



Clinical trial results:

A Phase III, double-blind, randomised, controlled, multi-country, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to GSK Biologicals' trivalent influenza vaccine Fluarix®, administered intramuscularly to children 6 to 35 months of age.

Summary

EudraCT number	2013-003155-38
Trial protocol	Outside EU/EEA
Global end of trial date	19 June 2013

Results information

Result version number	v1
This version publication date	18 April 2016
First version publication date	04 July 2015

Trial information

Trial identification

Sponsor protocol code	250116926
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01711736
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, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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	23 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2013
Global end of trial reached?	Yes
Global end of trial date	19 June 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the immunogenicity of FLU Q-QIV based on Center for Biologics Evaluation and Research's (CBER)'s Seroconversion Rate (SCR) criterion for each of the four strains in children 6 to 35 months of age, approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively).

Criterion for determination of effective immunisation:

The lower limit of the two-sided 95% confidence interval (CI) for SCR should be $\geq 40\%$ for each strain.

- To describe the reactogenicity of FLU Q-QIV and Fluarix in terms of solicited local and general adverse events (AEs), during a 7-day follow-up period.

Protection of trial subjects:

The vaccine recipients were observed closely for at least 30 minutes following the administration of vaccine, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2012
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	Honduras: 210
Country: Number of subjects enrolled	Canada: 146
Country: Number of subjects enrolled	Dominican Republic: 250
Worldwide total number of subjects	606
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	402
Children (2-11 years)	204
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:

Primed subjects: Received 2 doses of seasonal influenza vaccine separated by at least one month during the last season or had received at least 1 dose prior to last season. Unprimed subjects: Did not receive any seasonal influenza vaccine in the past or received only 1 dose for the first time in the last influenza season.

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
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Data were collected in a double-blind manner. The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK2282512A Group

Arm description:

Subjects aged between 6 to 35 months inclusive received 1 dose (primed subjects) at Day 0 and 2 doses (unprimed subjects) at Days 0 and 28 of quadrivalent influenza GSK2282512A vaccine. Quadrivalent influenza GSK2282512A vaccine was administered intramuscularly in the left anterolateral thigh (subjects < 12 months of age) or the deltoid muscle (subjects ≥ 12 months of age).

Arm type	Experimental
Investigational medicinal product name	FLU Q-QIV (Quadrivalent influenza vaccine)
Investigational medicinal product code	GSK2282512A
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 or 2 doses administered intramuscularly (IM) in deltoid muscle or anterolateral thigh on Day 0 (primed subjects) and on Day 0 and Day 28 (unprimed subjects) respectively.

Arm title	Fluarix Group
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Arm description:

Subjects aged between 6 to 35 months inclusive received 1 dose (primed subjects) at Day 0 and 2 doses (unprimed subjects) at Days 0 and 28 of Fluarix vaccine. Fluarix vaccine was administered intramuscularly in the left anterolateral thigh (subjects < 12 months of age) or the deltoid muscle (subjects ≥ 12 months of age).

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

Dosage and administration details:

1 or 2 doses administered IM in deltoid muscle or anterolateral thigh, on Day 0 (primed subjects) and on Day 0 and Day 28 (unprimed subjects) respectively.

Number of subjects in period 1^[1]	GSK2282512A Group	Fluarix Group
Started	299	302
Completed	287	294
Not completed	12	8
Consent withdrawn by subject	6	6
Migrated/moved from study area	2	1
Lost to follow-up	4	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 5 subjects enrolled in the study were allocated subject numbers but the study vaccine dose was not administered.

Baseline characteristics

Reporting groups

Reporting group title	GSK2282512A Group
Reporting group description:	
Subjects aged between 6 to 35 months inclusive received 1 dose (primed subjects) at Day 0 and 2 doses (unprimed subjects) at Days 0 and 28 of quadrivalent influenza GSK2282512A vaccine. Quadrivalent influenza GSK2282512A vaccine was administered intramuscularly in the left anterolateral thigh (subjects < 12 months of age) or the deltoid muscle (subjects ≥ 12 months of age).	
Reporting group title	Fluarix Group
Reporting group description:	
Subjects aged between 6 to 35 months inclusive received 1 dose (primed subjects) at Day 0 and 2 doses (unprimed subjects) at Days 0 and 28 of Fluarix vaccine. Fluarix vaccine was administered intramuscularly in the left anterolateral thigh (subjects < 12 months of age) or the deltoid muscle (subjects ≥ 12 months of age).	

Reporting group values	GSK2282512A Group	Fluarix Group	Total
Number of subjects	299	302	601
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	18.2	18.1	
standard deviation	± 8.17	± 8.34	-
Gender categorical Units: Subjects			
Female	155	146	301
Male	144	156	300

End points

End points reporting groups

Reporting group title	GSK2282512A Group
Reporting group description: Subjects aged between 6 to 35 months inclusive received 1 dose (primed subjects) at Day 0 and 2 doses (unprimed subjects) at Days 0 and 28 of quadrivalent influenza GSK2282512A vaccine. Quadrivalent influenza GSK2282512A vaccine was administered intramuscularly in the left anterolateral thigh (subjects < 12 months of age) or the deltoid muscle (subjects ≥ 12 months of age).	
Reporting group title	Fluarix Group
Reporting group description: Subjects aged between 6 to 35 months inclusive received 1 dose (primed subjects) at Day 0 and 2 doses (unprimed subjects) at Days 0 and 28 of Fluarix vaccine. Fluarix vaccine was administered intramuscularly in the left anterolateral thigh (subjects < 12 months of age) or the deltoid muscle (subjects ≥ 12 months of age).	

Primary: Number of seroconverted subjects for anti- Haemagglutination Inhibition (HI) antibodies against each of the four vaccine influenza strains of quadrivalent influenza GSK2282512A vaccine.

End point title	Number of seroconverted subjects for anti- Haemagglutination Inhibition (HI) antibodies against each of the four vaccine influenza strains of quadrivalent influenza GSK2282512A vaccine. ^{[1][2]}
End point description: A seroconverted subject was defined as a vaccinated subject with either a pre-vaccination titer less than (<) 1:10 and a post-vaccination titer greater than or equal to (≥) 1:40, or a pre-vaccination titer ≥ 1:10 and at least a 4-fold increase in post-vaccination titer. The vaccine strains assessed were Flu A/CAL/7/09 (H1N1), Flu A/Victoria/361/11 (H3N2), Flu B/Hubei-Wujiagang/158/09 (Yamagata) and Flu B/Bri/60/08 (Victoria). This outcome concerns solely subjects in the GSK2282512A Group.	
End point type	Primary
End point timeframe: At Day 28 for primed subjects and at Day 56 for unprimed subjects.	

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.

[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 concerns solely subjects in the GSK2282512A Group.

End point values	GSK2282512A Group			
Subject group type	Reporting group			
Number of subjects analysed	284			
Units: Subjects				
[H1N1, Day 28 = primed and Day 56 = unprimed]	244			
[H3N2, Day 28 = primed and Day 56 = unprimed]	205			
[Yamagata, Day 28 = primed and Day 56 = unprimed]	224			
[Victoria, Day 28 = primed and Day 56 = unprimed]	210			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting any and grade 3 solicited local symptoms.

End point title	Number of subjects reporting any and grade 3 solicited local symptoms. ^[3]
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End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any was defined as occurrence of the specified solicited local symptom regardless of its intensity. Grade 3 pain was defined as pain that prevented normal everyday activities. Grade 3 swelling was greater than 100 millimeters (mm) i.e. >100mm.

End point type	Primary
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End point timeframe:

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

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.

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	291	297		
Units: Subjects				
Any Pain	95	91		
Grade 3 Pain	7	3		
Any Redness	6	6		
Grade 3 Redness	0	0		
Any Swelling	5	6		
Grade 3 Swelling	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting any, grade 3 and related solicited general symptoms (excluding fever).

End point title	Number of subjects reporting any, grade 3 and related solicited general symptoms (excluding fever). ^[4]
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End point description:

Solicited general symptoms assessed were drowsiness, irritability/fussiness and loss of appetite. Any was defined as any solicited general symptom reported irrespective of intensity and relationship to vaccination. Related was defined as symptoms assessed by the investigator to have a causal relationship to vaccination. Grade 3 irritability/fussiness was defined as crying that could not be

comforted/prevented normal activity. Grade 3 loss of appetite was defined as not eating at all. Grade 3 drowsiness was defined as drowsiness that prevented normal activity.

End point type	Primary
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End point timeframe:

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

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

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	296		
Units: Subjects				
Any Drowsiness	93	88		
Grade 3 Drowsiness	9	9		
Related Drowsiness	79	80		
Any Irritability/fussiness	118	123		
Grade 3 Irritability/fussiness	15	14		
Related Irritability/fussiness	104	106		
Any Loss of appetite	99	100		
Grade 3 Loss of appetite	16	14		
Related Loss of appetite	84	83		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting any, grade 3 and related fever.

End point title	Number of subjects reporting any, grade 3 and related fever. ^[5]
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End point description:

Any fever was defined as any fever ≥ 38.0 degrees Celsius ($^{\circ}\text{C}$) irrespective of intensity and relationship to vaccination. Related was defined as symptoms assessed by the investigator to have a causal relationship to vaccination. Grade 3 fever was defined as fever ≥ 39.0 $^{\circ}\text{C}$.

End point type	Primary
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End point timeframe:

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

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.

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	296		
Units: Subjects				
Any Fever	61	60		
Grade 3 Fever	23	13		

Related Fever	49	48		
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Statistical analyses

No statistical analyses for this end point

Secondary: Haemagglutination inhibition (HI) antibody titers against each of the four vaccine influenza strains.

End point title	Haemagglutination inhibition (HI) antibody titers against each of the four vaccine influenza strains.
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End point description:

HI antibody titers were expressed as Geometric mean titers (GMTs). The vaccine strains assessed were Flu A/CAL/7/09 (H1N1), Flu A/Victoria/361/11 (H3N2), Flu B/Hubei-Wujiagang/158/09 (Yamagata) and Flu B/Bri/60/08 (Victoria).

End point type	Secondary
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End point timeframe:

At Day 0 (for all subjects) and 28 days after the last vaccine dose (at Day 28 for primed subjects and at Day 56 for unprimed subjects).

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	287		
Units: Titers				
geometric mean (confidence interval 95%)				
[H1N1, Day 0]	9.6 (8.1 to 11.3)	9.8 (8.3 to 11.6)		
[H1N1, Day 28 = primed and Day 56 = unprimed]	157.1 (132.8 to 185.9)	61.2 (49.2 to 76.2)		
[H3N2, Day 0]	17.4 (14.1 to 21.5)	13.8 (11.4 to 16.8)		
[H3N2, Day 28 = primed and Day 56 = unprimed]	159.4 (129.4 to 196.3)	103 (83.7 to 126.7)		
[Yamagata, Day 0]	7.7 (6.9 to 8.7)	7.2 (6.5 to 8)		
[Yamagata, Day 28 = primed and Day 56 = unprimed]	114.2 (100 to 130.5)	107.2 (92.2 to 124.6)		
[Victoria, Day 0]	10.6 (9.1 to 12.4)	9.3 (8 to 10.7)		
[Victoria, Day 28 = primed and Day 56 = unprimed]	111.4 (91.9 to 135.2)	15.6 (13.3 to 18.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for anti- Haemagglutination Inhibition (HI) antibodies against each of the four vaccine influenza strains of Fluarix vaccine.

End point title	Number of seroconverted subjects for anti- Haemagglutination Inhibition (HI) antibodies against each of the four vaccine influenza strains of Fluarix vaccine. ^[6]
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End point description:

A seroconverted subject was defined as a vaccinated subject with either a pre-vaccination titer less than (<) 1:10 and a post-vaccination titer greater than or equal to (≥) 1:40, or a pre-vaccination titer ≥ 1:10 and at least a 4-fold increase in post-vaccination titer. The vaccine strains assessed were Flu A/CAL/7/09 (H1N1), Flu A/Victoria/361/11 (H3N2), Flu B/Hubei-Wujiagang/158/09 (Yamagata) and Flu B/Bri/60/08 (Victoria). This outcome concerns solely subjects in the Fluarix Group.

End point type	Secondary
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End point timeframe:

At Day 28 for primed subjects and at Day 56 for unprimed subjects.

Notes:

[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 concerns solely subjects in the Fluarix Group.

End point values	Fluarix Group			
Subject group type	Reporting group			
Number of subjects analysed	287			
Units: Subjects				
[H1N1, Day 28 = primed and Day 56 = unprimed]	154			
[H3N2, Day 28 = primed and Day 56 = unprimed]	160			
[Yamagata, Day 28 = primed and Day 56 = unprimed]	222			
[Victoria, Day 28 = primed and Day 56 = unprimed]	28			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who were seroprotected for haemagglutination inhibition (HI) antibodies against each of the four vaccine influenza strains.

End point title	Number of subjects who were seroprotected for haemagglutination inhibition (HI) antibodies against each of the four vaccine influenza strains.
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End point description:

A seroprotected subject was defined as a vaccinated subject with a serum HI titer greater than or equal to (≥) 1:40 that usually is accepted as indicating protection in adults. The vaccine strains assessed were Flu A/CAL/7/09 (H1N1), Flu A/Victoria/361/11 (H3N2), Flu B/Hubei-Wujiagang/158/09 (Yamagata) and Flu B/Bri/60/08 (Victoria).

End point type	Secondary
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End point timeframe:

At Day 0 (for all subjects) and Day 28 after last vaccine dose (Day 28 for primed subjects and Day 56 for unprimed subjects).

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	287		
Units: Subjects				
[H1N1, Day 0]	46	47		
[H1N1, Day 28 = primed and Day 56 = unprimed]	254	169		
[H3N2, Day 0]	93	74		
[H3N2, Day 28 = primed and Day 56 = unprimed]	231	191		
[Yamagata, Day 0]	26	24		
[Yamagata, Day 28 = primed and Day 56 = unprimed]	242	229		
[Victoria, Day 0]	56	45		
[Victoria, Day 28 = primed and Day 56 = unprimed]	216	74		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean geometric increase (MGI) for haemagglutination inhibition (HI) antibody titer against each of the four vaccine influenza strains.

End point title	Mean geometric increase (MGI) for haemagglutination inhibition (HI) antibody titer against each of the four vaccine influenza strains.
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End point description:

MGI was defined as the fold increase in serum haemagglutination inhibition (HI) GMTs post-vaccination compared to pre-vaccination (Day 0). The vaccine strains assessed were Flu A/CAL/7/09 (H1N1), Flu A/Victoria/361/11 (H3N2), Flu B/Hubei-Wujiagang/158/09 (Yamagata) and Flu B/Bri/60/08 (Victoria).

End point type	Secondary
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End point timeframe:

28 days after the last vaccine dose (at Day 28 for primed subjects and at Day 56 for unprimed subjects).

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	287		
Units: Fold increase				
geometric mean (confidence interval 95%)				
[H1N1, Day 28 = primed and Day 56 = unprimed]	16.4 (14.3 to 18.7)	6.2 (5.3 to 7.3)		
[H3N2, Day 28 = primed and Day 56 = unprimed]	9.1 (8 to 10.5)	7.5 (6.4 to 8.7)		

[Yamagata, Day 28 = primed and Day 56 = unprimed]	14.8 (12.8 to 17.1)	14.8 (12.8 to 17.2)		
[Victoria, Day 28 = primed and Day 56 = unprimed]	10.5 (9.2 to 11.9)	1.7 (1.5 to 1.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related fever.

End point title	Number of subjects reporting any, grade 3 and related fever.
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End point description:

Any fever was defined as any fever ≥ 38.0 °C irrespective of intensity and relationship to vaccination. Related was defined as symptoms considered by the investigator to have a causal relationship to vaccination. Grade 3 fever was defined as fever ≥ 39.0 °C.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period.

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	296		
Units: Subjects				
Any Fever	46	42		
Grade 3 Fever	16	8		
Related Fever	39	38		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any Medically Attended Adverse Events (MAEs).

End point title	Number of subjects reporting any Medically Attended Adverse Events (MAEs).
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End point description:

MAEs were defined as adverse events with medically-attended visits that were not routine visits for physical examination or vaccination, such as visits for hospitalization, an emergency room visit, or an otherwise unscheduled visit to or from medical personnel (medical doctor) for any reason. Any was defined as any occurrence of MAE(s).

End point type	Secondary
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End point timeframe:

During the entire study period (Day 0 to Day 180).

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	302		
Units: Subjects				
Any MAE(s)	156	156		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any potential Immune-Mediated Diseases (pIMDs).

End point title	Number of subjects reporting any potential Immune-Mediated Diseases (pIMDs).
End point description: Potential immune-mediated diseases (pIMDs) were defined as a subset of adverse events that included both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which might or might not have an autoimmune aetiology. Any pIMD was defined as at least one pIMD experienced by the study subject.	
End point type	Secondary
End point timeframe: During the entire study period (Day 0 to Day 180).	

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	302		
Units: Subjects				
Any pIMD(s)	0	2		
Related pIMD(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related unsolicited adverse events (AEs).

End point title	Number of subjects reporting any, grade 3 and related unsolicited adverse events (AEs).
End point description: An unsolicited AE was defined as an untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the	

medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination.

End point type	Secondary
End point timeframe:	
During the 28-day (Days 0-27) post-vaccination period.	

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	302		
Units: Subjects				
Any Unsolicited AEs	142	165		
Grade 3 Unsolicited AEs	9	5		
Related Unsolicited AEs	17	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and related serious adverse events (SAEs).

End point title	Number of subjects reporting any and related serious adverse events (SAEs).
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End point description:

A serious adverse event was defined as any untoward medical occurrence that: resulted in death, was life threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject. Any was defined as occurrence of any symptom regardless of intensity grade or relation to vaccination and related was an event assessed by the investigator as causally related to the study vaccination.

End point type	Secondary
End point timeframe:	
During the entire study period (Day 0 – Day 180).	

End point values	GSK2282512A Group	Fluarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	302		
Units: Subjects				
Any SAEs	9	8		
Related SAEs	1	0		

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events: From Day 0 to Day 180; Solicited local and general symptoms: During the 7-day (Days 0-6) post-vaccination period; Unsolicited adverse events: During the 28-day (Days 0-27) post-vaccination period.

Adverse event reporting additional description:

For the systematically assessed other (non-serious) adverse events, the number of participants at risk included those from Total Vaccinated Cohort who had the symptom sheet completed.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	GSK2282512A Group
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Reporting group description:

Subjects aged between 6 to 35 months inclusive received 1 dose (primed subjects) at Day 0 and 2 doses (unprimed subjects) at Days 0 and 28 of quadrivalent influenza GSK2282512A vaccine. Quadrivalent influenza GSK2282512A vaccine was administered intramuscularly in the left anterolateral thigh (subjects < 12 months of age) or the deltoid muscle (subjects ≥ 12 months of age).

Reporting group title	Fluarix Group
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Reporting group description:

Subjects aged between 6 to 35 months inclusive received 1 dose (primed subjects) at Day 0 and 2 doses (unprimed subjects) at Days 0 and 28 of Fluarix vaccine. Fluarix vaccine was administered intramuscularly in the left anterolateral thigh (subjects < 12 months of age) or the deltoid muscle (subjects ≥ 12 months of age).

Serious adverse events	GSK2282512A Group	Fluarix Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 299 (3.01%)	8 / 302 (2.65%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Febrile convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 299 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 299 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 299 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 299 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 299 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyperreactivity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 299 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 299 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 299 (0.00%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 299 (0.00%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amoebic dysentery			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 299 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial pyelonephritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 299 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blastocystis infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 299 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 299 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 299 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Peritonitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 299 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis streptococcal			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 299 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 299 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 299 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 299 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 299 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 299 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GSK2282512A Group	Fluarix Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	118 / 299 (39.46%)	123 / 302 (40.73%)	
General disorders and administration site conditions			
Pain			
subjects affected / exposed ^[1]	95 / 291 (32.65%)	91 / 297 (30.64%)	
occurrences (all)	95	91	
Drowsiness			
subjects affected / exposed ^[2]	93 / 290 (32.07%)	88 / 296 (29.73%)	
occurrences (all)	93	88	
Irritability/fussiness			
subjects affected / exposed ^[3]	118 / 290 (40.69%)	123 / 296 (41.55%)	
occurrences (all)	118	123	
Loss of appetite			
subjects affected / exposed ^[4]	99 / 290 (34.14%)	100 / 296 (33.78%)	
occurrences (all)	99	100	
Fever (Days 0-6)			
subjects affected / exposed ^[5]	61 / 290 (21.03%)	60 / 296 (20.27%)	
occurrences (all)	61	60	
Fever (Days 0-3)			
subjects affected / exposed ^[6]	46 / 290 (15.86%)	42 / 296 (14.19%)	
occurrences (all)	46	42	
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	38 / 299 (12.71%)	38 / 302 (12.58%)	
occurrences (all)	38	38	
Infections and infestations			

Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	78 / 299 (26.09%)	90 / 302 (29.80%)	
occurrences (all)	78	90	

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: 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: 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: 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: 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: 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: 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