Clinical trial results:
A phase I/II, partially blind, randomized, multicentre, age-stratified, dose-range study in healthy females aged 9 - 25 years to assess the safety and immunogenicity of GlaxoSmithKline Biologicals' HPV-16/18 L1 VLP AS04 vaccine administered intramuscularly according to a 2-dose schedule (0, 2-month or 0, 6-month) when compared to a standard 3-dose schedule of GlaxoSmithKline Biologicals' HPV-16/18 L1 VLP AS04 vaccine

Summary

EudraCT number	2007-002777-32
Trial protocol	DE
Global end of trial date	18 March 2013

Results information

Result version number	v3 (current)
This version publication date	09 May 2021
First version publication date	04 April 2015
Version creation reason	• Correction of full data set Minor corrections in safety section.

Trial information

Trial identification

Sponsor protocol code	110659

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00541970
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium,
Public contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 January 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 March 2013
Global end of trial reached?	Yes
Global end of trial date	18 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunogenicity of the HPV-16/18 L1 VLP AS04 vaccine one month after the last dose when administered at different dosages (20 or 40 µg of each HPV antigen) and on different schedules (0, 2- or 0, 6-months) compared with the standard HPV-16/18 L1 VLP AS04 vaccine administered on a 3-dose schedule (0, 1, 6-months).
To evaluate the reactogenicity of the HPV-16/18 L1 VLP AS04 vaccine when administered at different dosages (20 or 40 µg of each HPV type) and on different schedules (0, 2- or 0, 6-months) with respect to the occurrence, intensity and relationship to vaccination of solicited local and general symptoms reported within 7 days (Days 0 - 6) after each and any vaccination.

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	17 October 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	60 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 479
Country: Number of subjects enrolled	Canada: 482
Worldwide total number of subjects	961
EEA total number of subjects	479

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)	961
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study included two phases, an active vaccination phase (Months 0-7) followed by a safety follow-up phase (up to the end of the study at Month 60).

Pre-assignment

Screening details:

The study was run in an open manner for subjects in the groups receiving the Cervarix vaccine on a 3-dose vaccination schedule. For subjects in the group receiving the Cervarix vaccine on a 2-dose vaccination schedule, the study was run in an observer-blind manner until Month 24, and then in an open manner.

Pre-assignment period milestones

Number of subjects started	961
Number of subjects completed	960

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 1

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 1/Placebo Group

Arm description:

Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 2, and 1 dose of placebo at Month 6. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	Cervarix
Investigational medicinal product code	
Other name	GlaxoSmithKline (GSK) Biologicals' Human Papillomavirus (HPV) vaccine 580299
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, different dosing /schedule

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

Dosage and administration details:

Intramuscular injection, different dosing /schedule

Arm title	Cervarix 1/Placebo/Cervarix 1 Group

Arm description:

Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	Cervarix
Investigational medicinal product code	
Other name	GlaxoSmithKline (GSK) Biologicals' Human Papillomavirus (HPV) vaccine 580299
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, different dosing /schedule

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

Dosage and administration details:

Intramuscular injection, different dosing /schedule

Arm title	Cervarix 2/Placebo/Cervarix 2 Group

Arm description:

Subjects received 2 doses of the Cervarix vaccine, formulation 2, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	Cervarix
Investigational medicinal product code	
Other name	GlaxoSmithKline (GSK) Biologicals' Human Papillomavirus (HPV) vaccine 580299
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, different dosing /schedule

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

Dosage and administration details:

Intramuscular injection, different dosing /schedule

Arm title	Cervarix 2 Group

Arm description:

Subjects received 3 doses of the Cervarix vaccine, formulation 2, at Month 0, Month 2 and Month 6. The Cervarix vaccine was administered intramuscularly into the deltoid of the non-dominant arm.

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

Dosage and administration details:

Intramuscular injection, different dosing /schedule

Investigational medicinal product name	Cervarix
Investigational medicinal product code	
Other name	GlaxoSmithKline (GSK) Biologicals' Human Papillomavirus (HPV) vaccine 580299
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, different dosing /schedule

Number of subjects in period 1[1]	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group
Started	240	241	240
Month 7	240	241	240
Month 12	240	241	240
Month 18	240	241	240
Month 24	240	241	240
Month 36	240	241	240
Month 48	240	241	240
Completed	162	164	158
Not completed	78	77	82
Protocol deviation	78	77	82

Number of subjects in period 1[1]	Cervarix 2 Group
Started	239
Month 7	239
Month 12	239
Month 18	239
Month 24	239
Month 36	239
Month 48	239
Completed	167
Not completed	72
Protocol deviation	72

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: Although 961 subjects were enrolled, only 960 subjects were vaccinated and started the study.

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix 1/Placebo Group
Reporting group description:	
Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 2, and 1 dose of placebo at Month 6. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.	
Reporting group title	Cervarix 1/Placebo/Cervarix 1 Group
Reporting group description:	
Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.	
Reporting group title	Cervarix 2/Placebo/Cervarix 2 Group
Reporting group description:	
Subjects received 2 doses of the Cervarix vaccine, formulation 2, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.	
Reporting group title	Cervarix 2 Group
Reporting group description:	
Subjects received 3 doses of the Cervarix vaccine, formulation 2, at Month 0, Month 2 and Month 6. The Cervarix vaccine was administered intramuscularly into the deltoid of the non-dominant arm.	

Reporting group values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group
Number of subjects	240	241	240
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			
geometric mean	17.1	17.2	17.3
standard deviation	± 4.3	± 4.3	± 4.25
Gender categorical			
Units: Subjects			
Female	240	241	240
Male	0	0	0

Reporting group values	Cervarix 2 Group	Total	
Number of subjects	239	960	

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	17.2		
standard deviation	± 4.38	-	
Gender categorical Units: Subjects			
Female	239	960	
Male	0	0	

End points

End points reporting groups

Reporting group title	Cervarix 1/Placebo Group
Reporting group description:	
Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 2, and 1 dose of placebo at Month 6. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.	
Reporting group title	Cervarix 1/Placebo/Cervarix 1 Group
Reporting group description:	
Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.	
Reporting group title	Cervarix 2/Placebo/Cervarix 2 Group
Reporting group description:	
Subjects received 2 doses of the Cervarix vaccine, formulation 2, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.	
Reporting group title	Cervarix 2 Group
Reporting group description:	
Subjects received 3 doses of the Cervarix vaccine, formulation 2, at Month 0, Month 2 and Month 6. The Cervarix vaccine was administered intramuscularly into the deltoid of the non-dominant arm.	

Primary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

End point title	Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies[1]
End point description:	
Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL).	
End point type	Primary
End point timeframe:	
One month after vaccination with the last dose of the Cervarix vaccine (Cervarix 1/Placebo Group: Month 3; Other groups: 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 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	224	206	204	208
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 [N=224;204;204;208]	5844.6 (5259.6 to 6494.7)	10500.9 (9356.9 to 11784.8)	7741.6 (6868.2 to 8726.1)	13045.3 (11211.4 to 15179.2)
Anti-HPV-18 [N=223;206;204;208]	3543.2 (3126.6 to 4015.3)	5997.5 (5310.9 to 6772.8)	4811.4 (4282.7 to 5405.3)	5087.1 (4460.2 to 5802.1)

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with report of any, and grade 3 solicited local symptoms

End point title	Number of subjects with report of any, and grade 3 solicited local symptoms[2]

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the solicited local symptom irrespective of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling larger than (>) 50 millimeters (mm).

End point type	Primary

End point timeframe:

Within 7 days (Day 0-6) after vaccination.

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 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	238	239	238	238
Units: Subjects				
Any Pain	222	225	222	225
Grade 3 Pain	18	27	26	35
Any Redness	109	112	123	145
Redness > 50 mm	3	4	1	3
Any Swelling	92	88	83	118
Swelling > 50 mm	4	3	1	5

Statistical analyses

No statistical analyses for this end point

Primary: 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[3]

End point description:

Assessed solicited general symptoms were arthralgia, fatigue, fever (defined as axillary temperature equal or above (≥) 37.5 degrees Celsius (°C), gastrointestinal symptoms, which included nausea, vomiting, diarrhoea and/or abdominal pain, headache, myalgia, rash and urticaria. Grade 3 symptoms =

symptoms that prevented normal activity. Grade 3 fever = axillary temperature ≥ 39 °C. Grade 3 urticaria = urticaria distributed on at least 4 body areas. Related symptom = symptom assessed by the investigator to be causally related to vaccination.

End point type	Primary

End point timeframe:

Within 7 days (Day 0-6) after vaccination.

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.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	238	239	238	238
Units: Subjects				
Any Arthralgia	45	57	39	43
Related Arthralgia	39	43	35	35
Grade 3 Arthralgia	0	3	4	3
Any Fatigue	100	109	104	107
Related Fatigue	76	82	87	83
Grade 3 Fatigue	11	4	5	8
Any Fever (Axillary Temperature >= 37.5°C)	23	20	22	39
Related Fever	18	15	16	27
Grade 3 Fever (Axillary Temperature >= 39.0°C)	1	0	1	0
Any Gastrointestinal Symptoms	48	48	36	68
Related Gastrointestinal Symptoms	36	43	27	50
Grade 3 Gastrointestinal Symptoms	3	7	2	7
Any Headache	101	116	112	125
Related Headache	79	81	91	95
Grade 3 Headache	9	9	7	12
Any Myalgia	79	109	98	99
Related Myalgia	62	87	75	77
Grade 3 Myalgia	3	9	6	7
Any Rash	12	12	10	15
Related Rash	8	9	8	9
Grade 3 Rash	0	0	1	1
Any Urticaria	2	4	4	5
Related Urticaria	1	3	4	3
Grade 3 Urticaria	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies.

End point title	Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human

	Papillomavirus 18 (anti-HPV-18) antibodies.[4]

End point description:

Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). The analysis was performed on the subjects who were administered a 2-dose vaccination schedule.

End point type	Secondary

End point timeframe:

At Month 3, 1 month after the second dose of vaccine or placebo

Notes:

[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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	224	206	203	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 [N=224;204;203]	5844.6 (5259.6 to 6494.7)	397.9 (337.4 to 469.2)	266.4 (227.2 to 312.4)	
Anti-HPV-18 [N=223;206;203]	3543.2 (3126.6 to 4015.3)	228.3 (196.7 to 265)	181.9 (156.8 to 211.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

End point title	Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

End point description:

Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). Groups were stratified into 3 age strata: 9-14, 15-19 and 20-25 years of age at the time of first vaccination. The 15-19 years age stratum in the group receiving the Cervarix vaccine on a 3-dose vaccination schedule was considered an active comparator.

End point type	Secondary

End point timeframe:

At Month 7, 1 month after the last dose of vaccine or placebo.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	221	206	204	208
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
9-14 years, Anti-HPV-16 [N=76;62;69;75]	2003.9 (1635.7 to 2455)	15028.4 (12611.3 to 17908.6)	11058.6 (9273.8 to 13186.7)	22066.3 (18140.7 to 26841.2)
15-19 years, Anti-HPV-16 [N=72;74;70;66]	1168.5 (957.4 to 1426.2)	10818.7 (8979.8 to 13034.2)	7869.6 (6488.9 to 9543.9)	12817.4 (9723.2 to 16896.2)
20-25 years, Anti-HPV-16 [N=73;68;65;67]	1371.2 (1092.2 to 1721.6)	7331.4 (5965.2 to 9010.4)	5209.2 (4166.5 to 6512.7)	7370 (5673.6 to 9573.6)
9-14 years, Anti-HPV-18 [N=76;64;69;75]	1134.3 (922.8 to 1394.3)	8085.8 (6654.5 to 9825)	5630.7 (4772.1 to 6643.7)	7192.9 (5952.6 to 8691.6)
15-19 years, Anti-HPV-18 [N=72;74;69;66]	719.8 (571.2 to 907)	6170.1 (5046.8 to 7543.5)	5039.3 (4283.4 to 5928.5)	4907 (3780.8 to 6368.7)
20-25 years, Anti-HPV-18 [N=72;68;66;67]	656.5 (514.6 to 837.5)	4389.6 (3525.6 to 5465.4)	3889.2 (2980.9 to 5074.3)	3576.8 (2886.5 to 4432.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

End point title	Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

End point description:

Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

At Month 12, at Month 18, at Month 24, at Month 36, and at Month 48 during the safety follow-up phase.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	216	198	195	198
Units: EL.U/mL				
geometric mean (confidence interval 95%)				

Anti-HPV-16 at Month 12 [216;191;195;198]	1064.7 (937.5 to 1209.1)	3256 (2918.8 to 3632.1)	2438.7 (2167.2 to 2744.2)	4726.7 (4036.8 to 5534.6)
Anti-HPV-16 at Month 18 [212;196;194;197]	968.1 (845.2 to 1109)	2229.4 (1983.2 to 2506.2)	1659.1 (1466.9 to 1876.4)	3185.1 (2735.1 to 3709.2)
Anti-HPV-16 at Month 24 [199;184;186;190]	821.2 (718.5 to 938.5)	1756.4 (1556.6 to 1981.9)	1285.1 (1139.6 to 1449.2)	2425.9 (2071.1 to 2841.5)
Anti-HPV-16 at Month 36 [166;158;162;153]	688.3 (592.2 to 799.9)	1462.2 (1288.8 to 1658.8)	1094 (961.1 to 1245.1)	2195.4 (1850.8 to 2604.1)
Anti-HPV-16 at Month 48 [160;151;157;148]	649.5 (556 to 758.8)	1261.2 (1106.4 to 1437.7)	953.5 (835.5 to 1088.2)	1892.3 (1594.2 to 2246)
Anti-HPV-18 at Month 12 [215;193;194;198]	472.9 (410.5 to 544.8)	1760.1 (1531.5 to 2022.8)	1426.2 (1250.8 to 1626.1)	1714.5 (1469.7 to 2000)
Anti-HPV-18 at Month 18 [211;198;193;197]	389.2 (338.7 to 447.2)	1025.2 (889 to 1182.2)	883.1 (774.7 to 1006.8)	1096.6 (939.4 to 1280.1)
Anti-HPV-18 at Month 24 [198;186;185;190]	345.9 (299.3 to 399.8)	818.2 (706.5 to 947.5)	674.6 (591.8 to 769)	866.8 (741.2 to 1013.6)
Anti-HPV-18 at Month 36 [166;160;162;153]	302.2 (254.9 to 358.2)	712.8 (605.4 to 839.3)	617.9 (532.3 to 717.2)	874.2 (734.9 to 1040)
Anti-HPV-18 at Month 48 [160;153;157;148]	260.4 (218.5 to 310.2)	626.3 (531 to 738.7)	517 (446.2 to 599.1)	723.2 (607.2 to 861.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

End point title	Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

End point description:

Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

At Month 7, 1 month after the last dose of vaccine or placebo.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	221	206	204	208
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 [N=221;204;204;208]	1483 (1311 to 1677.5)	10500.9 (9356.9 to 11784.8)	7741.6 (6868.2 to 8726.1)	13045.3 (11211.4 to 15179.2)

Anti-HPV-18 [N=220;206;204;208]	817.3 (715.6 to 933.4)	5997.5 (5310.9 to 6772.8)	4811.4 (4282.7 to 5405.3)	5087.1 (4460.2 to 5802.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents BAS results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	223	221	221	225
Units: Subjects				
BAS, PRE NORMAL [N=222;219;218;220], M7 NORMAL	219	214	208	214
BAS, PRE NORMAL [N=222;219;218;220], M7 BELOW	0	0	0	0
BAS, PRE NORMAL [N=222;219;218;220], M7 ABOVE	2	3	6	3
BAS, PRE NORMAL [N=222;219;218;220], M7 MISSING	1	2	4	3
BAS, PRE BELOW [N=0;0;1;1], M7 NORMAL	0	0	1	0
BAS, PRE BELOW [N=0;0;1;1], M7 BELOW	0	0	0	1
BAS, PRE BELOW [N=0;0;1;1], M7 ABOVE	0	0	0	0
BAS, PRE ABOVE [N=1;2;2;4], M7 NORMAL	1	2	2	4
BAS, PRE ABOVE [N=1;2;2;4], M7 BELOW	0	0	0	0
BAS, PRE ABOVE [N=1;2;2;4], M7 ABOVE	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents EOS results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	226	223	223	226
Units: Subjects				
EOS, PRE NORMAL [N=209;214;212;214], M7 NORMAL	203	207	200	205
EOS, PRE NORMAL [N=209;214;212;214], M7 BELOW	0	0	0	0
EOS, PRE NORMAL [N=209;214;212;214], M7 ABOVE	5	6	8	6
EOS, PRE NORMAL [N=209;214;212;214], M7 MISSING	1	1	4	3
EOS, PRE BELOW [N=1;2;1;0], M7 NORMAL	0	1	0	0
EOS, PRE BELOW [N=1;2;1;0], M7 BELOW	0	1	1	0
EOS, PRE BELOW [N=1;2;1;0], M7 ABOVE	1	0	0	0
EOS, PRE ABOVE [N=16;7;10;12], M7 NORMAL	8	3	3	7
EOS, PRE ABOVE [N=16;7;10;12], M7 BELOW	0	0	0	0
EOS, PRE ABOVE [N=16;7;10;12], M7 ABOVE	8	3	7	5
EOS, PRE ABOVE [N=16;7;10;12], M7 MISSING	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range.This outcome presents CREA results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	226	225	228	229
Units: Subjects				
CREA, PRE NORMAL [N=215;211;215;218], M7 NORMAL	202	200	210	206
CREA, PRE NORMAL [N=215;211;215;218], M7 BELOW	7	4	3	6
CREA, PRE NORMAL [N=215;211;215;218], M7 ABOVE	5	7	1	4
CREA, PRE NORMAL [N=215;211;215;218], M7 MISSING	1	0	1	2
CREA, PRE BELOW [N=8;7;7;6], M7 NORMAL	6	3	3	2
CREA, PRE BELOW [N=8;7;7;6], M7 BELOW	2	4	4	3
CREA, PRE BELOW [N=8;7;7;6], M7 ABOVE	0	0	0	0
CREA, PRE BELOW [N=8;7;7;6], M7 MISSING	0	0	0	1
CREA, PRE ABOVE [N=3;7;6;5], M7 NORMAL	2	4	4	2
CREA, PRE ABOVE [N=3;7;6;5], M7 BELOW	0	0	0	0
CREA, PRE ABOVE [N=3;7;6;5], M7 ABOVE	1	3	2	3

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents ALT results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	229	227	229	233
Units: Subjects				
ALT, PRE NORMAL [N=215;219;225;218], M7 NORMAL	211	211	213	209
ALT, PRE NORMAL [N=215;219;225;218], M7 BELOW	3	2	4	4
ALT, PRE NORMAL [N=215;219;225;218], M7 ABOVE	1	6	7	5
ALT, PRE NORMAL [N=215;219;225;218], M7 MISSING	0	0	1	0
ALT, PRE BELOW [N=1;3;1;4], M7 NORMAL	0	2	0	2
ALT, PRE BELOW [N=1;3;1;4], M7 BELOW	1	1	1	2
ALT, PRE BELOW [N=1;3;1;4], M7 ABOVE	0	0	0	0
ALT, PRE ABOVE [N=13;5;3;11], M7 NORMAL	9	4	1	7
ALT, PRE ABOVE [N=13;5;3;11], M7 BELOW	0	0	0	0
ALT, PRE ABOVE [N=13;5;3;11], M7 ABOVE	4	1	2	3
ALT, PRE ABOVE [N=13;5;3;11], M7 MISSING	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents Hct results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	229	228	227	233
Units: Subjects				
Hct, PRE NORMAL [N=215;208;208;217], M7 NORMAL	196	193	189	208
Hct, PRE NORMAL [N=215;208;208;217], M7 BELOW	6	5	8	2
Hct, PRE NORMAL [N=215;208;208;217], M7 ABOVE	11	8	7	6
Hct, PRE NORMAL [N=215;208;208;217], M7 MISSING	2	2	4	1
Hct, PRE BELOW [N=6;7;7;3], M7 NORMAL	3	5	4	2
Hct, PRE BELOW [N=6;7;7;3], M7 BELOW	3	2	3	1
Hct, PRE BELOW [N=6;7;7;3], M7 ABOVE	0	0	0	0
Hct, PRE ABOVE [N=8;13;12;13], M7 NORMAL	7	8	10	7
Hct, PRE ABOVE [N=8;13;12;13], M7 BELOW	0	0	0	0
Hct, PRE ABOVE [N=8;13;12;13], M7 ABOVE	1	5	2	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents LYM results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	226	223	223	227
Units: Subjects				
LYM, PRE NORMAL [N=211;211;204;213], M7 NORMAL	201	202	192	202
LYM, PRE NORMAL [N=211;211;204;213], M7 BELOW	3	0	3	1
LYM, PRE NORMAL [N=211;211;204;213], M7 ABOVE	6	7	5	7
LYM, PRE NORMAL [N=211;211;204;213], M7 MISSING	1	2	4	3
LYM, PRE BELOW [N=6;3;5;5], M7 NORMAL	4	3	3	1
LYM, PRE BELOW [N=6;3;5;5], M7 BELOW	2	0	2	2
LYM, PRE BELOW [N=6;3;5;5], M7 ABOVE	0	0	0	2
LYM, PRE ABOVE [N=9;9;14;9], M7 NORMAL	5	7	8	5
LYM, PRE ABOVE [N=9;9;14;9], M7 BELOW	0	0	1	0
LYM, PRE ABOVE [N=9;9;14;9], M7 ABOVE	4	2	5	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents MON results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	226	223	223	227
Units: Subjects				
MON, PRE NORMAL [N=217;211;211;219], M7 NORMAL	212	202	197	208
MON, PRE NORMAL [N=217;211;211;219], M7 BELOW	0	1	2	2
MON, PRE NORMAL [N=217;211;211;219], M7 ABOVE	4	6	9	6
MON, PRE NORMAL [N=217;211;211;219], M7 MISSING	1	2	3	3
MON, PRE BELOW [N=3;2;0;2], M7 NORMAL	1	1	0	2
MON, PRE BELOW [N=3;2;0;2], M7 BELOW	2	1	0	0
MON, PRE BELOW [N=3;2;0;2], M7 ABOVE	0	0	0	0
MON, PRE ABOVE [N=6;10;12;6], M7 NORMAL	5	6	6	4
MON, PRE ABOVE [N=6;10;12;6], M7 BELOW	0	0	0	0
MON, PRE ABOVE [N=6;10;12;6], M7 ABOVE	1	4	5	2
MON, PRE ABOVE [N=6;10;12;6], M7 MISSING	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents NEU results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	224	223	223	226
Units: Subjects				
NEU, PRE NORMAL [N=206;207;202;204], M7 NORMAL	184	188	185	186
NEU, PRE NORMAL [N=206;207;202;204], M7 BELOW	16	16	9	9
NEU, PRE NORMAL [N=206;207;202;204], M7 ABOVE	5	1	1	3
NEU, PRE NORMAL [N=206;207;202;204], M7 MISSING	1	2	7	6
NEU, PRE BELOW [N=11;11;16;19], M7 NORMAL	8	6	9	15
NEU, PRE BELOW [N=11;11;16;19], M7 BELOW	2	4	7	3
NEU, PRE BELOW [N=11;11;16;19], M7 ABOVE	0	0	0	0
NEU, PRE ABOVE [N=7;5;5;3], M7 NORMAL	6	5	5	1
NEU, PRE ABOVE [N=7;5;5;3], M7 BELOW	0	0	0	2
NEU, PRE ABOVE [N=7;5;5;3], M7 ABOVE	1	0	0	0
NEU, PRE BELOW [N=11;11;16;19], M7 MISSING	1	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents RBC results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	229	228	228	233
Units: Subjects				
RBC, PRE NORMAL [N=214;215;204;225], M7 NORMAL	204	204	196	213
RBC, PRE NORMAL [N=214;215;204;225], M7 BELOW	7	7	2	7
RBC, PRE NORMAL [N=214;215;204;225], M7 ABOVE	2	3	2	3
RBC, PRE NORMAL [N=214;215;204;225], M7 MISSING	1	1	4	2
RBC, PRE BELOW [N=6;6;12;4], M7 NORMAL	4	3	2	1
RBC, PRE BELOW [N=6;6;12;4], M7 BELOW	2	3	10	3
RBC, PRE BELOW [N=6;6;12;4], M7 ABOVE	0	0	0	0
RBC, PRE ABOVE [N=9;7;12;4], M7 NORMAL	5	4	6	3
RBC, PRE ABOVE [N=9;7;12;4], M7 BELOW	0	0	0	0
RBC, PRE ABOVE [N=9;7;12;4], M7 ABOVE	4	3	6	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents WBC results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	229	228	229	233
Units: Subjects				
WBC, PRE NORMAL [N=207;213;211;225], M7 NORMAL	197	199	194	212
WBC, PRE NORMAL [N=207;213;211;225], M7 BELOW	4	9	5	9
WBC, PRE NORMAL [N=207;213;211;225], M7 ABOVE	5	4	8	3
WBC, PRE NORMAL [N=207;213;211;225], M7 MISSING	1	1	4	1
WBC, PRE BELOW [N=8;9;6;4], M7 NORMAL	4	5	3	3
WBC, PRE BELOW [N=8;9;6;4], M7 BELOW	4	4	3	1
WBC, PRE BELOW [N=8;9;6;4], M7 ABOVE	0	0	0	0
WBC, PRE ABOVE [N=14;6;12;4], M7 NORMAL	10	4	9	4
WBC, PRE ABOVE [N=14;6;12;4], M7 BELOW	0	0	0	0
WBC, PRE ABOVE [N=14;6;12;4], M7 ABOVE	4	2	3	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point title	Number of subjects reporting clinically relevant abnormalities in biochemical and haematological laboratory parameters assessed.

End point description:

Assessed parameters were alanine aminotransferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), haematocritis (Hct), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC) and white blood cells (WBC). Subjects were categorized according to their results at pre-vaccination at Month 0 (PRE) which were normal, above normal or below the normal range. Per parameter and range, it was assessed whether laboratory values of the subjects were normal, above normal or below the normal range. This outcome presents PLA results.

End point type	Secondary

End point timeframe:

At Month 7 (M7)

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	226	227	228	232
Units: Subjects				
PLA, PRE NORMAL [N=211;210;215;221], M7 NORMAL	204	204	206	218
PLA, PRE NORMAL [N=211;210;215;221], M7 BELOW	1	2	3	0
PLA, PRE NORMAL [N=211;210;215;221], M7 ABOVE	5	2	2	1
PLA, PRE NORMAL [N=211;210;215;221], M7 MISSING	1	2	4	2
PLA, PRE BELOW [N=0;3;0;3], M7 NORMAL	0	0	0	1
PLA, PRE BELOW [N=0;3;0;3], M7 BELOW	0	3	0	2
PLA, PRE BELOW [N=0;3;0;3], M7 ABOVE	0	0	0	0
PLA, PRE ABOVE [N=15;14;13;8], M7 NORMAL	9	11	8	4
PLA, PRE ABOVE [N=15;14;13;8], M7 BELOW	0	0	0	0
PLA, PRE ABOVE [N=15;14;13;8], M7 ABOVE	6	3	5	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects against human Papillomavirus 16 (HPV-16) and human Papillomavirus 18 (HPV-18)

End point title	Number of seroconverted subjects against human Papillomavirus 16 (HPV-16) and human Papillomavirus 18 (HPV-18)

End point description:

Seroconversion was defined as the appearance of antibodies (i.e.titers greater than or equal to (≥) cut-off value) in the serum of subjects seronegative before vaccination. Assay cut-off was defined as ≥ 8 ELISA units per milliliter (EL.U/mL) for HPV-16, and 7 EL.U/mL for HPV-18. Seronegative subjects are subjects who had an antibody concentration below cut-off value. Cut-off values were 8 EL.U/mL for antibody concentrations against HPV-16, and 7 EL.U/mL for antibody concentrations against HPV-18.

End point type	Secondary

End point timeframe:

At Month 12, at Month 18, at Month 24, at Month 36, and at Month 48 during the safety follow-up phase.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	216	198	195	198
Units: Subjects				
Anti-HPV-16 at Month 12 [N=216;191;195;198]	194	162	172	169
Anti-HPV-16 at Month 18 [N=212;196;194;197]	192	166	172	168
Anti-HPV-16 at Month 24 [N=199;184;186;190]	185	155	165	162
Anti-HPV-16 at Month 36 [N=166;158;162;153]	156	135	146	135
Anti-HPV-16 at Month 48 [N=160;151;157;148]	149	130	139	129
Anti-HPV-18 at Month 12 [N=215;193;194;198]	187	173	166	173
Anti-HPV-18 at Month 18 [N=211;198;193;197]	184	177	166	173
Anti-HPV-18 at Month 24 [N=198;186;185;190]	173	165	159	166
Anti-HPV-18 at Month 36 [N=166;160;162;153]	144	145	139	132
Anti-HPV-18 at Month 48 [N=160;153;157;148]	138	139	135	129

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

End point title	Titers of anti-Papillomavirus 16 (anti-HPV-16) and anti-human Papillomavirus 18 (anti-HPV-18) antibodies

End point description:

Titers are given as Geometric Mean Titers (GMTs) expressed in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). The assay cut-off for Month 60 was defined as ≥ 19 ELISA units per milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

At Month 60 of the safety follow-up phase

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	137	134	131	146
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 at Month 60 [N=137;132;131;146]	658 (560.4 to 772.5)	1254 (1088.5 to 1444.8)	976.1 (846.1 to 1126.1)	1858.5 (1586.2 to 2177.6)
Anti-HPV-18 at Month 60 [N=137;134;131;146]	269.4 (223 to 325.5)	622.2 (519 to 745.9)	557.9 (473.7 to 657)	745.3 (629.3 to 882.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects against human Papillomavirus 16 (HPV-16) and human Papillomavirus 18 (HPV-18)

End point title	Number of seroconverted subjects against human Papillomavirus 16 (HPV-16) and human Papillomavirus 18 (HPV-18)

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. titers greater than or equal to (≥) cut-off value) in the serum of subjects seronegative before vaccination. Assay cut-off was defined as ≥ 19 ELISA units per milliliter (EL.U/mL). Seronegative subjects are subjects who had an antibody concentration below cut-off value.

End point type	Secondary

End point timeframe:

At Month 60 of the safety follow-up phase

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	130	122	119	127
Units: Subjects				
Anti-HPV-16 at Month 60 [N=130;114;119;127]	130	114	119	127
Anti-HPV-18 at Month 60 [N=117;122;116;125]	116	122	116	125

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with pregnancy outcomes.

End point title	Number of subjects with pregnancy outcomes.

End point description:

Pregnancy outcomes were ectopic pregnancy, elective termination with no apparent congenital anomaly (ACA), elective termination with congenital anomaly (CA), lost to follow up, pregnancy ongoing, spontaneous abortion with no ACA and live infant with no ACA.

End point type	Secondary

End point timeframe:

From Month 0 to Month 48.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	16	24	20
Units: Subjects				
Ectopic pregnancy	1	0	0	0
Elective termination with NO ACA	5	3	3	5
Elective termination with CA	0	0	1	0
Live infant with NO ACA	15	12	15	12
Lost to follow up	1	0	0	0
Pregnancy ongoing	0	1	2	2
Spontaneous abortion with NO ACA	1	0	3	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with pregnancy outcomes.

End point title	Number of subjects with pregnancy outcomes.

End point description:

Pregnancy outcomes were ectopic pregnancy, elective termination with no apparent congenital anomaly (ACA), elective termination with congenital anomaly (CA), lost to follow up, pregnancy ongoing, spontaneous abortion with no ACA and live infant with no ACA.

End point type	Secondary

End point timeframe:

Throughout the study period, from Month 0 to Month 60.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	23	30	26
Units: Subjects				
Ectopic pregnancy	1	0	0	1
Elective termination NO apparent congenital anom.	5	6	4	6
Elective termination congenital anomaly	0	0	1	0
Live infant NO apparent congenital anomaly	22	16	22	18
Lost to follow up	1	0	0	0
Molar pregnancy	1	0	0	0
Spontaneous abortion NO apparent congenital anom.	2	1	3	1

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:

An unsolicited adverse event (AE) is any adverse event (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) 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 = an event that prevented normal activity. Related = an event assessed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
Any unsolicited AE(s)	83	85	76	107
Grade 3 unsolicited AE(s)	11	8	6	14
Related unsolicited AE(s)	26	20	16	27

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Medically Significant Conditions (MSCs).

End point title	Number of subjects with Medically Significant Conditions (MSCs).

End point description:

MSCs were defined as: AEs prompting emergency room or physician visits that were not (1) related to common diseases or (2) routine visits for physical examination or vaccination, or SAEs that were not related to common diseases. The following did not require reporting as long as they were not considered SAEs and occurred more than 30 days after each vaccination: upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervicovaginal yeast infections, menstrual cycle abnormalities, injury, visits for routine physical examination or visits for vaccination.

End point type	Secondary

End point timeframe:

From Month 0 to Month 7.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
MSCs reported up to Month 7 [Units:subjects]	40	48	45	42

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Medically Significant Conditions (MSCs).

End point title	Number of subjects with Medically Significant Conditions

	(MSCs).

End point description:

MSCs were defined as: AEs prompting emergency room or physician visits that were not (1) related to common diseases or (2) routine visits for physical examination or vaccination, or SAEs that were not related to common diseases. The following did not require reporting as long as they were not considered SAEs and occurred more than 30 days after each vaccination: upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervicovaginal yeast infections, menstrual cycle abnormalities, injury, visits for routine physical examination or visits for vaccination.

End point type	Secondary

End point timeframe:

From Month 0 to Month 48.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
MSCs reported up to Month 48	79	94	88	82

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Medically Significant Conditions (MSCs).

End point title	Number of subjects with Medically Significant Conditions (MSCs).

End point description:

MSCs were defined as: AEs prompting emergency room or physician visits that were not (1) related to common diseases or (2) routine visits for physical examination or vaccination, or SAEs that were not related to common diseases. The following did not require reporting as long as they were not considered SAEs and occurred more than 30 days after each vaccination: upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervicovaginal yeast infections, menstrual cycle abnormalities, injury, visits for routine physical examination or visits for vaccination.

End point type	Secondary

End point timeframe:

Throughout the study period, from Month 0 to Month 60.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
MSCs	85	97	92	89

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with New Onset of Autoimmune Diseases (NOADs)

End point title	Number of subjects with New Onset of Autoimmune Diseases (NOADs)

End point description:

NOADs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

End point type	Secondary

End point timeframe:

From Month 0 to Month 7.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
NOADs reported up to Month 7	1	1	2	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with New Onset of Autoimmune Diseases (NOADs)

End point title	Number of subjects with New Onset of Autoimmune Diseases (NOADs)

End point description:

NOADs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

End point type	Secondary

End point timeframe:

From Month 0 to Month 48.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
NOADs reported up to Month 48	3	4	5	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with New Onset of Autoimmune Diseases (NOADs)

End point title	Number of subjects with New Onset of Autoimmune Diseases (NOADs)

End point description:

NOADs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

End point type	Secondary

End point timeframe:

Throughout the study period, from Month 0 to Month 60.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
(NOADs)	4	4	5	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with New Onset of Chronic Diseases (NOCDs)

End point title	Number of subjects with New Onset of Chronic Diseases (NOCDs)

End point description:

NOCDs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

End point type	Secondary

End point timeframe:

From Month 0 to Month 7.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
NOCDs reported up to Month 7	4	2	6	3

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with New Onset of Chronic Diseases (NOCDs)

End point title	Number of subjects with New Onset of Chronic Diseases (NOCDs)

End point description:

NOCDs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

End point type	Secondary

End point timeframe:

From Month 0 to Month 48.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
NOCDs reported up to Month 48	8	11	13	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with New Onset of Chronic Diseases (NOCDs)

End point title	Number of subjects with New Onset of Chronic Diseases (NOCDs)

End point description:

NOCDs include conditions such as autoimmune disorders, asthma, type I diabetes, or allergies.

End point type	Secondary

End point timeframe:

Throughout the study period, from Month 0 to Month 60.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
(NOCDs)	8	11	14	7

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:

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.

End point type	Secondary

End point timeframe:

From Month 0 to Month 7.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
SAE(s) up to Month 7	4	4	4	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:

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.

End point type	Secondary

End point timeframe:

From Month 0 to Month 48.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
SAEs up to Month 48	10	13	19	13

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:

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.

End point type	Secondary

End point timeframe:

Throughout the study period, from Month 0 to Month 60.

End point values	Cervarix 1/Placebo Group	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	241	240	239
Units: Subjects				
(SAEs)	14	16	19	15

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events: From Month 0 to Month 60. Unsolicited adverse events: Within the 30-day (Days 0-29) follow-up period after vaccination. Solicited symptoms: Within the 7-day (Days 0-6) follow-up period after vaccination.

Adverse event reporting additional description:

3 among the serious adverse events (SAEs) listed below are SAEs reported for the subject's offsprings (Spina bifida, Foetal distress syndrome and Premature baby).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Cervarix 1/Placebo/Cervarix 1 Group

Reporting group description:

Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

Reporting group title	Cervarix 2/Placebo/Cervarix 2 Group

Reporting group description:

Subjects received 2 doses of the Cervarix vaccine, formulation 2, at Month 0 and Month 6, and 1 dose of placebo at Month 2. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

Reporting group title	Cervarix 2 Group

Reporting group description:

Subjects received 3 doses of the Cervarix vaccine, formulation 2, at Month 0, Month 2 and Month 6. The Cervarix vaccine was administered intramuscularly into the deltoid of the non-dominant arm.

Reporting group title	Cervarix 1/Placebo Group

Reporting group description:

Subjects received 2 doses of the Cervarix vaccine, formulation 1, at Month 0 and Month 2, and 1 dose of placebo at Month 6. The Cervarix vaccine and placebo were administered intramuscularly into the deltoid of the non-dominant arm.

Serious adverse events	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 241 (6.64%)	19 / 240 (7.92%)	15 / 239 (6.28%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroma			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Fibrosarcoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Malignant melanoma stage IV			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Uterine leiomyoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign hydatidiform mole			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	1 / 240 (0.42%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Abortion spontaneous incomplete			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	2 / 240 (0.83%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ectopic pregnancy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal distress syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Pre-eclampsia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Premature baby			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Abortion missed			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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

Reproductive system and breast disorders			
Adenomyosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hyperventilation			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorexia nervosa			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Bulimia nervosa			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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

Depression			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	1 / 240 (0.42%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Psychotic disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Suicide attempt			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Injury, poisoning and procedural complications			
Concussion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Ligament rupture			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Tibia fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	1 / 240 (0.42%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Fall			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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

Stab wound			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Atrial septal defect			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Spina bifida			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Basilar artery thrombosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Cerebrovascular accident			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Migraine with aura			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendix disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia, obstructive			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 241 (0.83%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Hepatobiliary disorders			
Bile duct stone			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Cholecystitis acute			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Hepatomegaly			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema multiforme			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Cystitis haemorrhagic			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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 colic			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal disorder			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Basedow’s disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Coccydynia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament laxity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyarthritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Appendicitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	2 / 241 (0.83%)	4 / 240 (1.67%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis decidual			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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
Pharyngitis streptococcal			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	0 / 239 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	2 / 239 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis bacterial			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	1 / 240 (0.42%)	0 / 239 (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
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 241 (0.00%)	0 / 240 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vestibular neuronitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 241 (0.41%)	0 / 240 (0.00%)	0 / 239 (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

Serious adverse events	Cervarix 1/Placebo Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 240 (5.83%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fibrosarcoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma stage IV			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Benign hydatidiform mole			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 240 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Circulatory collapse				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
Abortion spontaneous				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 240 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abortion spontaneous incomplete				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ectopic pregnancy				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 240 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Foetal distress syndrome				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pre-eclampsia				
alternative assessment type: Non-systematic				

subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Premature baby			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abortion missed			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Adenomyosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hyperventilation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal behaviour			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anorexia nervosa				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bulimia nervosa				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Major depression				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychotic disorder				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Injury, poisoning and procedural complications			
Concussion			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ligament rupture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multiple injuries			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Contusion				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fall				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stab wound				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 240 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Atrial septal defect				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spina bifida				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Basilar artery thrombosis				
alternative assessment type: Non-systematic				

subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Migraine with aura				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
alternative assessment type: Non-systematic				
subjects affected / exposed	3 / 240 (1.25%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Appendix disorder				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia, obstructive				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
alternative assessment type: Non-systematic				

subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Bile duct stone				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatomegaly				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 240 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Erythema multiforme				
alternative assessment type: Non-systematic				

subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Cystitis haemorrhagic			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal colic			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Basedow’s disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Coccydynia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ligament laxity			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Polyarthritis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Acute tonsillitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endometritis decidual				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis streptococcal				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pilonidal cyst				
alternative assessment type: Non-systematic				

subjects affected / exposed	1 / 240 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis bacterial				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 240 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 240 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vestibular neuronitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 240 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Cervarix 1/Placebo/Cervarix 1 Group	Cervarix 2/Placebo/Cervarix 2 Group	Cervarix 2 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	233 / 241 (96.68%)	228 / 240 (95.00%)	233 / 239 (97.49%)
General disorders and administration site conditions			
Pain			

subjects affected / exposed	225 / 241 (93.36%)	222 / 240 (92.50%)	225 / 239 (94.14%)
occurrences (all)	225	222	225
Redness			
subjects affected / exposed	112 / 241 (46.47%)	123 / 240 (51.25%)	145 / 239 (60.67%)
occurrences (all)	112	123	145
Swelling			
subjects affected / exposed	88 / 241 (36.51%)	83 / 240 (34.58%)	118 / 239 (49.37%)
occurrences (all)	88	83	118
Arthralgia			
subjects affected / exposed	57 / 241 (23.65%)	39 / 240 (16.25%)	43 / 239 (17.99%)
occurrences (all)	57	39	43
Fatigue			
alternative assessment type: Non-systematic			
subjects affected / exposed	109 / 241 (45.23%)	104 / 240 (43.33%)	107 / 239 (44.77%)
occurrences (all)	109	104	107
Fever			
subjects affected / exposed	20 / 241 (8.30%)	22 / 240 (9.17%)	39 / 239 (16.32%)
occurrences (all)	20	22	39
Gastrointestinal			
subjects affected / exposed	48 / 241 (19.92%)	36 / 240 (15.00%)	68 / 239 (28.45%)
occurrences (all)	48	36	68
Headache			
subjects affected / exposed	116 / 241 (48.13%)	112 / 240 (46.67%)	125 / 239 (52.30%)
occurrences (all)	116	112	125
Rash			
alternative assessment type: Non-systematic			
subjects affected / exposed	12 / 241 (4.98%)	10 / 240 (4.17%)	15 / 239 (6.28%)
occurrences (all)	12	10	15
Gastrointestinal disorders			
Myalgia			
subjects affected / exposed	109 / 241 (45.23%)	98 / 240 (40.83%)	99 / 239 (41.42%)
occurrences (all)	109	98	99
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	11 / 241 (4.56%)	9 / 240 (3.75%)	15 / 239 (6.28%)
occurrences (all)	11	9	15

Non-serious adverse events	Cervarix 1/Placebo Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	229 / 240 (95.42%)		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	222 / 240 (92.50%)		
occurrences (all)	222		
Redness			
subjects affected / exposed	109 / 240 (45.42%)		
occurrences (all)	109		
Swelling			
subjects affected / exposed	92 / 240 (38.33%)		
occurrences (all)	92		
Arthralgia			
subjects affected / exposed	45 / 240 (18.75%)		
occurrences (all)	45		
Fatigue			
alternative assessment type: Non-systematic			
subjects affected / exposed	100 / 240 (41.67%)		
occurrences (all)	100		
Fever			
subjects affected / exposed	23 / 240 (9.58%)		
occurrences (all)	23		
Gastrointestinal			
subjects affected / exposed	48 / 240 (20.00%)		
occurrences (all)	48		
Headache			
subjects affected / exposed	101 / 240 (42.08%)		
occurrences (all)	101		
Rash			
alternative assessment type: Non-systematic			

subjects affected / exposed occurrences (all)	12 / 240 (5.00%) 12		
Gastrointestinal disorders Myalgia subjects affected / exposed occurrences (all)	 79 / 240 (32.92%) 79		
Infections and infestations Nasopharyngitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	 10 / 240 (4.17%) 10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 June 2009	Amendment 1 • In the purpose of collecting long-term immunogenicity and safety data for the HPV-16/18 L1 VLP AS04 vaccine in an alternative 2-dose schedule versus the 3-dose schedule, the study was extended by three years to include three additional visits planned for Months 36, 48 and 60. • The protocol was amended to allow subjects who miss one or more follow-up study visits to be invited to attend the next visit. • Administrative changes were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported