



## Clinical trial results:

**A phase II, controlled, randomized, single centre, single blind study to evaluate the immunogenicity, safety and reactogenicity of the low dose influenza vaccine with various doses of AS03 adjuvant compared to Fluarix™ (GlaxoSmithKline Biologicals) administered intramuscularly in subjects aged 18-59 years old.**

### Summary

EudraCT number	2006-003769-15
Trial protocol	BE
Global end of trial date	29 November 2006

### Results information

Result version number	v1
This version publication date	13 May 2016
First version publication date	04 December 2014

### Trial information

#### Trial identification

Sponsor protocol code	108656
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00374842
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, 1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 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?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 November 2006
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 November 2006
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To assess the humoral immune response (anti-haemagglutinin antibody titres) elicited by the low dose influenza vaccine adjuvanted with AS03 (full or half dose of AS03) and by Fluarix given intramuscularly in subjects aged 18-59 years old, 21 days following vaccination.

Protection of trial subjects:

As with all injectable vaccines, appropriate medical treatment was always readily available in case of anaphylactic reactions following the administration of the vaccine.

For this reason, the vaccine remained under medical supervision for 30 minutes after vaccination.

Subjects were instructed to contact the investigator should they manifest any signs or symptoms they perceive as serious.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 300
Worldwide total number of subjects	300
EEA total number of subjects	300

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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	300
From 65 to 84 years	0



## Subject disposition

### Recruitment

Recruitment details:

A total of 300 subjects were enrolled in the study. Study duration was of approximately 1 month (30 days) for all subjects.

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

Number of subjects started	300
Number of subjects completed	300

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	GSK1247446A Formulation 1 Group

Arm description:

Subjects aged 18 - 59 years at the time of enrolment received one dose of the GSK1247446A vaccine adjuvanted with a full dose of adjuvant at Day 0. The adjuvanted GSK1247446A vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	GlaxoSmithKline Biologicals low dose influenza vaccine adjuvanted with AS03 (full dose of AS03)
Investigational medicinal product code	FLU-LD
Other name	GSK1247446A
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Low-dose GlaxoSmithKline Biologicals' GSK1247446A influenza vaccine

<b>Arm title</b>	GSK1247446A Formulation 2 Group
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Arm description:

Subjects aged 18 - 59 years at the time of enrolment received one dose of the GSK1247446A vaccine adjuvanted with a half dose of adjuvant at Day 0. The adjuvanted GSK1247446A vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	GlaxoSmithKline Biologicals low dose influenza vaccine adjuvanted with AS03 (half dose of AS03)
Investigational medicinal product code	FLU-LD
Other name	GSK1247446A
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Low-dose GlaxoSmithKline Biologicals' GSK1247446A influenza vaccine

<b>Arm title</b>	Fluarix Group
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Arm description:

Subjects aged 18 - 59 years at the time of enrolment received one dose of the Fluarix™ vaccine at Day 0. The Fluarix™ vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.

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

Dosage and administration details:

Intramuscularly in the deltoid region of the non-dominant arm.

<b>Number of subjects in period 1</b>	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group
Started	100	100	100
Completed	100	100	100

## Baseline characteristics

### Reporting groups

Reporting group title	GSK1247446A Formulation 1 Group
Reporting group description:	Subjects aged 18 - 59 years at the time of enrolment received one dose of the GSK1247446A vaccine adjuvanted with a full dose of adjuvant at Day 0. The adjuvanted GSK1247446A vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.
Reporting group title	GSK1247446A Formulation 2 Group
Reporting group description:	Subjects aged 18 - 59 years at the time of enrolment received one dose of the GSK1247446A vaccine adjuvanted with a half dose of adjuvant at Day 0. The adjuvanted GSK1247446A vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.
Reporting group title	Fluarix Group
Reporting group description:	Subjects aged 18 - 59 years at the time of enrolment received one dose of the Fluarix™ vaccine at Day 0. The Fluarix™ vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.

Reporting group values	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group
Number of subjects	100	100	100
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			
geometric mean	37.3	35	37.7
standard deviation	± 13.94	± 13.26	± 13.75
Gender categorical Units: Subjects			
Female	65	60	57
Male	35	40	43

Reporting group values	Total		
Number of subjects	300		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days)	0 0 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			
geometric mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	182		
Male	118		

## End points

### End points reporting groups

Reporting group title	GSK1247446A Formulation 1 Group
Reporting group description: Subjects aged 18 - 59 years at the time of enrolment received one dose of the GSK1247446A vaccine adjuvanted with a full dose of adjuvant at Day 0. The adjuvanted GSK1247446A vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.	
Reporting group title	GSK1247446A Formulation 2 Group
Reporting group description: Subjects aged 18 - 59 years at the time of enrolment received one dose of the GSK1247446A vaccine adjuvanted with a half dose of adjuvant at Day 0. The adjuvanted GSK1247446A vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.	
Reporting group title	Fluarix Group
Reporting group description: Subjects aged 18 - 59 years at the time of enrolment received one dose of the Fluarix™ vaccine at Day 0. The Fluarix™ vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.	

### Primary: Titers of serum haemagglutination-inhibition (HI) antibodies against each of the 3 influenza strains assessed.

End point title	Titers of serum haemagglutination-inhibition (HI) antibodies against each of the 3 influenza strains assessed. <sup>[1]</sup>
End point description: Influenza strains assessed were the A/New Caledonia (A/CAL), A/Wisconsin (A/WIS), B/Malaysia (B/MAL) strains. Titers were presented as geometric mean titers (GMTs) calculated on subjects with available results, and expressed in haemagglutination-inhibition unit (HIU), e. g. the dilution of a serum haemagglutination-inhibition containing the specific antibody each of the assessed influenza strains at which the solution retained the minimum level of activity needed to neutralize or precipitate the corresponding influenzae antigen. The seropositivity cut-off value of the assay was 10 HIU.	
End point type	Primary
End point timeframe: At Day 0 and 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.

End point values	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	99	98	
Units: HIU				
geometric mean (confidence interval 95%)				
A/CAL, Day 0	31.9 (23.5 to 43.4)	36.1 (26.9 to 48.5)	26.1 (20.5 to 33.2)	
A/CAL, Day 21	475.4 (352.2 to 641.6)	399 (294.7 to 540.2)	380.6 (274.2 to 528.4)	
A/WIS, Day 0	16.8 (13.1 to 21.5)	19.9 (15.2 to 25.9)	14.7 (11.6 to 18.6)	
A/WIS, Day 21	276.2 (223.5 to 341.3)	241.9 (192.9 to 303.4)	172.3 (136.4 to 217.6)	

B/MAL, Day 0	20.4 (15.9 to 26.1)	22.2 (17.6 to 27.9)	26.5 (20.9 to 33.6)	
B/MAL, Day 21	268.6 (221.3 to 326)	301.5 (246.1 to 369.4)	219.2 (171.4 to 280.2)	

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of seroprotected subjects against each of the 3 influenza strains assessed.

End point title	Number of seroprotected subjects against each of the 3 influenza strains assessed. <sup>[2]</sup>
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End point description:

A seroprotected subject was a subject whose antibody titer against each of the influenza strains assessed (A/New Caledonia (A/CAL), A/Wisconsin (A/WIS) and B/Malaysia (B/MAL) strains) was equal to or higher than ( $\geq$ ) the assay seroprotection cut-off value of 40 haemagglutination-inhibition units (HIU) (e. g. the dilution of a serum haemagglutination-inhibition containing the specific antibody each of the assessed influenza strains at which the solution retained the minimum level of activity needed to neutralize or precipitate the corresponding influenzae antigen).

End point type	Primary
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End point timeframe:

At Day 0 and at Day 21.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

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

End point values	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	99	98	
Units: Subjects				
A/CAL, Day 0	41	55	35	
A/CAL, Day 21	95	97	93	
A/WIS, Day 0	32	37	25	
A/WIS, Day 21	97	97	93	
B/MAL, Day 0	31	39	44	
B/MAL, Day 21	97	98	94	

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of seroconverted subjects against each of the 3 influenza strains assessed

End point title	Number of seroconverted subjects against each of the 3 influenza strains assessed <sup>[3]</sup>
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End point description:

Influenza strains assessed were the A/New Caledonia (A/CAL), A/Wisconsin (A/WIS), and B/Malaysia (B/MAL) strains. A seroconverted subject was a subject who had either a pre-vaccination serum HI antibody titer lower than 10 haemagglutination-inhibition units (HIU) (e. g. the dilution of a serum haemagglutination-inhibition containing the specific antibody each of the assessed influenza strains at which the solution retained the minimum level of activity needed to neutralize or precipitate the corresponding influenzae antigen) and a post-vaccination titer higher than or equal to 40 HIU, or a pre-vaccination titer  $\geq 10$  and at least a four-fold increase in post- vaccination titer.

End point type Primary

End point timeframe:

At 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.

End point values	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	99	98	
Units: Subjects				
A/CAL, Day 21	69	64	66	
A/WIS, Day 21	88	79	73	
B/MAL, Day 21	76	82	65	

## Statistical analyses

No statistical analyses for this end point

### Primary: Seroconversion factor against each of the 3 Influenza strains assessed.

End point title Seroconversion factor against each of the 3 Influenza strains assessed.<sup>[4]</sup>

End point description:

Influenza strains assessed were the A/New Caledonia (A/CAL), A/Wisconsin (A/WIS), and B/Malaysia (B/MAL) strains. The seroconversion factor (SCF) was defined as a ratio, as the fold increase in serum haemagglutination-inhibition geometric mean titers (GMTs) post-vaccination compared to Day 0 (with GMTs in the above calculation expressed in haemagglutination-inhibition units (HIU) [e. g. the dilution of a serum haemagglutination-inhibition containing the specific antibody each of the assessed influenza strains at which the solution retained the minimum level of activity needed to neutralize or precipitate the corresponding influenza antigen]).

End point type Primary

End point timeframe:

At Day 21.

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.

<b>End point values</b>	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	99	98	
Units: Fold increase				
geometric mean (confidence interval 95%)				
A/CAL, Day 21	14.9 (10.4 to 21.3)	11 (7.7 to 15.9)	14.6 (9.9 to 21.6)	
A/WIS, Day 21	16.5 (13 to 20.9)	12.2 (9.2 to 16.1)	11.7 (8.8 to 15.6)	
B/MAL, Day 21	13.2 (10 to 17.4)	13.6 (10.2 to 18)	8.3 (6.2 to 11)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any and grade 3 solicited local symptoms

End point title	Number of subjects with any and grade 3 solicited local symptoms
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End point description:

Assessed solicited local symptoms were ecchymosis, pain, redness and swelling the site of injection. Any = occurrence of a solicited local symptom regardless of intensity grade. Grade 3 pain = Pain which prevented normal activity. Grade 3 ecchymosis/redness/swelling = ecchymosis/redness/swelling at injection site with a diameter larger than (>) 50 millimeters (mm). All solicited local symptoms assessed were considered by the investigator as causally related to the study vaccination.

End point type	Secondary
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End point timeframe:

Within the 7-day follow-up period (Days 0-6) after vaccination

<b>End point values</b>	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	100	100	
Units: Subjects				
Any ecchymosis	6	11	6	
Grade 3 ecchymosis (> 50 mm)	0	0	0	
Any pain	92	89	64	
Grade 3 pain	10	0	0	
Any redness	24	12	15	
Grade 3 redness (> 50 mm)	6	2	1	
Any swelling	28	17	7	
Grade 3 swelling (> 50 mm)	7	4	2	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any, grade 3 and related solicited general symptoms

End point title	Number of subjects with any, grade 3 and related solicited general symptoms
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End point description:

Assessed solicited general symptoms were arthralgia, fatigue, fever (axillary temperature higher than or equal to ( $\geq$ ) 37.5 degrees Celsius ( $^{\circ}$ C)), headache, muscle aches, and shivering. Any = Occurrence of a particular symptom regardless of intensity or relationship to vaccination. Grade 3 symptom = Symptom which prevented normal activity. Related = Symptom assessed by the investigator as causally related to the study vaccination. Grade 3 fever = axillary temperature higher than 39.0 $^{\circ}$ C.

End point type	Secondary
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End point timeframe:

Within the 7-day follow-up period (Days 0-6) after vaccination

End point values	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	100	100	
Units: Subjects				
Any arthralgia	32	14	7	
Grade 3 arthralgia	3	1	0	
Related arthralgia	32	13	5	
Any fatigue	60	42	28	
Grade 3 fatigue	6	2	1	
Related fatigue	59	39	26	
Axillary fever ( $\geq$ 37.5 $^{\circ}$ C)	30	12	2	
Grade 3 axillary fever ( $>$ 39.0 $^{\circ}$ C)	2	0	0	
Related axillary fever ( $\geq$ 37.5 $^{\circ}$ C)	30	12	2	
Any headache	51	40	29	
Grade 3 headache	9	6	3	
Related headache	50	35	23	
Any muscle aches	48	30	12	
Grade 3 muscle aches	4	2	0	
Related muscle aches	47	29	11	
Any shivering	33	13	5	
Grade 3 shivering	2	2	0	
Related shivering	33	13	5	

## Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any, grade 3 and related unsolicited adverse events (AEs)
End point description: An unsolicited AE is any 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. Any AE = any occurrence of an AE, regardless of intensity or relationship to study vaccination. Grade 3 = an event that prevented normal activity. Related = event assessed by the investigator as causally related to the study vaccination.	
End point type	Secondary
End point timeframe: Within the 30-day follow-up period (Days 0-29) after vaccination	

<b>End point values</b>	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	100	100	
Units: Subjects				
Subject(s) with any unsolicited AE(s)	55	47	35	
Subject(s) with Grade 3 unsolicited AE(s)	11	5	6	
Subject(s) with related unsolicited AE(s)	33	22	16	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any and related serious adverse events (SAEs)

End point title	Number of subjects with any and related serious adverse events (SAEs)
End point description: SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject. Any SAE = any occurrence of an SAE, regardless of relationship to study vaccination. A related SAE = an SAE assessed by the investigator as causally related to the study vaccination.	
End point type	Secondary
End point timeframe: From study start to study end, from Day 0 to Day 30	

<b>End point values</b>	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	100	100	
Units: Subjects				
Subject(s) with any SAE(s)	1	0	0	
Subject(s) with related SAE(s)	0	0	0	

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: within the 7-day (Days 0-6) follow-up period after vaccination. Unsolicited adverse events: Within the 30-day (Days 0-29) follow-up period after vaccination. Serious adverse events: From study start to study end (Days 0-30)

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	10

### Reporting groups

Reporting group title	GSK1247446A Formulation 1 Group
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Reporting group description:

Subjects aged 18 - 59 years at the time of enrolment received one dose of the GSK1247446A vaccine adjuvanted with a full dose of adjuvant at Day 0. The adjuvanted GSK1247446A vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.

Reporting group title	GSK1247446A Formulation 2 Group
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Reporting group description:

Subjects aged 18 - 59 years at the time of enrolment received one dose of the GSK1247446A vaccine adjuvanted with a half dose of adjuvant at Day 0. The adjuvanted GSK1247446A vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.

Reporting group title	Fluarix Group
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Reporting group description:

Subjects aged 18 - 59 years at the time of enrolment received one dose of the Fluarix™ vaccine at Day 0. The Fluarix™ vaccine was administered intramuscularly in the deltoid region of the non-dominant arm.

<b>Serious adverse events</b>	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	0 / 100 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural nausea			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	0 / 100 (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

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

<b>Non-serious adverse events</b>	GSK1247446A Formulation 1 Group	GSK1247446A Formulation 2 Group	Fluarix Group
Total subjects affected by non-serious adverse events subjects affected / exposed	92 / 100 (92.00%)	89 / 100 (89.00%)	64 / 100 (64.00%)
Nervous system disorders Headache (unsolicited AE) subjects affected / exposed occurrences (all)	9 / 100 (9.00%) 9	6 / 100 (6.00%) 6	2 / 100 (2.00%) 2
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	5 / 100 (5.00%) 5	2 / 100 (2.00%) 2	0 / 100 (0.00%) 0
General disorders and administration site conditions Ecchymosis alternative assessment type: Systematic subjects affected / exposed occurrences (all)	6 / 100 (6.00%) 6	11 / 100 (11.00%) 11	6 / 100 (6.00%) 6
Pain alternative assessment type: Systematic subjects affected / exposed occurrences (all)	92 / 100 (92.00%) 92	89 / 100 (89.00%) 89	64 / 100 (64.00%) 64
Redness alternative assessment type: Systematic subjects affected / exposed occurrences (all)	24 / 100 (24.00%) 24	12 / 100 (12.00%) 12	15 / 100 (15.00%) 15
Swelling alternative assessment type: Systematic subjects affected / exposed occurrences (all)	28 / 100 (28.00%) 28	17 / 100 (17.00%) 17	7 / 100 (7.00%) 7
Arthralgia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	32 / 100 (32.00%) 32	14 / 100 (14.00%) 14	7 / 100 (7.00%) 7
Fatigue alternative assessment type: Systematic			

subjects affected / exposed	60 / 100 (60.00%)	42 / 100 (42.00%)	28 / 100 (28.00%)
occurrences (all)	60	42	28
Headache (solicited general symptom AE)			
alternative assessment type: Systematic			
subjects affected / exposed	51 / 100 (51.00%)	40 / 100 (40.00%)	29 / 100 (29.00%)
occurrences (all)	51	40	29
Muscle aches			
alternative assessment type: Systematic			
subjects affected / exposed	48 / 100 (48.00%)	30 / 100 (30.00%)	12 / 100 (12.00%)
occurrences (all)	48	30	12
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed	33 / 100 (33.00%)	13 / 100 (13.00%)	5 / 100 (5.00%)
occurrences (all)	33	13	5
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	7 / 100 (7.00%)	3 / 100 (3.00%)	2 / 100 (2.00%)
occurrences (all)	7	3	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	15 / 100 (15.00%)	8 / 100 (8.00%)	11 / 100 (11.00%)
occurrences (all)	15	8	11

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported