Clinical trial results:
A phase IIIb, randomized, open, multicentre study to evaluate the immunogenicity and safety of GlaxoSmithKline Biologicals' HPV-16/18 L1 AS04 vaccine co-administered with GlaxoSmithKline Biologicals' combined reduced-antigen diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis vaccine (Boostrix® Polio) in healthy female subjects aged 10–18 years.

Summary

EudraCT number	2006-003807-38
Trial protocol	DE FR ES
Global end of trial date	25 July 2008

Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	22 November 2014

Trial information

Trial identification

Sponsor protocol code	108464

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00426361
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 July 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 July 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To demonstrate non-inferiority of the dTpa-IPV immune response at Month 1 when dTpa-IPV is co-administered with HPV-16/18 L1 AS04 vaccine at Month 0 compared to when dTpa-IPV is administered alone at Month 0.

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 vaccinee remained under medical supervision for 30 minutes after vaccination.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	13 February 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 262
Country: Number of subjects enrolled	France: 183
Country: Number of subjects enrolled	Germany: 306
Worldwide total number of subjects	751
EEA total number of subjects	751

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)	751
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: -

Pre-assignment period milestones

Number of subjects started	751
Number of subjects completed	751

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervarix Group

Arm description:

Subjects who received GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 0, 1 and 6.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' HPV-16/18 L1 AS04 vaccine (Cervarix TM)
Investigational medicinal product code	Cervarix TM
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

Three doses of vaccine administered intramuscularly, with the second and third dose give one month and six months after the first dose respectively

Arm title	Cervarix + Boostrix Polio Group

Arm description:

Subjects who received GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 0, 1 and 6 with co-administration of Boostrix™ Polio at Month 0.

Arm type	Experimental
Investigational medicinal product name	Boostrix ® Polio
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

One dose of vaccine administered intramuscularly

Investigational medicinal product name	GSK Biologicals' HPV-16/18 L1 AS04 vaccine (Cervarix TM)
Investigational medicinal product code	Cervarix TM
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

Three doses of vaccine administered intramuscularly, with the second and third dose give one month

and six months after the first dose respectively

Arm title	Boostrix Polio Cervarix Group
Arm description:	
Subjects who received Boostrix™ Polio at Month 0 and GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 1, 2 and 7.	
Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' HPV-16/18 L1 AS04 vaccine (Cervarix TM)
Investigational medicinal product code	Cervarix TM
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular and intravenous use
Dosage and administration details:	
Three doses of vaccine administered intramuscularly, with the second and third dose give one month and six months after the first dose respectively	
Investigational medicinal product name	Boostrix ® Polio
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular and intravenous use
Dosage and administration details:	
One dose of vaccine administered intramuscularly	

Number of subjects in period 1	Cervarix Group	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group
Started	248	255	248
Completed	244	250	243
Not completed	4	5	5
Consent withdrawn by subject	1	3	-
Lost to follow-up	3	2	5

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix Group
Reporting group description:	
Subjects who received GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 0, 1 and 6.	
Reporting group title	Cervarix + Boostrix Polio Group
Reporting group description:	
Subjects who received GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 0, 1 and 6 with co-administration of Boostrix™ Polio at Month 0.	
Reporting group title	Boostrix Polio Cervarix Group
Reporting group description:	
Subjects who received Boostrix™ Polio at Month 0 and GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 1, 2 and 7.	

Reporting group values	Cervarix Group	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group
Number of subjects	248	255	248
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			
median	13.9	14	13.9
standard deviation	± 2.59	± 2.43	± 2.47
Gender categorical Units: Subjects			
Female	248	255	248
Male	0	0	0

Reporting group values	Total		
Number of subjects	751		
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			
median			
standard deviation	-		
Gender categorical Units: Subjects			
Female	751		
Male	0		

End points

End points reporting groups

Reporting group title	Cervarix Group
Reporting group description:	
Subjects who received GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 0, 1 and 6.	
Reporting group title	Cervarix + Boostrix Polio Group
Reporting group description:	
Subjects who received GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 0, 1 and 6 with co-administration of Boostrix™ Polio at Month 0.	
Reporting group title	Boostrix Polio Cervarix Group
Reporting group description:	
Subjects who received Boostrix™ Polio at Month 0 and GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 1, 2 and 7.	

Primary: Number of subjects seroprotected against diphtheria and tetanus

End point title	Number of subjects seroprotected against diphtheria and tetanus[1][2]
End point description:	
Seroprotection against diphtheria and tetanus is defined as anti-diphtheria and anti-tetanus antibody titres greater than or equal to 0.1 International Units per Milliliter (≥ 0.1 IU/mL).	
End point type	Primary
End point timeframe:	
One month after vaccination with Boostrix Polio	

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: Only subjects who had received DTPa vaccination were included in the analysis.

End point values	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240	233		
Units: Subjects				
Diphtheria	238	233		
Tetanus	240	233		

Statistical analyses

No statistical analyses for this end point

Primary: Titers of anti-pertussis toxoid (anti-PT), anti-pertactin toxoid (anti-PRN) and anti-filamentous hemagglutinin (anti-FHA) antibodies

End point title	Titers of anti-pertussis toxoid (anti-PT), anti-pertactin toxoid

	(anti-PRN) and anti-filamentous hemagglutinin (anti-FHA) antibodies[3][4]

End point description:

Titers are given as geometric mean titers (GMTs) calculated on all subjects and expressed as Enzyme-linked Immunosorbent Assay Units per Milliliter (EL.U/mL).

End point type	Primary

End point timeframe:

One month after vaccination with Boostrix Polio

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
[4] - 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: Only subjects who had received DTPa vaccination were included in the analysis.

End point values	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240	233		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT (n=238, 229)	84.2 (73.6 to 96.4)	75.4 (65.6 to 86.8)		
Anti-FHA (n=240, 233)	611.7 (553.6 to 675.9)	615.2 (552.3 to 685.2)		
Anti-PRN (n=239, 233)	426.2 (368.1 to 493.4)	360 (299.3 to 433.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects seroprotected against Poliovirus type 1 (Polio 1), Polio 2 and Polio 3

End point title	Number of subjects seroprotected against Poliovirus type 1 (Polio 1), Polio 2 and Polio 3[5][6]

End point description:

Seroprotection against polio 1, 2 and 3 is defined as anti-polio 1, 2 and 3 antibody titers greater than or equal to 8 Effective Dose 50% (≥ 8 ED50).

End point type	Primary

End point timeframe:

One month after vaccination with Boostrix Polio

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
[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: Only subjects who had received DTPa vaccination were included in the analysis.

End point values	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240	232		
Units: Subjects				
Polio 1 (n=240, 231)	239	231		
Polio 2 (n=240, 232)	240	232		
Polio 3 (n=239, 232)	239	232		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Seroconverted for Anti-human Papilloma Virus 16 (Anti-HPV-16) and Anti-HPV-18 Antibodies after completing the Cervarix vaccination course

End point title	Number of Subjects Seroconverted for Anti-human Papilloma Virus 16 (Anti-HPV-16) and Anti-HPV-18 Antibodies after completing the Cervarix vaccination course

End point description:

Seroconversion is defined as the appearance of antibodies with titers greater than or equal to the predefined cut-off value in the serum of subject seronegative before vaccination. Cut-off values assessed include 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:

One month post Cervarix Dose 3 (Month 7/8)

End point values	Cervarix Group	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	204	204	
Units: Subjects				
Anti-HPV-16 (n=198, 202, 204)	198	201	204	
Anti-HPV-18 (n=191, 204, 203)	191	203	203	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Seroconverted for Anti-HPV-16 and Anti-HPV-18 Antibodies after incomplete Cervarix vaccination course

End point title	Number of Subjects Seroconverted for Anti-HPV-16 and Anti-HPV-18 Antibodies after incomplete Cervarix vaccination course[7]

End point description:

Seroconversion is defined as the appearance of antibodies with titers greater than or equal to the predefined cut-off value in the serum of subject seronegative before vaccination. Cut-off values assessed include 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:

One month post Dose 1

Notes:

[7] - 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: Only subjects who had received HPV vaccination were included in the analysis.

End point values	Cervarix Group	Cervarix + Boostrix Polio Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	204		
Units: Subjects				
Anti-HPV-16 (n=198, 202)	198	201		
Anti-HPV-18 (n=191, 204)	191	203		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of anti-human Papilloma virus 16 (anti-HPV-16) and anti-human Papilloma virus 18 (anti-HPV-18) antibodies After Completing the Cervarix Vaccination Course

End point title	Titers of anti-human Papilloma virus 16 (anti-HPV-16) and anti-human Papilloma virus 18 (anti-HPV-18) antibodies After Completing the Cervarix Vaccination Course

End point description:

Titers are given as Geometric Mean Titers (GMTs) expressed as Enzyme-linked Immunosorbent Assay Units Per Milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

One month post Cervarix Dose 3 (Month 7/8)]

End point values	Cervarix Group	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	213	222	218	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (n= 213, 222, 218)	18363.6 (16243 to 20761)	15370.2 (13350.9 to 17694.8)	14089.5 (12460.9 to 15930.9)	

Anti-HPV-18 (n= 210, 218, 216)	7032.8 (6220.7 to 7950.9)	6630.4 (5768 to 7621.6)	5135 (4537.3 to 5811.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of anti-diphtheria and anti-tetanus antibodies

End point title	Titers of anti-diphtheria and anti-tetanus antibodies[8]

End point description:

Titers are given as Geometric Mean Titers (GMTs) and expressed as IU/mL.

End point type	Secondary

End point timeframe:

One month after vaccination with Boostrix-Polio

Notes:

[8] - 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: Only subjects who had received DTPa vaccination were included in the analysis.

End point values	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240	233		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-diphtheria	5.085 (4.551 to 5.681)	5.466 (4.896 to 6.103)		
Anti-tetanus	8.552 (7.889 to 9.272)	9.039 (8.321 to 9.818)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-diphtheria and anti-tetanus antibody titers above 1.0 International Units per Milliliter (IU/mL)

End point title	Number of subjects with anti-diphtheria and anti-tetanus antibody titers above 1.0 International Units per Milliliter (IU/mL)[9]

End point description:

Anti-diphtheria and anti-tetanus antibodies cut-off value assessed include 1.0 IU/mL.

End point type	Secondary

End point timeframe:

One month after vaccination with Boostrix Polio

Notes:

[9] - 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: Only subjects who had received DTPa vaccination were included in the analysis.

End point values	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240	233		
Units: Subjects				
Anti-diphtheria	231	226		
Anti-tetanus	239	233		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-poliovirus type 1 (anti-polio 1), anti-polio 2 and anti-polio 3 antibody titers

End point title	Anti-poliovirus type 1 (anti-polio 1), anti-polio 2 and anti-polio 3 antibody titers[10]

End point description:

Titers are given as Geometric Mean Titers (GMTs). The titer is a serum dilution giving 50 percent reduction of signal compared to control without serum.

End point type	Secondary

End point timeframe:

One month after vaccination with Boostrix Polio

Notes:

[10] - 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: Only subjects who had received DTPa vaccination were included in the analysis.

End point values	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240	232		
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-polio 1 (n=240, 231)	2045.1 (1714.7 to 2439.2)	2390.5 (2021.4 to 2826.9)		
Anti-polio 2 (n=240, 232)	2151.1 (1806.5 to 2561.6)	2158.1 (1821.3 to 2557.1)		
Anti-polio 3 (n=239, 232)	2777.2 (2376.5 to 3245.4)	2732.5 (2318 to 3221.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster response to diphtheria and tetanus

End point title	Number of subjects with booster response to diphtheria and tetanus[11]

End point description:

Booster responses to diphtheria and tetanus were defined as: - For initially seronegative subjects (pre-vaccination titer below cut-off value of 0.1 International Units per Milliliter): antibody titers at least four times the cut-off (post-vaccination titer greater than or equal to 0.4 IU/mL), and - For initially seropositive subjects (pre-vaccination titer greater than or equal to 0.1 IU/mL): an increase in antibody titers of at least four times the pre-vaccination titer.

End point type	Secondary

End point timeframe:

One month after vaccination with Boostrix Polio

Notes:

[11] - 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: Only subjects who had received DTPa vaccination were included in the analysis.

End point values	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240	232		
Units: Subjects				
Diphtheria	160	159		
Tetanus	167	161		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster response to pertussis toxoid (PT), pertactin toxoid (PRN) and filamentous hemagglutinin (FHA)

End point title	Number of subjects with booster response to pertussis toxoid (PT), pertactin toxoid (PRN) and filamentous hemagglutinin (FHA)[12]

End point description:

Booster response to PT, FHA and PRN were defined as: - For initially seronegative subjects [pre-vaccination titer below cut-off value of 5 enzyme-linked immunosorbent assay units per milliliter (EL.U/mL)]: antibody titers at least 4 times the cut-off, - For initially seropositive subjects with pre-vaccination titer above 5 EL.U/mL and < 20 EL.U/mL: an increase in antibody titers of at least 4 times the pre-vaccination titer, - For initially seropositive subjects with pre-vaccination titer above 20 EL.U/mL: an increase in antibody titers of at least 2 times the pre-vaccination titer.

End point type	Secondary

End point timeframe:

One month after vaccination with Boostrix Polio

Notes:

[12] - 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: Only subjects who had received DTPa vaccination were included in the analysis.

End point values	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	230		
Units: Subjects				
PT (n=236, 228)	199	182		
FHA (n=235, 226)	210	205		
PRN (n=238, 230)	222	207		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited symptoms

End point title	Number of subjects reporting solicited symptoms

End point description:

Solicited local symptoms assessed include pain, redness and swelling at the injection site. Solicited general symptoms assessed include arthralgia, fatigue, fever (above 37.5 degree Celsius), gastrointestinal symptoms, headache, myalgia, rash and urticaria.

End point type	Secondary

End point timeframe:

During the 7-day period (Day 0-6) following each vaccination

End point values	Cervarix Group	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	246	253	247	
Units: Subjects				
Pain	225	237	233	
Redness	110	128	140	
Swelling	124	125	123	
Arthralgia	58	71	77	
Fatigue	109	135	121	
Fever	30	46	37	
Gastrointestinal symptoms	51	63	61	
Headache	111	138	122	
Myalgia	107	144	127	
Rash	20	27	17	
Urticaria	12	11	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events

End point title	Number of subjects reporting unsolicited adverse events

End point description:

Unsolicited adverse event = Any adverse event (AE) reported in addition to those solicited during the clinical study. Also any "solicited" symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

End point type	Secondary

End point timeframe:

During the 30-day period (Day 0-29) following vaccination

End point values	Cervarix Group	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	248	255	248	
Units: Subjects				
unsolicited adverse events	85	74	99	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Unsolicited Adverse Events as New Onset Chronic Diseases (NOCDs) and Other Medically Significant Adverse Events (MSAEs)

End point title	Number of Subjects Reporting Unsolicited Adverse Events as New Onset Chronic Diseases (NOCDs) and Other Medically Significant Adverse Events (MSAEs)

End point description:

NOCDs assessed include e.g. autoimmune disorders, asthma, type I diabetes. MSAEs assessed include AEs prompting emergency room or physician visits that are not related to common diseases or SAEs that are not related to common diseases.

End point type	Secondary

End point timeframe:

During the active phase of the study (up to Month 7/8) and during the safety follow-up (up to Month 12/13)

End point values	Cervarix Group	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	248	255	248	
Units: Subjects				
NOCDs [Active phase] (n=248, 255, 248)	5	9	9	
NOCDs [Safety follow-up] (n=244, 250, 243)	0	0	0	
MSAEs [Active phase] (n=248, 255, 248)	35	27	49	

MSAEs [Safety follow-up] (n=244, 250, 243)	7	3	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

End point title	Number of subjects reporting serious adverse events (SAEs)

End point description:

Serious adverse events assessed include medical occurrences that results 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.

End point type	Secondary

End point timeframe:

During the active phase of the study (up to Month 7/8) and during the safety follow-up (up to Month 12/13)

End point values	Cervarix Group	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	248	255	248	
Units: Subjects				
Active phase (n=248, 255, 248)	2	4	2	
Safety follow-up (n=244, 250, 243)	1	0	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the 7 day follow-up period after any vaccination for other (non-serious) adverse events. During the entire study period (12 months for Cervarix and Cervarix + Boostrix groups and 13 months for Cervarix Boostrix group) for serious adverse events.

Adverse event reporting additional description:

For other (non-serious) adverse events collected by systematic assessment, the number of subjects at risk corresponds to the number of subjects from the Total Vaccinated Cohort with a documented dose.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Cervarix Group

Reporting group description:

Subjects who received GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 0, 1 and 6.

Reporting group title	Cervarix + Boostrix Polio Group

Reporting group description:

Subjects who received GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 0, 1 and 6 with co-administration of Boostrix™ Polio at Month 0.

Reporting group title	Boostrix Polio Cervarix Group

Reporting group description:

Subjects who received Boostrix™ Polio at Month 0 and GSK Biologicals HPV 16/18 vaccine 580299 (CervarixTM) at Month 1, 2 and 7.

Serious adverse events	Cervarix Group	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 248 (1.21%)	4 / 255 (1.57%)	3 / 248 (1.21%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Muscle rupture			
subjects affected / exposed	0 / 248 (0.00%)	1 / 255 (0.39%)	0 / 248 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 248 (0.00%)	0 / 255 (0.00%)	1 / 248 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pregnancy, puerperium and perinatal conditions			
Imminent abortion			
subjects affected / exposed	0 / 248 (0.00%)	1 / 255 (0.39%)	0 / 248 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 248 (0.00%)	0 / 255 (0.00%)	1 / 248 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst ruptured			
subjects affected / exposed	1 / 248 (0.40%)	0 / 255 (0.00%)	0 / 248 (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
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 248 (0.40%)	0 / 255 (0.00%)	0 / 248 (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
Musculoskeletal and connective tissue disorders			
Scoliosis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 255 (0.39%)	0 / 248 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 248 (0.00%)	1 / 255 (0.39%)	0 / 248 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 248 (0.40%)	0 / 255 (0.00%)	0 / 248 (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
Tonsillitis streptococcal			

subjects affected / exposed	0 / 248 (0.00%)	0 / 255 (0.00%)	1 / 248 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cervarix Group	Cervarix + Boostrix Polio Group	Boostrix Polio Cervarix Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	225 / 248 (90.73%)	237 / 255 (92.94%)	233 / 248 (93.95%)
Nervous system disorders			
Headache (unsolicited AE)			
subjects affected / exposed	4 / 248 (1.61%)	6 / 255 (2.35%)	14 / 248 (5.65%)
occurrences (all)	4	6	14
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	225 / 246 (91.46%)	237 / 253 (93.68%)	233 / 247 (94.33%)
occurrences (all)	225	237	233
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	110 / 246 (44.72%)	128 / 253 (50.59%)	140 / 247 (56.68%)
occurrences (all)	110	128	140
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	124 / 246 (50.41%)	125 / 253 (49.41%)	123 / 247 (49.80%)
occurrences (all)	124	125	123
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed[4]	58 / 246 (23.58%)	71 / 253 (28.06%)	77 / 247 (31.17%)
occurrences (all)	58	71	77
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed[5]	109 / 246 (44.31%)	135 / 253 (53.36%)	121 / 247 (48.99%)
occurrences (all)	109	135	121
Fever (above 37.5 degree Celsius)			

alternative assessment type: Systematic			
subjects affected / exposed[6]	30 / 246 (12.20%)	46 / 253 (18.18%)	37 / 247 (14.98%)
occurrences (all)	30	46	37
Gastrointestinal symptoms			
alternative assessment type: Systematic			
subjects affected / exposed[7]	51 / 246 (20.73%)	63 / 253 (24.90%)	61 / 247 (24.70%)
occurrences (all)	51	63	61
Headache (solicited general symptom AE)			
alternative assessment type: Systematic			
subjects affected / exposed[8]	111 / 246 (45.12%)	138 / 253 (54.55%)	122 / 247 (49.39%)
occurrences (all)	111	138	122
Myalgia			
subjects affected / exposed[9]	107 / 246 (43.50%)	144 / 253 (56.92%)	127 / 247 (51.42%)
occurrences (all)	107	144	127
Rash			
subjects affected / exposed[10]	20 / 246 (8.13%)	27 / 253 (10.67%)	17 / 247 (6.88%)
occurrences (all)	20	27	17
Urticaria			
alternative assessment type: Systematic			
subjects affected / exposed[11]	12 / 246 (4.88%)	11 / 253 (4.35%)	15 / 247 (6.07%)
occurrences (all)	12	11	15
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	14 / 248 (5.65%)	4 / 255 (1.57%)	10 / 248 (4.03%)
occurrences (all)	14	4	10

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: The analysis was performed on subjects with symptom sheets completed.

[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: The analysis was performed on subjects with symptom sheets completed.

[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: The analysis was performed on subjects with symptom sheets completed.

[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: The analysis was performed on subjects with symptom sheets completed.

[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: The analysis was performed on subjects with symptom sheets completed.

[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: The analysis was performed on subjects with symptom sheets completed.

[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: The analysis was performed on subjects with symptom sheets completed.

[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: The analysis was performed on subjects with symptom sheets completed.

[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: The analysis was performed on subjects with symptom sheets completed.

[10] - 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: The analysis was performed on subjects with symptom sheets completed.

[11] - 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: The analysis was performed on subjects with symptom sheets completed.

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