Clinical trial results:
A phase IIIb, randomized, open, multicentre study to evaluate the immunogenicity and safety of GlaxoSmithKline Biologicals' HPV-16/18 L1 VLP AS04 vaccine (Cervarix) co-administrated with GlaxoSmithKline Biologicals' Hepatitis B vaccine (Engerix-B) in healthy female subjects aged 9 - 15 years.

Summary

EudraCT number	2007-007783-14
Trial protocol	NL SE
Global end of trial date	08 January 2010

Results information

Result version number	v2 (current)
This version publication date	12 August 2022
First version publication date	22 November 2014
Version creation reason	• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	111507

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00652938
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, 1330-B
Public contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, 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	11 May 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 August 2009
Global end of trial reached?	Yes
Global end of trial date	08 January 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To demonstrate non-inferiority of the hepatitis B immune response at Month 7 when hepatitis B vaccine is co-administered with HPV-16/18 vaccine at Months 0, 1 and 6 (HPV+HepB group) as compared to when hepatitis B vaccine is administered alone at Months 0, 1 and 6 (HepB group).
•To demonstrate non-inferiority of the HPV immune response at Month 7 when the HPV-16/18 vaccine is co-administered with hepatitis B vaccine (HPV+HepB group) as compared to when the HPV-16/18 vaccine is administered alone (HPV group).

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	09 April 2008
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	Netherlands: 325
Country: Number of subjects enrolled	Sweden: 419
Worldwide total number of subjects	744
EEA total number of subjects	744

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)	744

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:

While the total numbers of subjects enrolled in the study was 744, the total number of subjects that entered the study was 741. The remaining 3 subjects received a subject number but no vaccine dose and were therefore excluded from the analysis and group assignment.

Pre-assignment period milestones

Number of subjects started	744
Number of subjects completed	741

Pre-assignment subject non-completion reasons

Reason: Number of subjects	No vaccination received: 3

Period 1

Period 1 title	Overall period (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&Engerix Group

Arm description:

Subjects received 3 doses of Cervarix (Human Papillomavirus [HPV] vaccine) co-administered with Engerix (Hepatitis B [HBV] vaccine) according to a 0, 1, 6-month schedule.

Arm type	Active comparator
Investigational medicinal product name	HPV Vaccine (GSK580299) Cervarix,Engerix B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 doses of Cervarix (Human Papillomavirus [HPV] vaccine) co-administered with Engerix (Hepatitis B [HBV] vaccine) according to a 0, 1, 6-month schedule.

Arm title	Cervarix Group

Arm description:

Subjects received 3 doses of Cervarix (Human Papillomavirus [HPV] vaccine) according to a 0, 1, 6-month schedule.

Arm type	Experimental
Investigational medicinal product name	HPV Vaccine (GSK580299) Cervarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 doses of Cervarix (Human Papillomavirus [HPV] vaccine) according to a 0, 1, 6-month schedule.

Arm title	Engerix Group

Arm description:

Subjects received 3 doses of Engerix (Hepatitis B [HBV] vaccine) according to a 0, 1, 6-month schedule.

Arm type	Active comparator
Investigational medicinal product name	Engerix B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 doses of Engerix (Hepatitis B [HBV] vaccine) according to a 0, 1, 6-month schedule.

Number of subjects in period 1[1]	Cervarix&Engerix Group	Cervarix Group	Engerix Group
Started	247	247	247
Completed	246	240	242
Not completed	1	7	5
Consent withdrawn by subject	-	6	1
Fear of blood sampling	-	1	-
Adverse event, non-fatal	1	-	2
Lost to follow-up	-	-	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: While the total numbers of subjects enrolled in the study was 744, the total number of subjects that entered the study was 741. The remaining 3 subjects received a subject number but no vaccine dose and were therefore excluded from the analysis and group assignment.

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix&Engerix Group
Reporting group description:	
Subjects received 3 doses of Cervarix (Human Papillomavirus [HPV] vaccine) co-administered with Engerix (Hepatitis B [HBV] vaccine) according to a 0, 1, 6-month schedule.	
Reporting group title	Cervarix Group
Reporting group description:	
Subjects received 3 doses of Cervarix (Human Papillomavirus [HPV] vaccine) according to a 0, 1, 6-month schedule.	
Reporting group title	Engerix Group
Reporting group description:	
Subjects received 3 doses of Engerix (Hepatitis B [HBV] vaccine) according to a 0, 1, 6-month schedule.	

Reporting group values	Cervarix&Engerix Group	Cervarix Group	Engerix Group
Number of subjects	247	247	247
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	11.4	11.3	11.4
standard deviation	± 2.17	± 2.14	± 2.17
Gender categorical Units: Subjects			
Female	247	247	247
Male	0	0	0

Reporting group values	Total		
Number of subjects	741		
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	741		
Male	0		

End points

End points reporting groups

Reporting group title	Cervarix&Engerix Group
Reporting group description:	
Subjects received 3 doses of Cervarix (Human Papillomavirus [HPV] vaccine) co-administered with Engerix (Hepatitis B [HBV] vaccine) according to a 0, 1, 6-month schedule.	
Reporting group title	Cervarix Group
Reporting group description:	
Subjects received 3 doses of Cervarix (Human Papillomavirus [HPV] vaccine) according to a 0, 1, 6-month schedule.	
Reporting group title	Engerix Group
Reporting group description:	
Subjects received 3 doses of Engerix (Hepatitis B [HBV] vaccine) according to a 0, 1, 6-month schedule.	

Primary: Number of subjects with anti-Hepatitis B surface antigen (anti-HBs) Antibody Concentrations above the cut-off value for seroprotection

End point title	Number of subjects with anti-Hepatitis B surface antigen (anti-HBs) Antibody Concentrations above the cut-off value for seroprotection[1][2]
End point description:	
Only groups which had received the HBV vaccine were included in the analysis. Subjects included were seronegative for anti-HBs (antibody titer <3.3 milli International Units per milliliter (mIU/mL)) prior to vaccination. Anti-HBs antibody cut-off value for seroprotection assessed included 10 mIU/mL. The analysis was performed on the According-to-Protocol (ATP) Cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.	
End point type	Primary
End point timeframe:	
Month 7	

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 groups which had received the HBV vaccine were included in the analysis.

End point values	Cervarix&Engerix Group	Engerix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	181		
Units: Subjects	190	181		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Anti-human Papillomavirus 16 and 18 (Anti-HPV-

16 and Anti-HPV-18) Antibody Concentrations Above the Cut-off Value for seroconversion

End point title	Number of Subjects With Anti-human Papillomavirus 16 and 18 (Anti-HPV-16 and Anti-HPV-18) Antibody Concentrations Above the Cut-off Value for seroconversion[3][4]

End point description:

Only groups which had received the HPV vaccine were included in the analysis. Anti-HPV-16 antibody cut-off value assessed included 8 Enzyme-linked Immunosorbent Assay (ELISA) units per milliliter (EL.U/mL) and anti-HPV-18 antibody cut-off value assessed included 7 EL.U/mL. Subjects included were seronegative for anti-HPV-16 (antibody titer <8 EL.U/mL) and anti-HPV-18 (antibody titer <7 EL.U/mL) prior to vaccination.
The analysis was performed on the According-to-Protocol (ATP) Cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.

End point type	Primary

End point timeframe:

Month 7

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 groups which had received the HPV vaccine were included in the analysis.

End point values	Cervarix&Engerix Group	Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	207	202		
Units: Subjects				
Anti-HPV-16 (N= 207; 200)	205	200		
Anti-HPV-18 (N= 200; 202)	199	202		

Statistical analyses

No statistical analyses for this end point

Primary: Anti-HPV-16/18 antibody titres

End point title	Anti-HPV-16/18 antibody titres[5][6]

End point description:

Antibody titers for Anti-HPV-16 and Anti-HPV-18 were expressed as Geometric Mean Titers (GMTs). Only groups which had received the HPV vaccine were included in the analysis. Subjects included were seronegative for anti-HPV-16 (antibody titer <8 EL.U/mL) and anti-HPV-18 (antibody titer <7 EL.U/mL) prior to vaccination.
The analysis was performed on the According-to-Protocol (ATP) Cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.

End point type	Primary

End point timeframe:

Month 7

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 groups which had received the HPV vaccine were included in the analysis.

End point values	Cervarix&Engerix Group	Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	207	202		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (N=207; 200)	19819.8 (16856.9 to 23303.6)	21712.6 (19460.2 to 24225.6)		
Anti-HPV-18 (N=200; 202)	8835.1 (7636.3 to 10222.1)	8838.6 (7948.5 to 9828.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-HBs Antibody Concentrations Above the Cut-off Value for Seroconversion

End point title	Number of Subjects With Anti-HBs Antibody Concentrations Above the Cut-off Value for Seroconversion[7]

End point description:

Only groups which had received the HBV vaccine were included in the analysis. Subjects included were seronegative for anti-HBs (antibody titer <3.3 mIU/mL) prior to vaccination. Anti-HBs antibody cut-off value for seroconversion assessed included 3.3 mIU/mL.
The analysis was performed on the According-to-Protocol (ATP) Cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.

End point type	Secondary

End point timeframe:

Month 7

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 groups which had received the HBV vaccine were included in the analysis.

End point values	Cervarix&Engerix Group	Engerix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	181		
Units: Subjects	192	181		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs Antibody Titres

End point title	Anti-HBs Antibody Titres[8]

End point description:

Antibody titers for anti-HBs were given as Geometric Mean Titers (GMTs) in mIU/mL. Only groups which had received the HBV vaccine were included in the analysis. Subjects included were seronegative for anti-HBs (antibody titer <3.3 mIU/mL) prior to vaccination.
The analysis was performed on the According-to-Protocol (ATP) Cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.

End point type	Secondary

End point timeframe:

Month 7

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 groups which had received the HBV vaccine were included in the analysis.

End point values	Cervarix&Engerix Group	Engerix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	181		
Units: mIU/mL				
geometric mean (confidence interval 95%)	1280.9 (973.3 to 1685.7)	3107.7 (2473.1 to 3905.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-HPV-16 and Anti-HPV-18 Antibody Concentrations Above the Cut-off Value for Seroconversion

End point title	Number of Subjects With Anti-HPV-16 and Anti-HPV-18 Antibody Concentrations Above the Cut-off Value for Seroconversion[9]

End point description:

Only groups which had received the HPV vaccine were included in the analysis. Anti-HPV-16 antibody cut-off value assessed included 8 Enzyme-linked Immunosorbent Assay (ELISA) units per milliliter (EL.U/mL) and anti-HPV-18 antibody cut-off value assessed included 7 EL.U/mL. Subjects included were seronegative for anti-HPV-16 (antibody titer <8 EL.U/mL) and anti-HPV-18 (antibody titer <7 EL.U/mL) prior to vaccination.
The analysis was performed on the According-to-Protocol (ATP) Cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.

End point type	Secondary

End point timeframe:

Month 2

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 groups which had received the HPV vaccine were included in the analysis.

End point values	Cervarix&Engerix Group	Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	207	201		
Units: Subjects				
Anti-HPV-16 (N= 207; 199)	207	199		
Anti-HPV-18 (N= 200; 201)	200	201		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16/18 Antibody Titres

End point title	Anti-HPV-16/18 Antibody Titres[10]

End point description:

Antibody titers for Anti-HPV-16 and Anti-HPV-18 are expressed as Geometric Mean Titers (GMTs). Only groups which had received the HPV vaccine were included in the analysis. Subjects included were seronegative for anti-HPV-16 (antibody titer <8 EL.U/mL) and anti-HPV-18 (antibody titer <7 EL.U/mL) prior to vaccination.
The analysis was performed on the According-to-Protocol (ATP) Cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.

End point type	Secondary

End point timeframe:

Month 2

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 groups which had received the HPV vaccine were included in the analysis.

End point values	Cervarix&Engerix Group	Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	207	201		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (N= 207; 199)	4894.7 (4472.5 to 5356.7)	5069.2 (4581.2 to 5609.1)		
Anti-HPV-18 (N= 200; 201)	4790.4 (4338.9 to 5288.8)	4663.8 (4228.2 to 5144.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-Hepatitis B Surface Antigen (Anti-HBs) Antibody Concentrations Above the Cut-off Value for Seroconversion

End point title	Number of Subjects With Anti-Hepatitis B Surface Antigen (Anti-HBs) Antibody Concentrations Above the Cut-off Value for Seroconversion[11]

End point description:

Only groups which had received the HBV vaccine were included in the analysis. Subjects included were seronegative for anti-HBs (antibody titer <3.3 mIU/mL) prior to vaccination. Anti-HBs antibody cut-off value for seroconversion assessed included 3.3 mIU/mL.
The analysis was performed on the According-to-Protocol (ATP) Cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.

End point type	Secondary

End point timeframe:

Month 2

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 groups which had received the HBV vaccine were included in the analysis.

End point values	Cervarix&Engerix Group	Engerix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	178		
Units: Subjects	165	168		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-Hepatitis B Surface Antigen (Anti-HBs) Antibody Concentrations Above the Cut-off Value for Seroprotection

End point title	Number of Subjects With Anti-Hepatitis B Surface Antigen (Anti-HBs) Antibody Concentrations Above the Cut-off Value for Seroprotection[12]

End point description:

Only groups which had received the HBV vaccine were included in the analysis. Subjects included were seronegative for anti-HBs (antibody titer <3.3 milli International Units per milliliter (mIU/mL)) prior to vaccination vaccination. Anti-HBs antibody cut-off value for seroprotection assessed included 10 mIU/mL.
The analysis was performed on the According-to-Protocol (ATP) Cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.

End point type	Secondary

End point timeframe:

Month 2

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 groups which had received the HBV vaccine were included in the analysis.

End point values	Cervarix&Engerix Group	Engerix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	178		
Units: Subjects	128	142		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody titers

End point title	Anti-HBs antibody titers[13]

End point description:

Anti-HBs antibody titers are given as GMTs in mIU/mL. Only groups which had received the HBV vaccine were included in the analysis. Subjects included were seronegative for anti-HBs (antibody titer <3.3 mIU/mL) prior to vaccination.
The analysis was performed on the According-to-Protocol (ATP) Cohort for immunogenicity, which included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.

End point type	Secondary

End point timeframe:

Month 2

Notes:

[13] - 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 groups which had received the HBV vaccine were included in the analysis.

End point values	Cervarix&Engerix Group	Engerix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	178		
Units: mIU/mL				
geometric mean (confidence interval 95%)	13.6 (11.4 to 16.2)	26.9 (22.1 to 32.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Any Solicited Local Symptoms

End point title	Number of Subjects Reporting Any Solicited Local Symptoms

End point description:

Solicited local symptoms included injection site pain, redness and swelling. Any solicited local symptom is occurrence of a symptom regardless of its intensity.
Analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects for whom data were available.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix&Engerix Group	Cervarix Group	Engerix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	245	246	
Units: Subjects				
Pain	244	238	182	
Redness	122	127	63	
Swelling	120	111	47	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting grade 3 solicited local symptoms

End point title	Number of subjects reporting grade 3 solicited local symptoms

End point description:

Solicited local symptoms included injection site pain, redness and swelling. Grade 3 pain is pain that prevented normal everyday activities. Grade 3 redness is redness that was >50 mm. Grade 3 swelling is swelling that was >50 mm.
Analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects for whom data were available.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix&Engerix Group	Cervarix Group	Engerix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	245	246	
Units: Subjects				
Pain	54	35	4	
Redness	12	5	1	
Swelling	17	13	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited general symptoms

End point title	Number of subjects reporting any solicited general symptoms

End point description:

Solicited general symptoms included arthralgia, fatigue, gastrointestinal, headache, myalgia, rash,

temperature in degrees Celsius (axillary) and urticaria. Any solicited general symptom is the occurrence of the symptom regardless of its intensity or relationship to study vaccination.
Analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects for whom data were available.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix&Engerix Group	Cervarix Group	Engerix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	245	246	
Units: Subjects				
Arthralgia	31	23	26	
Fatigue	130	107	104	
Gastrointestinal	65	67	70	
Headache	136	131	129	
Myalgia	55	55	53	
Rash	10	14	11	
Temperature	32	23	36	
Urticaria	5	5	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting grade 3 solicited general symptoms

End point title	Number of subjects reporting grade 3 solicited general symptoms

End point description:

Solicited general symptoms included arthralgia, fatigue, gastrointestinal, headache, myalgia, rash, temperature in degrees Celsius (axillary) and urticaria. Grade 3 arthralgia, fatigue, gastrointestinal, headache, myalgia and rash were symptoms that prevented normal activity. Grade 3 temperature was temperature >39 degrees Celsius. Grade 3 urticaria was urticaria distributed on at least 4 body areas.
Analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects for whom data were available.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix&Engerix Group	Cervarix Group	Engerix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	245	246	
Units: Subjects				
Arthralgia	1	0	0	
Fatigue	8	8	9	

Gastrointestinal	4	6	8	
Headache	13	11	4	
Myalgia	2	2	1	
Rash	0	1	0	
Temperature	3	2	3	
Urticaria	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting related solicited general symptoms

End point title	Number of subjects reporting related solicited general symptoms

End point description:

Solicited general symptoms included arthralgia, fatigue, gastrointestinal, headache, myalgia, rash, temperature in degrees Celsius (axillary) and urticaria. Related solicited general symptoms were those symptoms assessed by the investigators as related to the study vaccination.
Analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects for whom data were available.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix&Engerix Group	Cervarix Group	Engerix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	245	246	
Units: Subjects				
Arthralgia	18	16	12	
Fatigue	89	70	51	
Gastrointestinal	35	40	25	
Headache	77	71	57	
Myalgia	40	40	20	
Rash	8	8	4	
Temperature	13	10	6	
Urticaria	4	4	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects reporting any, grade 3 and causally related to vaccination unsolicited adverse events (AEs)

End point title	Number of Subjects reporting any, grade 3 and causally related to vaccination 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. Grade 3 AE was an AE that prevented normal activities. Related AE was an AE that was assessed by the investigator as related to the study vaccination.
Analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects for whom data were available.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix&Engerix Group	Cervarix Group	Engerix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	247	247	
Units: Subjects				
Any AEs	130	99	99	
Grade 3 AEs	19	19	16	
Related AEs	43	19	25	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and causally related to vaccination serious adverse events (SAEs)

End point title	Number of subjects reporting any and causally related to vaccination 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. Related SAEs were SAEs assessed by the investigators as related to the vaccination. * Grade 3 SAEs were not assessed.
Analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects for whom data were available.

End point type	Secondary

End point timeframe:

Throughout the active phase of the study (up to Month 7)

End point values	Cervarix&Engerix Group	Cervarix Group	Engerix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	247	247	
Units: Subjects				
Any	2	1	0	
Related	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and causally related to vaccination SAEs

End point title	Number of subjects reporting any and causally related to vaccination 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. * Grade 3 SAEs were not assessed.
Analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects for whom data were available.

End point type	Secondary

End point timeframe:

Throughout the safety follow-up (month 7 up to Month 12)

End point values	Cervarix&Engerix Group	Cervarix Group	Engerix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	247	247	
Units: Subjects				
Any	1	1	1	
Related	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting medically significant conditions

End point title	Number of subjects reporting medically significant conditions

End point description:

Medically significant conditions (i.e., 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 SAEs that are not related to common diseases).
Analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects for whom data were available.

End point type	Secondary

End point timeframe:

Throughout the active phase of the study (up to Month 7)

End point values	Cervarix&Engerix Group	Cervarix Group	Engerix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	247	247	
Units: Subjects	31	28	22	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting medically significant conditions

End point title	Number of subjects reporting medically significant conditions

End point description:

Medically significant conditions (i.e., 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 SAEs that are not related to common diseases).
Analysis was performed on the Total Vaccinated Cohort, which included all vaccinated subjects for whom data were available.

End point type	Secondary

End point timeframe:

Throughout the safety follow-up (month 7 up to Month 12)

End point values	Cervarix&Engerix Group	Cervarix Group	Engerix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	247	247	
Units: Subjects	0	2	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms were collected during the 7-day period (Days 0 - 6) following vaccination, unsolicited AEs during the 30-day period (Days 0 - 29) following any vaccination and SAEs during the whole study period, up to Month 12.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Cervarix&Engerix Group

Reporting group description:

Subjects received 3 doses of Cervarix (Human Papillomavirus [HPV] vaccine) co-administered with Engerix (Hepatitis B [HBV] vaccine) according to a 0, 1, 6-month schedule.

Reporting group title	Cervarix Group

Reporting group description:

Subjects received 3 doses of Cervarix (Human Papillomavirus [HPV] vaccine) according to a 0, 1, 6-month schedule.

Reporting group title	Engerix Group

Reporting group description:

Subjects received 3 doses of Engerix (Hepatitis B [HBV] vaccine) according to a 0, 1, 6-month schedule.

Serious adverse events	Cervarix&Engerix Group	Cervarix Group	Engerix Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 247 (1.21%)	2 / 247 (0.81%)	1 / 247 (0.40%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Traumatic brain injury			
subjects affected / exposed	1 / 247 (0.40%)	0 / 247 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 247 (0.00%)	0 / 247 (0.00%)	1 / 247 (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
Forearm fracture			

subjects affected / exposed	0 / 247 (0.00%)	1 / 247 (0.40%)	0 / 247 (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	1 / 247 (0.40%)	0 / 247 (0.00%)	0 / 247 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 247 (0.00%)	1 / 247 (0.40%)	0 / 247 (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	1 / 247 (0.40%)	0 / 247 (0.00%)	0 / 247 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cervarix&Engerix Group	Cervarix Group	Engerix Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	244 / 247 (98.79%)	238 / 247 (96.36%)	182 / 247 (73.68%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	244 / 247 (98.79%)	238 / 247 (96.36%)	182 / 247 (73.68%)
occurrences (all)	244	238	182
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	122 / 247 (49.39%)	127 / 247 (51.42%)	63 / 247 (25.51%)
occurrences (all)	122	127	63
Swelling			

alternative assessment type: Systematic			
subjects affected / exposed	120 / 247 (48.58%)	111 / 247 (44.94%)	47 / 247 (19.03%)
occurrences (all)	120	111	47
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	31 / 247 (12.55%)	23 / 247 (9.31%)	26 / 247 (10.53%)
occurrences (all)	31	23	26
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	130 / 247 (52.63%)	107 / 247 (43.32%)	104 / 247 (42.11%)
occurrences (all)	130	107	104
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed	65 / 247 (26.32%)	67 / 247 (27.13%)	70 / 247 (28.34%)
occurrences (all)	65	67	70
Headache (Solicited Symptom)			
alternative assessment type: Systematic			
subjects affected / exposed	136 / 247 (55.06%)	131 / 247 (53.04%)	129 / 247 (52.23%)
occurrences (all)	136	131	129
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	55 / 247 (22.27%)	55 / 247 (22.27%)	53 / 247 (21.46%)
occurrences (all)	55	55	53
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 247 (4.05%)	14 / 247 (5.67%)	11 / 247 (4.45%)
occurrences (all)	10	14	11
Temperature			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 247 (12.96%)	23 / 247 (9.31%)	36 / 247 (14.57%)
occurrences (all)	32	23	36
Nasopharyngitis			
subjects affected / exposed	29 / 247 (11.74%)	27 / 247 (10.93%)	26 / 247 (10.53%)
occurrences (all)	29	27	26

Headache (AE)			
subjects affected / exposed	17 / 247 (6.88%)	19 / 247 (7.69%)	9 / 247 (3.64%)
occurrences (all)	17	19	9
Oropharyngeal pain			
subjects affected / exposed	13 / 247 (5.26%)	13 / 247 (5.26%)	7 / 247 (2.83%)
occurrences (all)	13	13	7

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