Clinical trial results:
A Phase 2, Randomized, Controlled, Observer-Blind, Clinical Study to Evaluate the Humoral and Cell Mediated Immunity and Safety of Two Intramuscular Doses of Fluad™ or Agrippal™ in Previously Unvaccinated Healthy Subjects Aged 6 to < 36 Months.

Summary

EudraCT number	2010-023791-63
Trial protocol	DE BE
Global end of trial date	14 February 2012
Results information	
Result version number	v2 (current)
This version publication date	28 July 2016
First version publication date	20 March 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	V70_34
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01342796
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 and Diagnostics S.r.l., RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l, 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	17 May 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 February 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the cell mediated immune (CMI) responses to two 0.25 mL Intramuscular (IM) injections of Thiomersal free MF59C.1-adjuvated influenza vaccine (aTIV) or to two 0.25 mL IM injections of non-adjuvated trivalent influenza vaccine (TIV) as determined by the quality and quantity of the antigen-specific T- cells responses after in-vitro restimulation of peripheral blood mononuclear cells in previously unvaccinated healthy children aged 6 to <36 months.

Protection of trial subjects:

This clinical study was designated, implemented and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations (CFR) Title 21, and Japanese Ministry of Health, Labor and Welfare), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	21 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 84
Worldwide total number of subjects	84
EEA total number of subjects	84

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)	43

Children (2-11 years)	41
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:

A total of 90 subjects were planned for this study. Overall, 84 subjects were enrolled .

Pre-assignment

Screening details:

Subjects were randomized into one of two treatment groups in a 1:1 ratio to receive either aTIV or TIV.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	aTIV (6 to < 24 months)

Arm description:

Subjects aged between 6 to <24 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.

Arm type	Experimental
Investigational medicinal product name	MF59C.1-adjuvanted subunit trivalent influenza vaccine (purified viral envelope-glycoproteins neuraminidase (NA) and hemagglutinin (HA))
Investigational medicinal product code	
Other name	Fluad
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of one 0.25 mL dose administered IM in the deltoid muscle, preferably of the non-dominant arm.

Arm title	aTIV (24 to <36 months)

Arm description:

Subjects aged between 24 to <36 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.

Arm type	Experimental
Investigational medicinal product name	MF59C.1-adjuvanted subunit trivalent influenza vaccine (purified viral envelope-glycoproteins neuraminidase (NA) and hemagglutinin (HA))
Investigational medicinal product code	
Other name	Fluad
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of one 0.25 mL dose administered IM in the deltoid muscle, preferably of the non-dominant arm.

Arm title	TIV (6 to <24 months)

Arm description:

Subjects aged between 6 to <24 months who received two doses of inactivated unadjuvanted trivalent influenza vaccine on days 1 and 29.

Arm type	Active comparator
Investigational medicinal product name	Egg-derived trivalent subunit influenza vaccine
Investigational medicinal product code	
Other name	Agrippal
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of one 0.25 mL dose administered IM in the deltoid muscle, preferably of the non-dominant arm.

Arm title	TIV (24 to <36 months)

Arm description:

Subjects aged between 24 to <36 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.

Arm type	Active comparator
Investigational medicinal product name	Egg-derived trivalent subunit influenza vaccine
Investigational medicinal product code	
Other name	Agrippal
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of one 0.25 mL dose administered IM in the deltoid muscle, preferably of the non-dominant arm.

Number of subjects in period 1	aTIV (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)
Started	22	21	21
Completed	21	19	20
Not completed	1	2	1
Consent withdrawn by subject	1	1	-
Inappropriate enrollment	-	1	-
Lost to follow-up	-	-	1

Number of subjects in period 1	TIV (24 to <36 months)
Started	20
Completed	18
Not completed	2
Consent withdrawn by subject	-
Inappropriate enrollment	-
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	aTIV (6 to < 24 months)
Reporting group description:	
Subjects aged between 6 to <24 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.	

Reporting group title	aTIV (24 to <36 months)
Reporting group description:	
Subjects aged between 24 to <36 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.	

Reporting group title	TIV (6 to <24 months)
Reporting group description:	
Subjects aged between 6 to <24 months who received two doses of inactivated unadjuvanted trivalent influenza vaccine on days 1 and 29.	

Reporting group title	TIV (24 to <36 months)
Reporting group description:	
Subjects aged between 24 to <36 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.	

Reporting group values	aTIV (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)
Number of subjects	22	21	21
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	13.1	27.6	13.1
standard deviation	± 5.4	± 2.8	± 5.6
Gender categorical			
Units: Subjects			
Female	9	7	11
Male	13	14	10

Reporting group values	TIV (24 to <36 months)	Total	
Number of subjects	20	84	

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	30		
standard deviation	± 3.7	-	
Gender categorical Units: Subjects			
Female	7	34	
Male	13	50	

End points

End points reporting groups

Reporting group title	aTIV (6 to < 24 months)

Reporting group description:

Subjects aged between 6 to <24 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.

Reporting group title	aTIV (24 to <36 months)

Reporting group description:

Subjects aged between 24 to <36 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.

Reporting group title	TIV (6 to <24 months)

Reporting group description:

Subjects aged between 6 to <24 months who received two doses of inactivated unadjuvanted trivalent influenza vaccine on days 1 and 29.

Reporting group title	TIV (24 to <36 months)

Reporting group description:

Subjects aged between 24 to <36 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.

Subject analysis set title	Per Protocol Set/Serology
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the full analysis set who received the relevant dose of vaccine correctly on Day 1, who provided evaluable serum samples with the relevant time windows and had no major protocol violations.

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the Exposed Set (all enrolled subjects who actually received a study vaccine) who provided post-baseline safety data.

Subject analysis set title	Per Protocol Set/CMI
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the full analysis set who received the relevant dose of vaccine correctly on Day 1, who provided evaluable serum samples with the relevant time windows and had no major protocol violations.

Primary: 1. Proportion of Cytokine Producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane strains/B/Florida/Staphylococcus enterotoxin B (SEB)/Tetanus toxoid strains.

End point title	1. Proportion of Cytokine Producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane strains/B/Florida/Staphylococcus enterotoxin B (SEB)/Tetanus toxoid strains.[1]

End point description:

Immunogenicity was measured in terms Proportion of Cytokine γ producing CD4+ T cells (Mean Cells per Million Total Cells (95% CI) in Response to In vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/Staphylococcus enterotoxin B (SEB) at day 1 and day 50. Data are reported based on the Per Protocol Set (PPS).

End point type	Primary

End point timeframe:

Day 1 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 (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Mean Cells per Million Total Cells				
arithmetic mean (confidence interval 95%)				
A/H1N1 (Day 1; N=16,8,17,8)	624 (422 to 826)	621 (405 to 836)	616 (420 to 812)	710 (495 to 926)
A/H1N1 (Day 50; N=16,8,17,8)	1262 (968 to 1556)	1953 (1189 to 2718)	1073 (788 to 1358)	1120 (356 to 1885)
A/H3N2 (Day 1; N=16,9,18,13)	438 (234 to 642)	613 (369 to 851)	506 (313 to 698)	398 (195 to 601)
A/H3N2 (Day 50; N=16,9,18,13)	1117 (861 to 1373)	1641 (1211 to 2071)	635 (394 to 876)	658 (603 to 1013)
B/Brisbane (Day 1; N=14,5,17,7)	644 (423 to 864)	526 (180 to 873)	623 (422 to 823)	966 (673 to 1258)
B/Brisbane (Day 50; N=14,5,17,7)	2184 (1750 to 2618)	2683 (1372 to 3994)	933 (539 to 1327)	1187 (113 to 2261)
B/Florida (Day 1; N=7,2,11,7)	708 (211 to 1205)	410 (-118.7 to 938)	791 (395 to 1187)	721 (439 to 1004)
B/Florida (Day 50; N=7,2,11,7)	1857 (1281 to 2433)	1008 (135 to 1881)	972 (513 to 1431)	1057 (615 to 1499)
SEB (Day 1; N=8,2,11,6)	75308 (50618 to 99997)	88595 (54063 to 123126)	111107 (90052 to 132162)	101313 (81376 to 121249)
SEB (Day 50; N=8,2,11,6)	88688 (63452 to 113924)	55772 (-2700 to 114244)	101174 (80115 to 122233)	111908 (78955 to 144861)
Tetanus Toxoid (Day 1; N=8,2,10,6)	1270 (719 to 1821)	1154 (-874.8 to 3183)	1351 (858 to 1844)	1397 (226 to 2568)
Tetanus Toxoid (Day 50; N=8,2,10,6)	1244 (772 to 1717)	860 (116 to 1604)	1177 (755 to 1600)	1328 (900 to 1757)

Statistical analyses

No statistical analyses for this end point

Primary: 2. Proportion of IL-2 Producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/Tetanus toxoid strains.

End point title	2. Proportion of IL-2 Producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/Tetanus toxoid strains.[2]

End point description:

Immunogenicity was measured in terms of the Proportion of IL-2 γproducing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/Tetanus toxoid at day 1 and day 50. Data are reported based on the Per Protocol Set (PPS).

End point type	Primary

End point timeframe:

Day 1 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 (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Mean Cells per Million Total Cells				
arithmetic mean (confidence interval 95%)				
A/H1N1 (Day 1; N=16,8,17,8)	285 (195 to 376)	242 (119 to 364)	167 (79 to 254)	356 (233 to 478)
A/H1N1 (Day 50; N=16,8,17,8)	891 (593 to 1189)	1308 (683 to 1932)	597 (308 to 886)	774 (149 to 1399)
A/H3N2 (Day 1; N=16,9,18,13)	199 (109 to 290)	216 (97 to 336)	153 (68 to 238)	219 (119 to 318)
A/H3N2 (Day 50; N=16,9,18,13)	754 (519 to 989)	1177 (810 to 1544)	407 (185 to 629)	342 (37 to 647)
B/Brisbane (Day 1; N=14,5,17,7)	294 (195 to 394)	179 (-112.5 to 470)	192 (101 to 283)	552 (306 to 798)
B/Brisbane (Day 50; N=14,5,17,7)	1612 (1187 to 2037)	1813 (798 to 2828)	618 (234 to 1002)	700 (-130.3 to 1531)
B/Florida (Day 1; N=7,2,11,7)	457 (159 to 755)	26 (-304.7 to 357)	181 (-57.24 to 419)	407 (231 to 584)
B/Florida (Day 50; N=7,2,11,7)	1404 (923 to 1885)	585 (-91.75 to 1262)	487 (109 to 865)	571 (264 to 878)
SEB (Day 1; N=8,2,11,16)	65580 (42981 to 88179)	81296 (46182 to 116409)	98178 (78905 to 117450)	86057 (65784 to 106330)
SEB (Day 50; N=8,2,11,16)	75418 (53564 to 97273)	48228 (-6205 to 102660)	89792 (71551 to 108033)	96476 (65156 to 127795)
Tetanus Toxoid (Day 1; N=8,2,10,6)	596 (288 to 905)	563 (-231.4 to 1360)	635 (359 to 911)	717 (256 to 1177)
Tetanus Toxoid (Day 50; N=8,2,10,6)	656 (285 to 1027)	584 (-496.8 to 1664)	681 (349 to 1013)	887 (268 to 1507)

Statistical analyses

No statistical analyses for this end point

Primary: 3. Proportion of IFN-γProducing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/Tetanus toxoid strains.

End point title	3. Proportion of IFN-γProducing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/Tetanus toxoid strains.[3]

End point description:

Immunogenicity was measured in terms of the Proportion of IFN-γproducing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/Tetanus toxoid strains at day 1 and day 50. Data are reported based on the Per Protocol Set (PPS).

End point type	Primary

End point timeframe:

Day 1 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 (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Mean Cells per Million Total Cells				
arithmetic mean (confidence interval 95%)				
A/H1N1 (Day 1; N=16,8,17,8)	110 (54 to 165)	66 (2.63 to 129)	115 (61 to 169)	127 (64 to 190)
A/H1N1 (Day 50; N=16,8,17,8)	186 (98 to 275)	348 (114 to 583)	166 (80 to 251)	303 (69 to 537)
A/H3N2 (Day 1; N=16,9,18,13)	76 (32 to 121)	75 (21 to 130)	65 (23 to 107)	92 (47 to 138)
A/H3N2 (Day 50; N=16,9,18,13)	82 (47 to 118)	357 (174 to 540)	117 (83 to 150)	117 (-35.01 to 269)
B/Brisbane (Day 1; N=14,5,17,7)	84 (47 to 122)	40 (-88.84 to 168)	80 (45 to 114)	192 (83 to 301)
B/Brisbane (Day 50; N=14,5,17,7)	373 (218 to 529)	204 (45 to 364)	119 (-22.68 to 260)	213 (82 to 344)
B/Florida (Day 1; N=7,2,11,7)	116 (55 to 177)	53 (-133 to 238)	61 (13 to 110)	135 (36 to 234)
B/Florida (Day 50; N=7,2,11,7)	196 (31 to 361)	181 (-9.667 to 372)	182 (52 to 312)	133 (34 to 231)
SEB (Day 1; N=8,2,11,6)	3252 (1877 to 4627)	2803 (-1842 to 7447)	3741 (2569 to 4914)	6056 (3375 to 8738)
SEB (Day 50; N=8,2,11,6)	3291 (1738 to 4844)	4674 (636 to 8712)	4098 (2775 to 5420)	5543 (3386 to 7700)
Tetanus Toxoid (Day 1; N=8,2,10,6)	98 (16 to 181)	305 (39 to 571)	145 (71 to 219)	136 (-17.56 to 289)
Tetanus Toxoid (Day 50; N=8,2,10,6)	129 (63 to 196)	73 (-79.23 to 225)	181 (121 to 240)	133 (51 to 215)

Statistical analyses

No statistical analyses for this end point

Primary: 4. Proportion of TNF-α Producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/Tetanus toxoid strains.

End point title	4. Proportion of TNF-α Producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/Tetanus toxoid strains.[4]

End point description:

Immunogenicity was measured in terms of Proportion of TNF-α producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/Tetanus toxoid strains at day 1 and day 50. Data are reported based on the Per Protocol Set (PPS).

End point type	Primary

End point timeframe:

Day 1 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 (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Mean Cells per Million Total Cells				
arithmetic mean (confidence interval 95%)				
A/H1N1 (Day 1; N=16,8,17,8)	109 (72 to 145)	139 (32 to 246)	96 (61 to 132)	180 (73 to 287)
A/H1N1 (Day 50; N=16,8,17,8)	372 (271 to 473)	614 (276 to 951)	212 (114 to 310)	369 (31 to 706)
A/H3N2 (Day 1; N=16,9,18,13)	56 (35 to 76)	115 (58 to 173)	64 (45 to 84)	69 (21 to 117)
A/H3N2 (Day 50; N=16,9,18,13)	394 (234 to 553)	542 (340 to 743)	179 (28 to 329)	203 (37 to 369)
B/Brisbane (Day 1; N=14,5,17,7)	118 (88 to 148)	49 (-116.5 to 214)	89 (62 to 117)	258 (118 to 397)
B/Brisbane (Day 50; N=14,5,17,7)	855 (550 to 1160)	1031 (410 to 1653)	247 (-29.07 to 522)	284 (-224.8 to 794)
B/Florida (Day 1; N=7,2,11,7)	152 (82 to 222)	44 (-275.1 to 362)	106 (50 to 162)	250 (80 to 421)
B/Florida (Day 50; N=7,2,11,7)	691 (366 to 1016)	398 (191 to 605)	229 (-27.79 to 487)	308 (204 to 412)
SEB (Day 1; N=8,2,11,6)	25901 (14384 to 37417)	23891 (4929 to 42852)	37632 (27811 to 47453)	38312 (27364 to 49259)
SEB (Day 50; N=8,2,11,6)	34801 (23595 to 46006)	22816 (-1592 to 47223)	33427 (23980 to 42874)	38540 (25651 to 51430)
Tetanus Toxoid (Day 1; N=8,2,10,6)	446 (171 to 722)	685 (18 to 1351)	486 (239 to 732)	587 (202 to 972)
Tetanus Toxoid (Day 50; N=8,2,10,6)	421 (224 to 618)	201 (-591.2 to 992)	581 (405 to 757)	802 (346 to 1257)

Statistical analyses

No statistical analyses for this end point

Primary: 5. Proportion of IL-21 Producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/ Tetanus toxoid strains.

End point title	5. Proportion of IL-21 Producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/ Tetanus toxoid strains.[5]

End point description:

Immunogenicity was measured in terms of Proportion of IL-21 producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/ Tetanus toxoid strains day 1 and day 50. Data are reported based on the Per Protocol Set (PPS).

End point type	Primary

End point timeframe:

Day 1 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 (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Mean Cells per Million Total Cells				
arithmetic mean (confidence interval 95%)				
A/H1N1 (Day 1; N=16,8,17,8)	128 (11 to 246)	126 (5.87 to 246)	177 (63 to 291)	218 (98 to 338)
A/H1N1 (Day 50; N=16,8,17,8)	209 (125 to 292)	423 (241 to 605)	164 (83 to 244)	168 (-13.7 to 350)
A/H3N2 (Day 1; N=16,9,18,13)	85 (-47.3 to 218)	104 (3.92 to 205)	188 (63 to 312)	104 (20 to 187)
A/H3N2 (Day 50; N=16,9,18,13)	121 (79 to 162)	381 (153 to 608)	76 (37 to 115)	156 (-33.04 to 345)
B/Brisbane (Day 1; N=14,5,17,7)	157 (12 to 301)	202 (-7.426 to 412)	246 (114 to 377)	230 (53 to 407)
B/Brisbane (Day 50; N=14,5,17,7)	353 (198 to 508)	306 (-37.86 to 650)	222 (82 to 363)	255 (-35.78 to 545)
B/Florida (Day 1; N=7,2,11,7)	141 (-239 to 520)	271 (-182.3 to 724)	466 (163 to 769)	243 (0.55 to 485)
B/Florida (Day 50; N=7,2,11,7)	519 (172 to 865)	152 (-360.9 to 664)	241 (-32.12 to 513)	386 (112 to 659)
SEB (Day 1; N=8,2,11,6)	625 (15 to 1236)	339 (-1215 to 1893)	637 (116 to 1157)	707 (-190.5 to 1603)
SEB (Day 50; N=8,2,11,6)	482 (292 to 672)	574 (115 to 1033)	370 (208 to 532)	500 (238 to 762)
Tetanus Toxoid (Day 1; N=8,2,10,6)	509 (-13.31 to 1032)	192 (-1376 to 1759)	632 (165 to 1100)	665 (-240.2 to 1570)
Tetanus Toxoid (Day 50; N=8,2,10,6)	581 (272 to 891)	253 (-69.17 to 576)	370 (93 to 646)	316 (132 to 499)

Statistical analyses

No statistical analyses for this end point

Primary: 6. Proportion of IL-13 Producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/ Tetanus toxoid strains.

End point title	6. Proportion of IL-13 Producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/ Tetanus toxoid strains.[6]

End point description:

Immunogenicity was measured in terms of Proportion of IL-13 producing CD4+ T cells in Response to In Vitro Pulse With A/H1N1/A/H3N2/B/Brisbane/B/Florida/SEB/ Tetanus toxoid at day 1 and day 50. Data are reported based on the Per Protocol Set (PPS).

End point type	Primary

End point timeframe:

Day 1 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 (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Mean Cells per Million Total Cells				
arithmetic mean (confidence interval 95%)				
A/H1N1 (Day 1; N=16,8,17,8)	251 (128 to 374)	228 (55 to 401)	217 (98 to 337)	107 (-66.17 to 279)
A/H1N1 (Day 50; N=16,8,17,8)	143 (-17.82 to 305)	395 (169 to 622)	398 (242 to 554)	198 (-28.8 to 425)
A/H3N2 (Day 1; N=16,9,18,13)	205 (94 to 317)	323 (147 to 500)	198 (93 to 304)	137 (-9.455 to 284)
A/H3N2 (Day 50; N=16,9,18,13)	239 (120 to 358)	509 (217 to 801)	229 (117 to 342)	231 (-8.971 to 471)
B/Brisbane (Day 1; N=14,5,17,7)	199 (52 to 346)	174 (-39.68 to 387)	188 (55 to 322)	144 (-36.68 to 324)
B/Brisbane (Day 50; N=14,5,17,7)	179 (104 to 255)	559 (174 to 944)	118 (50 to 187)	285 (-39.75 to 611)
B/Florida (Day 1; N=7,2,11,7)	203 (-30.97 to 438)	85 (-78.43 to 248)	132 (-54.71 to 319)	45 (-42.78 to 132)
B/Florida (Day 50; N=7,2,11,7)	85 (3.81 to 167)	136 (-95.56 to 367)	99 (34 to 164)	80 (-42.17 to 202)
SEB (Day 1; N=8,2,11,6)	934 (475 to 1394)	585 (-594.4 to 1718)	571 (179 to 963)	1433 (799 to 2088)
SEB (Day 50; N=8,2,11,6)	624 (422 to 826)	1565 (-238.8 to 3369)	728 (557 to 899)	1245 (290 to 2200)
Tetanus Toxoid (Day 1; N=8,2,10,6)	250 (46 to 454)	63 (-151 to 276)	294 (112 to 477)	154 (31 to 277)
Tetanus Toxoid (Day 50; N=8,2,10,6)	273 (-27.74 to 574)	142 (-543.2 to 827)	267 (-2.3 to 536)	321 (-62.18 to 704)

Statistical analyses

No statistical analyses for this end point

Primary: 12. Number of Subjects Reporting Unsolicited Adverse Events After Receiving two doses of aTIV and TIV.

End point title	12. Number of Subjects Reporting Unsolicited Adverse Events After Receiving two doses of aTIV and TIV.[7]

End point description:

The number of subjects reporting unsolicited AEs between Day 1 and the study termination i.e., Day 50, after receiving two doses of aTIV and TIV. Data are reported based on the Safety Set.

End point type	Primary

End point timeframe:

Day 1 to Day 50 post vaccination.

Notes:

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

End point values	aTIV (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Number of Subjects				
Any Adverse Event (AE)	9	11	11	7
At least possibly related AE	0	1	2	1
Any SAE	0	0	1	1
At least possibly related SAE	0	0	0	0
AE leading to discontinuation	0	0	0	0
Death	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Geometric mean HI titer (GMTs) against the three vaccine strains after two doses of aTIV and TIV.

End point title	7. Geometric mean HI titer (GMTs) against the three vaccine strains after two doses of aTIV and TIV.

End point description:

The immunogenicity was assessed in terms of GMT in subjects aged 6 to < 36 months against each of three vaccine strains after receiving two doses of aTIV and two doses of TIV. Data are reported based on the Per Protocol Set (PPS).

End point type	Secondary

End point timeframe:

Day 1 and Day 50.

End point values	aTIV (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Titers				
geometric mean (confidence interval 95%)				
A/H1N1 (Day 1; N=16,9,17,13)	16 (5.72 to 43)	43 (9.56 to 195)	16 (5.87 to 42)	152 (43 to 532)
A/H1N1 (Day 50; N=16,9,17,13)	944 (527 to 1690)	1709 (1068 to 2734)	209 (119 to 367)	893 (606 to 1317)
A/H3N2 (Day 1; N=16,9,17,13)	5.45 (3.51 to 8.46)	7.35 (4.42 to 12)	6.65 (4.34 to 10)	5 (3.28 to 7.63)
A/H3N2 (Day 50; N=16,9,17,13)	1115 (731 to 1700)	1377 (688 to 2757)	210 (140 to 316)	193 (109 to 343)
B/Brisbane (Day 1; N=16,9,17,13)	9.17 (5.69 to 15)	6.8 (3.14 to 15)	6.52 (4.1 to 10)	15 (8.06 to 29)

B/Brisbane (Day 50; N=16,9,17,13)	255 (146 to 444)	372 (170 to 812)	40 (23 to 68)	68 (36 to 130)

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Geometric Mean Ratio (GMRs) against the three vaccine strains after two doses of aTIV and TIV.

End point title	8. Geometric Mean Ratio (GMRs) against the three vaccine strains after two doses of aTIV and TIV.

End point description:

The immunogenicity was assessed in terms of GMR in subjects aged 6 to < 36 months against each of three vaccine strains after receiving two doses of aTIV and two doses of TIV. Data are reported based on the Per Protocol Set (PPS).

End point type	Secondary

End point timeframe:

Day 50 to Day 1.

End point values	aTIV (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Ratio				
geometric mean (confidence interval 95%)				
A/H1N1 (Day 50/Day 1; N=16,9,17,13)	60 (27 to 133)	27 (11 to 67)	13 (6.15 to 29)	7.59 (3.63 to 16)
A/H3N2 (Day 50/Day 1; N=16,9,17,13)	197 (119 to 327)	196 (90 to 426)	33 (20 to 53)	38 (20 to 72)
B/Brisbane (Day 50/Day 1; N=16,9,17,13)	33 (19 to 56)	35 (17 to 72)	5.21 (3.08 to 8.82)	6.13 (3.34 to 11)

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Percentage of subjects achieving seroconversion or a significant increase in HI antibody titer after receiving two doses of aTIV and TIV by age cohort.

End point title	9. Percentage of subjects achieving seroconversion or a significant increase in HI antibody titer after receiving two doses of aTIV and TIV by age cohort.

End point description:

The immunogenicity was assessed in terms of percentage of subjects aged 6 to<36 months with seroconversion (defined as a change in HI titer of <10 on day 1 to a HI titer > 40 at day 50) or

significant increase in HI titers (defined as a 4 fold or greater increase in titer in a subject with a day 1 titer > 10) after administration of two doses of aTIV against two doses of TIV. In the interpretation of HI immunogenicity results, the CHMP criteria (CPMP/BWP/214/96) for healthy adults were taken in consideration as the proportion of subjects achieving seroconversion or significant increase in HI titer should be > 40%. Data are reported based on the Per Protocol Set (PPS).

End point type	Secondary

End point timeframe:

Day 50.

End point values	aTIV (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Percentages of Subjects				
number (confidence interval 95%)				
A/H1N1 (Day 50; N=16,9,17,13)	100 (79 to 100)	100 (66 to 100)	76 (50 to 93)	69 (39 to 91)
A/H3N2 (Day 50; N=16,9,17,13)	100 (79 to 100)	100 (66 to 100)	88 (64 to 99)	100 (75 to 100)
B/Brisbane (Day 50; N=16,9,17,13)	100 (79 to 100)	100 (66 to 100)	47 (23 to 72)	62 (32 to 86)

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Percentage of subjects with a HI titer ≥ 40 against the three vaccine strains after two doses of aTIV and TIV.

End point title	10. Percentage of subjects with a HI titer ≥ 40 against the three vaccine strains after two doses of aTIV and TIV.

End point description:

The immunogenicity was assessed in terms of percentage of subjects aged 6 to < 36 months with seroprotection as measured by HI assay against each of three vaccine strains after receiving two doses of aTIV and two doses of TIV. In the interpretation of HI immunogenicity results, the CHMP criteria (CPMP/BWP/214/96) for healthy adults were taken in consideration which defined The proportion of subjects achieving an HI titer ≥ 40 should be > 70%. Data are reported based on the Per Protocol Set (PPS).

End point type	Secondary

End point timeframe:

Day 1 and Day 50.

End point values	aTIV (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Percentages of Subjects				
number (confidence interval 95%)				
A/H1N1 (Day 1; N=16,9,17,13)	25 (7 to 52)	56 (21 to 86)	24 (7 to 50)	77 (46 to 95)
A/H1N1 (Day 50; N=16,9,17,13)	100 (79 to 100)	100 (66 to 100)	88 (64 to 99)	100 (75 to 100)
A/H3N2 (Day 1; N=16,9,17,13)	0 (0 to 21)	11 (0 to 48)	6 (0 to 29)	0 (0 to 25)
A/H3N2 (Day 50; N=16,9,17,13)	100 (79 to 100)	100 (66 to 100)	94 (71 to 100)	100 (75 to 100)
B/Brisbane (Day 1; N=16,9,17,13)	25 (7 to 52)	11 (0 to 48)	12 (1 to 36)	31 (9 to 61)
B/Brisbane (Day 50; N=16,9,17,13)	100 (79 to 100)	100 (66 to 100)	47 (23 to 72)	69 (39 to 91)

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Number of Subjects Reporting Solicited Adverse Events and Other Indicators of Reactogenicity After Receiving two doses of aTIV and TIV by injection.

End point title	11. Number of Subjects Reporting Solicited Adverse Events and Other Indicators of Reactogenicity After Receiving two doses of aTIV and TIV by injection.

End point description:

The number of subjects reporting solicited local and systemic adverse events and other solicited adverse events after receiving two doses of aTIV and TIV are reported. Data are reported based on the Safety Set.

End point type	Secondary

End point timeframe:

Day 1 to Day 7 post vaccination.

End point values	aTIV (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)	TIV (24 to <36 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	21	20
Units: Number of Subjects				
Any Local (vac.1; N=22,21,20,19)	9	9	6	4
Injection site induration (vac.1; N=22,20,20,19)	1	1	1	1
Injection site erythema (vac.1; N=22,20,20,19)	4	3	0	0
Injection site ecchymosis (vac.1; N=22,20,20,19)	3	1	0	0
Injection site swelling (vac.1; N=22,20,20,19)	0	1	0	0
Injection site tenderness (vac.1; N=22,20,20,19)	4	6	5	4
Any Systemic (vac.1; N=22,20,20,19)	10	14	12	10

Diarrhea (vac.1; N=22,20,20,19)	2	6	6	2
Eat Change (vac.1; N=22,20,20,19)	2	5	5	3
Irritability (vac.1; N=22,20,20,19)	5	3	2	2
Shivering (vac.1; N=22,20,20,19)	1	1	1	0
Sleepiness (vac.1; N=22,20,20,19)	3	6	3	5
Unusual Crying (vac.1; N=22,20,20,19)	0	3	2	1
Vomiting (vac.1; N=22,20,20,19)	0	3	3	1
Other (vac.1; N=22,20,20,19)	2	9	5	3
Analgesic (vac.1; N=22,20,20,19)	2	6	5	3
Stayed home (vac.1; N=22,20,20,19)	2	6	1	1
Fever (≥ 38°C) (vac.1; N=22,20,20,19)	3	8	6	3
Any Local (vac.2; N=20,19,20,18)	6	4	4	3
Injection site induration (vac.2; N=20,19,20,18)	1	2	1	1
Injection site erythema (vac.2; N=20,19,20,18)	2	2	1	1
Injection site ecchymosis (vac.2; N=20,19,20,18)	0	0	1	1
Injection site swelling (vac.2; N=20,19,20,18)	1	0	1	0
Injection site tenderness (vac.2; N=20,19,20,18)	3	2	3	2
Any Systemic (vac.2; N=20,19,20,18)	10	9	10	6
Diarrhea (vac.2; N=20,19,20,18)	3	2	2	1
Eat Change (vac.2; N=20,19,20,18)	4	4	3	2
Irritability (vac.2; N=20,19,20,18)	3	3	4	2
Shivering (vac.2; N=20,19,20,18)	0	0	0	0
Sleepiness (vac.2; N=20,19,20,18)	2	5	5	2
Unusual Crying (vac.2; N=20,19,20,18)	2	4	2	2
Vomiting (vac.2; N=20,19,20,18)	0	2	0	0
Other (vac.2; N=20,19,20,18)	8	4	0	3
Analgesic (vac.2; N=20,19,20,18)	7	2	0	3
Stayed home (vac.2; N=20,19,20,18)	3	2	0	1
Fever (≥ 38°C) (vac.2; N=20,19,20,18)	6	5	2	3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
All solicited AEs and unsolicited AEs were collected from Day 1 to Day 7; all unsolicited SAEs, medically attended AEs, AEs leading to withdrawal from the study were collected from Day 1 to Day 50.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	aTIV (6 to < 24 months)
Reporting group description:	
Subjects aged between 6 to <24 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.	
Reporting group title	aTIV (24 to <36 months)
Reporting group description:	
Subjects aged between 24 to <36 months who received two doses of MF59C.1-adjuvanted subunit trivalent influenza vaccine on days 1 and 29.	
Reporting group title	TIV (6 to <24 months)
Reporting group description:	
Subjects aged between 6 to <24 months who received two doses of inactivated unadjuvanted trivalent influenza vaccine on days 1 and 29.	
Reporting group title	TIV (24 to <36 months)
Reporting group description:	
Subjects aged between 24 to <36 months who received two doses of inactivated unadjuvanted trivalent influenza vaccine on days 1 and 29.	

Serious adverse events	aTIV (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Varicella			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	TIV (24 to <36 months)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Varicella			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	aTIV (6 to < 24 months)	aTIV (24 to <36 months)	TIV (6 to <24 months)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 22 (86.36%)	18 / 21 (85.71%)	17 / 21 (80.95%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	4 / 22 (18.18%)	7 / 21 (33.33%)	7 / 21 (33.33%)
occurrences (all)	7	11	11
General disorders and administration site conditions			
Crying			
subjects affected / exposed	2 / 22 (9.09%)	4 / 21 (19.05%)	4 / 21 (19.05%)
occurrences (all)	2	7	6
Injection site erythema			
subjects affected / exposed	5 / 22 (22.73%)	3 / 21 (14.29%)	1 / 21 (4.76%)
occurrences (all)	6	5	1
Injection site haemorrhage			
subjects affected / exposed	3 / 22 (13.64%)	1 / 21 (4.76%)	1 / 21 (4.76%)
occurrences (all)	3	1	2
Injection site induration			

subjects affected / exposed	1 / 22 (4.55%)	2 / 21 (9.52%)	2 / 21 (9.52%)
occurrences (all)	2	3	3
Injection site pain			
subjects affected / exposed	5 / 22 (22.73%)	6 / 21 (28.57%)	5 / 21 (23.81%)
occurrences (all)	7	8	8
Pyrexia			
subjects affected / exposed	8 / 22 (36.36%)	11 / 21 (52.38%)	9 / 21 (42.86%)
occurrences (all)	13	18	12
Nasopharyngitis			
subjects affected / exposed	2 / 22 (9.09%)	3 / 21 (14.29%)	2 / 21 (9.52%)
occurrences (all)	2	3	2
Bronchitis			
subjects affected / exposed	1 / 22 (4.55%)	2 / 21 (9.52%)	0 / 21 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 22 (22.73%)	6 / 21 (28.57%)	8 / 21 (38.10%)
occurrences (all)	6	10	10
Vomiting			
subjects affected / exposed	0 / 22 (0.00%)	3 / 21 (14.29%)	3 / 21 (14.29%)
occurrences (all)	0	5	3
Psychiatric disorders			
Eating Disorder			
subjects affected / exposed	5 / 22 (22.73%)	6 / 21 (28.57%)	7 / 21 (33.33%)
occurrences (all)	6	9	10
Irritability			
subjects affected / exposed	6 / 22 (27.27%)	5 / 21 (23.81%)	5 / 21 (23.81%)
occurrences (all)	8	7	7
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 21 (4.76%)	2 / 21 (9.52%)
occurrences (all)	1	1	2
Tonsillitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			

subjects affected / exposed	0 / 22 (0.00%)	0 / 21 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Varicella			
subjects affected / exposed	2 / 22 (9.09%)	1 / 21 (4.76%)	0 / 21 (0.00%)
occurrences (all)	2	1	0

Non-serious adverse events	TIV (24 to <36 months)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 20 (60.00%)		
Nervous system disorders			
Somnolence			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	8		
General disorders and administration site conditions			
Crying			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	5		
Injection site erythema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injection site haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Injection site induration			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Injection site pain			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	7		
Pyrexia			
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	7		
Nasopharyngitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Bronchitis			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Psychiatric disorders			
Eating Disorder			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	6		
Irritability			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	5		
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Varicella			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 March 2011	1. Allowed for a 0.25 ml presentation of aTIV to be used; 2. Incorporated changes to safety reporting section in line with new SAE SOP effective from APR 11; 3. Removal of requirement to enter data in EDC following the day 8 and day 36 telephone calls; 4. Incorporated corrections to statistical section.
19 August 2011	1. Extension of study to new season 2011/2012; 2. Correction to visit windows; 3. Increase in sample size to 90 to make up for higher than expected number of nonevaluable subjects in season 1.

Notes:

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/25037034