Clinical trial results:
A phase IIIb open, randomized multi-center study to evaluate the immunogenicity and safety of GSK Biologicals HPV-16/18 L1 VLP AS04 vaccine when administered intramuscularly according to an alternative dosing schedule at, 0, 1 and 12 months as compared to the standard dosing schedule at 0, 1 and 6 months in young healthy female subjects aged 15-25 years.

Summary

EudraCT number	2007-003256-11
Trial protocol	IT SK
Global end of trial date	20 July 2009

Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	21 May 2015

Trial information

Trial identification

Sponsor protocol code	109179 (HPV-044 PRI)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00552279
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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	10 November 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 February 2009
Global end of trial reached?	Yes
Global end of trial date	20 July 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the immunogenicity of GSK Biologicals HPV-16/18 L1 VLP AS04 vaccine administered according to an alternative schedule of 0, 1, 12 months is non-inferior to that of the vaccine administered according to a standard schedule of 0, 1, 6 months one month after the third dose.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed-up for 30 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 November 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovakia: 268
Country: Number of subjects enrolled	Italy: 269
Country: Number of subjects enrolled	Romania: 268
Worldwide total number of subjects	805
EEA total number of subjects	805

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)	402
Adults (18-64 years)	403
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 805 subjects were enrolled and 804 subjects were vaccinated and included in the analyses.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervarix-12 Group

Arm description:

Women received 3 doses of Cervarix™ (human papillomavirus [HPV] vaccine) administered according to a 0, 1, 12-month schedule.

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

Dosage and administration details:

Intramuscular administration into the deltoid region of the non-dominant arm according to a 0, 1, 12-month schedule.

Arm title	Cervarix-6 Group

Arm description:

Women received 3 doses of Cervarix TM (HPV vaccine) administered according to a 0, 1, 6-month schedule.

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

Dosage and administration details:

Intramuscular administration into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule.

Number of subjects in period 1[1]	Cervarix-12 Group	Cervarix-6 Group
Started	403	401
Completed	389	398
Not completed	14	3
Consent withdrawn by subject	12	1
Adverse event, non-fatal	-	1
Other	1	1
Migrated/moved from study area	1	-

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: A total of 805 subjects were enrolled and only 804 subjects were vaccinated and included in the analyses.

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix-12 Group
Reporting group description:	
Women received 3 doses of Cervarix™ (human papillomavirus [HPV] vaccine) administered according to a 0, 1, 12-month schedule.	
Reporting group title	Cervarix-6 Group
Reporting group description:	
Women received 3 doses of Cervarix TM (HPV vaccine) administered according to a 0, 1, 6-month schedule.	

Reporting group values	Cervarix-12 Group	Cervarix-6 Group	Total
Number of subjects	403	401	804
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			
arithmetic mean	18.6	18.7	
standard deviation	± 2.98	± 3.13	-
Gender categorical			
Units: Subjects			
Female	403	401	804
Male	0	0	0

End points

End points reporting groups

Reporting group title	Cervarix-12 Group
Reporting group description:	
Women received 3 doses of Cervarix™ (human papillomavirus [HPV] vaccine) administered according to a 0, 1, 12-month schedule.	
Reporting group title	Cervarix-6 Group
Reporting group description:	
Women received 3 doses of Cervarix TM (HPV vaccine) administered according to a 0, 1, 6-month schedule.	

Primary: Number of Subjects Seroconverted for Anti-human Papilloma Virus 16 (Anti-HPV-16) and Anti-human Papilloma Virus 18 (Anti-HPV-18) Antibodies.

End point title	Number of Subjects Seroconverted for Anti-human Papilloma Virus 16 (Anti-HPV-16) and Anti-human Papilloma Virus 18 (Anti-HPV-18) Antibodies.
End point description:	
Seroconversion is defined as the appearance of anti-HPV-16 and/or anti- HPV-18 antibodies (i.e. antibody titer ≥ cut-off value) in the sera of subjects seronegative before vaccination. Cut-off values were 8 enzyme-linked immunosorbent assay units per milliliter (EL.U/mL) for anti-HPV-16 antibodies and 7 EL.U/mL for anti- HPV-18 antibodies.	
End point type	Primary
End point timeframe:	
One month after the third vaccine dose.	

End point values	Cervarix-12 Group	Cervarix-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	346	346		
Units: Subjects				
Anti-HPV-16 (N=337;342)	337	342		
Anti-HPV-18 (N=346;346)	345	346		

Statistical analyses

Statistical analysis title	Difference in seroconversion rates
Comparison groups	Cervarix-12 Group v Cervarix-6 Group
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Risk difference (RD)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.11
upper limit	1.13

Statistical analysis title	Difference in seroconversion rates
Comparison groups	Cervarix-12 Group v Cervarix-6 Group
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Risk difference (RD)
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	1.62

Primary: Titer of Anti-HPV-16 and Anti-HPV-18 Antibodies.

End point title	Titer of Anti-HPV-16 and Anti-HPV-18 Antibodies.
End point description:	
Titer given as geometric mean titer (GMT).	
End point type	Primary
End point timeframe:	
One month after the third vaccine dose.	

End point values	Cervarix-12 Group	Cervarix-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	346	346		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (N=337;342)	11337.2 (10238.2 to 12554.1)	10050.9 (9180.9 to 11003.3)		
Anti-HPV-18 (N=346;346)	4526.7 (4110.1 to 4985.6)	3879.9 (3532.7 to 4261.2)		

Statistical analyses

Statistical analysis title	Non-inferiority analysis for HPV-16 & HPV-18
Comparison groups	Cervarix-12 Group v Cervarix-6 Group
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Risk ratio (RR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1

Statistical analysis title	Non-inferiority analysis for HPV-16 & HPV-18
Comparison groups	Cervarix-12 Group v Cervarix-6 Group
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Risk ratio (RR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.01

Secondary: Number of Subjects Seroconverted for Anti-HPV-16 and Anti-HPV-18 Antibodies.

End point title	Number of Subjects Seroconverted for Anti-HPV-16 and Anti-HPV-18 Antibodies.

End point description:

Seroconversion is defined as the appearance of anti-HPV-16 and/or anti- HPV-18 antibodies (i.e. antibody titer ≥ cut-off value) in the sera of subjects seronegative before vaccination. Cut-off values were 8 enzyme-linked immunosorbent assay units per milliliter (EL.U/mL) for anti-HPV-16 antibodies and 7 EL.U/mL for anti- HPV-18 antibodies.

End point type	Secondary

End point timeframe:

One month after the second vaccine dose.

End point values	Cervarix-12 Group	Cervarix-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	346	346		
Units: Subjects				
Anti-HPV-16 (N=337;342)	337	342		
Anti-HPV-18 (N=346;346)	346	346		

Statistical analyses

No statistical analyses for this end point

Secondary: Titer of Anti-HPV-16 and Anti-HPV-18 Antibodies.

End point title	Titer of Anti-HPV-16 and Anti-HPV-18 Antibodies.
End point description:	
Titer given as GMT.	
End point type	Secondary
End point timeframe:	
One month after the second vaccine dose.	

End point values	Cervarix-12 Group	Cervarix-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	346	346		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (N=337;342)	3307 (3051 to 3584.5)	3184.1 (2938.3 to 3450.5)		
Anti-HPV-18 (N=346;346)	2382.3 (2179.2 to 2604.3)	2256.3 (2070.7 to 2458.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Solicited Local Symptoms.

End point title	Number of Subjects Reporting Solicited Local Symptoms.
End point description:	
Solicited local symptoms assessed include pain, redness and swelling at the injection site.	
End point type	Secondary
End point timeframe:	
During the 7-day (Days 0-6) period following each vaccination.	

End point values	Cervarix-12 Group	Cervarix-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402	401		
Units: Subjects				
Any pain, D1	362	367		
Any redness, D1	100	99		
Any swelling, D1	57	63		
Any pain, D2	337	354		
Any redness, D2	119	99		
Any swelling, D2	74	74		
Any pain, D3	326	335		
Any redness, D3	145	127		
Any swelling, D3	120	101		
Any pain, overall	385	386		
Any redness, overall	201	182		
Any swelling, overall	158	145		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Solicited General Symptoms.

End point title	Number of Subjects Reporting Solicited General Symptoms.

End point description:

Solicited general symptoms assessed include arthralgia, fatigue, fever, gastrointestinal symptoms, headache, myalgia, rash, and urticaria.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix-12 Group	Cervarix-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402	401		
Units: Subjects				
Any arthralgia, D1	41	36		
Any fatigue, D1	175	174		
Any temperature ≥ 37.5°C, D1	9	9		
Any gastro-intestinal symptoms, D1	45	58		
Any headache, D1	128	126		
Any myalgia, D1	105	116		
Any rash, D1	12	18		

Any urticaria, D1	6	13		
Any arthralgia, D2	29	34		
Any fatigue, D2	150	147		
Any temperature ≥ 37.5°C, D2	16	12		
Any gastro-intestinal symptoms, D2	30	35		
Any headache, D2	104	114		
Any myalgia, D2	87	94		
Any rash, D2	11	13		
Any urticaria, D2	3	6		
Any arthralgia, D3	43	44		
Any fatigue, D3	157	143		
Any temperature ≥ 37.5°C, D3	12	12		
Any gastro-intestinal symptoms, D3	32	22		
Any headache, D3	119	110		
Any myalgia, D3	109	103		
Any rash, D3	15	15		
Any urticaria, D3	5	3		
Any arthralgia, overall	85	78		
Any fatigue, overall	245	237		
Any temerature ≥ 37.5°C, overall	37	29		
Any gastro-intestinal symptoms, overall	85	86		
Any headache, overall	203	199		
Any myalgia, overall	167	168		
Any rash, overall	30	34		
Any urticaria, overall	12	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Unsolicited Adverse Events (AE).

End point title	Number of Subjects Reporting Unsolicited Adverse Events (AE).

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix-12 Group	Cervarix-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	401		
Units: Subjects				
Any AE(s)	117	129		
Grade 3 AE(s)	8	8		
Related AE(s)	6	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting New Onset of Chronic Diseases (NOCDs), New Onset autoimmune diseases (NOADs), serious adverse events (SAEs), and Medically Significant Conditions (MSCs).

End point title	Number of Subjects Reporting New Onset of Chronic Diseases (NOCDs), New Onset autoimmune diseases (NOADs), serious adverse events (SAEs), and Medically Significant Conditions (MSCs).

End point description:

Entire study period = up to Month 18 Cervarix-12 & Month 12 Cervarix-6. NOCDs assessed include eg. autoimmune disorders (NOADs), asthma, type I diabetes. MSCs assessed include AEs prompting emergency room visits and physician office visits not related to common illnesses. An SAE is any untoward medical occurrence that: results in death, is lifethreatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

End point type	Secondary

End point timeframe:

During the entire study period (up to Month 18 or up to Month 12).

End point values	Cervarix-12 Group	Cervarix-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	401		
Units: Subjects				
MSCs	42	44		
NOCDs	0	5		
NOADs	0	2		
SAEs	12	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with pregnancies and their outcomes.

End point title	Number of subjects with pregnancies and their outcomes.

End point description:

Entire study period = up to Month 18 Cervarix-12 & Month 12 Cervarix-6 Number of pregnancies and pregnancy outcomes.

End point type	Secondary

End point timeframe:

During the entire study period (up to Month 18 or Month 12).

End point values	Cervarix-12 Group	Cervarix-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	3		
Units: Subjects				
Normal infant	2	1		
Elective abortion	0	2		
Abortion threatened	1	0		
Ongoing	1	0		
Foetal distress syndrome	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects completing the 3-dose vaccination schedule.

End point title	Number of subjects completing the 3-dose vaccination schedule.

End point description:

End point type	Secondary

End point timeframe:

After the third vaccine dose.

End point values	Cervarix-12 Group	Cervarix-6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	401		
Units: Subjects				
D3	388	397		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

- Solicited local and general symptoms: during the 7 day - (Day 0-Day 6) after each vaccination.
- Unsolicited adverse events: during the 30 day (Day 0 - Day 29) after each vaccination.
- Serious adverse event: up to Month 12 and up to Month 18.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Cervarix-12 Group

Reporting group description:

Women received 3 doses of Cervarix™ (human papillomavirus [HPV] vaccine) administered according to a 0, 1, 12-month schedule.

Reporting group title	Cervarix-6 Group

Reporting group description:

Women received 3 doses of Cervarix™ (HPV vaccine) administered according to a 0, 1, 6-month schedule.

Serious adverse events	Cervarix-12 Group	Cervarix-6 Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 403 (2.98%)	9 / 401 (2.24%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer female			
subjects affected / exposed	0 / 403 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion threatened			

subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cephalhaematoma			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal distress syndrome			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Cyst			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Brain hypoxia			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 403 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			

subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 403 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 403 (0.50%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 403 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Thyroiditis			

subjects affected / exposed	0 / 403 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Chondropathy			
subjects affected / exposed	0 / 403 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 403 (0.50%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 403 (0.00%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 403 (0.25%)	1 / 401 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheitis			
subjects affected / exposed	1 / 403 (0.25%)	0 / 401 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cervarix-12 Group	Cervarix-6 Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	385 / 403 (95.53%)	386 / 401 (96.26%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	385 / 403 (95.53%)	386 / 401 (96.26%)	
occurrences (all)	385	386	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	201 / 403 (49.88%)	182 / 401 (45.39%)	
occurrences (all)	201	182	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	158 / 403 (39.21%)	145 / 401 (36.16%)	
occurrences (all)	158	145	
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	85 / 403 (21.09%)	78 / 401 (19.45%)	
occurrences (all)	85	78	
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	245 / 403 (60.79%)	237 / 401 (59.10%)	
occurrences (all)	245	237	
Temperature ≥ 37.5°C			
alternative assessment type: Systematic			
subjects affected / exposed	37 / 403 (9.18%)	29 / 401 (7.23%)	
occurrences (all)	37	29	
Gastrointestinal symptoms			

alternative assessment type: Systematic			
subjects affected / exposed	85 / 403 (21.09%)	86 / 401 (21.45%)	
occurrences (all)	85	86	
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	203 / 403 (50.37%)	199 / 401 (49.63%)	
occurrences (all)	203	199	
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	167 / 403 (41.44%)	168 / 401 (41.90%)	
occurrences (all)	167	168	
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 403 (7.44%)	34 / 401 (8.48%)	
occurrences (all)	30	34	
Urticaria			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 403 (2.98%)	18 / 401 (4.49%)	
occurrences (all)	12	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported