Clinical trial results:
A phase II, randomized, observer blind, multicenter study to evaluate the safety and immunogenicity of a single low dose of AS03-adjuvanted, Quebec- or Dresden- manufactured monovalent A/California/7/2009 (H1N1)v-like vaccine in children 3 to less than 10 years old

Summary

EudraCT number	2011-003512-23
Trial protocol	Outside EU/EEA
Global end of trial date	31 January 2011

Results information

Result version number	v1
This version publication date	18 April 2016
First version publication date	23 July 2015

Trial information

Trial identification

Sponsor protocol code	114495

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01161160
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.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	09 May 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 August 2010
Global end of trial reached?	Yes
Global end of trial date	31 January 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether vaccination with 1 dose of 0.9 µg monovalent A/California/7/2009 (H1N1)v-like HA antigen produced in Quebec adjuvanted with AS03B and 1 dose of monovalent A/California/7/2009 (H1N1)v-like HA antigen produced in Dresden adjuvanted with AS03B; results in an immune response to the vaccine-homologous virus that meets or exceeds the U.S Food and Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER) and the European Medicines Agency (EMA), Committee for Medicinal Products for Human Use (CHMP) guidance targets for pandemic vaccine serocon-version rate (SCR), rate of induction of vaccine-homologous reciprocal hemagglutination inhibition (HI) titers >= 40 (potential seroprotection rate [SPR]) and geo-metric mean fold rise (GMFR) 21 days after vaccination in children 3 to < 10 years of age.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 July 2010
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	Philippines: 102
Country: Number of subjects enrolled	Thailand: 107
Worldwide total number of subjects	209
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	0

months)	
Children (2-11 years)	209
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: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	FluQ half Goup

Arm description:

Subjects received 1 half-pediatric dose of FluQ vaccine at Day 0

Arm type	Experimental
Investigational medicinal product name	Arepanrix™
Investigational medicinal product code	GSK2340274A
Other name	Q-PAN H1N1-AS03 (FluQ)
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.

Arm title	FluD half Group

Arm description:

Subjects received 1 half-pediatric dose of FluD vaccine at Day 0

Arm type	Experimental
Investigational medicinal product name	Pandemrix™
Investigational medicinal product code	GSK2340272A
Other name	D-PAN H1N1-AS03 (FluD)
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.

Arm title	FluQ Group

Arm description:

Subjects received 1 pediatric dose of FluQ vaccine at Day 0

Arm type	Experimental
Investigational medicinal product name	Arepanrix™
Investigational medicinal product code	GSK2340274A
Other name	Q-PAN H1N1-AS03 (FluD)
Pharmaceutical forms	Emulsion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered intramuscularly in the deltoid of the non-dominant arm.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: This is an observer-blind study which means that during the course of the study, the vaccine recipient (subject) and those responsible for the evaluation of any study endpoint, were all unaware of which vaccine was administered to a particular subject. To do so, vaccine preparation and vaccination was done by authorized medical personnel who did not participate in any of the study clinical evaluation (i.e. assessor).

Number of subjects in period 1	FluQ half Goup	FluD half Group	FluQ Group
Started	76	75	58
Completed	76	75	58

Baseline characteristics

Reporting groups	
Reporting group title	FluQ half Goup
Reporting group description:	
Subjects received 1 half-pediatric dose of FluQ vaccine at Day 0	
Reporting group title	FluD half Group
Reporting group description:	
Subjects received 1 half-pediatric dose of FluD vaccine at Day 0	
Reporting group title	FluQ Group
Reporting group description:	
Subjects received 1 pediatric dose of FluQ vaccine at Day 0	

Reporting group values	FluQ half Goup	FluD half Group	FluQ Group
Number of subjects	76	75	58
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: years			
arithmetic mean	6	6	6
standard deviation	± 2.03	± 2.02	± 2
Gender categorical Units: Subjects			
Female	30	38	27
Male	46	37	31

Reporting group values	Total		
Number of subjects	209		
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: years arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	95		
Male	114		

End points

End points reporting groups

Reporting group title	FluQ half Goup
Reporting group description:	
Subjects received 1 half-pediatric dose of FluQ vaccine at Day 0	
Reporting group title	FluD half Group
Reporting group description:	
Subjects received 1 half-pediatric dose of FluD vaccine at Day 0	
Reporting group title	FluQ Group
Reporting group description:	
Subjects received 1 pediatric dose of FluQ vaccine at Day 0	

Primary: Number of seroconverted subjects for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Number of seroconverted subjects for HI antibodies against Flu A/CAL/7/09 H1N1 strain[1][2]
End point description:	
Seroconversion rate (SCR) was defined as the proportion of subjects who had either a pre-vaccination reciprocal HI titre < 10 and a post-vaccination reciprocal titre ≥ 40, or a pre-vaccination reciprocal HI titre ≥ 10 and at least a 4-fold increase in post vaccination reciprocal titre against the vaccine virus.	
End point type	Primary
End point timeframe:	
At Day 21	

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
The CBER Criteria were fulfilled for this study if after vaccination in FluQ half and FluD half groups:
- the lower limit (LL) of the 95% confidence interval (CI) for SCR was >40%,
- the LL of the 95% CI for SPR was >70%.
The CHMP Criteria were fulfilled if:
– the point estimate for SCR is >40%,
– the post-vaccination point estimate for SPR is >70%
– the point estimate for GMFR was >2.5

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure specifically covers the results of the subjects that received the FluQ half or FluD half pediatric vaccine (i.e. FluQ half Group and FluD half Group).

End point values	FluQ half Goup	FluD half Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	75		
Units: Subjects				
Flu A/CAL/7/09	75	74		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Number of seroprotected subjects for HI antibodies against Flu A/CAL/7/09 H1N1 strain[3][4]

End point description:

A seroprotected subject was defined as a subject with a serum HI titre greater than or equal to 1:40 that usually is accepted as indicating protection.

End point type	Primary

End point timeframe:

At Day 0 and Day 21

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
The CBER Criteria were fulfilled for this study if after vaccination in FluQ half and FluD half groups:
- the lower limit (LL) of the 95% confidence interval (CI) for SCR was >40%,
- the LL of the 95% CI for SPR was >70%.
The CHMP Criteria were fulfilled if:
– the point estimate for SCR is >40%,
– the post-vaccination point estimate for SPR is >70%
– the point estimate for GMFR was >2.5

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure specifically covers the results of the subjects that received the FluQ half or FluD half pediatric vaccine (i.e. FluQ half Group and FluD half Group).

End point values	FluQ half Goup	FluD half Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	75		
Units: Subjects				
Day 0 (PRE)	28	24		
Day 21 (POST)	75	74		

Statistical analyses

No statistical analyses for this end point

Primary: Seroconversion factor for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Seroconversion factor for HI antibodies against Flu A/CAL/7/09 H1N1 strain[5][6]

End point description:

Seroconversion factors [as known as Geometric Mean Fold Rise (GMFR)] were defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.

End point type	Primary

End point timeframe:

At day 21

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was

performed.
The CBER Criteria were fulfilled for this study if after vaccination in FluQ half and FluD half groups:
- the lower limit (LL) of the 95% confidence interval (CI) for SCR was >40%,
- the LL of the 95% CI for SPR was >70%.
The CHMP Criteria were fulfilled if:
– the point estimate for SCR is >40%,
– the post-vaccination point estimate for SPR is >70%
– the point estimate for GMFR was >2.5
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure specifically covers the results of the subjects that received the FluQ half or FluD half pediatric vaccine (i.e. FluQ half Group and FluD half Group).

End point values	FluQ half Goup	FluD half Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	75		
Units: Fold increase				
geometric mean (confidence interval 95%)				
Flu A/CAL/7/09	25.7 (20.7 to 32)	27.1 (22.4 to 32.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Number of seroconverted subjects for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point description:

Seroconversion rate (SCR) was defined as the proportion of subjects who had either a pre-vaccination reciprocal HI titre < 10 and a post-vaccination reciprocal titre ≥ 40, or a pre-vaccination reciprocal HI titre ≥ 10 and at least a 4-fold increase in post vaccination reciprocal titre against the vaccine virus.

End point type	Secondary

End point timeframe:

At Day 182

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	74	58	
Units: Subjects				
Flu A/CAL/7/09	46	53	40	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Number of seroprotected subjects for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point description:

A seroprotected subject was defined as a subject with a serum HI titer greater than or equal to 1:40 that usually is accepted as indicating protection.

End point type	Secondary

End point timeframe:

At Day 0 and Day 182

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	74	58	
Units: Subjects				
Day 0 (PRE)	27	24	18	
Day 182 (POST)	55	63	46	

Statistical analyses

No statistical analyses for this end point

Secondary: Seroconversion factor for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point title	Seroconversion factor for HI antibodies against Flu A/CAL/7/09 H1N1 strain

End point description:

End point type	Secondary

End point timeframe:

At Day 182

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	74	58	
Units: Fold increase				
geometric mean (confidence interval 95%)				
Flu A/CAL/7/09	6.6 (5.4 to 8.2)	8 (6.4 to 10.1)	8.9 (6.8 to 11.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with HI antibody titers against Flu A/CAL/7/09 ≥ 1:10

End point title	Number of subjects with HI antibody titers against Flu A/CAL/7/09 ≥ 1:10

End point description:

End point type	Secondary

End point timeframe:

At Day 21

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Subjects				
Flu A/CAL/7/09 (POST)	76	75	58	

Statistical analyses

No statistical analyses for this end point

Secondary: HI antibody titres against Flu A/CAL/7/09 H1N1 strain

End point title	HI antibody titres against Flu A/CAL/7/09 H1N1 strain

End point description:

Antibody titres were expressed as Geometric mean titers (GMTs).

End point type	Secondary

End point timeframe:

At Day 21

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/CAL/7/09 (POST)	448.6 (323.9 to 621.3)	434.1 (321 to 587)	418.8 (297.6 to 589.1)	

Statistical analyses

Statistical analysis title	Adjusted ratios Flu A/CAL/7/09 H1N1.HA antibodies

Statistical analysis description:

To demonstrate immunological equivalence of HA antigen adjuvanted with AS03B manufactured in Quebec (FluQ) and HA antigen adjuvanted with AS03B manufactured in Dresden (FluD), 21 days after vaccination.

Comparison groups	FluQ half Goup v FluD half Group
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	equivalence[7]
Parameter estimate	Adjusted GMT ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.26

Notes:

[7] - Equivalence criteria were fulfilled if the 2-sided 95% confidence limits on the geometric mean titre (GMT) ratio was within the interval 0.5 to 2.0.

Secondary: Number of subjects with HI antibody titers against Flu A/CAL/7/09 ≥ 1:10

End point title	Number of subjects with HI antibody titers against Flu A/CAL/7/09 ≥ 1:10

End point description:

End point type	Secondary

End point timeframe:

At Day 182

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	74	58	
Units: Subjects				
Flu A/CAL/7/09 (POST)	72	72	58	

Statistical analyses

No statistical analyses for this end point

Secondary: HI antibody titres against Flu A/CAL/7/09 H1N1 strain

End point title	HI antibody titres against Flu A/CAL/7/09 H1N1 strain

End point description:

Antibody titers were expressed as GMTs.

End point type	Secondary

End point timeframe:

At Day 182

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	74	58	
Units: Titers				
geometric mean (confidence interval 95%)				
Flu A/CAL/7/09 (POST)	117.4 (84.5 to 163.1)	128.3 (95.8 to 171.9)	115.7 (80.7 to 166)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local Adverse events (AEs)

End point title	Number of subjects reporting any and grade 3 solicited local Adverse events (AEs)

End point description:

Any was defined as occurrence of any local symptom regardless of their intensity grade. Grade 3 redness and swelling = >100 millimeter (mm) and grade 3 pain = Cried when limb is moved/spontaneously painful.

End point type	Secondary

End point timeframe:

During a 7-day (Days 0-6) post-vaccination period

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Subjects				
Any Pain	41	41	23	
Grade 3 Pain	3	0	0	
Any Redness	0	1	0	
Grade 3 Redness	0	0	0	
Any Swelling	1	5	1	

Grade 3 Swelling	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general AEs aged 3 years to 5 years

End point title	Number of subjects reporting any, grade 3 and related solicited general AEs aged 3 years to 5 years

End point description:

Solicited general symptoms assessed were drowsiness, irritability, loss of appetite and fever (Fever = axillary temperature equal to or above 38.0 degrees Celsius (°C)). Any = any solicited general symptom reported irrespective of intensity and relationship to vaccination. Related = symptoms considered by the investigator to have a causal relationship to vaccination. Grade 3 symptoms = symptoms that prevented normal activity. Grade 3 fever = axillary temperature equal to or above (≥) 39.0°C.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	31	24	
Units: Subjects				
Any Drowsiness	5	3	1	
Grade 3 Drowsiness	0	0	0	
Related Drowsiness	1	2	0	
Any Irritability	2	7	1	
Grade 3 Irritability	0	0	0	
Related Irritability	0	2	0	
Any Loss of appetite	6	4	1	
Grade 3 Loss of appetite	1	1	0	
Related Loss of appetite	1	2	0	
Any Fever	2	5	5	
Grade 3 Fever	1	2	1	
Related Fever	1	5	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general symptoms on subjects aged 6 years to 10 years

End point title	Number of subjects reporting solicited general symptoms on subjects aged 6 years to 10 years

End point description:

Solicited general symptoms assessed were fatigue, gastrointestinal symptoms, headache, joint pain at other location, muscle aches, shivering, sweating and fever (Fever = axillary temperature equal to or above 38.0 degrees Celsius (°C)). Any = any solicited general symptom reported irrespective of intensity and relationship to vaccination. Related = symptoms considered by the investigator to have a causal relationship to vaccination. Grade 3 symptoms = symptoms that prevented normal activity. Grade 3 fever = axillary temperature equal to or above (≥) 39.0°C.

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	44	33	
Units: Subjects				
Any Fatigue	4	3	2	
Grade 3 Fatigue	1	0	0	
Related Fatigue	1	0	0	
Any Gastrointestinal	2	1	0	
Grade 3 Gastrointestinal	1	0	0	
Related Gastrointestinal	0	0	0	
Any Headache	7	9	4	
Grade 3 Headache	1	0	0	
Related Headache	0	2	0	
Any Joint pain at other location	5	1	4	
Grade 3 Joint pain at other location	1	0	0	
Related Joint pain at other location	1	0	0	
Any Muscle aches	6	7	5	
Grade 3 Muscle aches	0	0	0	
Related Muscle aches	1	1	0	
Any Shivering	4	2	0	
Grade 3 Shivering	1	0	0	
Related Shivering	0	0	0	
Any Sweating	2	1	0	
Grade 3 Sweating	1	0	0	
Related Sweating	0	0	0	
Any Fever	4	0	0	
Grade 3 Fever	1	0	0	
Related Fever	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with medically-attended adverse events (MAEs)

End point title	Number of subjects with medically-attended adverse events

	(MAEs)

End point description:

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Subjects				
Any MAE(s)	14	9	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with MAEs

End point title	Number of subjects with MAEs

End point description:

End point type	Secondary

End point timeframe:

During the entire study period (Day 0 to Day 182)

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Subjects				
Any MAE(s)	29	29	18	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potential immune-mediated diseases (pIMDs)

End point title	Number of subjects with potential immune-mediated diseases (pIMDs)

End point description:

End point type	Secondary

End point timeframe:

Up to Day 21

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Subjects				
pIMDs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with pIMDs

End point title	Number of subjects with pIMDs

End point description:

End point type	Secondary

End point timeframe:

During the entire study period (Day 0 to Day 182)

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Subjects				
pIMDs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

End point type	Secondary

End point timeframe:

Within the 21-day (Days 0-20) post-vaccination period

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Subjects				
Any AE(s)	22	21	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

End point type	Secondary

End point timeframe:

Within the 42-day (Days 0-41) post-vaccination period

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Subjects				
Any AE(s)	28	28	23	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

End point type	Secondary

End point timeframe:

Up to 21 days after vaccination

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Subjects				
Any SAE(s)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

End point type	Secondary

End point timeframe:

During the entire study period (Days 0 - 182)

End point values	FluQ half Goup	FluD half Group	FluQ Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	58	
Units: Subjects				
Any SAE(s)	1	0	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: Day 0 to 182; Unsolicted AEs: During the 42-day (Days 0-41) post-vaccination period; Solicited local and general symptoms: During the 7-day (Days 0-6) post-vaccination period.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	FluQ half Goup

Reporting group description:

Subjects received 1 half-pediatric dose of FluQ vaccine at Day 0

Reporting group title	FluD half Group

Reporting group description:

Subjects received 1 half-pediatric dose of FluD vaccine at Day 0

Reporting group title	FluQ Group

Reporting group description:

Subjects received 1 pediatric dose of FluQ vaccine at Day 0

Serious adverse events	FluQ half Goup	FluD half Group	FluQ Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	1 / 58 (1.72%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Dengue fever			
subjects affected / exposed	1 / 76 (1.32%)	0 / 75 (0.00%)	0 / 58 (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
Influenza			
subjects affected / exposed	0 / 76 (0.00%)	0 / 75 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	FluQ half Goup	FluD half Group	FluQ Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 76 (53.95%)	41 / 75 (54.67%)	23 / 58 (39.66%)
General disorders and administration site conditions			
Pyrexia (within the 21-day (Days 0-20) post-vaccination period)			
subjects affected / exposed	2 / 76 (2.63%)	6 / 75 (8.00%)	1 / 58 (1.72%)
occurrences (all)	2	6	1
Pyrexia (within the 42-day (Days 0-41) post-vaccination period)			
subjects affected / exposed	4 / 76 (5.26%)	9 / 75 (12.00%)	6 / 58 (10.34%)
occurrences (all)	4	9	6
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	41 / 76 (53.95%)	41 / 75 (54.67%)	23 / 58 (39.66%)
occurrences (all)	41	41	23
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 75 (1.33%)	0 / 58 (0.00%)
occurrences (all)	0	1	0
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 76 (1.32%)	5 / 75 (6.67%)	1 / 58 (1.72%)
occurrences (all)	1	5	1
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[1]	5 / 33 (15.15%)	3 / 31 (9.68%)	1 / 24 (4.17%)
occurrences (all)	5	3	1
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[2]	2 / 33 (6.06%)	7 / 31 (22.58%)	1 / 24 (4.17%)
occurrences (all)	2	7	1
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[3]	6 / 33 (18.18%)	4 / 31 (12.90%)	1 / 24 (4.17%)
occurrences (all)	6	4	1

Temperature/ (Axillary) (subjects aged 3 years to 5 years)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	2 / 33 (6.06%)	5 / 31 (16.13%)	5 / 24 (20.83%)
occurrences (all)	2	5	5
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed[5]	4 / 41 (9.76%)	3 / 44 (6.82%)	2 / 33 (6.06%)
occurrences (all)	4	3	2
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed[6]	2 / 41 (4.88%)	1 / 44 (2.27%)	0 / 33 (0.00%)
occurrences (all)	2	1	0
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[7]	7 / 41 (17.07%)	9 / 44 (20.45%)	4 / 33 (12.12%)
occurrences (all)	7	9	4
Joint pain at other location			
alternative assessment type: Systematic			
subjects affected / exposed[8]	5 / 41 (12.20%)	1 / 44 (2.27%)	4 / 33 (12.12%)
occurrences (all)	5	1	4
Muscle aches			
alternative assessment type: Systematic			
subjects affected / exposed[9]	6 / 41 (14.63%)	7 / 44 (15.91%)	5 / 33 (15.15%)
occurrences (all)	6	7	5
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed[10]	4 / 41 (9.76%)	2 / 44 (4.55%)	0 / 33 (0.00%)
occurrences (all)	4	2	0
Sweating			
alternative assessment type: Systematic			
subjects affected / exposed[11]	2 / 41 (4.88%)	1 / 44 (2.27%)	0 / 33 (0.00%)
occurrences (all)	2	1	0
Temperature/ (Axillary) (subjects aged 6 years to <10 years)			
alternative assessment type: Systematic			

subjects affected / exposed[12]	4 / 41 (9.76%)	0 / 44 (0.00%)	0 / 33 (0.00%)
occurrences (all)	4	0	0
Eye disorders			
Conjunctivitis			
subjects affected / exposed	3 / 76 (3.95%)	1 / 75 (1.33%)	3 / 58 (5.17%)
occurrences (all)	3	1	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 76 (2.63%)	4 / 75 (5.33%)	3 / 58 (5.17%)
occurrences (all)	2	4	3
Infections and infestations			
Upper respiratory tract infection (within the 21-day (Days 0-20) post-vaccination period)			
subjects affected / exposed	5 / 76 (6.58%)	5 / 75 (6.67%)	1 / 58 (1.72%)
occurrences (all)	5	5	1
Nasopharyngitis (within the 21-day (Days 0-20) post-vaccination period)			
subjects affected / exposed	5 / 76 (6.58%)	1 / 75 (1.33%)	2 / 58 (3.45%)
occurrences (all)	5	1	2
Rhinitis (within the 21-day (Days 0-20) post-vaccination period)			
subjects affected / exposed	4 / 76 (5.26%)	2 / 75 (2.67%)	0 / 58 (0.00%)
occurrences (all)	4	2	0
Nasopharyngitis (within the 42-day (Days 0-41) post-vaccination period)			
subjects affected / exposed	7 / 76 (9.21%)	5 / 75 (6.67%)	5 / 58 (8.62%)
occurrences (all)	7	5	5
Upper respiratory tract infection (within the 42-day (Days 0-41) post-vaccination period)			
subjects affected / exposed	6 / 76 (7.89%)	6 / 75 (8.00%)	3 / 58 (5.17%)
occurrences (all)	6	6	3
Rhinitis (within the 42-day (Days 0-41) post-vaccination period)			
subjects affected / exposed	5 / 76 (6.58%)	2 / 75 (2.67%)	0 / 58 (0.00%)
occurrences (all)	5	2	0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the

vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on Total Vaccinated cohort which included all subjects with the vaccine administration documented and symptom sheet completed only on subjects that reported the specific symptom. Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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