Clinical trial results:
A Phase III, open, non-randomized, multi-centric, single dose study to assess immunogenicity and safety of Fluarix™ / Influsplit SSW® 2009/2010 injected intramuscularly in young adults (18 to 60 years) and in elderly (over 60 years).

Summary

EudraCT number	2009-010811-34
Trial protocol	DE
Global end of trial date	08 July 2009

Results information

Result version number	v1
This version publication date	11 May 2016
First version publication date	04 December 2014

Trial information

Trial identification

Sponsor protocol code	113018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00920374
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium,
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	08 July 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 July 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the humoral response (anti-hemagglutinin antibody tested by hemagglutination inhibition) against each vaccine strain in adults aged 18 years or above, 21 days after vaccination with Fluarix™/Influsplit SSW® 2009-2010.

Protection of trial subjects:

As with all injectable vaccines, appropriate medical treatment was always readily available in case of rare anaphylactic reactions following the administration of the vaccine.
For this reason, the vaccine remained under medical supervision for 30 minutes after vaccination.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	16 June 2009
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	Germany: 118
Worldwide total number of subjects	118
EEA total number of subjects	118

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)	61
From 65 to 84 years	57
85 years and over	0

Subject disposition

Recruitment	
Recruitment details: -	
Pre-assignment	
Screening details: -	
Pre-assignment period milestones	
Number of subjects started	118
Number of subjects completed	118

Period 1	
Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Fluarix Adult Group

Arm description:

Subjects who are 18-60 years of age received one dose of Fluarix™

Arm type	Experimental
Investigational medicinal product name	Fluarix™/Influsplit SSW®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

single intramuscular dose on Day 0

Arm title	Fluarix Elderly Group

Arm description:

Subjects who are > 60 years of age received one dose of Fluarix™

Arm type	Experimental
Investigational medicinal product name	Fluarix™/Influsplit SSW®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

single intramuscular dose on Day 0

Number of subjects in period 1	Fluarix Adult Group	Fluarix Elderly Group
Started	61	57
Completed	61	57

Baseline characteristics

Reporting groups	
Reporting group title	Fluarix Adult Group
Reporting group description:	
Subjects who are 18-60 years of age received one dose of Fluarix™	

Reporting group title	Fluarix Elderly Group
Reporting group description:	
Subjects who are > 60 years of age received one dose of Fluarix™	

Reporting group values	Fluarix Adult Group	Fluarix Elderly Group	Total
Number of subjects	61	57	118
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			
geometric mean	39.3	68.9	
standard deviation	± 12.18	± 6.57	-
Gender categorical			
Units: Subjects			
Female	32	28	60
Male	29	29	58

End points

End points reporting groups

Reporting group title	Fluarix Adult Group
Reporting group description:	
Subjects who are 18-60 years of age received one dose of Fluarix™	

Reporting group title	Fluarix Elderly Group
Reporting group description:	
Subjects who are > 60 years of age received one dose of Fluarix™	

Primary: Hemagglutination Inhibition (HI) Antibody Titre

End point title	Hemagglutination Inhibition (HI) Antibody Titre[1]
End point description:	
Titres given as geometric mean titer (GMT) were presented for all three vaccine influenza virus strains	
End point type	Primary
End point timeframe:	
Day 0 and 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	Fluarix Adult Group	Fluarix Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: titre				
geometric mean (confidence interval 95%)				
A/Brisbane (Day 0)	15.5 (11.7 to 20.6)	11.4 (9.2 to 14)		
A/Brisbane (Day 21)	139.7 (100.6 to 194)	55.8 (39.2 to 79.5)		
A/Uruguay (Day 0)	18.2 (13.7 to 24.1)	13.2 (10.1 to 17.2)		
A/Uruguay (Day 21)	151.7 (111.6 to 206.2)	112.4 (76.3 to 165.5)		
B/Brisbane (Day 0)	62.8 (45.4 to 86.8)	77.6 (57.3 to 105)		
B/Brisbane (Day 21)	393 (319.3 to 483.7)	371.3 (274.9 to 501.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With HI Antibody Titre Above the Cut-off Value

End point title	Number of Subjects With HI Antibody Titre Above the Cut-off Value[2]

End point description:

The cut-off value assessed was ≥ 1:10 and was presented for all three vaccine influenza virus strains

End point type	Primary

End point timeframe:

Day 0 and 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	Fluarix Adult Group	Fluarix Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: Subjects				
A/Brisbane (Day 0)	39	36		
A/Brisbane (Day 21)	58	56		
A/Uruguay (Day 0)	44	37		
A/Uruguay (Day 21)	59	56		
B/Brisbane (Day 0)	56	54		
B/Brisbane (Day 21)	59	56		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Seroprotected Subjects

End point title	Number of Seroprotected Subjects[3]

End point description:

A seroprotected subject is a subject with a serum HI antibody titre ≥ 1:40

End point type	Primary

End point timeframe:

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

End point values	Fluarix Adult Group	Fluarix Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: Subjects				
A/Brisbane (Day 0)	18	6		
A/Brisbane (Day 21)	53	35		

A/Uruguay (Day 0)	17	10		
A/Uruguay (Day 21)	52	46		
B/Brisbane (Day 0)	38	45		
B/Brisbane (Day 21)	59	56		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Seroconverted Subjects

End point title	Number of Seroconverted Subjects[4]

End point description:

A seroconverted subject is a subject with a pre-vaccination serum HI titre< 1:10 and a post-vaccination serum HI titre ≥ 1:40, or a pre-vaccination serum HI titre ≥ 1:10 and a fold increase (Day 21/Day 0) ≥ 4

End point type	Primary

End point timeframe:

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

End point values	Fluarix Adult Group	Fluarix Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: Subjects				
A/Brisbane	41	24		
A/Uruguay	40	41		
B/Brisbane	34	30		

Statistical analyses

No statistical analyses for this end point

Primary: Seroconversion Factor

End point title	Seroconversion Factor[5]

End point description:

Seroconversion factor, defined as the fold increase in serum HI GMT post-vaccination compared to pre-vaccination (Day 0), is presented for all three vaccine influenza virus strains

End point type	Primary

End point timeframe:

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

End point values	Fluarix Adult Group	Fluarix Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	56		
Units: fold increase				
geometric mean (confidence interval 95%)				
A/Brisbane	9 (6.2 to 13.1)	4.9 (3.5 to 6.9)		
A/Uruguay	8.3 (6 to 11.6)	8.5 (6.2 to 11.7)		
B/Brisbane	6.3 (4.5 to 8.7)	4.8 (3.6 to 6.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Seroprotection Power

End point title	Seroprotection Power[6]

End point description:

Seroprotection power is defined as the number of subject who had a pre-vaccination titre < 1:40 and a post-vaccination titre ≥ 1:40

End point type	Primary

End point timeframe:

Day 21

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	Fluarix Adult Group	Fluarix Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	50		
Units: Subjects				
A/Brisbane (N=41; 50)	35	29		
A/Uruguay (N=42; 46)	35	36		
B/Brisbane (N=21; 11)	21	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Solicited Local Symptoms

End point title	Number of Subjects Reporting Solicited Local Symptoms

End point description:

Solicited local symptoms assessed include ecchymosis, induration, pain, redness, and swelling.

End point type	Secondary

End point timeframe:

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

End point values	Fluarix Adult Group	Fluarix Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	57		
Units: Subjects				
Ecchymosis	3	2		
Induration	14	13		
Pain	41	21		
Redness	22	16		
Swelling	9	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Solicited General Symptoms

End point title	Number of Subjects Reporting Solicited General Symptoms

End point description:

Solicited general symptoms assessed include arthralgia, fatigue, headache, myalgia, shivering, sweating, and fever

End point type	Secondary

End point timeframe:

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

End point values	Fluarix Adult Group	Fluarix Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	57		
Units: Subjects				
Arthralgia	5	8		
Fatigue	13	6		
Headache	12	3		
Myalgia	14	7		
Shivering	2	2		
Sweating	6	5		
Fever	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Unsolicited Adverse Events (AE)

End point title	Number of Subjects Reporting Unsolicited Adverse Events (AE)

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:

During the 21-day (Day 0-20) post-vaccination period

End point values	Fluarix Adult Group	Fluarix Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	57		
Units: Subjects				
AE	9	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Serious Adverse Events (SAE)

End point title	Number of Subjects Reporting Serious Adverse Events (SAE)

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

End point values	Fluarix Adult Group	Fluarix Elderly Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	57		
Units: Subjects				
(SAE)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Serious Adverse Events: From Day 0 to Day 21; Solicited local and general symptoms: During the 4-day (Days 0-3) post-vaccination period; Unsolicited symptoms: During the 21-day (Day 0-20) post-vaccination period	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	Fluarix Adult Group
Reporting group description:	
Subjects who are 18-60 years of age received one dose of Fluarix™	
Reporting group title	Fluarix Elderly Group
Reporting group description:	
Subjects who are > 60 years of age received one dose of Fluarix™	

Serious adverse events	Fluarix Adult Group	Fluarix Elderly Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 61 (0.00%)	0 / 57 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Fluarix Adult Group	Fluarix Elderly Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 61 (67.21%)	21 / 57 (36.84%)	
General disorders and administration site conditions			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 61 (8.20%)	8 / 57 (14.04%)	
occurrences (all)	5	8	
Fatigue			
alternative assessment type: Systematic			

subjects affected / exposed	13 / 61 (21.31%)	6 / 57 (10.53%)	
occurrences (all)	13	6	
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 61 (19.67%)	3 / 57 (5.26%)	
occurrences (all)	12	3	
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 61 (22.95%)	7 / 57 (12.28%)	
occurrences (all)	14	7	
Sweating			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 61 (9.84%)	5 / 57 (8.77%)	
occurrences (all)	6	5	
Induration			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 61 (22.95%)	13 / 57 (22.81%)	
occurrences (all)	14	13	
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	41 / 61 (67.21%)	21 / 57 (36.84%)	
occurrences (all)	41	21	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 61 (36.07%)	16 / 57 (28.07%)	
occurrences (all)	22	16	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 61 (14.75%)	9 / 57 (15.79%)	
occurrences (all)	9	9	

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