 (3.15 to 5.59)		
A/H3N2 Day 50/Day 1	23 (17 to 29)	9.63 (7.4 to 12)		
B Strain Day 29/Day 1	1.9 (1.6 to 2.27)	1.31 (1.1 to 1.56)		
B Strain Day 50/Day 1	3.86 (3.2 to 4.64)	1.82 (1.52 to 2.19)		

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of Antibody Responses of aTIV With TIV in Terms of Percentage of Subjects Achieving Seroconversion or 4-fold Increase in HI Titers Against mismatched Strains (Drifted Strains)

End point title	Comparison of Antibody Responses of aTIV With TIV in Terms of Percentage of Subjects Achieving Seroconversion or 4-fold Increase in HI Titers Against mismatched Strains (Drifted Strains)[6]

End point description:

Seroconversion rate is defined as either pre-vaccination HI titer <10 and a post-vaccination HI titer ≥40 or a prevaccination HI titer ≥10 and a minimum four-fold rise in post-vaccination HI antibody titer

End point type	Primary

End point timeframe:

Day 1, Day 29 and Day 50

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: There were no statistical analysis done.

End point values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)	TIV (≥36 to ≤60 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	102	23	20
Units: Percentages of subjects				
number (confidence interval 95%)				
A/H1N1 Day 29	47 (37 to 58)	45 (35 to 55)	74 (52 to 90)	70 (46 to 88)
A/H1N1 Day 50	87 (78 to 93)	73 (63 to 81)	74 (52 to 90)	80 (56 to 94)

A/H3N2 Day 29	63 (52 to 72)	43 (33 to 53)	83 (61 to 95)	85 (62 to 97)
A/H3N2 Day 50	96 (90 to 99)	79 (70 to 87)	91 (72 to 99)	90 (68 to 99)
B Strain Day 29	9 (4 to 17)	6 (2 to 12)	43 (23 to 66)	20 (6 to 44)
B Strain Day 50	55 (44 to 65)	19 (12 to 28)	70 (47 to 87)	45 (23 to 68)

End point values	aTIV (≥6to ≤60 months)	TIV (≥6 to ≤60 months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	120	122		
Units: Percentages of subjects				
number (confidence interval 95%)				
A/H1N1 Day 29	53 (43 to 62)	49 (40 to 58)		
A/H1N1 Day 50	84 (76 to 90)	74 (65 to 81)		
A/H3N2 Day 29	67 (57 to 75)	50 (41 to 59)		
A/H3N2 Day 50	95 (89 to 98)	81 (73 to 88)		
B Strain Day 29	16 (10 to 24)	8 (4 to 15)		
B Strain Day 50	58 (48 to 66)	23 (12 to 31)		

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of Antibody Responses of aTIV With TIV in Terms of Percentage of Subjects Achieving Seroprotection as measured by HI Titers Against mismatched Strains (Drifted Strains)

End point title	Comparison of Antibody Responses of aTIV With TIV in Terms of Percentage of Subjects Achieving Seroprotection as measured by HI Titers Against mismatched Strains (Drifted Strains)[7]

End point description:

Seroprotection is defined as an HI titer ≥40.

End point type	Primary

End point timeframe:

Day 1, Day 29 and Day 50

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

End point values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)	TIV (≥36 to ≤60 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	102	23	20
Units: Percentages of subjects				
number (confidence interval 95%)				
A/H1N1 Day 1	80 (71 to 88)	75 (65 to 83)	74 (52 to 90)	95 (75 to 100)
A/H1N1 Day 29	93 (86 to 97)	92 (85 to 97)	96 (78 to 100)	100 (83 to 100)

A/H1N1 Day 50	100 (96 to 100)	98 (93 to 100)	96 (78 to 100)	100 (83 to 100)
A/H3N2 Day 1	36 (27 to 46)	33 (24 to 43)	48 (27 to 69)	65 (41 to 85)
A/H3N2 Day 29	65 (55 to 74)	48 (38 to 58)	91 (72 to 99)	85 (62 to 97)
A/H3N2 Day 50	100 (96 to 199)	91 (84 to 96)	100 (85 to 100)	100 (83 to 100)
B Strain Day 1	16 (10 to 25)	14 (8 to 22)	35 (16 to 57)	35 (15 to 59)
B Strain Day 29	34 (25 to 44)	21 (13 to 30)	52 (31 to 73)	45 (23 to 68)
B Strain Day 50	90 (82 to 95)	56 (46 to 66)	78 (56 to 93)	80 (56 to 94)

End point values	aTIV (≥6to ≤60 months)	TIV (≥6 to ≤60 months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	120	122		
Units: Percentages of subjects				
number (confidence interval 95%)				
A/H1N1 Day 1	79 (71 to 86)	78 (69 to 85)		
A/H1N1 Day 29	93 (87 to 97)	93 (87 to 97)		
A/H1N1 Day 50	99 (95 to 100)	98 (94 to 100)		
A/H3N2 Day 1	38 (30 to 48)	39 (30 to 48)		
A/H3N2 Day 29	70 (61 to 78)	54 (45 to 63)		
A/H3N2 Day 50	100 (97 to 100)	93 (86 to 97)		
B Strain Day 1	20 (13 to 28)	17 (11 to 25)		
B Strain Day 29	38 (29 to 47)	25 (17 to 33)		
B Strain Day 50	88 (80 to 93)	60 (51 to 69)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Reporting Solicited Local and Systemic Adverse Events, After Any Vaccination

End point title	Number of Subjects Reporting Solicited Local and Systemic Adverse Events, After Any Vaccination[8]

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic adverse events, 3 weeks after the primary course with aTIV and TIV vaccine

End point type	Primary

End point timeframe:

From day 1 through day 50 after any vaccination

Notes:

[8] - 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: There were no statistical analysis done.

End point values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)	TIV (≥36 to ≤60 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	130	44[9]	48[10]
Units: Number				
Injection Site Ecchymosis	18	18	11	9
Injection Site Erythema	31	18	21	19
Injection Site Induration	13	5	19	12
Injection Site Swelling	8	5	12	6
Tenderness	30	25	30	20
Changing Eat Habits	22	18	0	0
Sleepiness	9	8	0	0
Unusual Crying	32	28	0	0
Irritability	23	20	0	0
Vomiting	12	8	0	0
Chills	0	0	7	5
Diarrhea	16	9	0	0
Shivering	7	2	0	0
Malaise	0	0	15	13
Myalgia	0	0	7	5
Arthralgia	0	0	4	1
Headache	0	0	9	11
Sweating	0	0	2	4
Fatigue	0	0	7	5
Fever (≥38°C)	89	100	41	39
Temp (≥40°C)	0	0	0	1
Stayed Home	30	22	8	6
Analg.Antipy. Med. Used	46	30	17	11

Notes:

[9] - A total of 6 subjects were erroneously randomized in the 36 to < 60 aTIV months age group

[10] - A total of 2 subjects were errneously randomized to 36 to < 60 TIV months of age group

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Reporting Unsolicited Adverse Events after any vaccination

End point title	Number of Subjects Reporting Unsolicited Adverse Events after any vaccination[11]

End point description:

All AEs and concomitant medications were collected from visit 1 (day 1) to visit 5 (day 50

End point type	Primary

End point timeframe:

Day 1 through day 50

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

End point values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)	TIV (≥36 to ≤60 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	136	132	44	48
Units: Number of subjects				
Any AE	57	47	16	23
At least possibly related AEs	6	3	1	1
Any SAE	0	0	0	0
At least possibly related SAEs	0	0	0	0
AE leading to discontinuation	0	0	1	1
Death	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of Antibody Responses of aTIV With TIV in Terms of Geometric Mean Titers (GMTs) Against mismatched Strains (Drifted Strains)

End point title	Comparison of Antibody Responses of aTIV With TIV in Terms of Geometric Mean Titers (GMTs) Against mismatched Strains (Drifted Strains)

End point description:

The Hemagglutination Inhibition (HI) antibody responses of aTIV compared to TIV assessed in terms of post vaccination GMTs at three weeks after last vaccination against the three homologous vaccine strains.

End point type	Secondary

End point timeframe:

Day 1, Day 29 and Day 50

End point values	aTIV (≥6to ≤36 months)	TIV (≥6 to ≤36 months)	aTIV (≥36 to ≤60 months)	TIV (≥36 to ≤60 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	102	23	20
Units: Titers				
geometric mean (confidence interval 95%)				
A/HINI Day 1	43 (36 to 52)	45 (37 to 54)	39 (25 to 62)	61 (37 to 100)
A/H1N1 Day 29	207 (143 to 300)	157 (109 to 225)	430 (189 to 977)	381 (155 to 933)
A/H1N1 Day 50	394 (298 to 522)	279 (213 to 367)	458 (259 to 809)	426 (228 to 793)
A/H3N2 Day 1	19 (13 to 28)	16 (11 to 23)	40 (20 to 81)	64 (30 to 138)
A/H3N2 Day 29	168 (104 to 273)	56 (35 to 90)	393 (167 to 925)	827 (325 to 2107)
A/H3N2 Day 50	475 (346 to 651)	56 (35 to 90)	629 (363 to 1091)	1014 (556 to 1850)
B Strain Day 1	15 (13 to 17)	14 (12 to 16)	16 (12 to 22)	36 (25 to 51)
B Strain Day 29	25 (21 to 30)	18 (16 to 22)	57 (35 to 94)	53 (31 to 92)
B Strain Day 50	55 (47 to 65)	25 (21 to 29)	73 (45 to 119)	80 (47 to 136)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 to Day 50	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups	
Reporting group title	TIV (≥6 to ≤36 months)
Reporting group description:	
Children 6 to <36 months of age received two 0.25 mL doses of non-adjuvanted split influenza vaccine (TIV), administered four weeks apart	
Reporting group title	aTIV (≥6to ≤36 months)
Reporting group description:	
Children 6 to <36 months of age received two 0.25 mL doses of MF59 adjuvanted trivalent influenza vaccine(aTIV), administered four weeks apart	
Reporting group title	aTIV (≥36 to ≤60 months)
Reporting group description:	
Children 36 to <60 months of age received two 0.5 mL doses of aTIV, administered four weeks apart	
Reporting group title	TIV (≥36 to ≤60 months)
Reporting group description:	
Children 36 to <60 months of age received two 0.5 mL doses of either TIV, administered four weeks apart.	
Reporting group title	aTIV (≥6to ≤60 months)
Reporting group description:	
Children aged 6 to <36 months received two doses of 0.25 mL and those aged 36 to <60 received two doses of 0.5 mL of aTIV, administered four weeks apart.	
Reporting group title	TIV (≥6 to ≤60 months)
Reporting group description:	
Children aged 6 to <36 months received two doses of 0.25 mL and those aged 36 to <60 received two doses of 0.5 mL of TIV, administered four weeks apart	

Serious adverse events	TIV (≥6 to ≤36 months)	aTIV (≥6to ≤36 months)	aTIV (≥36 to ≤60 months)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 132 (0.76%)	1 / 136 (0.74%)	0 / 44 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Multiple injuries			
subjects affected / exposed	1 / 132 (0.76%)	0 / 136 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Pleural cyst			
subjects affected / exposed	0 / 132 (0.00%)	1 / 136 (0.74%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lobar pneumonia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 136 (0.74%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	TIV (≥36 to ≤60 months)	aTIV (≥6to ≤60 months)	TIV (≥6 to ≤60 months)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	1 / 180 (0.56%)	1 / 180 (0.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Multiple injuries			
subjects affected / exposed	0 / 48 (0.00%)	0 / 180 (0.00%)	1 / 180 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural cyst			
subjects affected / exposed	0 / 48 (0.00%)	1 / 180 (0.56%)	0 / 180 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lobar pneumonia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 180 (0.56%)	0 / 180 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	TIV (≥6 to ≤36 months)	aTIV (≥6to ≤36 months)	aTIV (≥36 to ≤60 months)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 132 (57.58%)	101 / 136 (74.26%)	40 / 44 (90.91%)
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 132 (1.52%)	0 / 136 (0.00%)	9 / 44 (20.45%)
occurrences (all)	2	0	13
Somnolence			
subjects affected / exposed	8 / 132 (6.06%)	9 / 136 (6.62%)	0 / 44 (0.00%)
occurrences (all)	9	11	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	2 / 132 (1.52%)	8 / 136 (5.88%)	6 / 44 (13.64%)
occurrences (all)	2	8	6
Crying			
subjects affected / exposed	28 / 132 (21.21%)	32 / 136 (23.53%)	0 / 44 (0.00%)
occurrences (all)	40	43	0
Fatigue			
subjects affected / exposed	0 / 132 (0.00%)	0 / 136 (0.00%)	7 / 44 (15.91%)
occurrences (all)	0	0	10
Injection site haemmorhage			
subjects affected / exposed	18 / 132 (13.64%)	18 / 136 (13.24%)	11 / 44 (25.00%)
occurrences (all)	22	22	13
Injection site induration			
subjects affected / exposed	5 / 132 (3.79%)	14 / 136 (10.29%)	18 / 44 (40.91%)
occurrences (all)	5	18	25
Injection site pain			
subjects affected / exposed	25 / 132 (18.94%)	31 / 136 (22.79%)	29 / 44 (65.91%)
occurrences (all)	32	38	43
Injection site swelling			
subjects affected / exposed	5 / 132 (3.79%)	8 / 136 (5.88%)	12 / 44 (27.27%)
occurrences (all)	6	10	12
Malaise			
subjects affected / exposed	0 / 132 (0.00%)	0 / 136 (0.00%)	15 / 44 (34.09%)
occurrences (all)	0	0	18
Pyrexia			

subjects affected / exposed	34 / 132 (25.76%)	44 / 136 (32.35%)	11 / 44 (25.00%)
occurrences (all)	44	56	12
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 132 (9.09%)	20 / 136 (14.71%)	0 / 44 (0.00%)
occurrences (all)	14	25	0
Vomiting			
subjects affected / exposed	8 / 132 (6.06%)	12 / 136 (8.82%)	2 / 44 (4.55%)
occurrences (all)	8	14	2
Injection site erythema			
subjects affected / exposed	18 / 132 (13.64%)	32 / 136 (23.53%)	20 / 44 (45.45%)
occurrences (all)	23	41	28
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
subjects affected / exposed	5 / 132 (3.79%)	8 / 136 (5.88%)	1 / 44 (2.27%)
occurrences (all)	5	9	1
Cough			
subjects affected / exposed	5 / 132 (3.79%)	6 / 136 (4.41%)	5 / 44 (11.36%)
occurrences (all)	5	6	6
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 132 (0.00%)	0 / 136 (0.00%)	2 / 44 (4.55%)
occurrences (all)	0	0	3
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	18 / 132 (13.64%)	22 / 136 (16.18%)	0 / 44 (0.00%)
occurrences (all)	24	29	0
Irritability			
subjects affected / exposed	20 / 132 (15.15%)	23 / 136 (16.91%)	0 / 44 (0.00%)
occurrences (all)	21	37	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 132 (0.00%)	0 / 136 (0.00%)	4 / 44 (9.09%)
occurrences (all)	0	0	5
Myalgia			

subjects affected / exposed	0 / 132 (0.00%)	0 / 136 (0.00%)	7 / 44 (15.91%)
occurrences (all)	0	0	10
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 132 (2.27%)	7 / 136 (5.15%)	5 / 44 (11.36%)
occurrences (all)	3	7	5
Nasopharyngitis			
subjects affected / exposed	7 / 132 (5.30%)	16 / 136 (11.76%)	1 / 44 (2.27%)
occurrences (all)	9	16	2
Otitis Media			
subjects affected / exposed	6 / 132 (4.55%)	8 / 136 (5.88%)	3 / 44 (6.82%)
occurrences (all)	6	10	3
Pharyngitis streptococcal			
subjects affected / exposed	5 / 132 (3.79%)	5 / 136 (3.68%)	0 / 44 (0.00%)
occurrences (all)	6	5	0
Tonsillitis			
subjects affected / exposed	2 / 132 (1.52%)	7 / 136 (5.15%)	0 / 44 (0.00%)
occurrences (all)	2	7	0
Upper respiratory tract infection			
subjects affected / exposed	9 / 132 (6.82%)	11 / 136 (8.09%)	1 / 44 (2.27%)
occurrences (all)	9	13	1
Varicella			
subjects affected / exposed	4 / 132 (3.03%)	9 / 136 (6.62%)	2 / 44 (4.55%)
occurrences (all)	4	9	2

Non-serious adverse events	TIV (≥36 to ≤60 months)	aTIV (≥6to ≤60 months)	TIV (≥6 to ≤60 months)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 48 (83.33%)	141 / 180 (78.33%)	116 / 180 (64.44%)
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 48 (22.92%)	9 / 180 (5.00%)	13 / 180 (7.22%)
occurrences (all)	17	13	19
Somnolence			
subjects affected / exposed	0 / 48 (0.00%)	9 / 180 (5.00%)	8 / 180 (4.44%)
occurrences (all)	0	11	9
General disorders and administration site conditions			

Chills			
subjects affected / exposed	5 / 48 (10.42%)	14 / 180 (7.78%)	7 / 180 (3.89%)
occurrences (all)	6	14	8
Crying			
subjects affected / exposed	0 / 48 (0.00%)	32 / 180 (17.78%)	28 / 180 (15.56%)
occurrences (all)	0	43	40
Fatigue			
subjects affected / exposed	5 / 48 (10.42%)	7 / 180 (3.89%)	5 / 180 (2.78%)
occurrences (all)	6	10	6
Injection site haemmorhage			
subjects affected / exposed	9 / 48 (18.75%)	29 / 180 (16.11%)	27 / 180 (15.00%)
occurrences (all)	11	35	33
Injection site induration			
subjects affected / exposed	12 / 48 (25.00%)	32 / 180 (17.78%)	17 / 180 (9.44%)
occurrences (all)	16	43	21
Injection site pain			
subjects affected / exposed	20 / 48 (41.67%)	60 / 180 (33.33%)	45 / 180 (25.00%)
occurrences (all)	27	81	59
Injection site swelling			
subjects affected / exposed	6 / 48 (12.50%)	20 / 180 (11.11%)	11 / 180 (6.11%)
occurrences (all)	7	22	13
Malaise			
subjects affected / exposed	13 / 48 (27.08%)	15 / 180 (8.33%)	13 / 180 (7.22%)
occurrences (all)	20	18	20
Pyrexia			
subjects affected / exposed	13 / 48 (27.08%)	55 / 180 (30.56%)	47 / 180 (26.11%)
occurrences (all)	15	68	59
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 48 (4.17%)	20 / 180 (11.11%)	14 / 180 (7.78%)
occurrences (all)	0	25	16
Vomiting			
subjects affected / exposed	0 / 48 (0.00%)	14 / 180 (7.78%)	8 / 180 (4.44%)
occurrences (all)	0	16	8
Injection site erythema			

subjects affected / exposed	19 / 48 (39.58%)	52 / 180 (28.89%)	37 / 180 (20.56%)
occurrences (all)	24	69	47
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
subjects affected / exposed	1 / 48 (2.08%)	9 / 180 (5.00%)	6 / 180 (3.33%)
occurrences (all)	2	10	7
Cough			
subjects affected / exposed	8 / 48 (16.67%)	11 / 180 (6.11%)	13 / 180 (7.22%)
occurrences (all)	10	12	15
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	4 / 48 (8.33%)	2 / 180 (1.11%)	4 / 180 (2.22%)
occurrences (all)	4	3	4
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	0 / 48 (0.00%)	22 / 180 (12.22%)	18 / 180 (10.00%)
occurrences (all)	0	29	24
Irritability			
subjects affected / exposed	0 / 48 (0.00%)	23 / 180 (12.78%)	20 / 180 (11.11%)
occurrences (all)	0	31	27
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 48 (2.08%)	4 / 180 (2.22%)	1 / 180 (0.56%)
occurrences (all)	1	5	1
Myalgia			
subjects affected / exposed	5 / 48 (10.42%)	7 / 180 (3.89%)	5 / 180 (2.78%)
occurrences (all)	6	10	6
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 48 (4.17%)	12 / 180 (6.67%)	5 / 180 (2.78%)
occurrences (all)	2	12	5
Nasopharyngitis			
subjects affected / exposed	2 / 48 (4.17%)	17 / 180 (9.44%)	9 / 180 (5.00%)
occurrences (all)	2	18	11
Otitis Media			

subjects affected / exposed	3 / 48 (6.25%)	11 / 180 (6.11%)	9 / 180 (5.00%)
occurrences (all)	3	13	9
Pharyngitis streptococcal			
subjects affected / exposed	5 / 48 (10.42%)	5 / 180 (2.78%)	10 / 180 (5.56%)
occurrences (all)	5	5	11
Tonsillitis			
subjects affected / exposed	4 / 48 (8.33%)	7 / 180 (3.89%)	6 / 180 (3.33%)
occurrences (all)	4	7	6
Upper respiratory tract infection			
subjects affected / exposed	3 / 48 (6.25%)	12 / 180 (6.67%)	12 / 180 (6.67%)
occurrences (all)	4	14	13
Varicella			
subjects affected / exposed	2 / 48 (4.17%)	11 / 180 (6.11%)	6 / 180 (3.33%)
occurrences (all)	2	11	6

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/20813217