Clinical trial results:
A Phase II, Observer-Blind, Randomized, Parallel Groups, Single Center, Exploratory Clinical Study to Evaluate the Immunogenicity and Safety of One and Two 0.25 mL Intramuscular Doses of FLUAD™ versus Two 0.25 mL Intramuscular Doses of Vaxigrip™ Influenza Vaccines in Healthy Subjects Aged 6 to <36 Months.

Summary

EudraCT number	2006-003181-34
Trial protocol	FI
Global end of trial date	24 August 2007

Results information

Result version number	v2 (current)
This version publication date	28 July 2016
First version publication date	31 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	V70P2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00408395
WHO universal trial number (UTN)	-
Other trial identifiers	Sample data: Sample data

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics S.r.l.
Sponsor organisation address	Via Fiorentina, 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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 December 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 August 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunogenicity of one 0.25 mL intramuscular (IM) injection of Fluad™ influenza vaccine and that of two 0.25 mL IM injections of the conventional influenza vaccine Vaxigrip™, in terms of post-immunization geometric mean titers (GMTs), as measured by Hemagglutination Inhibition (HI) test.

Protection of trial subjects:

Study vaccines were not administered to individuals with known hypersensitivity to any component of the vaccines. 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 systemic steroids was available in case of any anaphylactic reactions. Care was taken to ensure that the vaccine was not injected into a blood vessel.

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	14 November 2006
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: 281
Worldwide total number of subjects	281
EEA total number of subjects	281

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)	171
Children (2-11 years)	110
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:

All subjects were enrolled from Finland.

Pre-assignment

Screening details:

All the enrolled subject participated in 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

Blinding implementation details:

NA

Arms

Are arms mutually exclusive?	Yes
Arm title	aTIV

Arm description:

Subjects aged 6 to < 36 months received one or two doses of adjuvanted trivalent influenza vaccine (aTIV) administered on day 1 and/or day 29.

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

Dosage and administration details:

One or two doses of 0.25 mL IM injections of aTIV

Arm title	Control_TIV

Arm description:

Subjects aged 6 to < 36 months received one or two doses of non–adjuvanted trivalent influenza vaccine (TIV) administered on day 1 and/or day 29.

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

Dosage and administration details:

One or two doses of 0.25 mL IM injections of TIV.

Number of subjects in period 1	aTIV	Control_TIV
Started	139	142
Completed	111	123
Not completed	28	19
Consent withdrawn by subject	14	9
Administrative Reason	1	-
Unable To Classify	2	3
Adverse Events	1	-
Lost to follow-up	2	3
Inappropriate Enrollment	5	2
Protocol deviation	3	2

Baseline characteristics

Reporting groups	
Reporting group title	aTIV
Reporting group description:	
Subjects aged 6 to < 36 months received one or two doses of adjuvanted trivalent influenza vaccine (aTIV) administered on day 1 and/or day 29.	
Reporting group title	Control_TIV
Reporting group description:	
Subjects aged 6 to < 36 months received one or two doses of non–adjuvanted trivalent influenza vaccine (TIV) administered on day 1 and/or day 29.	

Reporting group values	aTIV	Control_TIV	Total
Number of subjects	139	142	281
Age categorical			
Units: Subjects			

Age continuous			
Subjects aged 6 to < 36 months received one or two doses of adjuvanted trivalent influenza vaccine (aTIV) or non –adjuvanted trivalent influenza vaccine (TIV) administered on day 1 and/or day 29.			
Units: months			
arithmetic mean	20.9	20.7	
standard deviation	± 8.9	± 8.6	-
Gender categorical			
Subjects aged 6 to < 36 months received one or two dose of aTIV and TIV administered on day 1 and/or day 29.			
Units: Subjects			
Female	65	60	125
Male	74	82	156

End points

End points reporting groups

Reporting group title	aTIV
Reporting group description:	
Subjects aged 6 to < 36 months received one or two doses of adjuvanted trivalent influenza vaccine (aTIV) administered on day 1 and/or day 29.	
Reporting group title	Control_TIV
Reporting group description:	
Subjects aged 6 to < 36 months received one or two doses of non–adjuvanted trivalent influenza vaccine (TIV) administered on day 1 and/or day 29.	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects with at least one vaccination and with some post-baseline safety data.	
Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects in the ITT population who received all the injections of vaccine correctly, and provide evaluable serum samples at the relevant time points, and have no major protocol violation as defined prior to unblinding.	

Primary: Geometric Mean Titers (GMT) after one dose of aTIV and two doses of TIV.

End point title	Geometric Mean Titers (GMT) after one dose of aTIV and two doses of TIV.[1]
End point description:	
The immunogenicity was assessed in subjects aged 6 to < 36 months in terms of GMT against each of three vaccine strains, four weeks after receiving one dose of aTIV and after two doses of TIV.	
End point type	Primary
End point timeframe:	
Day 29 and Day 50 post vaccination.	

Notes:

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

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	118		
Units: Titers				
geometric mean (confidence interval 95%)				
Day1 (H1N1)	5.93 (5.01 to 7)	6.4 (5.47 to 7.49)		
aTIV Day 29 and TIV Day 50 (H1N1)	34 (26 to 44)	92 (76 to 111)		
Day 1 (H3N2)	8.24 (6.25 to 11)	8.79 (6.78 to 11)		
aTIV Day 29 and TIV Day 50 (H3N2)	100 (74 to 135)	195 (160 to 237)		
Day 1 (B strain)	5.42 (5.08 to 5.77)	5.18 (4.88 to 5.5)		
aTIV Day 29 and TIV Day 50 (B strain)	8.11 (6.75 to 9.74)	20 (17 to 24)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs against the three vaccine strains after two doses of aTIV and two doses of TIV.

End point title	GMTs against the three vaccine strains after two doses of aTIV and two doses of 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.

End point type	Secondary

End point timeframe:

Day 50 post vaccination.

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	118		
Units: Titers				
geometric mean (confidence interval 95%)				
Day1 (H1N1)	5.93 (5.01 to 7)	6.4 (5.47 to 7.49)		
Day 50 (H1N1)	195 (159 to 240)	92 (76 to 111)		
Day 1 (H3N2)	8.24 (6.25 to 11)	8.79 (6.78 to 11)		
Day 50 (H3N2)	507 (412 to 623)	195 (160 to 237)		
Day 1 (B strain)	5.42 (5.08 to 5.77)	5.18 (4.88 to 5.5)		
Day 50 (B strain)	105 (88 to 127)	20 (17 to 24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects in terms of seroprotection in antibody titer against the three vaccine strains after two doses of aTIV and two doses of TIV.

End point title	Percentage of subjects in terms of seroprotection in antibody titer against the three vaccine strains after two doses of aTIV and two doses of 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.
Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

Day 50

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	118		
Units: Percentage of subjects				
number (confidence interval 95%)				
Day1 (H1N1)	5 (2 to 11)	7 (3 to 13)		
Day 50 (H1N1)	100 (97 to 100)	86 (79 to 92)		
Day 1 (H3N2)	12 (6 to 19)	13 (7 to 20)		
Day 50 (H3N2)	100 (97 to 100)	99 (95 to 100)		
Day 1 (B strain)	3 (1 to 8)	1 (0.021 to 5)		
Day 50 (B strain)	99 (95 to 100)	33 (25 to 42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with seroconversion or significant increase in HI antibody titer after receiving two doses of aTIV and two doses of TIV.

End point title	Percentages of subjects with seroconversion or significant increase in HI antibody titer after receiving two doses of aTIV and two doses of TIV.

End point description:

The immunogenicity was assessed in percentage of subjects aged 6 to 36 months with seroconversions or significant increase in HI antibody titer after two doses of aTIV against two doses of TIV.
Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

Day 50

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	118		
Units: Percentages of subjects				
number (confidence interval 95%)				
H1N1	100 (97 to 100)	86 (78 to 91)		
H3N2	98 (93 to 100)	96 (90 to 99)		
B strain	99 (95 to 100)	33 (25 to 42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects in terms of HI titer against the three vaccine strains after one dose of aTIV and two doses of TIV.

End point title	Percentage of subjects in terms of HI titer against the three vaccine strains after one dose of aTIV and two doses of TIV.

End point description:

The immunogenicity was assessed in terms of percentage of subjects aged 6 to < 36 months HI titer antibody response against each of three vaccine strains, after receiving one dose of aTIV and two doses of TIV.
Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

Day 29 and Day 50

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	118		
Units: Percentages of subjects				
number (confidence interval 95%)				
Day1 (H1N1)	5 (2 to 11)	7 (3 to 13)		
aTIV Day 29 and TIV Day 50 (H1N1)	51 (41 to 61)	86 (79 to 92)		
Day 1 (H3N2)	12 (6 to 19)	13 (7 to 20)		
aTIV Day 29 and TIV Day 50 (H3N2)	91 (84 to 96)	99 (95 to 100)		
Day 1 (B strain)	3 (1 to 8)	1 (0.021 to 5)		
aTIV Day 29 and TIV Day 50 (B strain)	5 (2 to 11)	33 (25 to 42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with seroconversion or significant increase in HI antibody titer after receiving one dose of aTIV and two doses of TIV.

End point title	Percentages of subjects with seroconversion or significant increase in HI antibody titer after receiving one dose of aTIV and two doses of TIV.

End point description:

The immunogenicity was assessed in percentage of subjects aged 6 to 36 months with seroconversions or significant increase in HI antibody titer after a single dose of aTIV against two doses of TIV.
Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

Day 29 and Day 50

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	118		
Units: Percentages of subjects				
number (confidence interval 95%)				
aTIV Day 29 and TIV Day 50 (H1N1)	51 (41 to 61)	86 (78 to 91)		
aTIV Day 29 and TIV Day 50 (H3N2)	89 (82 to 95)	96 (90 to 99)		
aTIV Day 29 and TIV Day 50 (B strain)	5 (2 to 11)	33 (25 to 42)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMT against the three vaccine strains after one dose of aTIV and one dose of TIV.

End point title	GMT against the three vaccine strains after one dose of aTIV and one dose of TIV.

End point description:

The immunogenicity was assessed in terms of GMT against each of three vaccine strains, 29 days after receiving one dose of aTIV and one dose of TIV.
Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

Day 29

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	118		
Units: Titers				
geometric mean (confidence interval 95%)				
Day1 (H1N1)	5.93 (5.01 to 7)	6.4 (5.47 to 7.49)		
Day 29 (H1N1)	34 (26 to 44)	17 (13 to 21)		

Day 1 (H3N2)	8.24 (6.25 to 11)	8.79 (6.78 to 11)		
Day 29 (H3N2)	100 (74 to 135)	38 (28 to 50)		
Day 1 (B strain)	5.42 (5.08 to 5.77)	5.18 (4.88 to 5.5)		
Day 29 (B strain)	8.11 (6.75 to 9.74)	5.79 (4.87 to 6.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects in terms of HI titer against the three vaccine strains after one dose of aTIV and one dose of TIV.

End point title	Percentage of subjects in terms of HI titer against the three vaccine strains after one dose of aTIV and one dose of TIV.

End point description:

The immunogenicity was assessed in terms of percentage of subjects aged 6 to < 36 months with HI titer against each of three vaccine strains, after receiving one dose of aTIV and one dose of TIV. Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

Day 29

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	118		
Units: Percentages of subjects				
number (confidence interval 95%)				
Day1 (H1N1)	5 (2 to 11)	7 (3 to 13)		
Day 29 (H1N1)	51 (41 to 61)	18 (11 to 26)		
Day 1 (H3N2)	12 (6 to 19)	13 (7 to 20)		
Day 29 (H3N2)	91 (84 to 96)	49 (40 to 59)		
Day 1 (B strain)	3 (1 to 8)	1 (0.021 to 5)		
Day 29 (B strain)	5 (2 to 11)	3 (1 to 7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with seroconversion or significant increase in HI antibody titer after receiving one dose of aTIV and one dose of TIV.

End point title	Percentages of subjects with seroconversion or significant increase in HI antibody titer after receiving one dose of aTIV and one dose of TIV.

End point description:

The immunogenicity was assessed in percentage of subjects aged 6 to <36 months with seroconversions or significant increase in HI antibody titer after administration of one dose of aTIV against one dose of TIV.
Analysis was done on the Per Protocol Set.

End point type	Secondary

End point timeframe:

Day 29

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	118		
Units: Percentages of subjects				
number (confidence interval 95%)				
H1N1	51 (41 to 61)	17 (11 to 25)		
H3N2	89 (82 to 95)	45 (36 to 54)		
B Strain	5 (2 to 11)	3 (1 to 7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Solicited Local and Systemic Adverse Events After Receiving two doses of aTIV and two doses of TIV, four weeks apart.

End point title	Number of Subjects Reporting Solicited Local and Systemic Adverse Events After Receiving two doses of aTIV and two doses of TIV, four weeks apart.

End point description:

The number of subjects aged 6 to <36 months reporting solicited local and systemic adverse events and other solicited adverse events after receiving two doses of aTIV and two doses of TIV, administered four weeks apart, are reported.
Analysis was done on the Safety Set.

End point type	Secondary

End point timeframe:

Day1 through Day 7

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	139		
Units: Number				
number (not applicable)				
Any Local	74	61		
Ecchymosis	18	19		
Erythema	46	38		
Induration	21	20		

Swelling	16	7		
Tenderness	58	47		
Any systemic	63	56		
Change in eat. habits	32	30		
Sleepiness	35	26		
Unusual Crying	24	19		
Irritability	53	46		
Vomiting	8	8		
Diarrhea	17	17		
Fever (>= 38C)	16	13		
Axill. Temp. (C) >= 40.0 C	0	0		
Analg. Antipyr. Med. Used	34	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Unsolicited Adverse Events After Receiving two doses of aTIV and two doses of TIV, four weeks apart.

End point title	Number of Subjects Reporting Unsolicited Adverse Events After Receiving two doses of aTIV and two doses of TIV, four weeks apart.

End point description:

The number of subjects 6months to <36 months of age reporting any unsolicited adverse event (AEs) between Day 1 to 7 and serious adverse events (SAEs), medically attended AEs, AEs leading to withdrawal from the study between Day 1 to Day 209 after receiving two doses of aTIV and two doses of TIV, administered four weeks apart are reported.
Analysis was done on the Safety Set.

End point type	Secondary

End point timeframe:

Day1 through Day 209

End point values	aTIV	Control_TIV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	139		
Units: Number of Subjects				
number (not applicable)				
Any AE	107	111		
At least possibly related AEs	21	21		
Serious AEs	2	6		
AEs leading to withdrawal	1	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study (solicited and unsolicited from Day 1 to Day 209).

Adverse event reporting additional description:

Any solicited and unsolicited adverse events were reported up to day 7 post vaccination. Unsolicited SAE, medically attended AEs, AEs leading to withdrawal from the study were collected from day 1 through day 209.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	aTIV

Reporting group description:

Subjects aged 6 to < 36 months received one or two dose of aTIV administered on day 1 and/or day 29.

Reporting group title	Control_TIV

Reporting group description:

Subjects aged 6 to < 36 months received one or two dose of non –adjuvanted trivalent influenza vaccine (TIV) administered on day 1 and/or day 29.

Serious adverse events	aTIV	Control_TIV	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 130 (1.54%)	6 / 139 (4.32%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 130 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 130 (0.00%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis Media			

subjects affected / exposed	0 / 130 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Syncytial Virus Infection			
subjects affected / exposed	0 / 130 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 130 (1.54%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis Chronic			
subjects affected / exposed	0 / 130 (0.00%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	aTIV	Control_TIV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 130 (89.23%)	125 / 139 (89.93%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	35 / 130 (26.92%)	27 / 139 (19.42%)	
occurrences (all)	35	27	
General disorders and administration site conditions			
Crying			
subjects affected / exposed	26 / 130 (20.00%)	21 / 139 (15.11%)	
occurrences (all)	26	21	
Injection Site Haemorrhage			
subjects affected / exposed	18 / 130 (13.85%)	19 / 139 (13.67%)	
occurrences (all)	18	19	
Injection Site Erythema			

subjects affected / exposed	46 / 130 (35.38%)	38 / 139 (27.34%)	
occurrences (all)	46	38	
Injection Site Induration			
subjects affected / exposed	21 / 130 (16.15%)	20 / 139 (14.39%)	
occurrences (all)	21	20	
Injection Site Pain			
subjects affected / exposed	58 / 130 (44.62%)	47 / 139 (33.81%)	
occurrences (all)	58	47	
Injection Site Swelling			
subjects affected / exposed	16 / 130 (12.31%)	7 / 139 (5.04%)	
occurrences (all)	16	7	
Pyrexia			
subjects affected / exposed	44 / 130 (33.85%)	39 / 139 (28.06%)	
occurrences (all)	44	39	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	23 / 130 (17.69%)	20 / 139 (14.39%)	
occurrences (all)	23	20	
Vomiting			
subjects affected / exposed	10 / 130 (7.69%)	11 / 139 (7.91%)	
occurrences (all)	10	11	
Teething			
subjects affected / exposed	7 / 130 (5.38%)	6 / 139 (4.32%)	
occurrences (all)	7	6	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	26 / 130 (20.00%)	30 / 139 (21.58%)	
occurrences (all)	26	30	
Psychiatric disorders			
Irritability			
subjects affected / exposed	53 / 130 (40.77%)	47 / 139 (33.81%)	
occurrences (all)	53	47	
Eating Disorder			
subjects affected / exposed	32 / 130 (24.62%)	30 / 139 (21.58%)	
occurrences (all)	32	30	
Infections and infestations			

Bronchitis			
subjects affected / exposed	13 / 130 (10.00%)	5 / 139 (3.60%)	
occurrences (all)	13	5	
Conjunctivitis			
subjects affected / exposed	13 / 130 (10.00%)	16 / 139 (11.51%)	
occurrences (all)	13	16	
Gastroenteritis			
subjects affected / exposed	11 / 130 (8.46%)	9 / 139 (6.47%)	
occurrences (all)	11	9	
Ear Infection			
subjects affected / exposed	8 / 130 (6.15%)	7 / 139 (5.04%)	
occurrences (all)	8	7	
Otitis Media			
subjects affected / exposed	33 / 130 (25.38%)	43 / 139 (30.94%)	
occurrences (all)	33	43	
Respiratory Tract Infection			
subjects affected / exposed	9 / 130 (6.92%)	11 / 139 (7.91%)	
occurrences (all)	9	11	
Rhinitis			
subjects affected / exposed	35 / 130 (26.92%)	23 / 139 (16.55%)	
occurrences (all)	35	23	
Upper Respiratory Tract Infection			
subjects affected / exposed	29 / 130 (22.31%)	28 / 139 (20.14%)	
occurrences (all)	29	28	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2006	Amendment to permit an interim analysis after all day 7 reactogenicity data have been collected from the first 100 children enrolled.
26 February 2007	Amendment to permit a preliminary analysis after day 29 data, 1 month after the first injection.
27 April 2007	Amendment to permit diary cards to collect information on all the AEs and Concomitant Medications which occurred during the follow up period, between day 50 and 209.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None

Notes: