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	v1
This version publication date	11 May 2016
First version publication date	08 January 2015

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)	0
Adolescents (12-17 years)	270
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:

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: -

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: -

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: -	
Reporting group title	Engerix-B Group
Reporting group description: -	

Reporting group values	Cervarix Group	Engerix-B Group	Total
Number of subjects	181	89	270
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			
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: -	
Reporting group title	Engerix-B Group
Reporting group description: -	

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 ≥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: Anti-HPV-16 and HPV-18 antibody titers

End point title	Anti-HPV-16 and HPV-18 antibody titers[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: Anti-HPV-16 and HPV-18 antibody titers

End point title	Anti-HPV-16 and HPV-18 antibody titers

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 > 50 mm.

End point type	Secondary

End point timeframe:

Within 7 days (Day 0 - 6) after each and any vaccination

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, Overall (N=180, 88)	159	39		
Grade 3, Pain, Overall (N=180, 88)	8	0		
Redness, Overall (N=180, 88)	51	15		
Grade 3, Redness, Overall (N=180, 88)	0	0		
Swelling, Overall (N=180, 88)	36	7		
Grade 3, Swelling, Overall (N=180, 88)	2	1		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any and Grade 3 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 (Day 0 - 6) after each and any vaccination

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, Overall (N=180, 88)	29	10		
Grade 3, Arthralgia, Overall (N=180, 88)	0	1		
Related, Arthralgia, Overall (N=180, 88)	22	5		
Fatigue, Overall (N=180, 88)	82	42		
Grade 3, Fatigue, Overall (N=180, 88)	4	0		
Related, Fatigue, Overall (N=180, 88)	52	33		
Fever (axillary), Overall (N=180, 88)	35	17		
Grade 3, Fever, Overall (N=180, 88)	0	0		
Related, Fever, Overall (N=180, 88)	3	1		
Gastrointestinal, Overall (N=180, 88)	40	14		
Grade 3, Gastrointestinal, Overall (N=180, 88)	4	1		
Related, Gastrointestinal, Overall (N=180, 88)	19	7		
Headache, Overall (N=180, 88)	77	33		
Grade 3, Headache, Overall (N=180, 88)	5	1		
Realated, Headache, Overall (N=180, 88)	43	16		
Myalgia, Overall (N=180, 88)	88	23		
Grade 3, Mylagia, Overall (N=180, 88)	3	0		
Related, Mylagia, Overall (N=180, 88)	70	14		
Rash, Overall (N=180, 88)	16	5		
Grade 3, Rash, Overall (N=180, 88)	0	0		
Related, Rash, Overall (N=180, 88)	5	1		
Urticaria, Overall (N=180, 88)	4	2		
Grade 3, Urticaria, Overall (N=180, 88)	0	0		
Related, Urticaria, Overall (N=180, 88)	1	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:

Within 30 days (Day 0-29) after any vaccination

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:

End point type	Secondary

End point timeframe:

Up to Month 7 and 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:

End point type	Secondary

End point timeframe:

Up to Month 7 and 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 Alanine Transferase (Alt)

End point title	Number of subjects with clinically relevant abnormalities in Alanine Transferase (Alt)

End point description:

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	0		
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		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically relevant abnormalities in Basophils (Bas)

End point title	Number of subjects with clinically relevant abnormalities in Basophils (Bas)

End point description:

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	146	76		
Units: Subjects				
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		

Statistical analyses

No statistical analyses for this end point

Secondary: nmNumber of subjects with clinically relevant abnormalities in Eosinophils (Eos)

End point title	nmNumber of subjects with clinically relevant abnormalities in Eosinophils (Eos)

End point description:

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	125	68		
Units: Subjects				
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		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically relevant abnormalities in Hematocrit (Hem)

End point title	Number of subjects with clinically relevant abnormalities in Hematocrit (Hem)

End point description:

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	159	81		
Units: Subjects				
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 Lymphocytes (Lym)

End point title	Number of subjects with clinically relevant abnormalities in Lymphocytes (Lym)

End point description:

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	142	71		
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		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically relevant abnormalities in Monocytes (Mon)

End point title	Number of subjects with clinically relevant abnormalities in Monocytes (Mon)

End point description:

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	108	50		
Units: Subjects				
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		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically relevant abnormalities in Neutrophils (Neu)

End point title	Number of subjects with clinically relevant abnormalities in Neutrophils (Neu)

End point description:

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	152	74		
Units: Subjects				
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		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically relevant abnormalities in Platelets (Pla)

End point title	Number of subjects with clinically relevant abnormalities in Platelets (Pla)

End point description:

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	78		
Units: Subjects				
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		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically relevant abnormalities in Red Blood Cells (RBC)

End point title	Number of subjects with clinically relevant abnormalities in Red Blood Cells (RBC)

End point description:

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	154	82		
Units: Subjects				
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		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with clinically relevant abnormalities in White Blood Cells (WBC)

End point title	Number of subjects with clinically relevant abnormalities in White Blood Cells (WBC)

End point description:

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	155	75		
Units: Subjects				
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

Secondary: Number of subjects with clinically relevant abnormalities in Creatinine (Crea)

End point title	Number of subjects with clinically relevant abnormalities in Creatinine (Crea)

End point description:

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	163	82		
Units: Subjects				
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, Normal, Month 2, Normal (N=13, 5)	10	3		
Crea, Normal, Month 2, Below (N=13, 5)	0	0		
Crea, Normal, Month 2, Above (N=13, 5)	3	2		
Crea, Normal, Month 7, Normal (N=13, 5)	10	5		
Crea, Normal, Month 7, Below (N=13, 5)	0	0		

Crea, Normal, Month 7, Above (N=13, 5)	3	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited adverse events: 7 days post-vaccination. Unsolicited adverse events: 30 days post-vaccination. Serious adverse events: Throughout the study period: up to Month 12.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Cervarix Group

Reporting group description:

Subjects aged between 10 and 18 years at the time of the first vaccination, who received 3 doses of Cervarix vaccine, administered by intramuscular injection in the upper deltoid site of the left arm according to a 0, 1 and 6-month schedule and were followed up for 7 months after the first dose.

Reporting group title	Engerix-B Group

Reporting group description:

Subjects aged between 10 and 18 years at the time of the first vaccination, who received 3 doses of Engerix-B vaccine, administered by intramuscular injection in the upper deltoid site of the left arm according to a 0, 1 and 6-month schedule and were followed up for 7 months after the first dose.

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

subjects affected / exposed	0 / 181 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 181 (0.55%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cervarix Group	Engerix-B Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	159 / 181 (87.85%)	42 / 89 (47.19%)	
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 181 (0.00%)	2 / 89 (2.25%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Headache (unsolicited)			
subjects affected / exposed	17 / 181 (9.39%)	9 / 89 (10.11%)	
occurrences (all)	17	9	
Pyrexia			
subjects affected / exposed	4 / 181 (2.21%)	3 / 89 (3.37%)	
occurrences (all)	4	3	
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	159 / 181 (87.85%)	39 / 89 (43.82%)	
occurrences (all)	159	39	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	51 / 181 (28.18%)	15 / 89 (16.85%)	
occurrences (all)	51	15	
Swelling			
alternative assessment type: Systematic			

subjects affected / exposed	36 / 181 (19.89%)	7 / 89 (7.87%)	
occurrences (all)	36	7	
Headache			
subjects affected / exposed[1]	77 / 180 (42.78%)	33 / 88 (37.50%)	
occurrences (all)	77	33	
Fatigue			
subjects affected / exposed[2]	82 / 180 (45.56%)	42 / 88 (47.73%)	
occurrences (all)	82	42	
Fever (axillary)			
subjects affected / exposed[3]	35 / 180 (19.44%)	17 / 88 (19.32%)	
occurrences (all)	35	17	
Gastrointestinal			
subjects affected / exposed[4]	40 / 180 (22.22%)	14 / 88 (15.91%)	
occurrences (all)	40	14	
Mylagia			
subjects affected / exposed[5]	88 / 180 (48.89%)	23 / 88 (26.14%)	
occurrences (all)	88	23	
Rash			
subjects affected / exposed[6]	16 / 180 (8.89%)	5 / 88 (5.68%)	
occurrences (all)	16	5	
Urticaria			
subjects affected / exposed[7]	4 / 180 (2.22%)	2 / 88 (2.27%)	
occurrences (all)	4	2	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 181 (1.10%)	0 / 89 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 181 (1.10%)	0 / 89 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Pharyngolaryngeal pain			
subjects affected / exposed	8 / 181 (4.42%)	3 / 89 (3.37%)	
occurrences (all)	8	3	
Cough			

subjects affected / exposed	4 / 181 (2.21%)	4 / 89 (4.49%)	
occurrences (all)	4	4	
Epistaxis			
subjects affected / exposed	1 / 181 (0.55%)	2 / 89 (2.25%)	
occurrences (all)	1	2	
Asthma			
subjects affected / exposed	0 / 181 (0.00%)	2 / 89 (2.25%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 181 (1.10%)	2 / 89 (2.25%)	
occurrences (all)	2	2	
Neck pain			
subjects affected / exposed	3 / 181 (1.66%)	1 / 89 (1.12%)	
occurrences (all)	3	1	
Arthralgia (unsolicited)			
subjects affected / exposed	3 / 181 (1.66%)	0 / 89 (0.00%)	
occurrences (all)	3	0	
Arthralgia			
subjects affected / exposed[8]	29 / 180 (16.11%)	10 / 88 (11.36%)	
occurrences (all)	29	10	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 181 (6.63%)	3 / 89 (3.37%)	
occurrences (all)	12	3	
Acute tonsillitis			
subjects affected / exposed	0 / 181 (0.00%)	2 / 89 (2.25%)	
occurrences (all)	0	2	
Influenza			
subjects affected / exposed	2 / 181 (1.10%)	0 / 89 (0.00%)	
occurrences (all)	2	0	
Sinusitis			
subjects affected / exposed	2 / 181 (1.10%)	0 / 89 (0.00%)	
occurrences (all)	2	0	
Varicella			

subjects affected / exposed occurrences (all)	2 / 181 (1.10%) 2	0 / 89 (0.00%) 0	

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.

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