Clinical trial results:
A Phase IIIb open-label, randomised, multi-centre primary immunization study to evaluate the immunogenicity and safety of GSK Biologicals' HPV-16/18 L1 VLP AS04 vaccine when administered intramuscularly according to alternative 2-dose schedules in 9 - 14 year old healthy females compared to the standard 3-dose schedule for GSK Biologicals' HPV-16/18 L1 VLP AS04 vaccine in 15 - 25 year old healthy females

Summary

EudraCT number	2011-000757-22
Trial protocol	DE IT
Global end of trial date	13 November 2014

Results information

Result version number	v3 (current)
This version publication date	04 June 2020
First version publication date	28 May 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	114700

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01381575
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	07 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 June 2012
Global end of trial reached?	Yes
Global end of trial date	13 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the immunogenicity (as determined by [enzyme-linked immunosorbent assay] ELISA) of GSK Biologicals' HPV-16/18 L1 VLP AS04 vaccine administered according to a 2-dose schedule of 0,6 months in 9-14-year old females is non-inferior to that administered according to the standard 3-dose schedule of 0,1,6 months in 15-25-year old females,1 month after the last dose of study vaccine.

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	29 June 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 190
Country: Number of subjects enrolled	Taiwan: 318
Country: Number of subjects enrolled	Thailand: 314
Country: Number of subjects enrolled	Germany: 325
Country: Number of subjects enrolled	Italy: 300
Worldwide total number of subjects	1447
EEA total number of subjects	625

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	0

months)	
Children (2-11 years)	476
Adolescents (12-17 years)	628
Adults (18-64 years)	343
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted by 33 principal investigators in five countries (Canada, Germany, Italy, Taiwan and Thailand).

Pre-assignment

Screening details:

All 1447 subjects enrolled in the study were vaccinated and included in the Total vaccinated cohort (TVC).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervarix 1 Group

Arm description:

Female subjects aged 9 to 14 years at the time of the first vaccination, who received 2 doses of the Cervarix vaccine at Day 0 and at Month 6, respectively. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals' HPV vaccine 580299
Investigational medicinal product code	
Other name	Cervarix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses of HPV vaccine administered intramuscularly.

Arm title	Cervarix 2 Group

Arm description:

Female subjects aged 15 to 25 years at the time of the first vaccination, who received 3 doses of the Cervarix vaccine at Day 0, at Month 1 and at Month 6, respectively. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.

Arm type	Active comparator
Investigational medicinal product name	GSK Biologicals' HPV vaccine 580299
Investigational medicinal product code	
Other name	Cervarix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 doses of HPV vaccine administered intramuscularly.

Arm title	Cervarix 3 Group

Arm description:

Female subjects aged 9 to 14 years at the time of the first vaccination, who received 2 doses of the Cervarix vaccine at Day 0 and at Month 12, respectively. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.

Arm type	Experimental

Investigational medicinal product name	GSK Biologicals' HPV vaccine 580299
Investigational medicinal product code	
Other name	Cervarix
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses of HPV vaccine administered intramuscularly.

Number of subjects in period 1	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group
Started	550	482	415
Completed	524	443	395
Not completed	26	39	20
Consent withdrawn by subject	15	9	7
Non-Serious Adverse Event	-	-	1
Migrated/moved from study area	2	12	2
Lost to follow-up	8	17	9
Serious Adverse Event	1	-	-
Protocol deviation	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix 1 Group
Reporting group description:	
Female subjects aged 9 to 14 years at the time of the first vaccination, who received 2 doses of the Cervarix vaccine at Day 0 and at Month 6, respectively. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.	
Reporting group title	Cervarix 2 Group
Reporting group description:	
Female subjects aged 15 to 25 years at the time of the first vaccination, who received 3 doses of the Cervarix vaccine at Day 0, at Month 1 and at Month 6, respectively. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.	
Reporting group title	Cervarix 3 Group
Reporting group description:	
Female subjects aged 9 to 14 years at the time of the first vaccination, who received 2 doses of the Cervarix vaccine at Day 0 and at Month 12, respectively. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.	

Reporting group values	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group
Number of subjects	550	482	415
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	264	0	212
Adolescents (12-17 years)	286	139	203
Adults (18-64 years)	0	343	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	11.6	19.6	11.4
standard deviation	± 1.59	± 3.05	± 1.55
Sex: Female, Male Units: Subjects			
Female	550	482	415
Male	0	0	0
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	6	3	6
Asian - Central/South Asian Heritage	1	1	4
Asian - East Asian Heritage	141	105	74
Asian - South East Asian Heritage	108	106	104
White - Arabic / North African Heritage	1	0	1

White - Caucasian / European Heritage	288	263	223
Mixed origin	5	4	3

Reporting group values	Total		
Number of subjects	1447		
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)	476		
Adolescents (12-17 years)	628		
Adults (18-64 years)	343		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	1447		
Male	0		
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	15		
Asian - Central/South Asian Heritage	6		
Asian - East Asian Heritage	320		
Asian - South East Asian Heritage	318		
White - Arabic / North African Heritage	2		
White - Caucasian / European Heritage	774		
Mixed origin	12		

End points

End points reporting groups

Reporting group title	Cervarix 1 Group
Reporting group description:	
Female subjects aged 9 to 14 years at the time of the first vaccination, who received 2 doses of the Cervarix vaccine at Day 0 and at Month 6, respectively. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.	
Reporting group title	Cervarix 2 Group
Reporting group description:	
Female subjects aged 15 to 25 years at the time of the first vaccination, who received 3 doses of the Cervarix vaccine at Day 0, at Month 1 and at Month 6, respectively. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.	
Reporting group title	Cervarix 3 Group
Reporting group description:	
Female subjects aged 9 to 14 years at the time of the first vaccination, who received 2 doses of the Cervarix vaccine at Day 0 and at Month 12, respectively. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.	

Primary: Number of seroconverted subjects for Anti- Human Papilloma virus 16 (Anti-HPV-16) and Anti-Human Papilloma Virus 18 (Anti-HPV-18) antibodies in Cervarix 1 Group and Cervarix 2 Group at Month 7

End point title	Number of seroconverted subjects for Anti- Human Papilloma virus 16 (Anti-HPV-16) and Anti-Human Papilloma Virus 18 (Anti-HPV-18) antibodies in Cervarix 1 Group and Cervarix 2 Group at Month 7[1]
End point description:	
Seroconversion was defined as the appearance of antibodies (anti-HPV-16 concentrations greater than or equal to (≥) 8 enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL) and anti-HPV-18 concentrations ≥ 7 EL.U/mL) in the serum of subjects seronegative before vaccination. A seronegative subject was a subject with anti-HPV-16/18 antibody concentration lower than (<) 8/7 EL.U/mL, respectively.	
End point type	Primary
End point timeframe:	
At Month 7 (i.e. one month after the last dose of study vaccine)	

Notes:

[1] - 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: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 1 Group	Cervarix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	493	382		
Units: Subjects				
Anti-HPV-16 (N=488, 352)	488	352		
Anti-HPV-18 (N=493, 382)	493	382		

Statistical analyses

Statistical analysis title	Immune response to anti-HPV-16 in terms of SCR

Statistical analysis description:

Immune response to anti-HPV-16 in terms of seroconversion (SCR) rates: To evaluate sequentially if the immunogenicity (as determined by ELISA) of Cervarix vaccine administered according to a 2-dose schedule of 0,6 months in 9-14 year old females was non-inferior to that administered according to the standard 3-dose schedule of 0,1,6 months in 15-25 year old females, 1 month after the last dose of study vaccine, in initially seronegative subjects.

Comparison groups	Cervarix 1 Group v Cervarix 2 Group
Number of subjects included in analysis	875
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in SCR
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	0.78

Notes:

[2] - Non-inferiority with respect to seroconversion was demonstrated if, 1 month after the last dose, for both anti-HPV-16 and anti-HPV-18, the upper limit of the 95% Confidence Interval (CI) for the difference (Cervarix 2 Group minus Cervarix 1 Group) was below 5%.

Statistical analysis title	Immune response to anti-HPV-18 in terms of SCR

Statistical analysis description:

Immune response to anti-HPV-18 in terms of seroconversion (SCR) rates: To evaluate sequentially if the immunogenicity (as determined by ELISA) of Cervarix vaccine administered according to a 2-dose schedule of 0,6 months in 9-14 year old females was non-inferior to that administered according to the standard 3-dose schedule of 0,1,6 months in 15-25 year old females, 1 month after the last dose of study vaccine, in initially seronegative subjects.

Comparison groups	Cervarix 1 Group v Cervarix 2 Group
Number of subjects included in analysis	875
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in SCR
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.77

Notes:

[3] - Non-inferiority with respect to seroconversion was demonstrated if, 1 month after the last dose, for both anti-HPV-16 and anti-HPV-18, the upper limit of the 95% Confidence Interval (CI) for the difference (Cervarix 2 Group minus Cervarix 1 Group) was below 5%.

Primary: Anti-HPV-16 and anti-HPV-18 antibody concentrations (by ELISA) in Cervarix 1 Group and Cervarix 2 Group at Month 7

End point title	Anti-HPV-16 and anti-HPV-18 antibody concentrations (by ELISA) in Cervarix 1 Group and Cervarix 2 Group at Month 7[4]

End point description:

Antibody concentrations were assessed by ELISA and expressed as geometric mean concentrations (GMCs) in EL.U/mL.

End point type	Primary

End point timeframe:

At Month 7 (i.e. one month after the last dose of study vaccine)

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: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 1 Group	Cervarix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	493	382		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (N=488, 352)	9400.1 (8818.3 to 10020.4)	10234.5 (9258.3 to 11313.6)		
Anti-HPV-18 (N=493, 382)	5909.1 (5508.9 to 6338.4)	5002.6 (4572.6 to 5473.1)		

Statistical analyses

Statistical analysis title	Immune response to anti-HPV-16 in terms of GMCs

Statistical analysis description:

Immune response to anti-HPV-16 in terms of Geometric Mean Concentrations (GMCs): To evaluate sequentially if the immunogenicity (as determined by ELISA) of Cervarix vaccine administered according to a 2-dose schedule at 0, 6 months in 9-14 year old females was non-inferior to that administered according to the standard 3-dose schedule of 0,1,6 months in 15-25 year old females, 1 month after the last dose of study vaccine, in initially seronegative subjects.

Comparison groups	Cervarix 1 Group v Cervarix 2 Group
Number of subjects included in analysis	875
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Geometric mean ratio
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.22

Notes:

[5] - Non-inferiority with respect to Geometric Mean Concentrations (GMCs) was demonstrated if, 1 month after the last dose, for both anti-HPV-16 and anti-HPV-18, the upper limit of 95% CI for the GMT ratio (Cervarix 2 Group divided by Cervarix 1 Group) was below 2.

Statistical analysis title	Immune response to anti-HPV-18 in terms of GMCs

Statistical analysis description:

Immune response to anti-HPV-18 in terms of Geometric Mean Concentrations (GMCs): To evaluate sequentially if the immunogenicity (as determined by ELISA) of Cervarix vaccine administered according to a 2-dose schedule at 0, 6 months in 9-14 year old females was non-inferior to that administered according to the standard 3-dose schedule of 0,1,6 months in 15-25 year old females, 1 month after the last dose of study vaccine, in initially seronegative subjects.

Comparison groups	Cervarix 1 Group v Cervarix 2 Group

Number of subjects included in analysis	875
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Geometric mean ratio
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	0.95

Notes:

[6] - Non-inferiority with respect to Geometric Mean Concentrations (GMCs) was demonstrated if, 1 month after the last dose, for both anti-HPV-16 and anti-HPV-18, the upper limit of 95% CI for the GMT ratio (Cervarix 2 Group divided by Cervarix 1 Group) was below 2.

Secondary: Number of Seroconverted Subjects for Anti-HPV-16 and Anti-HPV-18 Antibodies in Cervarix 1 Group and Cervarix 2 Group at Day 0 and at Months 7, 12, 18, 24 and 36

End point title	Number of Seroconverted Subjects for Anti-HPV-16 and Anti-HPV-18 Antibodies in Cervarix 1 Group and Cervarix 2 Group at Day 0 and at Months 7, 12, 18, 24 and 36[7]

End point description:

Seroconversion was defined as the appearance of antibodies (anti-HPV-16 concentrations ≥ 8 EL.U/mL and anti-HPV-18 concentrations ≥ 7 EL.U/mL [applicable for Day 0, Month 7 and Month 12 time points] and anti-HPV-16 concentrations ≥ 19 EL.U/mL and anti-HPV-18 concentrations ≥ 18 EL.U/mL [applicable for Month 18, Month 24 and Month 36 timepoints]) in the serum of subjects seronegative before vaccination.
A seronegative subject was a subject with an anti-HPV-16/18 antibody concentration below (<) the aforementioned cut-offs.
Note: In order to increase the ELISA precision, the assay cut-off value was changed from 8 EL.U/mL to 19 EL.U/mL for HPV-16 and from 7 EL.U/mL to 18 EL.U/mL for HPV-18 from Month 18 onwards.

End point type	Secondary

End point timeframe:

At Day 0 and at Months 7, 12, 18, 24 and 36

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 1 Group	Cervarix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	462	356		
Units: Subjects				
Anti-HPV-16, Day 0 (N=455, 330)	0	0		
Anti-HPV-16, Month 7 (N=455, 330)	455	330		
Anti-HPV-16, Month 12 (N=455, 330)	455	330		
Anti-HPV-16, Month 18 (N=453, 329)	453	329		
Anti-HPV-16, Month 24 (N=454, 326)	454	326		
Anti-HPV-16, Month 36 (N=455, 330)	455	330		
Anti-HPV-18, Day 0 (N=462, 356)	0	0		
Anti-HPV-18, Month 7 (N=462, 356)	462	356		
Anti-HPV-18, Month 12 (N=462, 356)	462	356		
Anti-HPV-18, Month 18 (N=459, 355)	458	355		
Anti-HPV-18, Month 24 (N=460, 352)	459	352		
Anti-HPV-18, Month 36 (N=462, 356)	461	355		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16 and Anti-HPV-18 Antibody Concentrations (by ELISA) in Cervarix 1 Group and Cervarix 2 Group at Day 0 and at Months 7, 12, 18, 24 and 36

End point title	Anti-HPV-16 and Anti-HPV-18 Antibody Concentrations (by ELISA) in Cervarix 1 Group and Cervarix 2 Group at Day 0 and at Months 7, 12, 18, 24 and 36[8]

End point description:

Antibody concentrations were assessed by ELISA and expressed as geometric mean concentrations (GMCs) in EL.U/mL.

End point type	Secondary

End point timeframe:

At Day 0 and at Months 7, 12, 18, 24 and 36

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 1 Group	Cervarix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	462	356		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16, Day 0 (N=455, 330)	4.0 (4.0 to 4.0)	4.0 (4.0 to 4.0)		
Anti-HPV-16, Month 7 (N=455, 330)	9402.9 (8792.4 to 10055.8)	10120.2 (9162.7 to 11177.9)		
Anti-HPV-16, Month 12 (N=455, 330)	2653.5 (2473.5 to 2846.6)	3290.4 (2956.5 to 3662.0)		
Anti-HPV-16, Month 18 (N=453, 329)	1730.7 (1608.6 to 1862.0)	1931.2 (1735.4 to 2149.1)		
Anti-HPV-16, Month 24 (N=454, 326)	1483.8 (1382.1 to 1592.9)	1575.9 (1418.2 to 1751.2)		
Anti-HPV-16, Month 36 (N=455, 330)	1210.2 (1124.8 to 1302.1)	1326.4 (1193.9 to 1473.5)		
Anti-HPV-18, Day 0 (N=462, 356)	3.5 (3.5 to 3.5)	3.5 (3.5 to 3.5)		
Anti-HPV-18, Month 7 (N=462, 356)	5935.6 (5519.4 to 6383.3)	4984.2 (4543.9 to 5467.1)		
Anti-HPV-18, Month 12 (N=462, 356)	1523.6 (1403.7 to 1653.7)	1491.5 (1339.0 to 1661.4)		

Anti-HPV-18, Month 18 (N=459, 355)	864.6 (793.1 to 942.7)	830.6 (742.9 to 928.5)		
Anti-HPV-18, Month 24 (N=460, 352)	715.5 (658.1 to 777.9)	654.3 (582.9 to 734.5)		
Anti-HPV-18, Month 36 (N=462, 356)	562.8 (516.4 to 613.4)	552.6 (494.1 to 618.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Seroconverted Subjects for Anti-HPV-16 and Anti-HPV-18 Antibodies in Cervarix 3 Group

End point title	Number of Seroconverted Subjects for Anti-HPV-16 and Anti-HPV-18 Antibodies in Cervarix 3 Group[9]

End point description:

Seroconversion was defined as the appearance of antibodies (anti-HPV-16 concentrations ≥ 8 EL.U/mL and anti-HPV-18 concentrations ≥ 7 EL.U/mL [applicable for Day 0 and Month 13 time points] and anti-HPV-16 concentrations ≥ 19 EL.U/mL and anti-HPV-18 concentrations ≥ 18 EL.U/mL [applicable for Month 18, Month 24 and Month 36 timepoints]) in the serum of subjects seronegative before vaccination.
A seronegative subject was a subject with an anti-HPV-16/18 antibody concentration below (<) the aforementioned cut-offs.
Note: In order to increase the ELISA precision, the assay cut-off value was changed from 8 EL.U/mL to 19 EL.U/mL for HPV-16 and from 7 EL.U/mL to 18 EL.U/mL for HPV-18 from Month 18 onwards.

End point type	Secondary

End point timeframe:

At Day 0 and at Months 13, 18, 24 and 36

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 3 Group			
Subject group type	Reporting group			
Number of subjects analysed	355			
Units: Subjects				
Anti-HPV-16, Day 0 (N=339)	0			
Anti-HPV-16, Month 13 (N=339)	339			
Anti-HPV-16, Month 18 (N=339)	339			
Anti-HPV-16, Month 24 (N=337)	337			
Anti-HPV-16, Month 36 (N=339)	339			
Anti-HPV-18, Day 0 (N=355)	0			
Anti-HPV-18, Month 13 (N=355)	355			
Anti-HPV-18, Month 18 (N=355)	355			
Anti-HPV-18, Month 24 (N=353)	353			
Anti-HPV-18, Month 36 (N=355)	355			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16 and Anti-HPV-18 Antibody Concentrations (by ELISA) in Cervarix 3 Group

End point title	Anti-HPV-16 and Anti-HPV-18 Antibody Concentrations (by ELISA) in Cervarix 3 Group[10]

End point description:

Antibody concentrations were assessed by ELISA and expressed as geometric mean concentrations (GMCs) in EL.U/mL.

End point type	Secondary

End point timeframe:

At Day 0 and at Months 13, 18, 24 and 36

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 3 Group			
Subject group type	Reporting group			
Number of subjects analysed	355			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16, Day 0 (N=339)	4.0 (4.0 to 4.0)			
Anti-HPV-16, Month 13 (N=339)	11329.4 (10509.3 to 12213.5)			
Anti-HPV-16, Month 18 (N=339)	3248.2 (2974.2 to 3547.4)			
Anti-HPV-16, Month 24 (N=337)	2191.0 (2003.9 to 2395.5)			
Anti-HPV-16, Month 36 (N=339)	1559.3 (1431.2 to 1699.0)			
Anti-HPV-18, Day 0 (N=355)	3.5 (3.5 to 3.5)			
Anti-HPV-18, Month 13 (N=355)	6580.0 (6075.8 to 7126.0)			
Anti-HPV-18, Month 18 (N=355)	1860.3 (1699.4 to 2036.4)			
Anti-HPV-18, Month 24 (N=353)	1174.7 (1067.1 to 1293.2)			
Anti-HPV-18, Month 36 (N=355)	804.0 (731.8 to 883.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16 and Anti-HPV-18 antibody Titers [by Pseudovirion-Based Neutralisation Assay (PBNA)] in a subset of subjects from Cervarix 3 Group

End point title	Anti-HPV-16 and Anti-HPV-18 antibody Titers [by Pseudovirion-Based Neutralisation Assay (PBNA)] in a subset of subjects from Cervarix 3 Group[11]

End point description:

Antibody titers were expressed as geometric mean titers (GMTs). The cut-off of the assay was 40 ED50 for both anti-HPV-16 and anti-HPV-18. The assay was performed on a subset of 100 subjects from Cervarix 3 Group.

End point type	Secondary

End point timeframe:

At Day 0 and at Months 13, 18, 24 and 36

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 3 Group			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-HPV-16, Day 0 (N=88)	20.0 (20.0 to 20.0)			
Anti-HPV-16, Month 13 (N=88)	74848.0 (60521.9 to 92565.1)			
Anti-HPV-16, Month 18 (N=88)	16576.6 (13127.4 to 20932.0)			
Anti-HPV-16, Month 24 (N=87)	10003.7 (8114.1 to 12333.4)			
Anti-HPV-16, Month 36 (N=88)	9214.3 (7112.3 to 11937.5)			
Anti-HPV-18, Day 0 (N=88)	20.0 (20.0 to 20.0)			
Anti-HPV-18, Month 13 (N=88)	39994.7 (33327.2 to 47996.1)			
Anti-HPV-18, Month 18 (N=88)	9495.4 (7744.4 to 11642.2)			
Anti-HPV-18, Month 24 (N=87)	5464.1 (4377.8 to 6819.8)			
Anti-HPV-18, Month 36 (N=88)	4046.4 (3278.0 to 4994.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16 and Anti-HPV-18 Antibody Titers (by PBNA) in a Subset of Subjects From Cervarix 1 Group and Cervarix 2 Group

End point title	Anti-HPV-16 and Anti-HPV-18 Antibody Titers (by PBNA) in a Subset of Subjects From Cervarix 1 Group and Cervarix 2 Group[12]

End point description:

Antibody titers were expressed as GMTs. The cut-off of the assay was 40 ED50 for both anti-HPV-16 and anti-HPV-18. The assay was performed on a subset of 100 subjects per study group.

End point type	Secondary

End point timeframe:

At Day 0 and Months 7, 12, 18, 24 and 36

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 1 Group	Cervarix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	92		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-HPV-16, Day 0 (N=96, 92)	21.3 (18.8 to 24.2)	23.5 (20.7 to 26.6)		
Anti-HPV-16, Month 7 (N=96, 92)	82975.9 (67377.4 to 102185.6)	31407.6 (24181.5 to 40793.0)		
Anti-HPV-16, Month 12 (N=96, 92)	14872.1 (12025.5 to 18392.4)	15801.8 (12069.8 to 20687.8)		
Anti-HPV-16, Month 18 (N=95, 92)	7393.6 (5986.6 to 9131.1)	8246.4 (6224.6 to 10925.0)		
Anti-HPV-16, Month 24 (N=96, 92)	6216.5 (5111.0 to 7561.1)	7267.5 (5423.4 to 9738.6)		
Anti-HPV-16, Month 36 (N=96, 92)	7762.7 (6218.6 to 9690.1)	5063.7 (3800.4 to 6746.9)		
Anti-HPV-18, Day 0 (N=96, 92)	21.0 (19.0 to 23.5)	22.4 (20.4 to 24.5)		
Anti-HPV-18, Month 7 (N=96, 92)	24833.1 (20777.0 to 29681.1)	13935.6 (10991.0 to 17669.0)		
Anti-HPV-18, Month 12 (N=96, 92)	5914.5 (4756.0 to 7355.4)	5066.5 (3818.9 to 6721.7)		
Anti-HPV-18, Month 18 (N=95, 92)	3961.2 (3153.8 to 4975.4)	2958.2 (2213.9 to 3952.6)		
Anti-HPV-18, Month 24 (N=96, 92)	2849.4 (2276.0 to 3567.2)	2524.3 (1860.4 to 3425.2)		
Anti-HPV-18, Month 36 (N=95, 92)	2416.4 (1905.9 to 3063.5)	1956.2 (1488.5 to 2570.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cell-mediated immunogenicity related to anti-HPV-16 specific T cell-mediated immune response (CMI) for Cervarix 1 Group and Cervarix 2 Group in a sub-cohort of subjects

End point title	Cell-mediated immunogenicity related to anti-HPV-16 specific T cell-mediated immune response (CMI) for Cervarix 1 Group and Cervarix 2 Group in a sub-cohort of subjects[13]

End point description:

The CMI response represents the measure of the cytokines production [i.e. interleukin-2 (IL-2), interferon gamma (IFN-γ), tumor necrosis factor alpha (TNF-α) and the cluster of differentiation 40 Ligand (CD40L)] by HPV-antigen specific T lymphocytes and measured by intracellular cytokine staining (ICS) assay for HPV-16. The frequency was presented as number of cytokine-positive cluster of differentiation (CD)4 i.e. CD4+/CD8+ cells per million CD4+/CD8+ cells. All doubles = T cell expressing at least 2 cytokines. Results were tabulated by the pre-vaccination status of the subjects, where S- = seronegative subjects (antibody concentration < cut-off value) prior to vaccination. S+ = seropositive subjects (antibody concentration ≥ cut-off value) prior to vaccination. The assay was performed on a subset of 100 subjects per study group.

End point type	Secondary

End point timeframe:

At Day 0 and Months 7, 12, 24 and 36

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 1 Group	Cervarix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	70		
Units: cells/million T cells				
median (inter-quartile range (Q1-Q3))				
Anti-HPV-16, CD4 all doubles, S-, Day 0 (N=81, 68)	88.0 (62.0 to 152.0)	120.0 (67.0 to 185.5)		
Anti-HPV-16, CD4 all doubles, S-, Mth 7 (N=69, 50)	3953.0 (1866.0 to 7025.0)	3426.0 (1889.0 to 5214.0)		
Anti-HPV-16,CD4 all doubles, S-, Mth 12 (N=84, 70)	2491.0 (1387.5 to 5543.5)	2278.5 (1225.0 to 3363.0)		
Anti-HPV-16,CD4 all doubles, S-, Mth 24 (N=78, 67)	2698.0 (1231.0 to 5147.0)	2401 (1231.0 to 3641.0)		
Anti-HPV-16,CD4 all doubles, S-, Mth 36 (N=75, 57)	1951.0 (1085.0 to 5130.0)	2073.0 (1012.0 to 2836.0)		
Anti-HPV-16, CD4 all doubles, S+, Day 0 (N=8, 14)	77.5 (57.0 to 192.0)	100.0 (60.0 to 269.0)		

Anti-HPV-16, CD4 all doubles, S+, Mth 7 (N=8, 13)	5019.5 (1353.0 to 7343.0)	1820.0 (1311.0 to 3021.0)		
Anti-HPV-16, CD4 all doubles, S+, Mth 12 (N=9, 14)	2603.0 (1003.0 to 3350.0)	1423.5 (876.0 to 3747.0)		
Anti-HPV-16,CD4 all doubles, S+, Mth 24 (N=9, 12)	2552.0 (1156.0 to 3963.0)	1404.0 (1050.0 to 2856.5)		
Anti-HPV-16,CD4 all doubles, S+, Mth 36 (N=7, 12)	2180.0 (1293.0 to 3383.0)	1310.0 (939.0 to 2614.5)		
Anti-HPV-16, CD4-d-CD40L, S-, Day 0 (N=81, 68)	70.0 (42.0 to 130.0)	97.0 (49.0 to 144.0)		
Anti-HPV-16, CD4-d-CD40L, S-, Month 7 (N=69, 50)	3531.0 (1676.0 to 6528.0)	3196.0 (1692.0 to 4771.0)		
Anti-HPV-16, CD4-d-CD40L, S-, Month 12 (N=84, 70)	2439.5 (1342.5 to 5376.0)	2255.5 (1185.0 to 3290.0)		
Anti-HPV-16, CD4-d-CD40L, S-, Month 24 (N=78, 67)	2443.0 (1111.0 to 4922.0)	2344.0 (1031.0 to 3323.0)		
Anti-HPV-16, CD4-d-CD40L, S-, Month 36 (N=75, 57)	1935.0 (1048.0 to 5061.0)	2027.0 (978.0 to 2806.0)		
Anti-HPV-16, CD4-d-CD40L, S+, Day 0 (N=8, 14)	57.5 (39.5 to 162.0)	72.5 (40.0 to 186.0)		
Anti-HPV-16, CD4-d-CD40L, S+, Month 7 (N=8, 13)	4979.5 (1290.5 to 7001.5)	1655.0 (1050.0 to 2440.0)		
Anti-HPV-16, CD4-d-CD40L, S+, Month 12 (N=9, 14)	2587.0 (975.0 to 3305.0)	1412.5 (832.0 to 3677.0)		
Anti-HPV-16, CD4-d-CD40L, S+, Month 24 (N=9, 12)	2456.0 (945.0 to 3931.0)	1285.0 (962.5 to 1953.5)		
Anti-HPV-16, CD4-d-CD40L, S+, Month 36 (N=7, 12)	2109.0 (1178.0 to 3343.0)	1279.0 (928.0 to 2496.5)		
Anti-HPV-16, CD4-d-IFNγ, S-, Day 0 (N=81, 68)	44.0 (19.0 to 67.0)	39.5 (19.5 to 72.0)		
Anti-HPV-16, CD4-d-IFNγ, S-, Month 7 (N=69, 50)	840.0 (503.0 to 1538.0)	657.0 (474.0 to 1185.0)		
Anti-HPV-16, CD4-d-IFNγ, S-, Month 12 (N=84, 70)	546.0 (176.5 to 1007.5)	362.0 (202.0 to 644.0)		
Anti-HPV-16, CD4-d-IFNγ, S-, Month 24 (N=78, 67)	644.5 (294.0 to 1318.0)	449.0 (204.0 to 884.0)		
Anti-HPV-16, CD4-d-IFNγ, S-, Month 36 (N=75, 57)	562.0 (273.0 to 1334.0)	391.0 (215.0 to 824.0)		
Anti-HPV-16, CD4-d-IFNγ, S+, Day 0 (N=8, 14)	38.5 (26.5 to 86.0)	50.5 (31.0 to 75.0)		
Anti-HPV-16, CD4-d-IFNγ, S+, Month 7 (N=8, 13)	881.5 (462.5 to 2704.0)	489.0 (244.0 to 814.0)		
Anti-HPV-16, CD4-d-IFNγ, S+, Month 12 (N=9, 14)	533.0 (336.0 to 827.0)	329.0 (183.0 to 481.0)		
Anti-HPV-16, CD4-d-IFNγ, S+, Month 24 (N=9, 12)	579.0 (398.0 to 897.0)	310.5 (221.5 to 595.5)		
Anti-HPV-16, CD4-d-IFNγ, S+, Month 36 (N=7, 12)	651.0 (520.0 to 998.0)	564.0 (185.5 to 714.5)		
Anti-HPV-16, CD4-d-IL-2, S-, Day 0 (N=81, 68)	59.0 (35.0 to 103.0)	85.5 (43.5 to 143.0)		
Anti-HPV-16, CD4-d-IL-2, S-, Month 7 (N=69, 50)	3808.0 (1728.0 to 6787.0)	3212.5 (1788.0 to 5010.0)		

Anti-HPV-16, CD4-d-IL-2, S-, Month 12 (N=84, 70)	2402.5 (1308.5 to 5242.0)	2184.5 (1156.0 to 3238.0)		
Anti-HPV-16, CD4-d-IL-2, S-, Month 24 (N=78, 67)	2477.0 (1140.0 to 4680.0)	2282.0 (1138.0 to 3392.0)		
Anti-HPV-16, CD4-d-IL-2, S-, Month 36 (N=75, 57)	1881.0 (958.0 to 4912.0)	1922.0 (892.0 to 2708.0)		
Anti-HPV-16, CD4-d-IL-2, S+, Day 0 (N=8, 14)	68.0 (23.0 to 147.5)	77.5 (39.0 to 229.0)		
Anti-HPV-16, CD4-d-IL-2, S+, Month 7 (N=8, 13)	4886.0 (1162.5 to 6906.0)	1573.0 (1202.0 to 2924.0)		
Anti-HPV-16, CD4-d-IL-2, S+, Month 12 (N=9, 14)	2339.0 (877.0 to 3166.0)	1372.0 (868.0 to 3692.0)		
Anti-HPV-16, CD4-d-IL-2, S+, Month 24 (N=9, 12)	2454.0 (1026.0 to 3931.0)	1226.5 (969.0 to 2392.5)		
Anti-HPV-16, CD4-d-IL-2, S+, Month 36 (N=7, 12)	2135.0 (1221.0 to 3291.0)	1243.0 (910.5 to 2382.5)		
Anti-HPV-16, CD4-d-TNFα, S-, Day 0 (N=81, 68)	59.0 (37.0 to 93.0)	68.0 (29.5 to 110.5)		
Anti-HPV-16, CD4-d-TNFα, S-, Month 7 (N=69, 50)	2474.0 (1311.0 to 4800.0)	2575.5 (1224.0 to 3675.0)		
Anti-HPV-16, CD4-d-TNFα, S-, Month 12 (N=84, 70)	1944.0 (814.5 to 4150.0)	1726.0 (919.0 to 2481.0)		
Anti-HPV-16, CD4-d-TNFα, S-, Month 24 (N=78, 67)	2181.5 (886.0 to 4177.0)	1970.0 (773.0 to 2758.0)		
Anti-HPV-16, CD4-d-TNFα, S-, Month 36 (N=75, 57)	1595.0 (700.0 to 3836.0)	1390.0 (672.0 to 2092.0)		
Anti-HPV-16, CD4-d-TNFα, S+, Day 0 (N=8, 14)	47.0 (32.0 to 131.0)	64.0 (49.0 to 120.0)		
Anti-HPV-16, CD4-d-TNFα, S+, Month 7 (N=8, 13)	2058.5 (1047.0 to 3933.0)	1273.0 (949.0 to 2372.0)		
Anti-HPV-16, CD4-d-TNFα, S+, Month 12 (N=9, 14)	1826.0 (875.0 to 2703.0)	1171.0 (733.0 to 2828.0)		
Anti-HPV-16, CD4-d-TNFα, S+, Month 24 (N=9, 12)	1851.0 (1039.0 to 2259.0)	1061.5 (878.5 to 2421.5)		
Anti-HPV-16, CD4-d-TNFα, S+, Month 36 (N=7, 12)	1138.0 (1031.0 to 2506.0)	1057.0 (732.0 to 2009.0)		
Anti-HPV-16, CD8-all doubles, S-, Day 0 (N=81, 68)	11.0 (11.0 to 41.0)	11.0 (11.0 to 44.0)		
Anti-HPV-16, CD8-all doubles, S-, Mth 7 (N=69, 50)	11.0 (11.0 to 41.0)	11.0 (11.0 to 36.0)		
Anti-HPV-16,CD8 all doubles, S-, Mth 12 (N=84, 70)	30.5 (11.0 to 45.5)	29.5 (11.0 to 50.0)		
Anti-HPV-16,CD8-all doubles, S-, Mth 24 (N=78, 67)	11.0 (11.0 to 53.0)	11.0 (11.0 to 54.0)		
Anti-HPV-16,CD8-all doubles, S-, Mth 36 (N=75, 57)	37.0 (11.0 to 72.0)	35.0 (11.0 to 59.0)		
Anti-HPV-16, CD8-all doubles, S+, Day 0 (N=8, 14)	11.0 (11.0 to 49.0)	35.5 (26.0 to 41.0)		
Anti-HPV-16, CD8-all doubles, S+, Mth 7 (N=8, 13)	11.0 (11.0 to 30.5)	33.0 (11.0 to 43.0)		
Anti-HPV-16,CD8 all doubles, S+, Mth 12 (N=9, 14)	52.0 (49.0 to 77.0)	29.0 (11.0 to 57.0)		
Anti-HPV-16,CD8-all doubles, S+, Mth 24 (N=9, 12)	49.0 (12.0 to 63.0)	11.0 (11.0 to 56.0)		

Anti-HPV-16,CD8-all doubles, S+, Mth 36 (N=7, 12)	27.0 (11.0 to 123.0)	11.0 (11.0 to 49.0)		
Anti-HPV-16, CD8-d-CD40L, S-, Day 0 (N=81, 68)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-16, CD8-d-CD40L, S-, Month 7 (N=69, 50)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-16, CD8-d-CD40L, S-, Month 12 (N=84, 70)	7.0 (7.0 to 32.0)	7.0 (7.0 to 37.0)		
Anti-HPV-16, CD8-d-CD40L, S-, Month 24 (N=78, 68)	7.0 (7.0 to 7.0)	7.0 (7.0 to 31.0)		
Anti-HPV-16, CD8-d-CD40L, S-, Month 36 (N=75, 57)	11.0 (7.0 to 52.0)	7.0 (7.0 to 32.0)		
Anti-HPV-16, CD8-d-CD40L, S+, Day 0 (N=8, 14)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-16, CD8-d-CD40L, S+, Month 7 (N=8, 13)	7.0 (7.0 to 7.0)	7.0 (7.0 to 22.0)		
Anti-HPV-16, CD8-d-CD40L, S+, Month 12 (N=9, 14)	45.0 (7.0 to 48.0)	15.0 (7.0 to 37.0)		
Anti-HPV-16, CD8-d-CD40L, S+, Month 24 (N=9, 12)	7.0 (7.0 to 46.0)	7.0 (7.0 to 17.0)		
Anti-HPV-16, CD8-d-CD40L, S+, Month 36 (N=7, 12)	7.0 (7.0 to 27.0)	7.0 (7.0 to 15.0)		
Anti-HPV-16, CD8-d-IFNγ, S-, Day 0 (N=81, 68)	7.0 (7.0 to 32.0)	7.0 (7.0 to 37.0)		
Anti-HPV-16, CD8-d-IFNγ, S-, Month 7 (N=69, 50)	7.0 (7.0 to 35.0)	7.0 (7.0 to 26.0)		
Anti-HPV-16, CD8-d-IFNγ, S-, Month 12 (N=84, 70)	7.0 (7.0 to 38.0)	7.0 (7.0 to 46.0)		
Anti-HPV-16, CD8-d-IFNγ, S-, Month 24 (N=78, 67)	7.0 (7.0 to 37.0)	7.0 (7.0 to 42.0)		
Anti-HPV-16, CD8-d-IFNγ, S-, Month 36 (N=75, 57)	11.0 (7.0 to 44.0)	25.0 (7.0 to 44.0)		
Anti-HPV-16, CD8-d-IFNγ, S+, Day 0 (N=8, 14)	7.0 (7.0 to 45.0)	31.5 (22.0 to 37.0)		
Anti-HPV-16, CD8-d-IFNγ, S+, Month 7 (N=8, 13)	7.0 (7.0 to 7.0)	22.0 (7.0 to 30.0)		
Anti-HPV-16, CD8-d-IFNγ, S+, Month 12 (N=9, 14)	46.0 (31.0 to 54.0)	15.0 (7.0 to 40.0)		
Anti-HPV-16, CD8-d-IFNγ, S+, Month 24 (N=9, 12)	8.0 (7.0 to 46.0)	7.0 (7.0 to 23.0)		
Anti-HPV-16, CD8-d-IFNγ, S+, Month 36 (N=7, 12)	7.0 (7.0 to 63.0)	7.0 (7.0 to 45.0)		
Anti-HPV-16, CD8-d-IL-2, S-, Day 0 (N=81, 68)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-16, CD8-d-IL-2, S-, Month 7 (N=69, 50)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-16, CD8-d-IL-2, S-, Month 12 (N=84, 70)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-16, CD8-d-IL-2, S-, Month 24 (N=78, 67)	7.0 (7.0 to 30.0)	7.0 (7.0 to 30.0)		
Anti-HPV-16, CD8-d-IL-2, S-, Month 36 (N=75, 57)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-16, CD8-d-IL-2, S+, Day 0 (N=8, 14)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-16, CD8-d-IL-2, S+, Month 7 (N=8, 13)	7.0 (7.0 to 7.0)	7.0 (7.0 to 28.0)		
Anti-HPV-16, CD8-d-IL-2, S+, Month 12 (N=9, 14)	7.0 (7.0 to 31.0)	7.0 (7.0 to 23.0)		
Anti-HPV-16, CD8-d-IL-2, S+, Month 24 (N=9, 12)	7.0 (7.0 to 45.0)	7.0 (7.0 to 13.0)		
Anti-HPV-16, CD8-d-IL-2, S+, Month 36 (N=7, 12)	7 (7.0 to 23.0)	7 (7.0 to 7.0)		

Anti-HPV-16, CD8-d-TNFα, S-, Day 0 (N=81, 68)	7.0 (7.0 to 29.0)	7.0 (7.0 to 28.5)		
Anti-HPV-16, CD8-d-TNFα, S-, Month 7 (N=69, 50)	7.0 (7.0 to 33.0)	7.0 (7.0 to 32.0)		
Anti-HPV-16, CD8-d-TNFα, S-, Month 12 (N=84, 70)	7.0 (7.0 to 38.0)	7.0 (7.0 to 33.0)		
Anti-HPV-16, CD8-d-TNFα, S-, Month 24 (N=78, 67)	7.0 (7.0 to 37.0)	7.0 (7.0 to 24.0)		
Anti-HPV-16, CD8-d-TNFα, S-, Month 36 (N=75, 57)	7 (7.0 to 36.0)	7 (7.0 to 32.0)		
Anti-HPV-16, CD8-d-TNFα, S+, Day 0 (N=8, 14)	7.0 (7.0 to 30.5)	14.5 (7.0 to 31.0)		
Anti-HPV-16, CD8-d-TNFα, S+, Month 7 (N=8, 13)	7.0 (7.0 to 26.5)	22.0 (7.0 to 30.0)		
Anti-HPV-16, CD8-d-TNFα, S+, Month 12 (N=9, 14)	8.0 (7.0 to 54.0)	23.0 (7.0 to 30.0)		
Anti-HPV-16, CD8-d-TNFα, S+, Month 24 (N=9, 12)	8.0 (7.0 to 42.0)	7.0 (7.0 to 7.0)		
Anti-HPV-16, CD8-d-TNFα, S+, Month 36 (N=7, 12)	7.0 (7.0 to 119.0)	7.0 (7.0 to 7.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cell-mediated immunogenicity related to anti-HPV-18 specific T CMI response for Cervarix 1 Group and Cervarix 2 Group in a sub-cohort of subjects

End point title	Cell-mediated immunogenicity related to anti-HPV-18 specific T CMI response for Cervarix 1 Group and Cervarix 2 Group in a sub-cohort of subjects[14]

End point description:

The CMI response represents the measure of the cytokines production [IL-2, IFN-γ, TNF-α, and CD40L] by HPV-antigen specific T lymphocytes and measured by ICS assay for HPV-18. The frequency was presented as a number of cytokine-producing CD4+/CD8+ cells per million CD4+/CD8+ cells. All doubles = T cell expressing at least 2 cytokines. Results were tabulated by the pre-vaccination status of the subjects, where S- = seronegative subjects (antibody concentration < the cut-off value) prior to vaccination. S+ = seropositive subjects (antibody concentration ≥ cut-off value) prior to vaccination. The assay was performed on a subset of 100 subjects per study group.

End point type	Secondary

End point timeframe:

At Day 0 and Months 7, 12, 24 and 36

Notes:

[14] - 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: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 1 Group	Cervarix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	72		
Units: cells/million T cells				
median (inter-quartile range (Q1-Q3))				
Anti-HPV-18, CD4 all doubles, S-, Day 0 (N=77, 69)	86.0 (61.0 to 129.0)	112.0 (75.0 to 177)		

Anti-HPV-18, CD4 all doubles, S-,Mth 7 (N=65, 53)	2780.0 (1606.0 to 4289.0)	1864.0 (1158.0 to 2565.0)		
Anti-HPV-18,CD4 all doubles, S-,Mth 12 (N=83, 72)	2039.0 (1053.0 to 3481.0)	1246.5 (814.0 to 2045.5)		
Anti-HPV-18,CD4 all doubles, S-,Mth 24 (N=76, 68)	1815.5 (877.5 to 3193.0)	1355.0 (638.5 to 2106.0)		
Anti-HPV-18,CD4 all doubles, S-,Mth 36 (N= 72, 56)	1609.0 (716.0 to 3322.0)	1246.0 (676.5 to 1751.0)		
Anti-HPV-18, CD4 all doubles, S+, Day 0 (N=11, 14)	125.0 (61.0 to 227.0)	128.0 (71.0 to 153.0)		
Anti-HPV-18, CD4 all doubles, S+, Mth 7 (N=11, 11)	1593.0 (786.0 to 4012.0)	1498.0 (808.0 to 2727.0)		
Anti-HPV-18,CD4 all doubles, S+, Mth 12 (N=10, 13)	868.0 (576.0 to 2069.0)	787.0 (597.0 to 1771.0)		
Anti-HPV-18,CD4 all doubles, S+, Mth 24 (N=10, 12)	710.5 (523.0 to 2329.0)	885.0 (475.5 to 2147.5)		
Anti-HPV-18,CD4 all doubles, S+, Mth 36 (N=10, 13)	808.5 (624.0 to 1764.0)	598.0 (367.0 to 1414.0)		
Anti-HPV-18, CD4-d-CD40L, S-, Day 0 (N=77, 69)	62.0 (35.0 to 105.0)	88.0 (49.0 to 155.0)		
Anti-HPV-18, CD4-d-CD40L, S-, Month 7 (N=65, 53)	2634.0 (1331.0 to 3748.0)	1700.0 (993.0 to 2324.0)		
Anti-HPV-18, CD4-d-CD40L, S-, Month 12 (N=83, 72)	1967.0 (1019.0 to 3362.0)	1206.5 (797.5 to 2006.0)		
Anti-HPV-18, CD4-d-CD40L, S-, Month 24 (N=76, 68)	1632.0 (807.0 to 3133.0)	1290.5 (600.5 to 1911.0)		
Anti-HPV-18, CD4-d-CD40L, S-, Month 36 (N=72, 56)	1543.0 (686.0 to 3258.0)	1222.0 (670.0 to 1665.0)		
Anti-HPV-18, CD4-d-CD40L, S+, Day 0 (N=11, 14)	121.0 (50.0 to 223.0)	110.5 (44.0 to 142.0)		
Anti-HPV-18, CD4-d-CD40L, S+, Month 7 (N=11, 11)	1419.0 (729.0 to 3704.0)	1377.0 (703.0 to 2511.0)		
Anti-HPV-18, CD4-d-CD40L, S+, Month 12 (N=10, 13)	830.0 (572.0 to 2008.0)	767.0 (539.0 to 1724.0)		
Anti-HPV-18, CD4-d-CD40L, S+, Month 24 (N=10, 12)	652.0 (475.0 to 2151.0)	867.0 (431.0 to 1963.5)		
Anti-HPV-18, CD4-d-CD40L, S+, Month 36 (N=10, 13)	794.0 (604.0 to 1721.0)	594.0 (350.0 to 1356.0)		
Anti-HPV-18, CD4-d-IFNγ, S-, Day 0 (N=77, 69)	32.0 (19.0 to 55.0)	32.0 (19.0 to 68.0)		
Anti-HPV-18, CD4-d-IFNγ, S-, Month 7 (N=65, 53)	562.0 (220.0 to 952.0)	350.0 (192.0 to 554.0)		
Anti-HPV-18, CD4-d-IFNγ, S-, Month 12 (N=83, 72)	354.0 (132.0 to 669.0)	216.5 (111.5 to 390.0)		
Anti-HPV-18, CD4-d-IFNγ, S-, Month 24 (N=76, 68)	326.5 (166.5 to 799.5)	205.5 (108.5 to 538.0)		
Anti-HPV-18, CD4-d-IFNγ, S-, Month 36 (N=72, 56)	304.5 (168.5 to 757.0)	233.5 (114.5 to 485.5)		
Anti-HPV-18, CD4-d-IFNγ, S+, Day 0 (N=11, 14)	55.0 (19.0 to 70.0)	28.0 (19.0 to 48.0)		
Anti-HPV-18, CD4-d-IFNγ, S+, Month 7 (N=11, 11)	628.0 (186.0 to 1186.0)	376.0 (234.0 to 580.0)		
Anti-HPV-18, CD4-d-IFNγ, S+, Month 12 (N=10, 13)	244.5 (120.0 to 535.0)	161.0 (85.0 to 344.0)		
Anti-HPV-18, CD4-d-IFNγ, S+, Month 24 (N=10, 12)	295.5 (108.0 to 636.0)	270.5 (94.5 to 455.5)		
Anti-HPV-18, CD4-d-IFNγ, S+, Month 36 (N=10, 13)	356.0 (278.0 to 417.0)	239.0 (102.0 to 422.0)		

Anti-HPV-18, CD4-d-IL-2, S-, Day 0 (N=77, 69)	57.0 (30.0 to 96.0)	81.0 (36.0 to 127.0)		
Anti-HPV-18, CD4-d-IL-2, S-, Month 7 (N=65, 53)	2611.0 (1452.0 to 3953.0)	1725.0 (1026.0 to 2329.0)		
Anti-HPV-18, CD4-d-IL-2, S-, Month 12 (N=83, 72)	1959.0 (1009.0 to 3269.0)	1172.5 (755.5 to 1916.0)		
Anti-HPV-18, CD4-d-IL-2, S-, Month 24 (N=76, 68)	1638.5 (851.5 to 3084.0)	1306.0 (589.0 to 1977.5)		
Anti-HPV-18, CD4-d-IL-2, S-, Month 36 (N=72, 56)	1495.0 (661.0 to 3065.0)	1183.5 (586.5 to 1684.5)		
Anti-HPV-18, CD4-d-IL-2, S+, Day 0 (N=11, 14)	65.0 (31.0 to 137.0)	96.5 (48.0 to 102.0)		
Anti-HPV-18, CD4-d-IL-2, S+, Month 7 (N=11, 11)	1470.0 (691.0 to 3887.0)	1231.0 (690.0 to 2313.0)		
Anti-HPV-18, CD4-d-IL-2, S+, Month 12 (N=10, 13)	847.5 (556.0 to 2022.0)	783.0 (514.0 to 1650.0)		
Anti-HPV-18, CD4-d-IL-2, S+, Month 24 (N=10, 12)	652.5 (448.0 to 2269.0)	705.5 (433.0 to 2041.5)		
Anti-HPV-18, CD4-d-IL-2, S+, Month 36 (N=10, 13)	777.0 (589.0 to 1669.0)	554.0 (333.0 to 1370.0)		
Anti-HPV-18, CD4-d-TNFα, S-, Day 0 (N=77, 69)	49.0 (31.0 to 72.0)	73.0 (27.0 to 138.0)		
Anti-HPV-18, CD4-d-TNFα, S-, Month 7 (N=65, 53)	1699.0 (979.0 to 2832.0)	1394.0 (824.0 to 2060.0)		
Anti-HPV-18, CD4-d-TNFα, S-, Month 12 (N=83, 72)	1573.0 (715.0 to 2662.0)	991.0 (599.0 to 1617.0)		
Anti-HPV-18, CD4-d-TNFα, S-, Month 24 (N=76, 68)	1434.0 (637.5 to 2506.0)	1102.5 (543.0 to 1580.0)		
Anti-HPV-18, CD4-d-TNFα, S-, Month 36 (N=72, 56)	1268.0 (473.5 to 2130.0)	868.5 (520.0 to 1296.5)		
Anti-HPV-18, CD4-d-TNFα, S+, Day 0 (N=11, 14)	51.0 (44.0 to 159.0)	68.0 (32.0 to 137.0)		
Anti-HPV-18, CD4-d-TNFα, S+, Month 7 (N=11, 11)	1337.0 (437.0 to 3141.0)	1137.0 (648.0 to 2211.0)		
Anti-HPV-18, CD4-d-TNFα, S+, Month 12 (N=10, 13)	604.0 (391.0 to 1696.0)	684.0 (443.0 to 1284.0)		
Anti-HPV-18, CD4-d-TNFα, S+, Month 24 (N=10, 12)	601.0 (462.0 to 2122.0)	768.5 (370.5 to 1673.0)		
Anti-HPV-18, CD4-d-TNFα, S+, Month 36 (N=10, 13)	652.5 (489.0 to 1590.0)	444.0 (294.0 to 996.0)		
Anti-HPV-18, CD8-all doubles, S-, Day 0 (N=77, 69)	11.0 (11.0 to 36.0)	11.0 (11.0 to 33.0)		
Anti-HPV-18, CD8-all doubles, S-, Mth 7 (N=65, 53)	11.0 (11.0 to 37.0)	11.0 (11.0 to 32.0)		
Anti-HPV-18,CD8 all doubles, S-, Mth 12 (N=83, 72)	28.0 (11.0 to 47.0)	37.0 (11.0 to 51.5)		
Anti-HPV-18,CD8-all doubles, S-, Mth 24 (N=76, 68)	11.0 (11.0 to 51.0)	11.0 (11.0 to 43.0)		
Anti-HPV-18,CD8-all doubles, S-, Mth 36 (N=72, 56)	32.0 (11.0 to 45.5)	29.0 (11.0 to 51.0)		
Anti-HPV-18, CD8-all doubles, S+, Day 0 (N=11, 14)	11.0 (11.0 to 27.0)	11.0 (11.0 to 34.0)		
Anti-HPV-18, CD8-all doubles, S+, Mth 7 (N=11, 11)	11.0 (11.0 to 78.0)	11.0 (11.0 to 73.0)		
Anti-HPV-18,CD8 all doubles, S+, Mth 12 (N=10, 13)	44.0 (11.0 to 73.0)	11.0 (11.0 to 33.0)		
Anti-HPV-18,CD8-all doubles, S+, Mth 24 (N=10, 12)	19.5 (11.0 to 47.0)	11.0 (11.0 to 36.0)		
Anti-HPV-18,CD8-all doubles, S+, Mth 36 (N=10, 13)	45.0 (11.0 to 85.0)	34.0 (11.0 to 50.0)		

Anti-HPV-18, CD8-d-CD40L, S-, Day 0 (N=77, 69)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-CD40L, S-, Month 7 (N=65, 53)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-CD40L, S-, Month 12 (N=83, 72)	7.0 (7.0 to 32.0)	7.0 (7.0 to 36.5)		
Anti-HPV-18, CD8-d-CD40L, S-, Month 24 (N=76, 68)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-CD40L, S-, Month 36 (N=72, 56)	7.0 (7.0 to 35.5)	7.0 (7.0 to 37.5)		
Anti-HPV-18, CD8-d-CD40L, S+, Day 0 (N=11, 14)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-CD40L, S+, Month 7 (N=11, 11)	7.0 (7.0 to 7.0)	7.0 (7.0 to 27.0)		
Anti-HPV-18, CD8-d-CD40L, S+, Month 12 (N=10, 13)	34.5 (7.0 to 48.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-CD40L, S+, Month 24 (N=10, 12)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-CD40L, S+, Month 36 (N=10, 13)	25.0 (7.0 to 61.0)	7.0 (7.0 to 30.0)		
Anti-HPV-18, CD8-d-IFNγ, S-, Day 0 (N=77, 69)	7.0 (7.0 to 29.0)	7.0 (7.0 to 24.0)		
Anti-HPV-18, CD8-d-IFNγ, S-, Month 7 (N=65, 53)	7.0 (7.0 to 26.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-IFNγ, S-, Month 12 (N=83, 72)	7.0 (7.0 to 34.0)	7.0 (7.0 to 39.5)		
Anti-HPV-18, CD8-d-IFNγ, S-, Month 24 (N=76, 68)	7.0 (7.0 to 29.5)	7.0 (7.0 to 33.5)		
Anti-HPV-18, CD8-d-IFNγ, S-, Month 36 (N=72, 56)	7.0 (7.0 to 40.5)	7.0 (7.0 to 34.5)		
Anti-HPV-18, CD8-d-IFNγ, S+, Day 0 (N=11, 14)	7.0 (7.0 to 23.0)	7.0 (7.0 to 30.0)		
Anti-HPV-18, CD8-d-IFNγ, S+, Month 7 (N=11, 11)	7.0 (7.0 to 74.0)	7.0 (7.0 to 39.0)		
Anti-HPV-18, CD8-d-IFNγ, S+, Month 12 (N=10, 13)	16.0 (7.0 to 38.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-IFNγ, S+, Month 24 (N=10, 12)	7.0 (7.0 to 9.0)	7.0 (7.0 to 32.0)		
Anti-HPV-18, CD8-d-IFNγ, S+, Month 36 (N=10, 13)	7.0 (7.0 to 39.0)	7.0 (7.0 to 40.0)		
Anti-HPV-18, CD8-d-IL-2, S-, Day 0 (N=77, 69)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-IL-2, S-, Month 7 (N=65, 53)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-IL-2, S-, Month 12 (N=83, 72)	7.0 (7.0 to 26.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-IL-2, S-, Month 24 (N=76, 68)	7.0 (7.0 to 27.0)	7.0 (7.0 to 14.5)		
Anti-HPV-18, CD8-d-IL-2, S-, Month 36 (N=72, 56)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-IL-2, S+, Day 0 (N=11, 14)	7.0 (7.0 to 7.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-IL-2, S+, Month 7 (N=11, 11)	7.0 (7.0 to 24.0)	7.0 (7.0 to 34.0)		
Anti-HPV-18, CD8-d-IL-2, S+, Month 12 (N=10, 13)	7.0 (7.0 to 7.0)	7.0 (7.0 to 23.0)		
Anti-HPV-18, CD8-d-IL-2, S+, Month 24 (N=10, 12)	7.0 (7.0 to 24.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-IL-2, S+, Month 36 (N=10, 13)	7.0 (7.0 to 39.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-TNFα, S-, Day 0 (N=77, 69)	7.0 (7.0 to 7.0)	7.0 (7.0 to 8.0)		

Anti-HPV-18, CD8-d-TNFα, S-, Month 7 (N=65, 53)	7.0 (7.0 to 31.0)	7.0 (7.0 to 27.0)		
Anti-HPV-18, CD8-d-TNFα, S-, Month 12 (N=83, 72)	7.0 (7.0 to 31.0)	7.0 (7.0 to 35.0)		
Anti-HPV-18, CD8-d-TNFα, S-, Month 24 (N=76, 68)	7.0 (7.0 to 32.5)	7.0 (7.0 to 33.0)		
Anti-HPV-18, CD8-d-TNFα, S-, Month 36 (N=72, 56)	7.0 (7.0 to 32.0)	7.0 (7.0 to 35.0)		
Anti-HPV-18, CD8-d-TNFα, S+, Day 0 (N=11, 14)	7.0 (7.0 to 23.0)	7.0 (7.0 to 30.0)		
Anti-HPV-18, CD8-d-TNFα, S+, Month 7 (N=11, 11)	7.0 (7.0 to 74.0)	7.0 (7.0 to 62.0)		
Anti-HPV-18, CD8-d-TNFα, S+, Month 12 (N=10, 13)	7.0 (7.0 to 38.0)	7.0 (7.0 to 7.0)		
Anti-HPV-18, CD8-d-TNFα, S+, Month 24 (N=10, 12)	7.0 (7.0 to 31.0)	7.0 (7.0 to 16.5)		
Anti-HPV-18, CD8-d-TNFα, S+, Month 36 (N=10, 13)	17.0 (7.0 to 57.0)	7.0 (7.0 to 29.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cell-mediated immunogenicity related to anti-HPV-16 specific T CMI response for Cervarix 3 Group in a sub-cohort of subjects

End point title	Cell-mediated immunogenicity related to anti-HPV-16 specific T CMI response for Cervarix 3 Group in a sub-cohort of subjects[15]

End point description:

The CMI response was the measure of the cytokines production (IL-2, IFN-γ, TNF-α, and CD40L) by HPV-antigen specific T lymphocytes and measured by ICS assay for HPV-16. The frequency was presented as a number of cytokine-positive cluster of differentiation (CD)4 i.e.CD4+/CD8+ cells per million CD4+/CD8+ cells. All doubles= T cell expressing at least 2 cytokines. Results were tabulated by the pre-vaccination status of the subjects, where S- = seronegative subjects (antibody concentration < cut-off value) prior to vaccination. S+ = seropositive subjects (antibody concentration ≥ cut-off value) prior to vaccination. The assay was performed on a subset of 100 subjects from Cervarix 3 Group.

End point type	Secondary

End point timeframe:

At Day 0 and at Months 13, 18 and 36

Notes:

[15] - 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: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 3 Group			
Subject group type	Reporting group			
Number of subjects analysed	77			
Units: cells/million T cells				
median (inter-quartile range (Q1-Q3))				
Anti-HPV-16, CD4 all doubles, S-, Day 0 (N=77)	96.0 (61.0 to 170.0)			
Anti-HPV-16, CD4 all doubles, S-, Month 13 (N=73)	2399.0 (1514.0 to 4223.0)			

Anti-HPV-16, CD4 all doubles, S-, Month 18 (N=73)	1879.0 (1124.0 to 3449.0)			
Anti-HPV-16, CD4 all doubles, S-, Month 36 (N=70)	1786.5 (1064.0 to 3285.0)			
Anti-HPV-16, CD4 all doubles, S+, Day 0 (N=7)	169.0 (77.0 to 277.0)			
Anti-HPV-16, CD4 all doubles, S+, Month 13 (N=6)	2507.5 (1067.0 to 4212.0)			
Anti-HPV-16, CD4 all doubles, S+, Month 18 (N=6)	2717.5 (1597.0 to 4103.0)			
Anti-HPV-16, CD4 all doubles, S+, Month 36 (N=7)	1521.0 (297.0 to 3794.0)			
Anti-HPV-16, CD4-d-CD40L, S-, Day 0 (N=77)	89.0 (48.0 to 133.0)			
Anti-HPV-16, CD4-d-CD40L, S-, Month 13 (N=73)	2356.0 (1510.0 to 4165.0)			
Anti-HPV-16, CD4-d-CD40L, S-, Month 18 (N=73)	1831.0 (1070.0 to 3272.0)			
Anti-HPV-16, CD4-d-CD40L, S-, Month 36 (N=70)	1763.0 (1048.0 to 3239.0)			
Anti-HPV-16, CD4-d-CD40L, S+, Day 0 (N=7)	141.0 (73.0 to 261.0)			
Anti-HPV-16, CD4-d-CD40L, S+, Month 13 (N=6)	2450.5 (1036.0 to 4139.0)			
Anti-HPV-16, CD4-d-CD40L, S+, Month 18 (N=6)	2614.5 (1580.0 to 3862.0)			
Anti-HPV-16, CD4-d-CD40L, S+, Month 36 (N=7)	1426.0 (280.0 to 3697.0)			
Anti-HPV-16, CD4-d-IFNγ, S-, Day 0 (N=77)	35.0 (20.0 to 60.0)			
Anti-HPV-16, CD4-d-IFNγ, S-, Month 13 (N=73)	651.0 (328.0 to 1356.0)			
Anti-HPV-16, CD4-d-IFNγ, S-, Month 18 (N=73)	405.0 (208.0 to 821.0)			
Anti-HPV-16, CD4-d-IFNγ, S-, Month 36 (N=70)	646.0 (276.0 to 1282.0)			
Anti-HPV-16, CD4-d-IFNγ, S+, Day 0 (N=7)	68.0 (33.0 to 203.0)			
Anti-HPV-16, CD4-d-IFNγ, S+, Month 13 (N=6)	644.0 (204.0 to 1163.0)			
Anti-HPV-16, CD4-d-IFNγ, S+, Month 18 (N=6)	708.5 (361.0 to 1218.0)			
Anti-HPV-16, CD4-d-IFNγ, S+, Month 36 (N=7)	310.0 (72.0 to 1783.0)			
Anti-HPV-16, CD4-d-IL-2, S-, Day 0 (N=77)	63.0 (34.0 to 111.0)			
Anti-HPV-16, CD4-d-IL-2, S-, Month 13 (N=73)	2220.0 (1406.0 to 4107.0)			
Anti-HPV-16, CD4-d-IL-2, S-, Month 18 (N=73)	1830.0 (1084.0 to 3221.0)			

Anti-HPV-16, CD4-d-IL-2, S-, Month 36 (N=70)	1670.5 (1009.0 to 3169.0)			
Anti-HPV-16, CD4-d-IL-2, S+, Day 0 (N=7)	121.0 (47.0 to 191.0)			
Anti-HPV-16, CD4-d-IL-2, S+, Month 13 (N=6)	2442.0 (835.0 to 4006.0)			
Anti-HPV-16, CD4-d-IL-2, S+, Month 18 (N=6)	2659.5 (1510.0 to 3870.0)			
Anti-HPV-16, CD4-d-IL-2, S+, Month 36 (N=7)	1028.0 (267.0 to 3629.0)			
Anti-HPV-16, CD4-d-TNFα, S-, Day 0 (N=77)	63.0 (37.0 to 99.0)			
Anti-HPV-16, CD4-d-TNFα, S-, Month 13 (N=73)	1643.0 (907.0 to 2988.0)			
Anti-HPV-16, CD4-d-TNFα, S-, Month 18 (N=73)	1326.0 (807.0 to 2627.0)			
Anti-HPV-16, CD4-d-TNFα, S-, Month 36 (N=70)	1300.5 (693.0 to 2267.0)			
Anti-HPV-16, CD4-d-TNFα, S+, Day 0 (N=7)	140.0 (32.0 to 164.0)			
Anti-HPV-16, CD4-d-TNFα, S+, Month 13 (N=6)	1843.0 (584.0 to 2657.0)			
Anti-HPV-16, CD4-d-TNFα, S+, Month 18 (N=6)	2085.0 (1380.0 to 2700.0)			
Anti-HPV-16, CD4-d-TNFα, S+, Month 36 (N=7)	1202.0 (169.0 to 2745.0)			
Anti-HPV-16, CD8-all doubles, S-, Day 0 (N=77)	27.0 (11.0 to 54.0)			
Anti-HPV-16, CD8-all doubles, S-, Month 13 (N=73)	11.0 (11.0 to 43.0)			
Anti-HPV-16, CD8-all doubles, S-, Month 18 (N=73)	11.0 (11.0 to 53.0)			
Anti-HPV-16, CD8-all doubles, S-, Month 36 (N=70)	21.5 (11.0 to 52.0)			
Anti-HPV-16, CD8-all doubles, S+, Day 0 (N=7)	33.0 (11.0 to 59.0)			
Anti-HPV-16, CD8-all doubles, S+, Month 13 (N=6)	43.0 (11.0 to 57.0)			
Anti-HPV-16, CD8-all doubles, S+, Month 18 (N=6)	27.0 (11.0 to 52.0)			
Anti-HPV-16, CD8-all doubles, S+, Month 36 (N=7)	11.0 (11.0 to 89.0)			
Anti-HPV-16, CD8-d-CD40L, S-, Day 0 (N=77)	7.0 (7.0 to 35.0)			
Anti-HPV-16, CD8-d-CD40L, S-, Month 13 (N=73)	7.0 (7.0 to 29.0)			
Anti-HPV-16, CD8-d-CD40L, S-, Month 18 (N=73)	7.0 (7.0 to 34.0)			
Anti-HPV-16, CD8-d-CD40L, S-, Month 36 (N=70)	7.0 (7.0 to 30.0)			
Anti-HPV-16, CD8-d-CD40L, S+, Day 0 (N=7)	7.0 (7.0 to 35.0)			
Anti-HPV-16, CD8-d-CD40L, S+, Month 13 (N=6)	7.0 (7.0 to 34.0)			
Anti-HPV-16, CD8-d-CD40L, S+, Month 18 (N=6)	7.0 (7.0 to 7.0)			
Anti-HPV-16, CD8-d-CD40L, S+, Month 36 (N=7)	7.0 (7.0 to 46.0)			

Anti-HPV-16, CD8-d-IFNγ, S-, Day 0 (N=77)	7.0 (7.0 to 44.0)			
Anti-HPV-16, CD8-d-IFNγ, S-, Month 13 (N=73)	7.0 (7.0 to 35.0)			
Anti-HPV-16, CD8-d-IFNγ, S-, Month 18 (N=73)	7.0 (7.0 to 37.0)			
Anti-HPV-16, CD8-d-IFNγ, S-, Month 36 (N=70)	7.0 (7.0 to 38.0)			
Anti-HPV-16, CD8-d-IFNγ, S+, Day 0 (N=7)	29.0 (7.0 to 55.0)			
Anti-HPV-16, CD8-d-IFNγ, S+, Month 13 (N=6)	25.5 (7.0 to 53.0)			
Anti-HPV-16, CD8-d-IFNγ, S+, Month 18 (N=6)	7.0 (7.0 to 33.0)			
Anti-HPV-16, CD8-d-IFNγ, S+, Month 36 (N=7)	7.0 (7.0 to 46.0)			
Anti-HPV-16, CD8-d-IL-2, S-, Day 0 (N=77)	7.0 (7.0 to 7.0)			
Anti-HPV-16, CD8-d-IL-2, S-, Month 13 (N=73)	7.0 (7.0 to 7.0)			
Anti-HPV-16, CD8-d-IL-2, S-, Month 18 (N=73)	7.0 (7.0 to 29.0)			
Anti-HPV-16, CD8-d-IL-2, S-, Month 36 (N=70)	7.0 (7.0 to 7.0)			
Anti-HPV-16, CD8-d-IL-2, S+, Day 0 (N=7)	7.0 (7.0 to 7.0)			
Anti-HPV-16, CD8-d-IL-2, S+, Month 13 (N=6)	7.0 (7.0 to 7.0)			
Anti-HPV-16, CD8-d-IL-2, S+, Month 18 (N=6)	7.0 (7.0 to 7.0)			
Anti-HPV-16, CD8-d-IL-2, S+, Month 36 (N=7)	7.0 (7.0 to 46.0)			
Anti-HPV-16, CD8-d-TNFα, S-, Day 0 (N=77)	7.0 (7.0 to 27.0)			
Anti-HPV-16, CD8-d-TNFα, S-, Month 13 (N=73)	7.0 (7.0 to 29.0)			
Anti-HPV-16, CD8-d-TNFα, S-, Month 18 (N=73)	7.0 (7.0 to 41.0)			
Anti-HPV-16, CD8-d-TNFα, S-, Month 36 (N=70)	7.0 (7.0 to 38.0)			
Anti-HPV-16, CD8-d-TNFα, S+, Day 0 (N=7)	7.0 (7.0 to 7.0)			
Anti-HPV-16, CD8-d-TNFα, S+, Month 13 (N=6)	20.5 (7.0 to 44.0)			
Anti-HPV-16, CD8-d-TNFα, S+, Month 18 (N=6)	20.0 (7.0 to 39.0)			
Anti-HPV-16, CD8-d-TNFα, S+, Month 36 (N=7)	7.0 (7.0 to 7.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cell-mediated immunogenicity related to anti-HPV-18 specific T CMI response for Cervarix 3 Group in a sub-cohort of subjects

End point title	Cell-mediated immunogenicity related to anti-HPV-18 specific T CMI response for Cervarix 3 Group in a sub-cohort of subjects[16]

End point description:

The CMI response was the measure of the cytokines production (IL-2, IFN-γ, TNF-α, and CD40L) by HPV-antigen specific T lymphocytes and measured by ICS assay for HPV-18. The frequency was presented as a number of cytokine-producing CD4+/CD8+ cells per million CD4+/CD8+ cells. All doubles= T cell expressing at least 2 cytokines. Results were tabulated by the pre-vaccination status of the subjects, where S- = seronegative subjects (antibody concentration < cut-off value) prior to vaccination. S+ = seropositive subjects (antibody concentration ≥ cut-off value) prior to vaccination. The assay was performed on a subset of 100 subjects from Cervarix 3 Group.

End point type	Secondary

End point timeframe:

At Day 0 and at Months 13, 18 and 36

Notes:

[16] - 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: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 3 Group			
Subject group type	Reporting group			
Number of subjects analysed	82			
Units: cells/million T-cells				
median (inter-quartile range (Q1-Q3))				
Anti-HPV-18, CD4 all doubles, S-, Day 0 (N=82)	99.0 (61.0 to 149.0)			
Anti-HPV-18, CD4 all doubles, S-, Month 13 (N=77)	1499.0 (1033.0 to 2928.0)			
Anti-HPV-18, CD4 all doubles, S-, Month 18 (N=77)	1222.0 (796.0 to 2116.0)			
Anti-HPV-18, CD4 all doubles, S-, Month 36 (N=75)	1158.0 (606.0 to 2185.0)			
Anti-HPV-18, CD4 all doubles, S+, Day 0 (N=2)	107.5 (69.0 to 146.0)			
Anti-HPV-18, CD4 all doubles, S+, Month 13 (N=2)	1968.5 (1753.0 to 2184.0)			
Anti-HPV-18, CD4 all doubles, S+, Month 18 (N=2)	1250.0 (1156.0 to 1344.0)			
Anti-HPV-18, CD4 all doubles, S+, Month 36 (N=2)	1399.5 (1004.0 to 1795.0)			
Anti-HPV-18, CD4-d-CD40L, S-, Day 0 (N=82)	82.5 (42.0 to 125.0)			
Anti-HPV-18, CD4-d-CD40L, S-, Month 13 (N=77)	1472.0 (1003.0 to 2880.0)			
Anti-HPV-18, CD4-d-CD40L, S-, Month 18 (N=77)	1199.0 (748.0 to 2098.0)			
Anti-HPV-18, CD4-d-CD40L, S-, Month 36 (N=75)	1154.0 (563.0 to 2157.0)			
Anti-HPV-18, CD4-d-CD40L, S+, Day 0 (N=2)	103.5 (65.0 to 142.0)			
Anti-HPV-18, CD4-d-CD40L, S+, Month 13 (N=2)	1904.5 (1656.0 to 2153.0)			
Anti-HPV-18, CD4-d-CD40L, S+, Month 18 (N=2)	1174.5 (1110.0 to 1239.0)			

Anti-HPV-18, CD4-d-CD40L, S+, Month 36 (N=2)	1320.0 (918.0 to 1722.0)			
Anti-HPV-18, CD4-d-IFNγ, S-, Day 0 (N=82)	35.0 (23.0 to 61.0)			
Anti-HPV-18, CD4-d-IFNγ, S-, Month 13 (N=77)	349.0 (173.0 to 1221.0)			
Anti-HPV-18, CD4-d-IFNγ, S-, Month 18 (N=77)	226.0 (108.0 to 575.0)			
Anti-HPV-18, CD4-d-IFNγ, S-, Month 36 (N=75)	318.0 (140.0 to 766.0)			
Anti-HPV-18, CD4-d-IFNγ, S+, Day 0 (N=2)	33.5 (24.0 to 43.0)			
Anti-HPV-18, CD4-d-IFNγ, S+, Month 13 (N=2)	378.0 (307.0 to 449.0)			
Anti-HPV-18, CD4-d-IFNγ, S+, Month 18 (N=2)	157.5 (136.0 to 179.0)			
Anti-HPV-18, CD4-d-IFNγ, S+, Month 36 (N=2)	389.0 (231.0 to 547.0)			
Anti-HPV-18, CD4-d-IL-2, S-, Day 0 (N=82)	58.5 (32.0 to 98.0)			
Anti-HPV-18, CD4-d-IL-2, S-, Month 13 (N=77)	1398.0 (812.0 to 2743.0)			
Anti-HPV-18, CD4-d-IL-2, S-, Month 18 (N=77)	1102.0 (719.0 to 1924.0)			
Anti-HPV-18, CD4-d-IL-2, S-, Month 36 (N=75)	1086.0 (535.0 to 1974.0)			
Anti-HPV-18, CD4-d-IL-2, S+, Day 0 (N=2)	46.5 (33.0 to 60.0)			
Anti-HPV-18, CD4-d-IL-2, S+, Month 13 (N=2)	1845.0 (1544.0 to 2146.0)			
Anti-HPV-18, CD4-d-IL-2, S+, Month 18 (N=2)	1151.0 (1078.0 to 1224.0)			
Anti-HPV-18, CD4-d-IL-2, S+, Month 36 (N=2)	1160.0 (827.0 to 1493.0)			
Anti-HPV-18, CD4-d-TNFα, S-, Day 0 (N=82)	60.5 (34.0 to 97.0)			
Anti-HPV-18, CD4-d-TNFα, S-, Month 13 (N=77)	1029.0 (649.0 to 2051.0)			
Anti-HPV-18, CD4-d-TNFα, S-, Month 18 (N=77)	921.0 (539.0 to 1783.0)			
Anti-HPV-18, CD4-d-TNFα, S-, Month 36 (N=75)	812.0 (384.0 to 1545.0)			
Anti-HPV-18, CD4-d-TNFα, S+, Day 0 (N=2)	66.5 (29.0 to 104.0)			
Anti-HPV-18, CD4-d-TNFα, S+, Month 13 (N=2)	1449.5 (1317.0 to 1582.0)			
Anti-HPV-18, CD4-d-TNFα, S+, Month 18 (N=2)	954.5 (873.0 to 1036.0)			
Anti-HPV-18, CD4-d-TNFα, S+, Month 36 (N=2)	1127.0 (847.0 to 1407.0)			
Anti-HPV-18, CD8-all doubles, S-, Day 0 (N=82)	11.0 (11.0 to 47.0)			
Anti-HPV-18, CD8-all doubles, S-, Month 13 (N=77)	32.0 (11.0 to 49.0)			
Anti-HPV-18, CD8-all doubles, S-, Month 18 (N=77)	34.0 (11.0 to 50.0)			
Anti-HPV-18, CD8-all doubles, S-, Month 36 (N=75)	33.0 (11.0 to 56.0)			

Anti-HPV-18, CD8-all doubles, S+, Day 0 (N=2)	29.0 (11.0 to 47.0)			
Anti-HPV-18, CD8-all doubles, S+, Month 13 (N=2)	63.5 (39.0 to 88.0)			
Anti-HPV-18, CD8-all doubles, S+, Month 18 (N=2)	11.0 (11.0 to 11.0)			
Anti-HPV-18, CD8-all doubles, S+, Month 36 (N=2)	45.0 (11.0 to 79.0)			
Anti-HPV-18, CD8-d-CD40L, S-, Day 0 (N=82)	7.0 (7.0 to 30.0)			
Anti-HPV-18, CD8-d-CD40L, S-, Month 13 (N=77)	7.0 (7.0 to 38.0)			
Anti-HPV-18, CD8-d-CD40L, S-, Month 18 (N=77)	7.0 (7.0 to 34.0)			
Anti-HPV-18, CD8-d-CD40L, S-, Month 36 (N=75)	7.0 (7.0 to 38.0)			
Anti-HPV-18, CD8-d-CD40L, S+, Day 0 (N=82)	25.0 (7.0 to 43.0)			
Anti-HPV-18, CD8-d-CD40L, S+, Month 13 (N=2)	21.0 (7.0 to 35.0)			
Anti-HPV-18, CD8-d-CD40L, S+, Month 18 (N=2)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-CD40L, S+, Month 36 (N=2)	41.0 (7.0 to 75.0)			
Anti-HPV-18, CD8-d-IFNγ, S-, Day 0 (N=82)	7.0 (7.0 to 41.0)			
Anti-HPV-18, CD8-d-IFNγ, S-, Month 13 (N=77)	7.0 (7.0 to 40.0)			
Anti-HPV-18, CD8-d-IFNγ, S-, Month 18 (N=77)	7.0 (7.0 to 37.0)			
Anti-HPV-18, CD8-d-IFNγ, S-, Month 36 (N=75)	7.0 (7.0 to 44.0)			
Anti-HPV-18, CD8-d-IFNγ, S+, Day 0 (N=2)	25.0 (7.0 to 43.0)			
Anti-HPV-18, CD8-d-IFNγ, S+, Month 13 (N=2)	59.5 (35.0 to 84.0)			
Anti-HPV-18, CD8-d-IFNγ, S+, Month 18 (N=2)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-IFNγ, S+, Month 36 (N=2)	41.0 (7.0 to 75.0)			
Anti-HPV-18, CD8-d-IL-2, S-, Day 0 (N=82)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-IL-2, S-, Month 13 (N=77)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-IL-2, S-, Month 18 (N=77)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-IL-2, S-, Month 36 (N=75)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-IL-2, S+, Day 0 (N=2)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-IL-2, S+, Month 13 (N=2)	45.5 (7.0 to 84.0)			
Anti-HPV-18, CD8-d-IL-2, S+, Month 18 (N=2)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-IL-2, S+, Month 36 (N=2)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-TNFα, S-, Day 0 (N=72)	7.0 (7.0 to 38.0)			
Anti-HPV-18, CD8-d-TNFα, S-, Month 13 (N=77)	7.0 (7.0 to 30.0)			
Anti-HPV-18, CD8-d-TNFα, S-, Month 18 (N=77)	7.0 (7.0 to 40.0)			

Anti-HPV-18, CD8-d-TNFα, S-, Month 36 (N=75)	7.0 (7.0 to 35.0)			
Anti-HPV-18, CD8-d-TNFα, S+, Day 0 (N=2)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-TNFα, S+, Month 13 (N=2)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-TNFα, S+, Month 18 (N=2)	7.0 (7.0 to 7.0)			
Anti-HPV-18, CD8-d-TNFα, S+, Month 36 (N=2)	7.0 (7.0 to 7.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cell-mediated immunogenicity related to anti-HPV-16 specific B CMI response for Cervarix 1 Group and Cervarix 2 Group in a sub-cohort of subjects

End point title	Cell-mediated immunogenicity related to anti-HPV-16 specific B CMI response for Cervarix 1 Group and Cervarix 2 Group in a sub-cohort of subjects[17]

End point description:

The CMI response was assessed as being the frequency of B-cell memory of HPV-16 antigen-specific memory B-cells per million memory B-cells in subjects with detectable B-cells. The results are presented by pre-vaccination status, where S- = seronegative subjects (antibody concentration < cut-off value) prior to vaccination and S+ = seropositive subjects (antibody concentration ≥ cut-off value) prior to vaccination. The assay was performed on a subset of 100 subjects per study group.

End point type	Secondary

End point timeframe:

At Day 0 and Months 7, 12, 24 and 36

Notes:

[17] - 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: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 1 Group	Cervarix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	63		
Units: cells/million B-cells				
median (inter-quartile range (Q1-Q3))				
Anti-HPV-16, S-, Day 0 (N=74, 63)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)		
Anti-HPV-16, S-, Month 7 (N=70, 46)	2155.0 (886.0 to 5421.0)	1510.0 (799.0 to 3114.0)		
Anti-HPV-16, S-, Month 12 (N=55, 42)	801.0 (361.0 to 2648.0)	1145.0 (371.0 to 3215.0)		
Anti-HPV-16, S-, Month 24 (N=75, 60)	318.0 (95.0 to 697.0)	594.5 (147.5 to 1133.5)		
Anti-HPV-16, S-, Month 36 (N=70, 53)	560.5 (157.0 to 1012.0)	448.0 (219.0 to 821.0)		
Anti-HPV-16, S+, Day 0 (N=8, 13)	1.0 (1.0 to 16.0)	1.0 (1.0 to 51.0)		
Anti-HPV-16, S+, Month 7 (N=7, 11)	4838.0 (1513.0 to 11824.0)	477.0 (139.0 to 4928.0)		

Anti-HPV-16, S+, Month 12 (N=2, 9)	5056.0 (5018.0 to 5094.0)	539.0 (340.0 to 2111.0)		
Anti-HPV-16, S+, Month 24 (N=8, 12)	621.0 (324.5 to 1751.5)	568.5 (50.0 to 1955.0)		
Anti-HPV-16, S+, Month 36 (N=6, 13)	475.0 (414.0 to 822.0)	107.0 (1.0 to 1275.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cell-mediated immunogenicity related to anti-HPV-18 specific B CMI response for Cervarix 1 Group and Cervarix 2 Group in a sub-cohort of subjects

End point title	Cell-mediated immunogenicity related to anti-HPV-18 specific B CMI response for Cervarix 1 Group and Cervarix 2 Group in a sub-cohort of subjects[18]

End point description:

The cell-mediated immune response was assessed as being the frequency of B-cell memory of HPV-18 antigen-specific memory B-cells per million memory B-cells in subjects with detectable B-cells. The results are presented by pre-vaccination status, where S- = seronegative subjects (antibody concentration < cut-off value) prior to vaccination and S+ = seropositive subjects (antibody concentration ≥ cut-off value) prior to vaccination. The assay was performed on a subset of 100 subjects per study group.

End point type	Secondary

End point timeframe:

At Day 0 and at Months 7, 12, 24 and 36

Notes:

[18] - 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: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 1 Group	Cervarix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	63		
Units: cells/million B-cells				
median (inter-quartile range (Q1-Q3))				
Anti-HPV-18, S-, Day 0 (N=72, 63)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)		
Anti-HPV-18, S-, Month 7 (N=67, 48)	958.0 (386.0 to 2500.0)	817.5 (368.0 to 1894.5)		
Anti-HPV-18, S-, Month 24 (N=72, 61)	236.0 (61.5 to 710.0)	274.0 (71.0 to 829.0)		
Anti-HPV-18, S-, Month 36 (N=67, 54)	269.0 (62.0 to 732.0)	284.5 (90.0 to 582.0)		
Anti-HPV-18, S+, Day 0 (N=10, 14)	1.0 (1.0 to 44.0)	1.0 (1.0 to 22.0)		
Anti-HPV-18, S+, Month 7 (N=10, 10)	2016.5 (423.0 to 2797.0)	439.5 (31.0 to 1779.0)		
Anti-HPV-18, S+, Month 24 (N=11, 12)	299.0 (117.0 to 643.0)	338.5 (174.0 to 786.0)		
Anti-HPV-18, S+, Month 36 (N=9, 12)	154.0 (141.0 to 427.0)	93.0 (18.0 to 762.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cell-mediated immunogenicity related to anti-HPV-16 specific B CMI response for Cervarix 3 Group in a sub-cohort of subjects

End point title	Cell-mediated immunogenicity related to anti-HPV-16 specific B CMI response for Cervarix 3 Group in a sub-cohort of subjects[19]

End point description:

The cell-mediated immune response was assessed as being the frequency of B-cell memory of HPV-16 antigen-specific memory B-cells per million memory B-cells in subjects with detectable B-cells. The results are presented by pre-vaccination status, where S- = seronegative subjects (antibody concentration < cut-off value) prior to vaccination and S+ = seropositive subjects (antibody concentration ≥ cut-off value) prior to vaccination. The assay was performed on a subset of 100 subjects from Cervarix 3 Group.

End point type	Secondary

End point timeframe:

At Day 0 and at Months 13, 18 and 36

Notes:

[19] - 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: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 3 Group			
Subject group type	Reporting group			
Number of subjects analysed	68			
Units: cells/million B-cells				
median (inter-quartile range (Q1-Q3))				
Anti-HPV-16, S-, Day 0 (N=66)	1.0 (1.0 to 7.0)			
Anti-HPV-16, S-, Month 13 (N=68)	2809.5 (1402.5 to 5045.5)			
Anti-HPV-16, S-, Month 18 (N=60)	766.0 (412.0 to 1946.5)			
Anti-HPV-16, S-, Month 36 (N=67)	613.0 (322.0 to 1301.0)			
Anti-HPV-16, S+, Day 0 (N=5)	1.0 (1.0 to 20.0)			
Anti-HPV-16, S+, Month 13 (N=5)	5996.0 (919.0 to 7353.0)			
Anti-HPV-16, S+, Month 18 (N=5)	2130.0 (808.0 to 2271.0)			
Anti-HPV-16, S+, Month 36 (N=6)	425.0 (102.0 to 714.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cell-mediated immunogenicity related to anti-HPV-18 specific B CMI response for Cervarix 3 Group in a sub-cohort of subjects

End point title	Cell-mediated immunogenicity related to anti-HPV-18 specific B CMI response for Cervarix 3 Group in a sub-cohort of subjects[20]

End point description:

The cell-mediated immune response was assessed as being the frequency of B-cell memory of HPV-18 antigen-specific memory B-cells per million memory B-cells in subjects with detectable B-cells. The results are presented by pre-vaccination status, where S- = seronegative subjects (antibody concentration < cut-off value) prior to vaccination and S+ = seropositive subjects (antibody concentration ≥ cut-off value) prior to vaccination. The assay was performed on a subset of 100 subjects from Cervarix 3 Group.

End point type	Secondary

End point timeframe:

At Day 0 and at Months 13, 18 and 36

Notes:

[20] - 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: As Group Cervarix 3 received the last vaccination dose at Month 12, results were presented separately for Groups Cervarix 3 and for Cervarix 1 and 2.

End point values	Cervarix 3 Group			
Subject group type	Reporting group			
Number of subjects analysed	72			
Units: cells/million B-cells				
median (inter-quartile range (Q1-Q3))				
Anti-HPV-18, S-, Day 0 (N=70)	1.0 (1.0 to 1.0)			
Anti-HPV-18, S-, Month 13 (N=71)	1165.0 (602.0 to 1660.0)			
Anti-HPV-18, S-, Month 18 (N=64)	561.5 (132.0 to 1213.5)			
Anti-HPV-18, S-, Month 36 (N=72)	361.0 (112.0 to 724.0)			
Anti-HPV-18, S+, Day 0 (N=1)	48.0 (48.0 to 48.0)			
Anti-HPV-18, S+, Month 13 (N=2)	758.0 (114.0 to 1402.0)			
Anti-HPV-18, S+, Month 18 (N=1)	938.0 (938.0 to 938.0)			
Anti-HPV-18, S+, Month 36 (N=1)	1231.0 (1231.0 to 1231.0)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of any solicited local symptom regardless of their intensity grade. Grade 3 pain = significant pain at rest, that prevented normal every day activity. Grade 3 redness/swelling = redness/swelling above 50 millimeters (mm). Subjects from Cervarix 1 and Cervarix 3 Groups received only 2 doses of vaccine, therefore data are presented up to Dose 2.

End point type	Secondary

End point timeframe:

During the 7 day period (Days 0-6) after each vaccine dose and across doses

End point values	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	480	413	
Units: Subjects				
Any Pain - Dose 1 (N=549, 480, 411)	461	439	354	
Grade 3 Pain - Dose 1 (N=549, 480, 411)	24	21	21	
Any Pain - Dose 2 (N=544, 470, 404)	446	377	323	
Grade 3 Pain - Dose 2 (N=544, 470, 404)	33	25	31	
Any Pain - Dose 3 (N=0, 464, 0)	0	358	0	
Grade 3 Pain - Dose 3 (N=0, 464, 0)	0	20	0	
Any Pain - Across doses (N=550, 480, 413)	499	461	381	
Grade 3 Pain - Across doses (N=550, 480, 413)	50	53	48	
Any Redness - Dose 1 (N=549, 480, 411)	167	135	126	
Grade 3 Redness - Dose 1 (N=549, 480, 411)	0	2	2	
Any Redness - Dose 2 (N=544, 470, 404)	180	143	153	
Grade 3 Redness - Dose 2 (N=544, 470, 404)	4	5	1	
Any Redness - Dose 3 (N=0, 464, 0)	0	142	0	
Grade 3 Redness - Dose 3 (N=0, 464, 0)	0	5	0	
Any Redness - Across doses (N=550, 480, 413)	247	212	197	
Grade 3 Redness - Across doses (N=550, 480, 413)	4	10	3	
Any Swelling - Dose 1 (N=549, 480, 411)	141	105	101	
Grade 3 Swelling - Dose 1 (N=549, 480, 411)	3	1	4	
Any Swelling - Dose 2 (N=544, 470, 404)	166	131	135	
Grade 3 Swelling - Dose 2 (N=544, 470, 404)	2	4	2	
Any Swelling - Dose 3 (N=0, 464, 0)	0	136	0	
Grade 3 Swelling - Dose 3 (N=0, 464, 0)	0	3	0	
Any Swelling - Across doses (N=550, 480, 413)	225	204	171	

Grade 3 Swelling - Across doses (N=550, 480, 413)	5	6	6	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Assessed solicited general symptoms were arthralgia, fatigue, gastrointestinal symptoms, headache, myalgia, rash, fever and urticaria. Any = occurrence of any solicited general symptom regardless of intensity grade or relationship to vaccination. Any Fever = axillary temperature ≥ 37.5 degrees Celsius (°C). Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever greater than (>) 39.0 °C. Related = general symptom assessed by the investigator as causally related to the vaccination. Subjects from Cervarix 1 and Cervarix 3 Groups received only 2 doses of vaccine, therefore data are presented up to Dose 2.

End point type	Secondary

End point timeframe:

During the 7-day period (Days 0-6) after each vaccine dose and across doses

End point values	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	480	413	
Units: Subjects				
Any Artharlgia - Dose 1 (N=549, 480, 411)	61	53	52	
Grade 3 Arthralgia - Dose 1 (N=549, 480, 411)	8	3	3	
Related Arthralgia - Dose 1 (N=549, 480, 411)	56	50	45	
Any Artharlgia - Dose 2 (N=544, 470, 404)	71	56	64	
Grade 3 Arthralgia - Dose 2 (N=544, 470, 404)	2	1	3	
Related Arthralgia - Dose 2 (N=544, 470, 404)	64	50	57	
Any Artharlgia - Dose 3 (N=0, 464, 0)	0	49	0	
Grade 3 Arthralgia - Dose 3 (N=0, 464, 0)	0	3	0	
Related Arthralgia - Dose 3 (N=0, 464, 0)	0	42	0	
Any Artharlgia - Across doses (N=550, 480, 413)	111	107	93	
Grade 3 Arthralgia -Across doses (N=550, 480, 413)	9	6	6	
Related Arthralgia -Across doses (N=550, 480, 413)	105	102	83	

Any Fatigue - Dose 1 (N=549, 480, 411)	181	238	156	
Grade 3 Fatigue - Dose 1 (N=549, 480, 411)	7	9	10	
Related Fatigue - Dose 1 (N=549, 480, 411)	153	205	129	
Any Fatigue - Dose 2 (N=544, 470, 404)	167	168	144	
Grade 3 Fatigue - Dose 2 (N=544, 470, 404)	9	11	14	
Related Fatigue - Dose 2 (N=544, 470, 404)	149	142	119	
Any Fatigue - Dose 3 (N=0, 464, 0)	0	177	0	
Grade 3 Fatigue - Dose 3 (N=0, 464, 0)	0	12	0	
Related Fatigue - Dose 3 (N=0, 464, 0)	0	161	0	
Any Fatigue - Across doses (N=550, 480, 413)	247	310	215	
Grade 3 Fatigue - Across doses (N=550, 480, 413)	14	25	21	
Related Fatigue - Across doses (N=550, 480, 413)	221	294	185	
Any Gastrointestinal - Dose 1 (N=549, 480, 411)	59	88	44	
Grade 3 Gastrointestinal -Dose 1 (N=549, 480, 411)	1	2	3	
Related Gastrointestinal -Dose 1 (N=549, 480, 411)	49	67	32	
Any Gastrointestinal - Dose 2 (N=544, 470, 404)	51	50	48	
Grade 3 Gastrointestinal -Dose 2 (N=544, 470, 404)	6	2	4	
Related Gastrointestinal -Dose 2 (N=544, 470, 404)	34	36	40	
Any Gastrointestinal - Dose 3 (N=0, 464, 0)	0	45	0	
Grade 3 Gastrointestinal -Dose 3 (N=0, 464, 0)	0	7	0	
Related Gastrointestinal -Dose 3 (N=0, 464, 0)	0	35	0	
Any Gastrointestinal -Across doses (N=550,480,413)	98	134	77	
Grade 3 Gastroint. -Across doses (N=550, 480, 413)	7	11	7	
Related Gastroint. -Across doses (N=550, 480, 413)	77	106	62	
Any Headache - Dose 1 (N=549, 480, 411)	133	161	128	
Grade 3 Headache - Dose 1 (N=549, 480, 411)	9	10	10	
Related Headache - Dose 1 (N=549, 480, 411)	104	136	104	
Any Headache - Dose 2 (N=544, 470, 404)	128	129	130	
Grade 3 Headache - Dose 2 (N=544, 470, 404)	14	5	6	
Related Headache - Dose 2 (N=544, 470, 404)	107	108	100	
Any Headache - Dose 3 (N=0, 464, 0)	0	124	0	
Grade 3 Headache - Dose 3 (N=0, 464, 0)	0	11	0	

Related Headache - Dose 3 (N=0, 464, 0)	0	106	0	
Any Headache - Across doses (N=550, 480, 413)	204	246	185	
Grade 3 Headache - Across doses (N=550, 480, 413)	19	26	16	
Related Headache - Across doses (N=550, 480, 413)	176	219	148	
Any Myalgia - Dose 1 (N=549, 480, 411)	206	236	160	
Grade 3 Myalgia - Dose 1 (N=549, 480, 411)	16	12	8	
Related Myalgia - Dose 1 (N=549, 480, 411)	191	223	140	
Any Myalgia - Dose 2 (N=544, 470, 404)	196	182	150	
Grade 3 Myalgia - Dose 2 (N=544, 470, 404)	13	11	10	
Related Myalgia - Dose 2 (N=544, 470, 404)	182	171	136	
Any Myalgia - Dose 3 (N=0, 464, 0)	0	158	0	
Grade 3 Myalgia - Dose 3 (N=0, 464, 0)	0	8	0	
Related Myalgia - Dose 3 (N=0, 464, 0)	0	150	0	
Any Myalgia - Across doses (N=550, 480, 413)	278	295	221	
Grade 3 Myalgia - Across doses (N=550, 480, 413)	24	25	15	
Related Myalgia - Across doses (N=550, 480, 413)	265	285	201	
Any Rash - Dose 1 (N=549, 480, 411)	17	8	15	
Grade 3 Rash - Dose 1 (N=549, 480, 411)	1	0	0	
Related Rash - Dose 1 (N=549, 480, 411)	13	5	13	
Any Rash - Dose 2 (N=544, 470, 404)	17	11	16	
Grade 3 Rash - Dose 2 (N=544, 470, 404)	1	0	0	
Related Rash - Dose 2 (N=544, 470, 404)	13	10	16	
Any Rash - Dose 3 (N=0, 464, 0)	0	8	0	
Grade 3 Rash - Dose 3 (N=0, 464, 0)	0	0	0	
Related Rash - Dose 3 (N=0, 464, 0)	0	5	0	
Any Rash - Across doses (N=550, 480, 413)	33	25	29	
Grade 3 Rash - Across doses (N=550, 480, 413)	2	0	0	
Related Rash - Across doses (N=550, 480, 413)	26	18	28	
Any Fever - Dose 1 (N=549, 480, 411)	24	17	18	
Grade 3 Fever - Dose 1 (N=549, 480, 411)	1	0	0	
Related Fever - Dose 1 (N=549, 480, 411)	15	12	15	
Any Fever - Dose 2 (N=544, 470, 404)	21	15	25	
Grade 3 Fever - Dose 2 (N=544, 470, 404)	1	3	1	
Related Fever - Dose 2 (N=544, 470, 404)	17	12	18	
Any Fever - Dose 3 (N=0, 464, 0)	0	29	0	
Grade 3 Fever - Dose 3 (N=0, 464, 0)	0	0	0	

Related Fever - Dose 3 (N=0, 464, 0)	0	25	0	
Any Fever - Across doses (N=550, 480, 413)	41	48	42	
Grade 3 Fever - Across doses (N=550, 480, 413)	2	3	1	
Related Fever - Across doses (N=550, 480, 413)	29	39	32	
Any Urticaria - Dose 1 (N=549, 480, 411)	9	7	4	
Grade 3 Urticaria - Dose 1 (N=549, 480, 411)	1	1	0	
Related Urticaria - Dose 1 (N=549, 480, 411)	7	3	4	
Any Urticaria - Dose 2 (N=544, 470, 404)	7	9	9	
Grade 3 Urticaria - Dose 2 (N=544, 470, 404)	0	0	0	
Related Urticaria - Dose 2 (N=544, 470, 404)	6	7	8	
Any Urticaria - Dose 3 (N=0, 464, 0)	0	5	0	
Grade 3 Urticaria - Dose 3 (N=0, 464, 0)	0	0	0	
Related Urticaria - Dose 3 (N=0, 464, 0)	0	3	0	
Any Urticaria - Across doses (N=550, 480, 413)	15	15	13	
Grade 3 Urticaria - Across doses (N=550, 480, 413)	1	1	0	
Related Urticaria - Across doses (N=550, 480, 413)	13	11	12	

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 AE covers 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 and 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. Any = any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 = unsolicited AE preventing normal activity. Related = unsolicited AE assessed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	482	415	
Units: Subjects				
Any unsolicited AEs	97	167	74	
Grade 3 unsolicited AEs	2	17	6	
Related unsolicited AEs	11	24	13	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any potential Immune-Mediated Diseases (pIMDs)

End point title	Number of subjects with any potential Immune-Mediated Diseases (pIMDs)

End point description:

pIMDs are a subset of AEs that include both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which may or may not have an autoimmune etiology. The data for Cervarix 1 and 2 Groups are only presented up to Month 13, as the data were only collected up to Month 13 for those 2 groups.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 13 (for Cervarix 1 Group and Cervarix 2 Group) and from Day 0 up to Month 18 (for Cervarix 3 Group)

End point values	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	482	415	
Units: Subjects				
Any pIMDs,from Day 0 up to Month 13(N=550,482,415)	2	2	2	
Any pIMDs, from Day 0 up to Month 18 (N=0, 0, 415)	0	0	2	

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:

MSC include AEs prompting emergency room or physician visits that are not related to common diseases or routine visits for physical examination or vaccination, or serious adverse events (SAEs) that are not related to common diseases. Common diseases include upper respiratory infections, sinusitis,

pharyngitis, gastroenteritis, urinary tract infections, cervico-vaginal yeast infections, menstrual cycle abnormalities and injury.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 36 (throughout the study period)

End point values	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	482	415	
Units: Subjects	134	153	87	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, related and fatal serious adverse events (SAEs)

End point title	Number of subjects with any, related and fatal serious adverse events (SAEs)

End point description:

SAEs assessed include medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity or were a congenital anomaly/birth defect in the offspring of a study subject. Any = any SAE regardless of intensity grade or relation to vaccination. Related = SAE assessed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 36 (throughout the study period)

End point values	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	482	415	
Units: Subjects				
Any SAEs	20	28	24	
Related SAEs	0	0	1	
Fatal SAEs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting pregnancies and outcomes of reported pregnancies

End point title	Number of subjects reporting pregnancies and outcomes of reported pregnancies

End point description:

Outcomes of reported pregnancies were: Ectopic pregnancy, Elective termination NO apparent congenital anomaly (ACA), Live Infant NO ACA, Stillbirth NO ACA.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 36 (throughout the study period)

End point values	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	34	1	
Units: Subjects				
Ectopic pregnancy	0	1	0	
Elective termination NO ACA	0	2	0	
Live Infant NO ACA	1	30	1	
Stillbirth NO ACA	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects completing the vaccination course

End point title	Number of subjects completing the vaccination course

End point description:

The number of subjects completing the vaccination course was assessed as the number of subjects with at least one dose received during the study.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 13

End point values	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	482	415	
Units: Subjects	550	482	415	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms were collected during the 7-day period (Days 0-6) after vaccination. Unsolicited AEs were collected during the 30-day period (Days 0-29) after vaccination. SAEs were collected from Day 0 to Month 36.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and encoded as equal to the number of subjects affected. For the systematically assessed other (non-serious) adverse events, the number of exposed subjects included those from Total Vaccinated cohort who had the symptom sheet completed.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Cervarix 1 Group

Reporting group description:

Female subjects aged 9 to 14 years at the time of the first vaccination, who received 2 doses of the Cervarix vaccine at Months 0 and 6. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.

Reporting group title	Cervarix 2 Group

Reporting group description:

Female subjects aged 15 to 25 years at the time of the first vaccination, who received 3 doses of the Cervarix vaccine at Months 0, 1 and 6. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.

Reporting group title	Cervarix 3 Group

Reporting group description:

Female subjects aged 9 to 14 years at the time of the first vaccination, who received 2 doses of the Cervarix vaccine at Months 0 and 12. The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.

Serious adverse events	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 550 (3.64%)	28 / 482 (5.81%)	24 / 415 (5.78%)
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)			
Medulloblastoma			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Cholesteatoma			

subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Synovial sarcoma			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Ectopic pregnancy termination			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Pregnancy, puerperium and perinatal conditions			
Hyperemesis gravidarum			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Premature baby			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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 threatened			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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

Postpartum haemorrhage			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Stillbirth			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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			
Ovarian cyst ruptured			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Respiratory, thoracic and mediastinal disorders			
Transient tachypnoea of the newborn			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Respiratory disorder			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Tonsillar hypertrophy			

subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Schizoaffective disorder			
subjects affected / exposed	0 / 550 (0.00%)	2 / 482 (0.41%)	0 / 415 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Forearm fracture			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Carbon monoxide poisoning			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Intentional overdose			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Ligament rupture			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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

Road traffic accident			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Alcohol poisoning			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
VIIth nerve paralysis			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Strabismus			

subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Gastrointestinal disorders			
Abdominal strangulated hernia			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Abdominal pain			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Abdominal pain lower			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal haemorrhage			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Constipation			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Chronic gastritis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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			
Cholelithiasis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
IgA nephropathy			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Musculoskeletal and connective tissue disorders			
Synovial cyst			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Systemic lupus erythematosus			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Dengue fever			

subjects affected / exposed	1 / 550 (0.18%)	4 / 482 (0.83%)	3 / 415 (0.72%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis bacterial			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 550 (0.18%)	1 / 482 (0.21%)	0 / 415 (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
Tubo-ovarian abscess			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Tonsillitis			
subjects affected / exposed	1 / 550 (0.18%)	1 / 482 (0.21%)	2 / 415 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Infectious mononucleosis			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic inflammatory disease			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Peritonitis			

subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Salpingitis			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Salpingo-oophoritis			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Otitis media acute			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Pelvic infection			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	0 / 415 (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
Pharyngitis			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (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
Viral infection			
subjects affected / exposed	0 / 550 (0.00%)	0 / 482 (0.00%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			

subjects affected / exposed	0 / 550 (0.00%)	3 / 482 (0.62%)	5 / 415 (1.20%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 550 (0.36%)	1 / 482 (0.21%)	2 / 415 (0.48%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypovolaemia			
subjects affected / exposed	0 / 550 (0.00%)	1 / 482 (0.21%)	1 / 415 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 550 (0.18%)	0 / 482 (0.00%)	0 / 415 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cervarix 1 Group	Cervarix 2 Group	Cervarix 3 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	513 / 550 (93.27%)	466 / 482 (96.68%)	387 / 415 (93.25%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed[1]	499 / 550 (90.73%)	461 / 480 (96.04%)	381 / 413 (92.25%)
occurrences (all)	499	461	381
Redness			
subjects affected / exposed[2]	247 / 550 (44.91%)	212 / 480 (44.17%)	197 / 413 (47.70%)
occurrences (all)	247	212	197
Swelling			
subjects affected / exposed[3]	225 / 550 (40.91%)	204 / 480 (42.50%)	171 / 413 (41.40%)
occurrences (all)	225	204	171
Arthralgia			

subjects affected / exposed[4]	111 / 550 (20.18%)	107 / 480 (22.29%)	93 / 413 (22.52%)
occurrences (all)	111	107	93
Fatigue			
subjects affected / exposed[5]	247 / 550 (44.91%)	310 / 480 (64.58%)	215 / 413 (52.06%)
occurrences (all)	247	310	215
Gastrointestinal symptoms			
subjects affected / exposed[6]	98 / 550 (17.82%)	134 / 480 (27.92%)	77 / 413 (18.64%)
occurrences (all)	98	134	77
Headache			
subjects affected / exposed[7]	204 / 550 (37.09%)	246 / 480 (51.25%)	185 / 413 (44.79%)
occurrences (all)	204	246	185
Myalgia			
subjects affected / exposed[8]	278 / 550 (50.55%)	295 / 480 (61.46%)	221 / 413 (53.51%)
occurrences (all)	278	295	221
Rash			
subjects affected / exposed[9]	33 / 550 (6.00%)	25 / 480 (5.21%)	29 / 413 (7.02%)
occurrences (all)	33	25	29
Fever			
subjects affected / exposed[10]	41 / 550 (7.45%)	48 / 480 (10.00%)	42 / 413 (10.17%)
occurrences (all)	41	48	42
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	22 / 550 (4.00%)	27 / 482 (5.60%)	14 / 415 (3.37%)
occurrences (all)	22	27	14

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheet completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheet completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheet completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheet completed.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheet completed.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheet completed.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheet completed.
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheet completed.
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheet completed.
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheet completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2013	The HPV-070 protocol is being amended for the following reason: The assay used to measure anti-HPV-16/-18 antibody concentrations at the designated laboratory was improved to increase the assay precision by changing the assay cut-off value from 8 EL.U/mL to 19 EL.U/mL for HPV-16 and from 7 EL.U/mL to 18 EL.U/mL for HPV-18. This change in the assay was implemented for the testing of samples from Month 18 onwards.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported