Clinical trial results:
A phase III, double-blind, randomized, controlled study to evaluate the immunogenicity and safety of GlaxoSmithKline (GSK) Biologicals' HPV-16/18 L1 VLP AS04 vaccine administered intramuscularly according to a 0, 1, 6-month schedule in healthy Chinese female subjects aged 9-17 years.

Summary

EudraCT number	2012-003025-25
Trial protocol	Outside EU/EEA
Global end of trial date	08 December 2012

Results information

Result version number	v2 (current)
This version publication date	29 March 2023
First version publication date	12 July 2015
Version creation reason	• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	112022

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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 Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 March 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 December 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To demonstrate the non-inferiority of HPV immune response at one month post-dose 3 in Chinese female subjects aged 9-17 years from the current study versus Chinese women aged 18-25 years enrolled in the HPV-039 study (eTrack No. 107638).
Criteria for non-inferiority (one month after the third vaccine dose):
-The objective will be reached if for each HPV antigen (anti-HPV-16 and anti-HPV-18), the upper limit of the 95% confidence interval (CI) for the GMT ratio [GMTs in subjects aged 18-25 years with immunogenicity results at Month 7 who receive HPV-16/18 L1 VLP AS04 vaccine in the HPV-039 study divided by the GMTs of subjects aged 9-17 years who receive HPV-16/18 L1 VLP AS04 vaccine in the HPV-058 study] is below 2.
-This objective will be evaluated in the according-to-protocol (ATP) cohort for immunogenicity

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 October 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	China: 750
Worldwide total number of subjects	750
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)	0

Children (2-11 years)	0
Adolescents (12-17 years)	750
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total number of 750 subjects were enrolled in this study.

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, Monitor

Blinding implementation details:

Blinding was maintained for all subjects and investigators and their study staff participating in this study with regard to the individual subject treatment (vaccine or control) assignments allocated in this study. GSK personnel directly involved in the conduct of this study (e.g. site monitors, medical monitors, laboratory personnel, etc.) was also blinded to the subject's treatment assignments.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervarix Group

Arm description:

Subjects received 3 doses of Cervarix vaccine. Cervarix vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm according to a 0, 1, 6-month schedule.

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

Dosage and administration details:

Subjects received three doses of the Cervarix vaccine intramuscularly according to a 0, 1, 6-month schedule.

Arm title	Placebo Group

Arm description:

Subjects received 3 doses of placebo. Placebo vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm according to a 0, 1, 6-month schedule.

Arm type	Control
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received three doses of control intramuscularly according to a 0, 1, 6-month schedule.

Number of subjects in period 1	Cervarix Group	Placebo Group
Started	374	376
Completed	369	365
Not completed	5	11
Consent withdrawn by subject	4	3
Adverse event, non-fatal	-	2
Lost to follow-up	1	6

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix Group
Reporting group description:	
Subjects received 3 doses of Cervarix vaccine. Cervarix vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm according to a 0, 1, 6-month schedule.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 3 doses of placebo. Placebo vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm according to a 0, 1, 6-month schedule.	

Reporting group values	Cervarix Group	Placebo Group	Total
Number of subjects	374	376	750
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	13.1	13.1	
standard deviation	± 2.44	± 2.42	-
Gender categorical			
Units: Subjects			
Female	374	376	750
Male	0	0	0

End points

End points reporting groups

Reporting group title	Cervarix Group
Reporting group description:	
Subjects received 3 doses of Cervarix vaccine. Cervarix vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm according to a 0, 1, 6-month schedule.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 3 doses of placebo. Placebo vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm according to a 0, 1, 6-month schedule.	

Primary: Geometric mean titers (GMTs) for antibodies against Human Papillomavirus (HPV)-16/18 antigens

End point title	Geometric mean titers (GMTs) for antibodies against Human Papillomavirus (HPV)-16/18 antigens
End point description:	
Titers were given as geometric mean titers and were measured by Enzyme-linked Immunosorbent Assay (ELISA) and expressed as Enzyme-linked Immunosorbent Assay Units Per Milliliter (EL.U/mL).	
End point type	Primary
End point timeframe:	
One month after the third dose (at Month 7)	

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	362	363		
Units: titers				
geometric mean (confidence interval 95%)				
Anti-HPV-16	18347.1 (16915.2 to 19900.2)	5 (4.7 to 5.3)		
Anti-HPV-18	7960.2 (7181.3 to 8823.6)	4.1 (3.8 to 4.3)		

Statistical analyses

Statistical analysis title	Anti-HPV-016 immune response
Comparison groups	Cervarix Group v Placebo Group

Number of subjects included in analysis	725
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 2
Method	t-test, 2-sided
Parameter estimate	GMT ratio
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.43
Variability estimate	Standard deviation
Dispersion value	0.37

Statistical analysis title	Anti-HPV-018 immune response
Comparison groups	Cervarix Group v Placebo Group
Number of subjects included in analysis	725
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 2
Method	GMT ratio
Parameter estimate	GMT ratio
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.49
Variability estimate	Standard deviation
Dispersion value	0.42

Secondary: Number of subjects seroconverted for Anti-HPV-16 and Anti-HPV-18 antibodies

End point title	Number of subjects seroconverted for Anti-HPV-16 and Anti-HPV-18 antibodies

End point description:

Seroconversion is defined as the appearance of anti-HPV-16 and/or anti- HPV-18 antibodies (i.e. antibody titer ≥ cut-off value) in the sera of subjects seronegative before vaccination. Cut-off values were 8 enzyme-linked immunosorbent assay units per milliliter (EL.U/mL) for anti-HPV-16 antibodies and 7 EL.U/mL for anti- HPV-18 antibodies.

End point type	Secondary

End point timeframe:

At Month 7

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	338	344		
Units: Subjects				
Anti-HPV-16 (N=326;323)	326	8		
Anti-HPV-18 (N=338;344)	336	10		

Statistical analyses

No statistical analyses for this end point

Secondary: 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

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any was defined as any solicited local symptom reported irrespective of intensity. Grade 3 pain was defined as pain that prevented normal activity. Grade 3 redness and swelling were defined as redness/swelling above 50 millimeter (mm).

End point type	Secondary

End point timeframe:

During the 7 days (Days 0 – 6) following each vaccination

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	373	376		
Units: Subjects				
Any pain	350	299		
Grade 3 pain	38	16		
Any redness	113	52		
Grade 3 redness	2	1		
Any swelling	113	54		
Grade 3 swelling	13	2		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Solicited general symptoms assessed were arthralgia, fatigue, gastrointestinal, headache, myalgia, rash, urticaria and fever (= axillary temperature above 37.0 degrees Celsius (°C). Grade 3 fever = axillary

temperature above 39.0°C. Grade 3 urticaria = urticaria distributed on at least 4 body areas. For other symptoms, any = occurrence of any general symptom regardless of intensity grade or relation to vaccination and grade 3 = a general symptom that prevented normal activity. Related was a general symptom assessed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

During the 7 days (Days 0 – 6) following each vaccination

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	373	376		
Units: Subjects				
Any arthralgia	38	33		
Grade 3 arthralgia	0	2		
Related arthralgia	25	23		
Any fatigue	137	126		
Grade 3 fatigue	2	4		
Related fatigue	106	98		
Any gastrointestinal symptoms	57	45		
Grade 3 gastrointestinal symptoms	2	2		
Related gastrointestinal symptoms	21	31		
Any headache	123	99		
Grade 3 headache	5	3		
Related headache	80	70		
Any myalgia	110	93		
Grade 3 myalgia	1	1		
Related myalgia	96	83		
Any rash	9	4		
Grade 3 rash	0	0		
Related rash	3	2		
Any fever	86	74		
Grade 3 fever	2	0		
Related fever	40	27		
Any urticaria	8	3		
Grade 3 urticaria	0	0		
Related urticaria	7	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting medically significant conditions (MSCs)

End point title	Number of subjects reporting medically significant conditions (MSCs)

End point description:

Medically significant conditions (MSCs) are defined as: adverse events (AEs) prompting emergency room or physician visits that are not (1) related to common diseases or (2) routine visits for physical examination or vaccination, or serious adverse events (SAEs) that are not related to common diseases.

Common diseases include: upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervicovaginal yeast infections, menstrual cycle abnormalities and injury. MSCs were collected regardless of causal relationship to vaccination and intensity.

End point type	Secondary

End point timeframe:

Throughout the study period (from Day 0 up to Month 12)

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	376		
Units: Subjects				
Any MSC(s)	14	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting pregnancies and pregnancy outcomes

End point title	Number of subjects reporting pregnancies and pregnancy outcomes

End point description:

End point type	Secondary

End point timeframe:

Throughout the study period (from Day 0 up to Month 12)

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	376		
Units: Subjects				
Pregnancies	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:

Unsolicited AE covers any AE 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. Grade 3 was an event that prevented normal activities and related was defined as an unsolicited AE assessed by the investigator to be causally related to the study vaccination.

End point type	Secondary

End point timeframe:

Within 30 days (Days 0 – 29) after any vaccination

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	376		
Units: Subjects				
Any AEs	139	125		
Grade 3 AEs	0	3		
Related AEs	2	3		

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)

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 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:

Throughout the study period (from Day 0 up to Month 12)

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	376		
Units: Subjects				
Any SAEs	5	2		
Related SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events were assessed from Day 0 up to Month 12. Systematically assessed frequent adverse events (AEs) and non-systematically assessed frequent AEs were assessed during 7 days and 30 days post vaccination period respectively.

Adverse event reporting additional description:

For the systematically assessed other (non-serious) adverse events, the total participants at risk in Cervarix Group included those from Total Vaccinated cohort who had the symptom sheet completed and with at least one documented dose.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Cervarix Group

Reporting group description:

Subjects received 3 doses of Cervarix vaccine. Cervarix vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm according to a 0, 1, 6-month schedule.

Reporting group title	Placebo Group

Reporting group description:

Subjects received 3 doses of placebo. Placebo vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm according to a 0, 1, 6-month schedule.

Serious adverse events	Cervarix Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 374 (1.34%)	2 / 376 (0.53%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 374 (0.00%)	1 / 376 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 374 (0.00%)	1 / 376 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			

subjects affected / exposed	0 / 374 (0.00%)	1 / 376 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 374 (0.27%)	0 / 376 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 374 (0.27%)	0 / 376 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	1 / 374 (0.27%)	0 / 376 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Adnexa uteri cyst			
subjects affected / exposed	1 / 374 (0.27%)	0 / 376 (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			
Bronchopneumonia			
subjects affected / exposed	1 / 374 (0.27%)	0 / 376 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cervarix Group	Placebo Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	360 / 374 (96.26%)	339 / 376 (90.16%)	
General disorders and administration site conditions			

Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	350 / 373 (93.83%)	299 / 376 (79.52%)	
occurrences (all)	350	299	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	113 / 373 (30.29%)	52 / 376 (13.83%)	
occurrences (all)	113	52	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	113 / 373 (30.29%)	54 / 376 (14.36%)	
occurrences (all)	113	54	
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed[4]	38 / 373 (10.19%)	33 / 376 (8.78%)	
occurrences (all)	38	33	
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed[5]	137 / 373 (36.73%)	126 / 376 (33.51%)	
occurrences (all)	137	126	
Gastrointestinal symptoms			
alternative assessment type: Systematic			
subjects affected / exposed[6]	57 / 373 (15.28%)	45 / 376 (11.97%)	
occurrences (all)	57	45	
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[7]	123 / 373 (32.98%)	99 / 376 (26.33%)	
occurrences (all)	123	99	
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[8]	110 / 373 (29.49%)	93 / 376 (24.73%)	
occurrences (all)	110	93	
Fever			
alternative assessment type: Systematic			

subjects affected / exposed[9]	86 / 373 (23.06%)	74 / 376 (19.68%)	
occurrences (all)	86	74	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	101 / 374 (27.01%)	86 / 376 (22.87%)	
occurrences (all)	101	86	
Nasopharyngitis			
subjects affected / exposed	22 / 374 (5.88%)	18 / 376 (4.79%)	
occurrences (all)	22	18	

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: For a given subject cohort and the analysis of a given measurement, missing or non-evaluable measurements were not replaced. Therefore, an analysis excluded data points for subjects with missing or non-evaluable measurements i.e. analysis of solicited symptoms excluded vaccinated subjects without documented Diary Cards.

[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: For a given subject cohort and the analysis of a given measurement, missing or non-evaluable measurements were not replaced. Therefore, an analysis excluded data points for subjects with missing or non-evaluable measurements i.e. analysis of solicited symptoms excluded vaccinated subjects without documented Diary Cards.

[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: For a given subject cohort and the analysis of a given measurement, missing or non-evaluable measurements were not replaced. Therefore, an analysis excluded data points for subjects with missing or non-evaluable measurements i.e. analysis of solicited symptoms excluded vaccinated subjects without documented Diary Cards.

[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: For a given subject cohort and the analysis of a given measurement, missing or non-evaluable measurements were not replaced. Therefore, an analysis excluded data points for subjects with missing or non-evaluable measurements i.e. analysis of solicited symptoms excluded vaccinated subjects without documented Diary Cards.

[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: For a given subject cohort and the analysis of a given measurement, missing or non-evaluable measurements were not replaced. Therefore, an analysis excluded data points for subjects with missing or non-evaluable measurements i.e. analysis of solicited symptoms excluded vaccinated subjects without documented Diary Cards.

[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: For a given subject cohort and the analysis of a given measurement, missing or non-evaluable measurements were not replaced. Therefore, an analysis excluded data points for subjects with missing or non-evaluable measurements i.e. analysis of solicited symptoms excluded vaccinated subjects without documented Diary Cards.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: For a given subject cohort and the analysis of a given measurement, missing or non-evaluable measurements were not replaced. Therefore, an analysis excluded data points for subjects with missing or non-evaluable measurements i.e. analysis of solicited symptoms excluded vaccinated subjects without documented Diary Cards.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: For a given subject cohort and the analysis of a given measurement, missing or non-evaluable measurements were not replaced. Therefore, an analysis excluded data points for subjects with missing or non-evaluable measurements i.e. analysis of solicited symptoms excluded vaccinated subjects without documented Diary Cards.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: For a given subject cohort and the analysis of a given measurement, missing or non-evaluable measurements were not replaced. Therefore, an analysis excluded data points for subjects with missing or non-evaluable measurements i.e. analysis of solicited symptoms excluded vaccinated subjects without documented Diary Cards.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 November 2010	Amendment 1 • Due to a delay in the availability of the Month 7 serology data to be generated at the National Institute for Control of Pharmaceutical and Biological Products (NICPBP), the initial planned final analysis (for immunogenicity and safety data up to Month 7) and the annex analysis (for safety data collected during the 5-month extended safety follow-up (EFSU) period up to Month 12) will be conducted as one final analysis and will include all data up to Month 12. A clinical study report will be written to present the final analysis data. • The name of the coordinating authors and contributing authors have been updated in the title page.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported