Clinical trial results:
A phase IIa, observer-blind, multi-country, multicentre, randomised study to evaluate the immunogenicity, safety and reactogenicity of the GlaxoSmithKline Biologicals' quadrivalent influenza vaccine (QIV) adjuvanted with various doses of the AS03 (GSK2584786A), administered in children aged 6 to 35 months, and compared to non-adjuvanted QIV and Fluarix™.

Summary

EudraCT number	2010-020312-12
Trial protocol	ES FI
Global end of trial date	22 March 2011

Results information

Result version number	v1 (current)
This version publication date	18 April 2016
First version publication date	15 May 2015

Trial information

Trial identification

Sponsor protocol code	114294

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01195779
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	22 March 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 March 2011
Global end of trial reached?	Yes
Global end of trial date	22 March 2011
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To identify the optimal formulation (combination of HA dosage and AS03 dosage) of the FLU D-QIV-AS03 vaccine compared to non-adjuvanted QIV, given intramuscularly in children aged 6-35 months, based on immunogenicity (HI GMTs and neutralising antibodies GMTs for the four vaccine strains and frequency of influenza-specific CD4 T lymphocytes identified as producing immune markers like IFN-gamma, IL-2, IL-13, CD40L, or TNF-alpha upon in vitro stimulation 28 days following last dose of study vaccine) and reactogenicity (incidence of fever grade ≥2 within 7-days follow-up period after any vaccination).
Criteria: An overall desirability index based on both the immunogenicity and the reactogenicity endpoints will be computed for each formulation to identify the combination(s) having the most desirable profile.

Protection of trial subjects:

The vaccinees were be observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of anaphylaxis following the administration of vaccines. 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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 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	Spain: 4
Worldwide total number of subjects	4
EEA total number of subjects	4

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	3

months)	
Children (2-11 years)	1
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:

Note that only 4 of 1120 planned subjects were enrolled in the study before early termination.

Pre-assignment

Screening details:

Four subjects who were already enrolled in the study were followed for safety assessment until Day 180, i.e. during 6 months after vaccination (and not until Day 365 as it was planned in the protocol), because they only received a single dose of the study vaccines.

Period 1

Period 1 title	Overall Period (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:

Observer-blind controlled study

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK2584786A 1-A3 Group

Arm description:

Subjects received 1 dose of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation A3.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' influenza vaccine GSK2584786A, different formulations
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 Dose at Day 0 into the deltoid muscle.

Arm title	GSK2584786A 2-B1 Group

Arm description:

Subjects received 2 doses of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation B1.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' influenza vaccine GSK2584786A, different formulations
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 Doses at Days 0 and 28 into the deltoid muscle.

Arm title	GSK2584786A 2-B3 Group

Arm description:

Subjects received 2 doses of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation B3.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' influenza vaccine GSK2584786A, different formulations
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 Doses at Days 0 and 28 into the deltoid muscle.

Arm title	Fluarix Group

Arm description:

Subjects received 2 doses of GSK Biologicals' Fluarix vaccine (GSK2321138A).

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

Dosage and administration details:

2 Doses at Days 0 and 28 into the deltoid muscle.

Number of subjects in period 1	GSK2584786A 1-A3 Group	GSK2584786A 2-B1 Group	GSK2584786A 2-B3 Group
Started	1	1	1
Completed	1	1	1

Number of subjects in period 1	Fluarix Group
Started	1
Completed	1

Baseline characteristics

Reporting groups	
Reporting group title	GSK2584786A 1-A3 Group
Reporting group description:	
Subjects received 1 dose of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation A3.	
Reporting group title	GSK2584786A 2-B1 Group
Reporting group description:	
Subjects received 2 doses of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation B1.	
Reporting group title	GSK2584786A 2-B3 Group
Reporting group description:	
Subjects received 2 doses of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation B3.	
Reporting group title	Fluarix Group
Reporting group description:	
Subjects received 2 doses of GSK Biologicals' Fluarix vaccine (GSK2321138A).	

Reporting group values	GSK2584786A 1-A3 Group	GSK2584786A 2-B1 Group	GSK2584786A 2-B3 Group
Number of subjects	1	1	1
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: months			
arithmetic mean	28	17	14
standard deviation	± 0	± 0	± 0
Gender categorical			
Units: Subjects			
Female	0	1	0
Male	1	0	1

Reporting group values	Fluarix Group	Total	
Number of subjects	1	4	
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	14		
standard deviation	± 0	-	
Gender categorical			
Units: Subjects			
Female	1	2	
Male	0	2	

End points

End points reporting groups

Reporting group title	GSK2584786A 1-A3 Group
Reporting group description:	
Subjects received 1 dose of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation A3.	
Reporting group title	GSK2584786A 2-B1 Group
Reporting group description:	
Subjects received 2 doses of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation B1.	
Reporting group title	GSK2584786A 2-B3 Group
Reporting group description:	
Subjects received 2 doses of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation B3.	
Reporting group title	Fluarix Group
Reporting group description:	
Subjects received 2 doses of GSK Biologicals' Fluarix vaccine (GSK2321138A).	

Primary: Serum HI antibody titre against each of the 4 vaccine strains

End point title	Serum HI antibody titre against each of the 4 vaccine strains[1]
End point description:	
Data were not analyzed due to study early termination.	
End point type	Primary
End point timeframe:	
At Day 28/56.	

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 data were not analyzed due to the study early termination.

End point values	GSK2584786A 1-A3 Group	GSK2584786A 2-B1 Group	GSK2584786A 2-B3 Group	Fluarix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: Titre				
median (standard deviation)	()	()	()	()

Notes:

[2] - Data were not analyzed

[3] - Data were not analyzed

[4] - Data were not analyzed

[5] - Data were not analyzed

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:

End point type	Secondary

End point timeframe:

Within the 28-day (Days 0-27) post-vaccination period

End point values	GSK2584786A 1-A3 Group	GSK2584786A 2-B1 Group	GSK2584786A 2-B3 Group	Fluarix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	1	1
Units: Subjects				
Any AEs	0	1	1	1

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:

End point type	Secondary

End point timeframe:

Up to study end at Day 180

End point values	GSK2584786A 1-A3 Group	GSK2584786A 2-B1 Group	GSK2584786A 2-B3 Group	Fluarix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	1	1
Units: Subjects				
SAEs	0	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

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

End point description:

End point type	Secondary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each dose

End point values	GSK2584786A 1-A3 Group	GSK2584786A 2-B1 Group	GSK2584786A 2-B3 Group	Fluarix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	1	1
Units: Subjects				
Any Drowsiness	1	0	0	0
Grade 3 Drowsiness	0	0	0	0
Related Drowsiness	0	0	0	0
Any Fever	0	0	0	0
Grade 3 Fever	0	0	0	0
Related Fever	0	0	0	0
Any Irritability/Fussiness	1	0	0	0
Grade 3 Irritability/Fussiness	0	0	0	0
Related Irritability/Fussiness	0	0	0	0
Any Loss of appetite	0	0	0	0
Grade 3 Loss of appetite	0	0	0	0
Related Loss of appetite	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs: Days 0-27 post-vaccination. SAEs up to Day 180 post-vaccination.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	GSK2584786A 1-A3 Group
Reporting group description: Subjects received 1 dose of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation A3.	
Reporting group title	GSK2584786A 2-B1 Group
Reporting group description: Subjects received 2 doses of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation B1.	
Reporting group title	GSK2584786A 2-B3 Group
Reporting group description: Subjects received 2 doses of GSK Biologicals' adjuvanted quadrivalent influenza candidate vaccine (GSK2584786A) Formulation B3.	
Reporting group title	Fluarix Group
Reporting group description: Subjects received 2 doses of GSK Biologicals' Fluarix vaccine.	

Serious adverse events	GSK2584786A 1-A3 Group	GSK2584786A 2-B1 Group	GSK2584786A 2-B3 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Fluarix Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	GSK2584786A 1-A3 Group	GSK2584786A 2-B1 Group	GSK2584786A 2-B3 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	1 / 1 (100.00%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Fluarix Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Herpes zoster			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		

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? Yes

Date	Interruption	Restart date
22 March 2011	Since only 4 subjects were recruited in the study, the study was interrupted for logistical reasons.	-

Notes:

Limitations and caveats

None reported