Clinical trial results:
A phase I/II, observer-blind, randomized, controlled study to assess the immunogenicity and safety of GlaxoSmithKline Biologicals' HPV-16/18 L1/AS04 vaccine administered intramuscularly according to a 0, 1, 6 month schedule in healthy male subjects aged 10-18 years.

Summary

EudraCT number	2005-005943-24
Trial protocol	FI
Global end of trial date	19 June 2007

Results information

Result version number	v2 (current)
This version publication date	20 March 2023
First version publication date	08 January 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	580299/011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00309166
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, 1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 004 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 004 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	13 December 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 June 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate 1 month after the third dose (i.e. at Month 7), the immune responses to the candidate HPV-16/18 vaccine (as determined by anti-HPV-16/18 ELISA) in healthy male subjects aged 10-18 years old.

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	05 April 2006
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	Finland: 270
Worldwide total number of subjects	270
EEA total number of subjects	270

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)	11
Adolescents (12-17 years)	240
Adults (18-64 years)	19
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervarix Group

Arm description:

Healthy male subjects between and including 10 to 18 years of age at the time of the first vaccination, who were administered 3 doses of Cervarix (HPV-16/18 L1 VLP AS04) vaccine, intramuscularly into the deltoid region of the non-dominant arm, according to a 0, 1 and 6-month schedule. The subjects were followed up for 7 months after the first dose and an additional telephone contact was foreseen at Month 12.

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

Dosage and administration details:

All subjects received an intramuscular injection into the deltoid of the non-dominant arm according to a 0, 1 and 6-month schedule and were followed up for 7 months after the first dose. Additionally, a telephone contact was foreseen at Month 12.

Arm title	Engerix-B Group

Arm description:

Healthy male subjects between and including 10 to 18 years of age at the time of the first vaccination, who were administered 3 doses of Engerix-B (HBV) vaccine, intramuscularly into the deltoid region of the non-dominant arm, according to a 0, 1 and 6-month schedule. The subjects were followed up for 7 months after the first dose and an additional telephone contact was foreseen at Month 12.

Arm type	Active comparator
Investigational medicinal product name	Engerix-B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

All subjects received an intramuscular injection into the deltoid of the non-dominant arm according to a 0, 1 and 6-month schedule and were followed up for 7 months after the first dose. Additionally, a telephone contact was foreseen at Month 12.

Number of subjects in period 1	Cervarix Group	Engerix-B Group
Started	181	89
Completed	176	86
Not completed	5	3
Consent withdrawn by subject	4	3
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix Group
Reporting group description:	
Healthy male subjects between and including 10 to 18 years of age at the time of the first vaccination, who were administered 3 doses of Cervarix (HPV-16/18 L1 VLP AS04) vaccine, intramuscularly into the deltoid region of the non-dominant arm, according to a 0, 1 and 6-month schedule. The subjects were followed up for 7 months after the first dose and an additional telephone contact was foreseen at Month 12.	
Reporting group title	Engerix-B Group
Reporting group description:	
Healthy male subjects between and including 10 to 18 years of age at the time of the first vaccination, who were administered 3 doses of Engerix-B (HBV) vaccine, intramuscularly into the deltoid region of the non-dominant arm, according to a 0, 1 and 6-month schedule. The subjects were followed up for 7 months after the first dose and an additional telephone contact was foreseen at Month 12.	

Reporting group values	Cervarix Group	Engerix-B Group	Total
Number of subjects	181	89	270
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	9	2	11
Adolescents (12-17 years)	156	84	240
Adults (18-64 years)	16	3	19
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
geometric mean	14.4	14.4	
standard deviation	± 2.14	± 2.02	-
Gender categorical Units: Subjects			
Males	181	89	270

End points

End points reporting groups

Reporting group title	Cervarix Group

Reporting group description:

Healthy male subjects between and including 10 to 18 years of age at the time of the first vaccination, who were administered 3 doses of Cervarix (HPV-16/18 L1 VLP AS04) vaccine, intramuscularly into the deltoid region of the non-dominant arm, according to a 0, 1 and 6-month schedule. The subjects were followed up for 7 months after the first dose and an additional telephone contact was foreseen at Month 12.

Reporting group title	Engerix-B Group

Reporting group description:

Healthy male subjects between and including 10 to 18 years of age at the time of the first vaccination, who were administered 3 doses of Engerix-B (HBV) vaccine, intramuscularly into the deltoid region of the non-dominant arm, according to a 0, 1 and 6-month schedule. The subjects were followed up for 7 months after the first dose and an additional telephone contact was foreseen at Month 12.

Primary: Number of seroconverted subjects for anti-HPV-16 and HPV-18

End point title	Number of seroconverted subjects for anti-HPV-16 and HPV-

End point description:

Seroconversion was defined as the appearance of anti-HPV-16 and/or anti-HPV-18 antibodies (anti-HPV-16 titres ≥8 ELISA units per milliliter [EL.U/mL] and anti-HPV-18 titres greater than or equal to (≥) 7 EL.U/mL) in the serum of subjects seronegative before vaccination.

End point type	Primary

End point timeframe:

At 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.

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	86		
Units: Subjects				
HPV-16 (N=163, 83)	163	1		
HPV-18 (N=150, 86)	150	2		

Statistical analyses

No statistical analyses for this end point

Primary: Antibody titers against HPV-16 (anti-HPV-16) and HPV-18 (anti-HPV-18)

End point title	Antibody titers against HPV-16 (anti-HPV-16) and HPV-18 (anti-HPV-18)[2]

End point description:

Titers were given as geometric mean titers(GMT).

End point type	Primary

End point timeframe:

At Month 7

Notes:

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

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	86		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
HPV-16 (N=171, 86)	22564.8 (19800.3 to 25715.4)	4.2 (4 to 4.5)		
HPV-18 (N=170, 86)	8460.3 (7306.1 to 9796.8)	3.6 (3.4 to 3.8)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Seroconversion was defined as the appearance of anti-HPV-16 and/or anti-HPV-18 antibodies (anti-HPV-16 titres ≥8 ELISA units per milliliter [EL.U/mL] and anti-HPV-18 titres ≥7 EL.U/mL) in the serum of subjects seronegative before vaccination.

End point type	Secondary

End point timeframe:

At Month 2

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	86		
Units: Subjects				
HPV-16 (N=165, 83)	165	0		
HPV-18 (N=152, 86)	152	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers against HPV-16 (anti-HPV-16) and HPV-18 (anti-HPV-18)

End point title	Antibody titers against HPV-16 (anti-HPV-16) and HPV-18 (anti-HPV-18)

End point description:

Titers were given as GMTs.

End point type	Secondary

End point timeframe:

At Month 2

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	86		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
HPV-16 (N=173, 86)	5254.5 (4704.9 to 5868.2)	4.1 (4 to 4.3)		
HPV-18 (N=172, 86)	3696.9 (3275.9 to 4172.1)	3.7 (3.5 to 3.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms

End point title	Number of subjects with any and Grade 3 solicited local symptoms

End point description:

The solicited symptoms assessed were pain, redness and swelling. Any = any solicited local symptom irrespective of intensity grade; Grade 3 pain = pain that prevented normal activity; Grade 3 redness/swelling = redness/swelling beyond (>) 50 mm.

End point type	Secondary

End point timeframe:

Within 7 days (Day 0 - 6) after each dose and across doses, up to 7 months

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	88		
Units: Subjects				
Pain, Dose 1 (N=180, 88)	149	25		
Grade 3, Pain, Dose 1 (N=180, 88)	1	0		
Redness, Dose 1 (N=180, 88)	24	12		
Grade 3, Redness, Dose 1 (N=180, 88)	0	0		
Swelling, Dose 1 (N=180, 88)	7	3		
Grade 3, Swelling, Dose 1 (N=180, 88)	0	0		
Pain, Dose 2 (N=172, 86)	114	16		
Grade 3, Pain, Dose 2 (N=172, 86)	2	0		
Redness, Dose 2 (N=172, 86)	30	8		
Grade 3, Redness, Dose 2 (N=172, 86)	0	0		
Swelling, Dose 2 (N=172, 86)	20	2		
Grade 3, Swelling, Dose 2 (N=172, 86)	0	1		
Pain, Dose 3 (N=171, 85)	115	16		
Grade 3, Pain, Dose 3 (N=171, 85)	7	0		
Redness, Dose 3 (N=171, 85)	33	9		
Grade 3, Redness, Dose 3 (N=171, 85)	0	0		
Swelling, Dose 3 (N=171, 85)	29	3		
Grade 3, Swelling, Dose 3 (N=171, 85)	2	0		
Pain, Across doses (N=180, 88)	159	39		
Grade 3, Pain, Across doses (N=180, 88)	8	0		
Redness, Across doses (N=180, 88)	51	15		
Grade 3, Redness, Across doses (N=180, 88)	0	0		
Swelling, Across doses (N=180, 88)	36	7		
Grade 3, Swelling, Across doses (N=180, 88)	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, Grade 3 and related solicited general symptoms

End point title	Number of subjects with any, Grade 3 and related solicited general symptoms

End point description:

The solicited general symptoms assessed were Arthralgia, Fatigue, Fever (defined as axillary temperature ≥37.5 °C), Gastrointestinal, Headache, Myalgia, Rash and Urticaria. Any = any solicited general symptom irrespective of intensity grade or relationship to vaccination; Grade 3 = symptom that prevented normal activity; Grade 3 fever = temperature > 39.0 °C; Related = symptoms considered by the investigator to have a causal relationship to vaccination.

End point type	Secondary

End point timeframe:

Within 7 days (Days 0-6) after each dose and across doses, up to 7 months

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	88		
Units: Subjects				
Arthralgia, Dose 1 (N=180, 88)	17	7		
Grade 3, Athralgia, Dose 1 (N=180, 88)	0	0		
Related, Athralgia, Dose 1 (N=180, 88)	10	3		
Fatigue, Dose 1 (N=180, 88)	51	32		
Grade 3, Fatigue, Dose 1 (N=180, 88)	1	0		
Related, Fatigue, Dose 1 (N=180, 88)	26	18		
Fever (axillary), Dose 1 (N=180, 88)	24	11		
Grade 3, Fever, Dose 1 (N=180, 88)	0	0		
Related, Fever, Dose 1 (N=180, 88)	1	1		
Gastrointestinal, Dose 1 (N=180, 88)	33	10		
Grade 3, Gastrointestinal, Dose 1 (N=180, 88)	2	0		
Related, Gastrointestinal, Dose 1 (N=180, 88)	15	5		
Headache, Dose 1 (N=180, 88)	51	21		
Grade 3, Headache, Dose 1 (N=180, 88)	0	0		
Related, Headache, Dose 1 (N=180, 88)	24	7		
Myalgia, Dose 1 (N=180, 88)	67	16		
Grade 3, Mylagia, Dose 1 (N=180, 88)	1	0		
Related, Mylagia, Dose 1 (N=180, 88)	45	7		
Rash, Dose 1 (N=180, 88)	8	1		
Grade 3, Rash, Dose 1 (N=180, 88)	0	0		
Related, Rash, Dose 1 (N=180, 88)	2	1		
Urticaria, Dose 1 (N=180, 88)	3	0		
Grade 3, Urticaria, Dose 1 (N=180, 88)	0	0		
Related, Urticaria, Dose 1 (N=180, 88)	1	0		
Arthralgia, Dose 2 (N=173, 86)	6	3		
Grade 3, Arthralgia, Dose 2 (173, 86)	0	1		
Related, Arthralgia, Dose 2 (N=173, 86)	3	0		
Fatigue, Dose 2 (N=173, 86)	35	14		
Grade 3, Fatigue, Dose 2 (N=173, 86)	1	0		
Related, Fatigue, Dose 2 (N=173, 86)	21	9		
Fever (axillary), Dose 2 (N=173, 86)	14	6		
Grade 3, Fever, Dose 2 (N=173, 86)	0	0		
Related, Fever, Dose 2 (N=173, 86)	1	0		
Gastrointestinal, Dose 2 (N=173, 86)	18	4		
Grade 3, Gastrointestinal, Dose 2 (N=173, 86)	1	1		
Related, Gastrointestinal, Dose 2 (N=173, 86)	7	0		
Headache, Dose 2 (N=173, 86)	30	13		
Grade 3, Headache, Dose 2 (N=173, 86)	2	1		
Related, Headache, Dose 2 (N=173, 86)	14	7		

Myalgia, Dose 2 (N=173, 86)	35	8		
Grade 3, Maylagia, Dose 2 (N=173, 86)	1	0		
Related, Maylagia, Dose 2 (N=173, 86)	27	7		
Rash, Dose 2 (N=173, 86)	8	2		
Grade 3, Rash, Dose 2 (N=173, 86)	0	0		
Related, Rash, Dose 2 (N=173, 86)	3	0		
Urticaria, Dose 2 (N=173, 86)	1	2		
Grade 3, Urticaria, Dose 2 (N=173, 86)	0	0		
Related, Urticaria, Dose 2 (N=173, 86)	0	0		
Arthralgia, Dose 3 (N=170, 85)	12	3		
Grade 3, Arthralgia, Dose 3 (N=170, 85)	0	0		
Related, Arthtralgia, Dose 3 (N=170, 85)	12	3		
Fatigue, Dose 3 (N=170, 85)	44	15		
Grade 3, Fatigue, Dose 3 (N=170, 85)	2	0		
Related, Fatigue, Dose 3 (N=170, 85)	30	11		
Fever (axillary), Dose 3 (N=170, 85)	14	4		
Grade 3, Fever, Dose 3 (N=170, 85)	0	0		
Related, Fever, Dose 3 (N=170, 85)	1	0		
Gastrointestinal, Dose 3 (N=170, 85)	10	5		
Grade 3, Gastrointestinal, Dose 3 (N=170, 85)	1	0		
Related, Gastrointestinal, Dose 3 (N=170, 85)	8	4		
Headache, Dose 3 (N=170, 85)	30	11		
Grade 3, Headache, Dose 3 (N=170, 85)	3	0		
Related, Headache, Dose 3 (N=170, 85)	17	8		
Myalgia, Dose 3 (N=170, 85)	39	8		
Grade 3, Mylagia, Dose 3 (N=170, 85)	1	0		
Related, Mylagia, Dose 3 (N=170, 85)	35	6		
Rash, Dose 3 (N=170, 85)	3	2		
Grade 3, Rash, Dose 3 (N=170, 85)	0	0		
Related, Rash, Dose 3 (N=170, 85)	1	0		
Urticaria, Dose 3 (N=170, 85)	0	0		
Grade 3, Urticaria, Dose 3 (N=170, 85)	0	0		
Related, Urticaria, Dose 3 (N=170, 85)	0	0		
Arthralgia, Across doses (N=180, 88)	29	10		
Grade 3, Arthralgia, Across doses (N=180, 88)	0	1		
Related, Arthralgia, Across doses (N=180, 88)	22	5		
Fatigue, Across doses (N=180, 88)	82	42		
Grade 3, Fatigue, Across doses (N=180, 88)	4	0		
Fever (axillary), Across doses (N=180, 88)	35	17		
Grade 3, Fever, Across doses (N=180, 88)	0	0		
Related, Fever, Across doses (N=180, 88)	3	1		
Gastrointestinal, Across doses (N=180, 88)	40	14		
Grade 3, Gastrointestinal, Across dose (N=180, 88)	4	1		

Related, Gastrointestinal, Across dose (N=180, 88)	19	7		
Headache, Across doses (N=180, 88)	77	33		
Grade 3, Headache, Across doses (N=180, 88)	5	1		
Related, Headache, Across doses (N=180, 88)	43	16		
Related, Fatigue, Across doses (N=180, 88)	54	33		
Myalgia, Across doses (N=180, 88)	88	23		
Grade 3, Mylagia, Across doses (N=180, 88)	3	0		
Related, Mylagia, Across doses (N=180, 88)	70	14		
Rash, Across doses (N=180, 88)	16	5		
Grade 3, Rash, Across doses (N=180, 88)	0	0		
Related, Rash, Across doses (N=180, 88)	5	1		
Urticaria, Across doses (N=180, 88)	4	2		
Grade 3, Urticaria, Across doses (N=180, 88)	0	0		
Related, Urticaria, Across doses (N=180, 88)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, Grade 3 and related unsolicited adverse events (AEs)

End point title	Number of subjects with any, Grade 3 and related unsolicited adverse events (AEs)

End point description:

Solicited general symptoms assessed were arthralgia, fatigue, fever (defined as axillary temperature ≥37.5 °C), gastrointestinal, headache, myalgia, rash and urticaria. Any = any solicited general symptom irrespective of intensity grade or relationship to vaccination; Grade 3 = symptom that prevented normal activity; Grade 3 fever = temperature > 39.0 °C; Related = symptoms considered by the investigator to have a causal relationship to vaccination.

End point type	Secondary

End point timeframe:

Within 30 days (Day 0-29) after any vaccination, up to 7 months

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	89		
Units: Subjects				
Any AEs	68	31		
Grade 3 AEs	5	2		
Related AEs	5	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with New Onset of Chronic Diseases (NOCDs) and other medically significant conditions

End point title	Number of subjects with New Onset of Chronic Diseases (NOCDs) and other medically significant conditions

End point description:

NOCDs include asthma, Chron`s disease, dermatitis atopic. MSCs include AEs prompting emergency room or physician visits that are not related to common diseases or 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 and injury.

End point type	Secondary

End point timeframe:

Throughout the active phase of the study (up to Month 7) and the extended safety follow-up (from Month 7 up to Month 12)

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	89		
Units: Subjects				
NOCDs, Month 7 (N=181, 89)	2	1		
MSCs, Month 7 (N=181, 89)	22	10		
NOCDs, Month 7 to 12 (N=175,86)	0	0		
MSCs, Month 7 to 12 (N=175,86)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Serious adverse events (SAEs)

End point title	Number of subjects with Serious adverse events (SAEs)

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

Throughout the active phase of the study (up to Month 7) and the extended safety follow-up (from Month 7 up to Month 12)

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	89		
Units: Number				
SAEs, Month 7 (N=181,89)	2	0		
SAEs, Month 12 (N=175, 86)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters

End point title	Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters

End point description:

The occurence of clinically relevant abnormalities was assessed in the following biochemical and haematological parameters: alanine aminotransferase [ALT], basophils [BAS], creatinine [CREA], eosinophils [EOS] and hematocrit [Hem]. Levels of haematological/biochemical parameters assessed in terms of normal, below and above laboratory values were - normal, below, above and missing.

End point type	Secondary

End point timeframe:

At Month 2 and Month 7, post-vaccination

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	86		
Units: Subjects				
Alt, Normal, Month 2, Normal (N=172, 86)	166	79		
Alt, Normal, Month 2, Below (N=172, 86)	3	0		
Alt, Normal, Month 2, Above (N=172, 86)	3	2		
Alt, Normal, Month 2, Missing (N=172, 86)	0	5		
Alt, Normal, Month 7, Normal (N=171, 84)	165	81		
Alt, Normal, Month 7, Below (N=171, 84)	1	9		
Alt, Normal, Month 7, Above (N=171, 84)	5	3		
Alt, Below, Month 2, Normal (N=1, 0)	0	0		
Alt, Below, Month 2, Below (N=1, 0)	1	0		
Alt, Below, Month 2, Above (N=1, 0)	0	0		

Alt, Below, Month 7, Normal (N=1, 0)	0	0		
Alt, Below, Month 7, Below (N=1, 0)	1	0		
Alt, Below, Month 7, Above (N=1, 0)	0	0		
Alt, Above, Month 2, Normal (N=4, 1)	2	0		
Alt, Above, Month 2, Below (N=4, 1)	0	0		
Alt, Above, Month 2, Above (N=4, 1)	2	0		
Alt, Above, Month 2, Missing (N=4, 1)	0	1		
Alt, Above, Month 7, Normal (N=3, 1)	2	0		
Alt, Above, Month 7, Below (N=3, 1)	0	0		
Alt, Above, Month 7, Above (N=3, 1)	1	1		
BAS Normal, Month 2, Normal (N=146, 76)	140	65		
BAS Normal, Month 2, Below (N=146, 76)	0	0		
BAS Normal, Month 2, Above (N=146, 76)	3	3		
BAS Normal, Month 2, Missing (N=146, 76)	3	8		
BAS Normal, Month 7, Normal (N=145, 74)	134	66		
BAS Normal, Month 7, Below (N=145, 74)	0	0		
BAS Normal, Month 7, Above (N=145, 74)	11	8		
BAS Above, Month 2, Normal (N=18, 6)	12	5		
BAS Above, Month 2, Below (N=18, 6)	0	0		
BAS Above, Month 2, Above (N=18, 6)	6	1		
BAS Above, Month 7, Normal (N=18, 6)	14	4		
BAS Above, Month 7, Below (N=18, 6)	0	0		
BAS Above, Month 7, Above (N=18, 6)	4	2		
EOS Normal, Month 2, Normal (N=125, 68)	102	48		
EOS Normal, Month 2, Below (N=125, 68)	4	2		
EOS Normal, Month 2, Above (N=125, 68)	17	10		
EOS Normal, Month 2, Missing (N=125, 68)	2	8		
EOS Normal, Month 7, Normal (N=125, 67)	108	54		
EOS Normal, Month 7, Below (N=125, 67)	8	4		
EOS Normal, Month 7, Above (N=125, 67)	9	9		
EOS Below, Month 2, Normal (N=4, 3)	4	2		
EOS Below, Month 2, Below (N=4, 3)	0	1		
EOS Below, Month 2, Above (N=4, 3)	0	0		
EOS Below, Month 7, Normal (N=4, 2)	2	1		
EOS Below, Month 7, Below (N=4, 2)	2	1		
EOS Below, Month 7, Above (N=4, 2)	0	0		
EOS Above, Month 2, Normal (N=36, 11)	6	5		
EOS Above, Month 2, Below (N=36, 11)	0	0		
EOS Above, Month 2, Above (N=36, 11)	30	6		
EOS Above, Month 7, Normal (N=35, 11)	8	5		
EOS Above, Month 7, Below (N=35, 11)	0	0		

EOS Above, Month 7, Above (N=35, 11)	27	6		
CREA Normal, Month 2, Normal (N=163, 82)	158	76		
CREA Normal, Month 2, Below (N=163, 82)	0	0		
CREA Normal, Month 2, Above (N=163, 82)	5	0		
CREA Normal, Month 2, Missing (N=163, 82)	0	6		
CREA Normal, Month 7, Normal (N=161, 80)	159	79		
CREA Normal, Month 7, Below (N=161, 80)	0	0		
CREA Normal, Month 7, Above (N=161, 80)	2	1		
CREA Above, Month 2, Normal (N=13, 5)	10	3		
CREA Above, Month 2, Below (N=13, 5)	0	0		
CREA Above, Month 2, Above (N=13, 5)	3	2		
CREA Above, Month 7, Normal (N=13, 5)	10	5		
CREA Above, Month 7, Below (N=13, 5)	0	0		
CREA Above, Month 7, Above (N=13, 5)	3	0		
HEM Normal, Month 2, Normal (N=159, 81)	155	76		
HEM Normal, Month 2, Below (N=159, 81)	2	0		
HEM Normal, Month 2, Above (N=159, 81)	2	0		
HEM Normal, Month 2, Missing (N=159, 81)	0	5		
HEM Normal, Month 7, Normal (N=158, 79)	147	73		
HEM Normal, Month 7, Below (N=158, 79)	9	6		
HEM Normal, Month 7, Above (N=158, 79)	2	0		
HEM Below, Month 2, Normal (N=4, 1)	3	1		
HEM Below, Month 2, Below (N=4, 1)	1	0		
HEM Below, Month 2, Above (N=4, 1)	0	0		
HEM Below, Month 7, Normal (N=4, 1)	2	1		
HEM Below, Month 7, Below (N=4, 1)	2	0		
HEM Below, Month 7, Above (N=4, 1)	0	0		
HEM Above, Month 2, Normal (N=6, 2)	3	0		
HEM Above, Month 2, Below (N=6, 2)	0	0		
HEM Above, Month 2, Above (N=6, 2)	3	1		
HEM Above, Month 2, Missing (N=6, 2)	0	1		
HEM Above, Month 7, Normal (N=6, 2)	6	1		
HEM Above, Month 7, Below (N=6, 2)	0	0		
HEM Above, Month 7, Above (N=6, 2)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters

End point title	Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters

End point description:

The occurence of clinically relevant abnormalities was assessed in the following biochemical and haematological parameters: lymphocytes [LYM], monocytes [MON], neutrophils [NEU], platelets [PLA], red blood cells [RBC] and white blood cells [WBC]. Levels of haematological/biochemical parameters assessed in terms of normal, below and above laboratory values were - normal, below, above and missing.

End point type	Secondary

End point timeframe:

At Month 2 and Month 7, post-vaccination

End point values	Cervarix Group	Engerix-B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	82		
Units: Subjects				
Lym, Normal, Month 2, Normal (N=142, 71)	117	56		
Lym, Normal, Month 2, Below (N=142, 71)	5	1		
Lym, Normal, Month 2, Above (N=142, 71)	18	6		
Lym, Normal, Month 2, Missing (N=142, 71)	2	8		
Lym, Normal, Month 7, Normal (N=142, 69)	126	63		
Lym, Normal, Month 7, Below (N=142, 69)	4	1		
Lym, Normal, Month 7, Above (N=142, 69)	12	5		
Lym, Below , Month 2, Normal (N=3, 1)	1	1		
Lym, Below , Month 2, Below (N=3, 1)	2	0		
Lym, Below , Month 2, Above (N=3, 1)	0	0		
Lym, Below , Month 7, Normal (N=3, 1)	2	1		
Lym, Below , Month 7, Below (N=3, 1)	1	0		
Lym, Below , Month 7, Above (N=3, 1)	0	0		
Lym, Above, Month 2, Normal (N=20, 10)	11	5		
Lym, Above, Month 2, Below (N=20, 10)	1	0		
Lym, Above, Month 2, Above (N=20, 10)	8	5		
Lym, Above, Month 7, Normal (N=19, 10)	11	8		
Lym, Above, Month 7, Below (N=19, 10)	0	0		
Lym, Above, Month 7, Above (N=19, 10)	8	2		
MON Normal, Month 2, Normal (N=108, 50)	92	38		
MON Normal, Month 2, Below (N=108, 50)	0	0		
MON Normal, Month 2, Above (N=108, 50)	15	5		

MON Normal, Month 2, Missing (N=108, 50)	1	7		
MON Normal, Month 7, Normal (N=108, 48)	93	43		
MON Normal, Month 7, Below (N=108, 48)	0	1		
MON Normal, Month 7, Above (N=108, 48)	15	4		
MON Below, Month 2, Normal (N=1, 3)	1	3		
MON Below, Month 2, Below (N=1, 3)	0	0		
MON Below, Month 2, Above (N=1, 3)	0	0		
MON Below, Month 7, Normal (N=1, 3)	0	3		
MON Below, Month 7, Below (N=1, 3)	1	0		
MON Below, Month 7, Above (N=1, 3)	0	0		
MON Above, Month 2, Normal (N=56, 29)	7	8		
MON Above, Month 2, Below (N=56, 29)	0	0		
MON Above, Month 2, Above (N=56, 29)	48	20		
MON Above, Month 2, Missing (N=56, 29)	1	1		
MON Above, Month 7, Normal (N=55, 29)	13	7		
MON Above, Month 7, Below (N=55, 29)	0	0		
MON Above, Month 7, Above (N=55, 29)	42	22		
NEU Normal, Month 2, Normal (N=152, 74)	130	60		
NEU Normal, Month 2, Below (N=152, 74)	20	6		
NEU Normal, Month 2, Above (N=152, 74)	0	0		
NEU Normal, Month 2, Missing (N=152, 74)	2	8		
NEU Normal, Month 7, Normal (N=152, 72)	135	63		
NEU Normal, Month 7, Below (N=152, 72)	14	8		
NEU Normal, Month 7, Above (N=152, 72)	3	1		
NEU Below, Month 2, Normal (N=13, 8)	10	5		
NEU Below, Month 2, Below (N=13, 8)	3	3		
NEU Below, Month 2, Above (N=13, 8)	0	0		
NEU Below, Month 7, Normal (N=12, 8)	8	6		
NEU Below, Month 7, Below (N=12, 8)	3	2		
NEU Below, Month 7, Above (N=12, 8)	1	0		
PLA Normal, Month 2, Normal (N=164, 78)	158	68		
PLA Normal, Month 2, Below (N=164, 78)	3	2		
PLA Normal, Month 2, Above (N=164, 78)	3	2		
PLA Normal, Month 2, Missing (N=164, 78)	0	6		
PLA Normal, Month 7, Normal (N=163, 76)	156	71		
PLA Normal, Month 7, Below (N=163, 76)	2	1		
PLA Normal, Month 7, Above (N=163, 76)	5	4		
PLA Below, Month 2, Normal (N=2, 3)	0	2		

PLA Below, Month 2, Below (N=2, 3)	2	1		
PLA Below, Month 2, Above (N=2, 3)	0	0		
PLA Below, Month 7, Normal (N=2, 3)	1	0		
PLA Below, Month 7, Below (N=2, 3)	1	2		
PLA Below, Month 7, Above (N=2, 3)	0	0		
PLA Below, Month 7, Missing (N=2, 3)	0	1		
PLA Above, Month 2, Normal (N=3, 3)	2	1		
PLA Above, Month 2, Below (N=3, 3)	0	0		
PLA Above, Month 2, Above (N=3, 3)	1	2		
PLA Above, Month 7, Normal (N=3, 3)	0	0		
PLA Above, Month 7, Below (N=3, 3)	0	0		
PLA Above, Month 7, Above (N=3, 3)	3	3		
RBC Normal, Month 2, Normal (N=154, 82)	149	75		
RBC Normal, Month 2, Below (N=154, 82)	0	0		
RBC Normal, Month 2, Above (N=154, 82)	5	2		
RBC Normal, Month 2, Missing (N=154, 82)	0	5		
RBC Normal, Month 7, Normal (N=153, 80)	148	78		
RBC Normal, Month 7, Below (N=153, 80)	2	1		
RBC Normal, Month 7, Above (N=153, 80)	3	1		
RBC Below, Month 2, Normal (N=2, 0)	2	0		
RBC Below, Month 2, Below (N=2, 0)	0	0		
RBC Below, Month 2, Above (N=2, 0)	0	0		
RBC Below, Month 7, Normal (N=2, 0)	2	0		
RBC Below, Month 7, Below (N=2, 0)	0	0		
RBC Below, Month 7, Above (N=2, 0)	0	0		
RBC Above, Month 2, Normal (N=13, 2)	7	0		
RBC Above, Month 2, Below (N=13, 2)	0	0		
RBC Above, Month 2, Above (N=13, 2)	6	1		
RBC Above, Month 2, Missing (N=13, 2)	0	1		
RBC Above, Month 7, Normal (N=13, 2)	7	0		
RBC Above, Month 7, Below (N=13, 2)	0	0		
RBC Above, Month 7, Above (N=13, 2)	6	1		
RBC Above, Month 7, Missing (N=13, 2)	0	1		
WBC Normal, Month 2, Normal (N=155, 75)	142	62		
WBC Normal, Month 2, Below (N=155, 75)	7	3		
WBC Normal, Month 2, Above (N=155, 75)	6	4		
WBC Normal, Month 2, Missing (N=155, 75)	0	6		
WBC Normal, Month 7, Normal (N=154, 73)	133	66		
WBC Normal, Month 7, Below (N=154, 73)	4	2		
WBC Normal, Month 7, Above (N=154, 73)	17	4		
WBC Normal, Month 7, Missing (N=154, 73)	0	1		
WBC Below, Month 2, Normal (N=4, 2)	4	1		

WBC Below, Month 2, Below (N=4, 2)	0	1		
WBC Below, Month 2, Above (N=4, 2)	0	0		
WBC Below, Month 7, Normal (N=4, 2)	4	2		
WBC Below, Month 7, Below (N=4, 2)	0	0		
WBC Below, Month 7, Above (N=4, 2)	0	0		
WBC Above, Month 2, Normal (N=10, 7)	10	7		
WBC Above, Month 2, Below (N=10, 7)	0	0		
WBC Above, Month 2, Above (N=10, 7)	0	0		
WBC Above, Month 7, Normal (N=10, 7)	9	6		
WBC Above, Month 7, Below (N=10, 7)	0	0		
WBC Above, Month 7, Above (N=10, 7)	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: during the 7-day (Days 0-6) post-vaccination period. Unsolicited AEs: during the 30-day (Days 0-29) post-vaccination period. SAEs: Throughout the entire study period (active phase and extended safety follow-up): up to Month 12

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Engerix-B Group

Reporting group description:

Healthy male subjects between and including 10 to 18 years of age at the time of the first vaccination, who were administered 3 doses of Engerix-B (HBV) vaccine, intramuscularly into the deltoid region of the non-dominant arm, according to a 0, 1 and 6-month schedule. The subjects were followed up for 7 months after the first dose and an additional telephone contact was foreseen at Month 12.

Reporting group title	Cervarix Group

Reporting group description:

Healthy male subjects between and including 10 to 18 years of age at the time of the first vaccination, who were administered 3 doses of Cervarix (HPV-16/18 L1 VLP AS04) vaccine, intramuscularly into the deltoid region of the non-dominant arm, according to a 0, 1 and 6-month schedule. The subjects were followed up for 7 months after the first dose and an additional telephone contact was foreseen at Month 12.

Serious adverse events	Engerix-B Group	Cervarix Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 89 (1.12%)	3 / 181 (1.66%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Epilepsy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 89 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Crohn’s disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 89 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Osteochondrosis	Additional description: This serious adverse event was recorded during the ESFU phase, which only included subjects that could have been contacted by telephone for the Safety follow-up at Month 12, hence the number of participants at risk is different.		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 89 (1.12%)	0 / 181 (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			
Appendicitis	Additional description: This serious adverse event was recorded during the ESFU phase, which only included subjects that could have been contacted by telephone for the Safety follow-up at Month 12, hence the number of participants at risk is different.		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 89 (0.00%)	1 / 181 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Engerix-B Group	Cervarix Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 89 (82.02%)	170 / 181 (93.92%)	
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	40 / 89 (44.94%)	82 / 181 (45.30%)	
occurrences (all)	56	131	
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	19 / 89 (21.35%)	39 / 181 (21.55%)	
occurrences (all)	24	56	
Pain			
subjects affected / exposed	42 / 89 (47.19%)	159 / 181 (87.85%)	
occurrences (all)	61	130	
Swelling			

subjects affected / exposed	7 / 89 (7.87%)	36 / 181 (19.89%)	
occurrences (all)	8	56	
Fatigue			
alternative assessment type: Non-systematic			
subjects affected / exposed	42 / 89 (47.19%)	82 / 181 (45.30%)	
occurrences (all)	61	130	
Gastrointestinal disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	14 / 89 (15.73%)	40 / 181 (22.10%)	
occurrences (all)	19	61	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	15 / 89 (16.85%)	51 / 181 (28.18%)	
occurrences (all)	29	87	
Rash			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 89 (5.62%)	16 / 181 (8.84%)	
occurrences (all)	5	20	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 89 (11.24%)	31 / 181 (17.13%)	
occurrences (all)	13	38	
Myalgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	23 / 89 (25.84%)	88 / 181 (48.62%)	
occurrences (all)	32	142	
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 89 (3.37%)	12 / 181 (6.63%)	
occurrences (all)	3	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 November 2006	Human papillomavirus (HPV) infection has been clearly established as the central cause of cervical cancer. GlaxoSmithKline (GSK) Biological has developed a virus-like particle (VLP) vaccine against the oncogenic types HPV-16 and HPV-18 (which are the most common oncogenic HPV types, found in approximately 70% of all cervical cancers) formulated with the AS04 adjuvant system. AS04 is comprised of aluminum salts and 3-O-desacyl-4'-monophosphoryl lipid A (MPL). This vaccine (HPV-16/18 L1/AS04) has been shown to be safe and immunogenic in previous trials, and has prevented incident and persistent HPV 16/18 infection and their associated lesions in women in study 580299/001 (HPV-001).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported