Clinical trial results:
A Phase IIIb observer-blind, randomized, multicentre primary immunization study to evaluate the immunogenicity and safety of GSK Biologicals' HPV-16/18 L1 VLP AS04 vaccine and Merck's Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine, when administered intramuscularly according to alternative 2-dose schedules in 9-14-year-old healthy females.

Summary

EudraCT number	2011-002035-26
Trial protocol	FR SE
Global end of trial date	27 October 2015

Results information

Result version number	v3 (current)
This version publication date	12 April 2020
First version publication date	21 April 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	115411

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01462357
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	22 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 October 2015
Global end of trial reached?	Yes
Global end of trial date	27 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate sequentially if the immunogenicity (as determined by enzyme-linked immunosorbent assay [ELISA]) of GSK Biologicals' HPV-16/18 L1 Virus-like-particle (VLP) AS04 vaccine administered according to a 2-dose schedule at 0, 6 months is non-inferior/superior to that of Merck's HPV-6/11/16/18 L1 VLP recombinant vaccine administered according to a 2-dose schedule at 0, 6 months in 9-14 year-old females, 1 month after the last dose (Month 7).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 72
Country: Number of subjects enrolled	France: 231
Country: Number of subjects enrolled	Hong Kong: 534
Country: Number of subjects enrolled	Singapore: 242
Worldwide total number of subjects	1079
EEA total number of subjects	303

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	551
Adolescents (12-17 years)	528
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

1079 subjects entered this study, of which 4 subjects signed an informed consent but did not receive a single dose of the vaccine and were hence not counted as starting the study.

Pre-assignment period milestones

Number of subjects started	1079
Number of subjects completed	1075

Pre-assignment subject non-completion reasons

Reason: Number of subjects	No vaccine administered: 4

Period 1

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

Blinding implementation details:

Data was collected in an observer-blind manner. By observer-blind, it is meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint (e.g. immunogenicity, reactogenicity, and safety) were all unaware of which vaccine was administered. To do so, vaccine preparation and administration were be done by authorised medical personnel who did not participate in any of the study clinical evaluation assays.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervarix 2 dose Group

Arm description:

Subjects who received 2 doses of Cervarix vaccine at Day 0 and Month 6 and 1 dose of placebo at Month 2. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.

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

Dosage and administration details:

2 doses of 0.5 mL supplied as a liquid in individual pre-filled syringes administered intramuscularly in the deltoid muscle of the non-dominant arm at Day 0 and Month 6.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.5 mL supplied as a liquid in individual pre-filled syringes, administered intramuscularly in

the deltoid muscle of the non-dominant arm at Month 2 (Cervarix 2 dose Group and Gardasil 2 dose Group) to maintain blinding.

Arm title	Gardasil 2 dose Group

Arm description:

Subjects who received 2 doses of Gardasil vaccine at Day 0 and Month 6 and 1 dose of placebo at Month 2. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.5 mL supplied as a liquid in individual pre-filled syringes, administered intramuscularly in the deltoid muscle of the non-dominant arm at Month 2 (Cervarix 2 dose Group and Gardasil 2 dose Group) to maintain blinding.

Investigational medicinal product name	Gardasil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

2 or 3 doses of 0.5 mL supplied as a liquid in individual pre-filled syringes or vials to be administered intramuscularly in the deltoid muscle of the non-dominant arm at Day 0 and Month 6 (Gardasil 2 dose Group) or at Day 0, Month 2 and Month 6 (Gardasil 3 dose Group), respectively.

Arm title	Gardasil 3 dose Group

Arm description:

Subjects who received 3 doses of Gardasil vaccine at Day 0 and at Months 2 and 6. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.

Arm type	Experimental
Investigational medicinal product name	Gardasil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

2 or 3 doses of 0.5 mL supplied as a liquid in individual pre-filled syringes or vials to be administered intramuscularly in the deltoid muscle of the non-dominant arm at Day 0 and Month 6 (Gardasil 2 dose Group) or at Day 0, Month 2 and Month 6 (Gardasil 3 dose Group), respectively.

Number of subjects in period 1[1]	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group
Started	359	358	358
Completed	351	339	346
Not completed	8	19	12

Consent withdrawal (not due to an adverse event)	3	11	3
Death	-	-	1
Migrated/moved from study area	2	3	1
Lost to follow-up	3	5	7

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 1079 subjects entered this study, of which 4 subjects signed an informed consent but did not receive a single dose of the vaccine and were hence not counted as starting the study.

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix 2 dose Group
Reporting group description:	
Subjects who received 2 doses of Cervarix vaccine at Day 0 and Month 6 and 1 dose of placebo at Month 2. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.	
Reporting group title	Gardasil 2 dose Group
Reporting group description:	
Subjects who received 2 doses of Gardasil vaccine at Day 0 and Month 6 and 1 dose of placebo at Month 2. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.	
Reporting group title	Gardasil 3 dose Group
Reporting group description:	
Subjects who received 3 doses of Gardasil vaccine at Day 0 and at Months 2 and 6. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.	

Reporting group values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group
Number of subjects	359	358	358
Age categorical Units: Subjects			
Age Continuous Units: Years			
arithmetic mean	11.5	11.5	11.6
standard deviation	± 1.64	± 1.56	± 1.64
Sex: Female, Male Units: Subjects			
Female	359	358	358
Male	0	0	0
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	4	6	4
Asian - Central / South Asian Heritage	1	1	2
Asian - East Asian Heritage	179	178	179
Asian - South East Asian Heritage	81	78	83
White - Arabic / North African Heritage	5	7	7
White - Caucasian / European Heritage	89	86	83
White - Caucasian / African Heritage	0	1	0
African - White / Caucasian Heritage	0	1	0

Reporting group values	Total		
Number of subjects	1075		

Age categorical Units: Subjects			

Age Continuous Units: Years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: Subjects			
Female Male	1075 0		
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American Asian - Central / South Asian Heritage Asian - East Asian Heritage Asian - South East Asian Heritage White - Arabic / North African Heritage White - Caucasian / European Heritage White - Caucasian / African Heritage African - White / Caucasian Heritage	14 4 536 242 19 258 1 1		

End points

End points reporting groups

Reporting group title	Cervarix 2 dose Group
Reporting group description:	
Subjects who received 2 doses of Cervarix vaccine at Day 0 and Month 6 and 1 dose of placebo at Month 2. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.	
Reporting group title	Gardasil 2 dose Group
Reporting group description:	
Subjects who received 2 doses of Gardasil vaccine at Day 0 and Month 6 and 1 dose of placebo at Month 2. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.	
Reporting group title	Gardasil 3 dose Group
Reporting group description:	
Subjects who received 3 doses of Gardasil vaccine at Day 0 and at Months 2 and 6. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.	

Primary: Number of seroconverted subjects for anti-HPV-16/18 antibodies as assessed by Enzyme-Linked Immunosorbent Assay (ELISA) at Month 7 based on the ATP cohort for immunogenicity

End point title	Number of seroconverted subjects for anti-HPV-16/18 antibodies as assessed by Enzyme-Linked Immunosorbent Assay (ELISA) at Month 7 based on the ATP cohort for immunogenicity
End point description:	
Seroconversion was defined as the appearance of antibodies (i.e. anti-HPV-16 and anti-HPV-18 antibody titers greater than or equal to (≥) 19 and 18 ELISA units per milliliter (EL.U/mL), respectively), in the serum of subjects seronegative before vaccination.	
End point type	Primary
End point timeframe:	
At Month 7 (i.e. one month after the last dose of study vaccine)	

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	334	331	333	
Units: Subjects				
Anti-HPV-16 (N=330, 327, 322)	330	327	322	
Anti-HPV-18 (N=334, 331, 333)	334	331	333	

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 rates (SCR): To evaluate sequentially if the immunogenicity (as determined by ELISA) of Cervarix vaccine administered according to a 2-dose	

schedule at 0, 6 months is non-inferior to that of Gardasil vaccine administered according to a 2-dose schedule at 0, 6 months, 1 month after the last dose (Month 7), in initially seronegative subjects.

Comparison groups	Cervarix 2 dose Group v Gardasil 2 dose Group
Number of subjects included in analysis	665
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in SCR
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.16
upper limit	1.15

Notes:

[1] - Non-inferiority with respect to seroconversion was shown if, one month after the last dose, for both anti-HPV-16 and anti-HPV-18 antibodies, the upper limit of the 95% confidence interval (CI) for the difference (Gardasil 2 dose Group minus Cervarix 2 dose 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 SCR: To evaluate sequentially if the immunogenicity (as determined by ELISA) of Cervarix vaccine administered according to a 2-dose schedule at 0, 6 months is non-inferior to that of Gardasil vaccine administered according to a 2-dose schedule at 0, 6 months, 1 month after the last dose (Month 7), in initially seronegative subjects.

Comparison groups	Gardasil 2 dose Group v Cervarix 2 dose Group
Number of subjects included in analysis	665
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	-1.15
upper limit	1.14

Notes:

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

Primary: Anti-HPV-16/18 antibody titers as assessed by ELISA at Month 7 based on the ATP cohort for immunogenicity

End point title	Anti-HPV-16/18 antibody titers as assessed by ELISA at Month 7 based on the ATP cohort for immunogenicity

End point description:

Anti-HPV 16/18 antibody titers were presented as Geometric Mean Titers (GMTs) and expressed 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)

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	334	331	333	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (N=330,327,322)	8244.1 (7678.3 to 8851.7)	5056.0 (4596.5 to 5561.5)	4807.4 (4420.8 to 5227.7)	
Anti-HPV-18 (N=334,331,333)	5277.4 (4858.6 to 5732.4)	1207.2 (1092.9 to 1333.4)	1653.5 (1484.4 to 1841.8)	

Statistical analyses

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

Statistical analysis description:

Immune response to anti-HPV-16 in terms of Geometric Mean Titers (GMT): To evaluate sequentially if the immunogenicity (as determined by ELISA) of Cervarix vaccine administered according to a 2-dose schedule at 0, 6 months is non-inferior to that of Gardasil vaccine administered according to a 2-dose schedule at 0, 6 months, 1 month after the last dose (Month 7), in initially seronegative subjects.

Comparison groups	Gardasil 2 dose Group v Cervarix 2 dose Group
Number of subjects included in analysis	665
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.69

Notes:

[3] - Non-inferiority with respect to GMT was shown if, one month after the last dose, for both anti-HPV-16 and anti-HPV-18 antibodies, the upper limit of the 95% CI for the GMT ratio (Gardasil 2 dose Group divided by Cervarix 2 dose Group) was below 2.

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

Statistical analysis description:

Immune response to anti-HPV-18 in terms of GMT: To evaluate sequentially if the immunogenicity (as determined by ELISA) of Cervarix vaccine administered according to a 2-dose schedule at 0, 6 months is non-inferior to that of Gardasil vaccine administered according to a 2-dose schedule at 0, 6 months, 1 month after the last dose (Month 7), in initially seronegative subjects.

Comparison groups	Gardasil 2 dose Group v Cervarix 2 dose Group
Number of subjects included in analysis	665
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	0.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.26

Notes:

[4] - Non-inferiority with respect to GMT was shown if, one month after the last dose, for both anti-HPV-16 and anti-HPV-18 antibodies, the upper limit of the 95% confidence interval (CI) for the GMT ratio (Gardasil 2 dose Group divided by Cervarix 2 dose Group) was below 2.

Primary: Anti-HPV-16/18 antibody titers as assessed by ELISA at Month 7 based on the Total Vaccinated Cohort (TVC)

End point title	Anti-HPV-16/18 antibody titers as assessed by ELISA at Month 7 based on the Total Vaccinated Cohort (TVC)

End point description:

Anti-HPV 16/18 antibody titers were presented as Geometric Mean Titers (GMTs) and expressed 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)

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	357	353	351	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (N=357, 353, 351)	8256.4 (7650.3 to 8910.6)	4886.1 (4435.4 to 5382.6)	4789.2 (4409.6 to 5201.4)	
Anti-HPV-18 (N=357, 353, 351)	5267.8 (4857.1 to 5713.2)	1166.3 (1056 to 1288.2)	1635.8 (1470 to 1820.4)	

Statistical analyses

Statistical analysis title	Anti-HPV-18 immune response

Statistical analysis description:

Anti-HPV-18 immune response: To evaluate sequentially if the immunogenicity (as determined by ELISA) of Cervarix vaccine administered according to a 2-dose schedule at 0, 6 months is superior to that of Gardasil vaccine administered according to a 2-dose schedule at 0, 6 months, in 9-14 year-old females, 1 month after the last dose (Month 7) regardless of serostatus.

Comparison groups	Cervarix 2 dose Group v Gardasil 2 dose Group
Number of subjects included in analysis	710
Analysis specification	Pre-specified
Analysis type	superiority[5]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	4.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.97
upper limit	5.13

Notes:

[5] - Superiority was shown if the lower limit of the 95% CI for the ratio of GMTs (Cervarix 2 dose Group divided by Gardasil 2 dose Group) was above 1 for anti-HPV-18 antibodies.

Statistical analysis title	Anti-HPV-16 immune response

Statistical analysis description:

Anti-HPV-16 immune response: To evaluate sequentially if the immunogenicity (as determined by ELISA) of Cervarix vaccine administered according to a 2-dose schedule at 0, 6 months is superior to that of Gardasil vaccine administered according to a 2-dose schedule at 0, 6 months, in 9-14 year-old females, 1 month after the last dose (Month 7) regardless of serostatus.

Comparison groups	Cervarix 2 dose Group v Gardasil 2 dose Group
Number of subjects included in analysis	710
Analysis specification	Pre-specified
Analysis type	superiority[6]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.49
upper limit	1.91

Notes:

[6] - Superiority was shown if the lower limit of the 95% CI for the ratio of GMTs (Cervarix 2 dose Group divided by Gardasil 2 dose Group) was above 1 for anti-HPV-16 antibodies.

Secondary: Anti-HPV-16/18 seroconversion rates as assessed by ELISA

End point title	Anti-HPV-16/18 seroconversion rates as assessed by ELISA

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. anti-HPV-16 and anti-HPV-18 antibody titers ≥ 19 and 18 EL.U/mL, respectively) in the serum of subjects seronegative before vaccination.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	322	310	320	
Units: Subjects				
Anti-HPV-16, Day 0 (N=318, 306, 309)	0	0	0	
Anti-HPV-18, Day 0 (N=322, 310, 320)	0	0	0	
Anti-HPV-16, Month 12 (N=317, 305, 308)	316	305	308	
Anti-HPV-18, Month 12 (N=321, 309, 319)	320	309	319	

Anti-HPV-16, Month 18 (N=316, 305, 309)	316	304	309	
Anti-HPV-18, Month 18 (N=320, 309, 320)	320	294	313	
Anti-HPV-16, Month 24 (N=314, 304, 307)	314	303	307	
Anti-HPV-18, Month 24 (N=318, 308, 318)	318	287	308	
Anti-HPV-16, Month 36 (N=318, 306, 309)	318	304	308	
Anti-HPV-18, Month 36 (N=322, 310, 320)	322	267	297	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16/18 antibody titers as assessed by ELISA

End point title	Anti-HPV-16/18 antibody titers as assessed by ELISA

End point description:

Anti-HPV 16/18 antibody titers were presented as GMTs and expressed in EL.U/mL based on ELISA.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	322	310	320	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16, Day 0 (N=318, 306, 309)	9.5 (9.5 to 9.5)	9.5 (9.5 to 9.5)	9.5 (9.5 to 9.5)	
Anti-HPV-18, Day 0 (N=322, 310, 320)	9.0 (9.0 to 9.0)	9.0 (9.0 to 9.0)	9.0 (9.0 to 9.0)	
Anti-HPV-16, Month 12 (N=317, 305, 308)	2209.2 (2014 to 2423.4)	1294.8 (1160.4 to 1444.9)	1600.7 (1457.3 to 1758.2)	
Anti-HPV-18, Month 12 (N=321, 309, 319)	1299.3 (1176.2 to 1435.6)	266.6 (236.3 to 300.8)	478.5 (422.8 to 541.6)	
Anti-HPV-16, Month 18 (N=316, 305, 309)	1488.8 (1365.5 to 1623.3)	684.4 (605.8 to 773.2)	824.0 (744.4 to 912.2)	
Anti-HPV-18, Month 18 (N=320, 309, 320)	754.2 (682.6 to 833.2)	134.8 (118.1 to 154)	231.3 (202.4 to 264.4)	
Anti-HPV-16, Month 24 (N=314, 304, 307)	1285.0 (1181.1 to 1398.0)	514.1 (455.4 to 580.3)	637.1 (575.8 to 704.9)	
Anti-HPV-18, Month 24 (N=318, 308, 318)	613.7 (555.0 to 678.6)	106.3 (93.2 to 121.3)	182.0 (159.3 to 208.0)	
Anti-HPV-16, Month 36 (N=318, 306, 309)	1061.4 (971.8 to 1159.4)	379.8 (333.4 to 432.7)	472.4 (425 to 525.0)	

Anti-HPV-18, Month 36 (N=322, 310, 320)	486.5 (437.8 to 540.6)	71.0 (62.0 to 81.2)	119.1 (103.4 to 137.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16/18 antibody titers as assessed by ELISA at Month 36

End point title	Anti-HPV-16/18 antibody titers as assessed by ELISA at Month 36

End point description:

Data at Month 36 were also expressed as International Units per milliliter (IU)/mL. Conversion factor from EU/mL to IU/mL was determined to be 1/6.1 for HPV-16 and 1/5.7 for HPV-18, using the WHO International Standards (NIBSC codes 05-134 and 10-140 for HPV-16 and HPV-18, respectively). The assay cut-offs were therefore 3.1 IU/mL and 3.2 IU/mL for anti-HPV-16 and anti-HPV-18 antibodies, respectively.

End point type	Secondary

End point timeframe:

At Month 36

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	322	310	320	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (N=318,306,309)	174.0 (159.3 to 190.1)	62.3 (54.7 to 71.0)	77.4 (69.6 to 86.0)	
Anti-HPV-18 (N=322,310,320)	85.3 (76.7 to 94.8)	12.5 (10.9 to 14.3)	20.9 (18.2 to 24.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16/18 seroconversion rates as assessed by pseudovirion-based neutralization assay (PBNA) in a subset of subjects, based on the Month 36 ATP cohort for immunogenicity

End point title	Anti-HPV-16/18 seroconversion rates as assessed by pseudovirion-based neutralization assay (PBNA) in a subset of subjects, based on the Month 36 ATP cohort for immunogenicity

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. anti-HPV-16 and anti-HPV-18 antibody titers respectively ≥40 ED50) in the serum of subjects seronegative before vaccination. The assay was performed on a subset of approximately 100 subjects per study group.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	87	91	
Units: Subjects				
Anti-HPV-16, Day 0 (N=89, 85, 91)	0	0	0	
Anti-HPV-18, Day 0 (N=89, 87, 91)	0	0	0	
Anti-HPV-16, Month 7 (N=89, 85, 91)	89	85	91	
Anti-HPV-18, Month 7 (N=89, 87, 91)	89	87	91	
Anti-HPV-16, Month 12 (N=88, 85, 91)	88	85	91	
Anti-HPV-18, Month 12 (N=88, 87, 91)	88	86	91	
Anti-HPV-16, Month 18 (N=88, 85, 90)	88	83	89	
Anti-HPV-18, Month 18 (N=87, 87, 91)	87	77	89	
Anti-HPV-16, Month 24 (N=86, 83, 91)	86	83	90	
Anti-HPV-18, Month 24 (N=86, 83, 91)	86	75	88	
Anti-HPV-16, Month 36 (N=89, 85, 91)	89	85	91	
Anti-HPV-18, Month 36 (N=89, 87, 91)	89	75	86	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16/18 antibody titers as assessed by PBNA in a subset of subjects, based on the Month 36 ATP cohort for immunogenicity

End point title	Anti-HPV-16/18 antibody titers as assessed by PBNA in a subset of subjects, based on the Month 36 ATP cohort for immunogenicity

End point description:

Anti-HPV 16/18 antibody titers were presented as GMTs and expressed in titers using the PBNA. The assay was performed on a subset of approximately 100 subjects per study group.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	87	91	
Units: Titers				
geometric mean (confidence interval 95%)				

Anti-HPV-16, Day 0 (N=89, 85, 91)	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	
Anti-HPV-18, Day 0 (N=89, 87, 91)	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	
Anti-HPV-16, Month 7 (N=89, 85, 91)	52868.5 (44171.0 to 63278.5)	19130.1 (15166.8 to 24129.0)	22182.7 (17611.7 to 27940.1)	
Anti-HPV-18, Month 7 (N=89, 87, 91)	24068.5 (19293.2 to 30025.8)	4726.5 (3600.9 to 6204.0)	8243.9 (6276.2 to 10828.4)	
Anti-HPV-16, Month 12 (N=88, 85, 91)	10695.9 (8564.9 to 13357.1)	4280.1 (3245.9 to 5643.6)	5843.8 (4599.8 to 7424.1)	
Anti-HPV-18, Month 12 (N=88, 87, 91)	3683.3 (2914.4 to 4655.2)	689.0 (517.2 to 917.8)	1788.6 (1308.6 to 2444.7)	
Anti-HPV-16, Month 18 (N=88, 85, 90)	8436.3 (6650.6 to 10701.4)	2129.7 (1512.8 to 2998.1)	2987.2 (2218.5 to 4022.3)	
Anti-HPV-18, Month 18 (N=87, 87, 91)	2426.3 (1885.7 to 3121.7)	295.7 (217.0 to 402.8)	812.1 (577.0 to 1143.0)	
Anti-HPV-16, Month 24 (N=86, 83, 91)	5036.7 (4097.8 to 6190.7)	1211.8 (893.8 to 1642.9)	1967.2 (1507.5 to 2567.2)	
Anti-HPV-18, Month 24 (N=86, 83, 91)	1763.0 (1384.5 to 2245.0)	237.1 (177.2 to 317.1)	573.1 (421.5 to 779.3)	
Anti-HPV-16, Month 36 (N=89, 85, 91)	4357.8 (3577.8 to 5307.9)	1128.9 (857.4 to 1486.4)	1577.0 (1210.4 to 2054.5)	
Anti-HPV-18, Month 36 (N=89, 87, 91)	1613.9 (1267.6 to 2054.7)	185.8 (140.4 to 245.8)	472.8 (345.8 to 646.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16/18 seroconversion rates as assessed by PBNA in a subset of subjects, based on the Month 36 TVC

End point title	Anti-HPV-16/18 seroconversion rates as assessed by PBNA in a subset of subjects, based on the Month 36 TVC

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. anti-HPV-16 and anti-HPV-18 antibody titers ≥40 ED50) in the serum of subjects seronegative before vaccination. The assay was performed on a subset of approximately 100 subjects per study group.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	92	98	
Units: Subjects				
Anti-HPV-16, Day 0 (N=99, 90, 98)	0	0	0	
Anti-HPV-18, Day 0 (N=99, 92, 98)	0	0	0	
Anti-HPV-16, Month 7 (N= 99, 90, 98)	99	90	98	
Anti-HPV-18, Month 7 (N= 99, 92, 98)	99	92	98	
Anti-HPV-16, Month 12 (N= 98, 90, 98)	97	90	98	
Anti-HPV-18, Month 12 (N=98, 92, 98)	98	91	98	
Anti-HPV-16, Month 18 (N=98, 90, 97)	97	88	96	
Anti-HPV-18, Month 18 (N=97, 92, 98)	97	82	96	
Anti-HPV-16, Month 24 (N=96, 87, 98)	95	87	97	
Anti-HPV-18, Month 24 (N=96, 87, 98)	96	79	94	
Anti-HPV-16, Month 36 (N=98, 90, 98)	97	90	98	
Anti-HPV-18, Month 36 (N=97, 92, 98)	97	80	92	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16/18 antibody titers as assessed by PBNA in a subset of subjects, based on the Month 36 TVC

End point title	Anti-HPV-16/18 antibody titers as assessed by PBNA in a subset of subjects, based on the Month 36 TVC

End point description:

Anti-HPV 16/18 antibody titers were presented as GMT and expressed in titers using the PBNA. The assay was performed on a subset of approximately 100 subjects per study group.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	92	98	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-HPV-16, Day 0 (N=99, 90, 98)	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	
Anti-HPV-18, Day 0 (N=99, 92, 98)	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	
Anti-HPV-16, Month 7 (N=99, 90, 98)	50000.7 (39742.9 to 62906.0)	18573.7 (14876.8 to 23189.3)	22294.2 (17763.8 to 27980.0)	
Anti-HPV-18, Month 7 (N= 99, 92, 98)	23576.9 (18922.5 to 29376.2)	4563.7 (3519.5 to 5917.8)	8042.1 (6186.1 to 10454.8)	

Anti-HPV-16, Month 12 (N=98, 90, 98)	10039.6 (7884.1 to 12784.5)	4174.9 (3207.5 to 5434.2)	5766.0 (4573.8 to 7268.9)	
Anti-HPV-18, Month 12 (N= 98, 92, 98)	3546.9 (2829.7 to 4445.8)	670.3 (510.0 to 880.9)	1801.4 (1333.0 to 2434.2)	
Anti-HPV-16, Month 18 (N= 98, 90, 97)	7508.8 (5819.8 to 9688.0)	2070.2 (1494.9 to 2866.9)	2961.5 (2233.9 to 3926.2)	
Anti-HPV-18, Month 18 (N=97, 92, 98)	2240.5 (1763.3 to 2846.9)	294.5 (219.5 to 395.1)	797.6 (576.3 to 1104.0)	
Anti-HPV-16, Month 24 (N=96, 87, 98)	4609.1 (3673.5 to 5782.9)	1193.9 (889.6 to 1602.3)	1932.0 (1499.4 to 2489.5)	
Anti-HPV-18, Month 24 (N=96, 87, 98)	1638.6 (1297.9 to 2068.8)	239.7 (181.2 to 317.1)	564.6 (418.1 to 762.5)	
Anti-HPV-16, Month 36 (N=98, 90, 98)	4011.7 (3229.7 to 4983.0)	1111.4 (849.1 to 1454.6)	1517.2 (1174.7 to 1959.4)	
Anti-HPV-18, Month 36 (N=97, 92, 98)	1513.7 (1197.5 to 1913.2)	185.8 (142.2 to 242.7)	468.6 (346.3 to 634.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: T-cell-mediated immune responses in the sub-cohort for Cell-Mediated Immunity (CMI)

End point title	T-cell-mediated immune responses in the sub-cohort for Cell-Mediated Immunity (CMI)

End point description:

Among immune markers expressed were Interleukin-2 (IL-2), Interferon-gamma (IFN-γ), Tumor necrosis factor-alpha (TNF-α) and CD40-ligand (CD40-L). The assay was performed on a sub-cohort of approximately 100 subjects per study group.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	74	
Units: T-cells/million cells				
median (inter-quartile range (Q1-Q3))				
CD4+ All doubles, Anti-HPV-16,Day 0 (N=53, 42, 53)	10 (1 to 78)	22 (1 to 90)	33 (1 to 80)	
CD4+ All doubles, Anti-HPV-18,Day 0 (N=53, 42, 54)	28 (1 to 83)	47.5 (1 to 102)	26 (1 to 92)	
CD4+ All doubles,Anti-HPV-16,Month 7(N=63, 58, 62)	1662 (644 to 3221)	872 (479 to 1275)	1121 (694 to 1890)	

CD4+ All doubles,Anti-HPV-18,Month 7(N=63, 58, 63)	897 (496 to 2497)	427 (259 to 744)	640 (355 to 1304)	
CD4+All doubles,Anti-HPV-16,Month 12(N=67, 58, 66)	916 (641 to 2340)	585.5 (316 to 1250)	819.5 (554 to 1623)	
CD4+All doubles,Anti-HPV-18,Month 12(N=67, 59, 66)	789 (384 to 1492)	327 (184 to 658)	446 (205 to 824)	
CD4+All doubles,Anti-HPV-16,Month 24 N=66, 60, 74)	1068.5 (495 to 2410)	750.5 (366.5 to 1142.5)	968.5 (588 to 1830)	
CD4+All doubles Anti-HPV-18,Month 24(N=65, 60, 73)	645 (311 to 1406)	352 (196.5 to 503)	578 (267 to 972)	
CD4+All doubles.Anti-HPV-16,Month 36(N=58, 55, 64)	1012 (427 to 2373)	685 (385 to 1321)	842.5 (437.5 to 1624)	
CD4+All doubles,Anti-HPV-18,Month 36(N=57, 55, 63)	682 (313 to 1425)	350 (196 to 665)	516 (270 to 1029)	
CD4-d-CD40L, Anti-HPV-16, Day 0 (N=53, 42, 53)	1 (1 to 73)	14 (1 to 72)	30 (1 to 73)	
CD4-d-CD40L, Anti-HPV-18, Day 0 (N=53, 42, 54)	14 (1 to 83)	39.5 (1 to 102)	27.5 (1 to 70)	
CD4-d-CD40L, Anti-HPV-16, Month 7 (N=63, 58, 62)	1515 (638 to 3098)	779 (456 to 1211)	1025.5 (670 to 1848)	
CD4-d-CD40L, Anti-HPV-18, Month 7 (N=63, 58, 63)	866 (496 to 2483)	386.5 (237 to 708)	574 (328 to 1224)	
CD4-d-CD40L, Anti-HPV-16, Month 12 (N=67, 58, 66)	889 (591 to 2236)	524 (280 to 1135)	761.5 (484 to 1425)	
CD4-d-CD40L, Anti-HPV-18, Month 12 (N=67, 59, 66)	688 (344 to 1435)	317 (147 to 633)	383.5 (214 to 729)	
CD4-d-CD40L, Anti-HPV-16, Month 24 (N=66, 60, 74)	1045.5 (518 to 2269)	736 (348 to 1101.5)	937 (588 to 1801)	
CD4-d-CD40L, Anti-HPV-18, Month 24 (N=65, 60, 73)	639 (310 to 1374)	332 (204 to 510.5)	564 (289 to 940)	
CD4-d-CD40L, Anti-HPV-16, Month 36 (N=58, 55, 64)	957 (465 to 2303)	685 (349 to 1321)	778.5 (416.5 to 1560.5)	
CD4-d-CD40L, Anti-HPV-18, Month 36 (N=57, 55, 63)	671 (290 to 1435)	337 (204 to 648)	499 (264 to 1020)	
CD4-d- IFNγ, Anti-HPV-16, Day 0 (N=53, 42, 53)	12 (1 to 30)	19 (1 to 42)	1 (1 to 28)	
CD4-d- IFNγ, Anti-HPV-18, Day 0 (N=53, 42, 54)	14 (1 to 33)	13.5 (1 to 36)	3.5 (1 to 30)	
CD4-d- IFNγ, Anti-HPV-16, Month 7 (N=63, 58, 62)	365 (161 to 881)	320 (157 to 533)	422.5 (206 to 708)	
CD4-d- IFNγ, Anti-HPV-18, Month 7 (N=63, 58, 63)	242 (111 to 712)	133.5 (83 to 240)	181 (78 to 409)	
CD4-d- IFNγ, Anti-HPV-16, Month 12 (N=67, 58, 66)	326 (110 to 644)	235 (108 to 501)	356 (135 to 734)	
CD4-d- IFNγ, Anti-HPV-18, Month 12 (N=67, 59, 66)	175 (87 to 444)	112 (55 to 240)	164 (57 to 315)	
CD4-d- IFNγ, Anti-HPV-16, Month 24 (N=66, 60, 74)	300.5 (119 to 781)	317.5 (146.5 to 514)	421 (157 to 767)	
CD4-d- IFNγ, Anti-HPV-18, Month 24 (N=65, 60, 73)	171 (68 to 462)	112 (49.5 to 229.5)	220 (65 to 348)	
CD4-d-IFNγ, Anti-HPV-16, Month 36 (N=58, 55, 64)	253.5 (81 to 667)	301 (134 to 571)	270.5 (129 to 666.5)	
CD4-d-IFNγ, Anti-HPV-18, Month 36 (N=57, 55, 63)	193 (51 to 376)	109 (27 to 230)	155 (45 to 314)	
CD4-d-IL-2, Anti-HPV-16, Day 0 (N=53, 42, 53)	14 (1 to 52)	25 (1 to 72)	33 (1 to 56)	
CD4-d-IL-2, Anti-HPV-18, Day 0 (N=53, 42, 54)	1 (1 to 49)	36.5 (1 to 76)	22 (1 to 60)	
CD4-d-IL-2, Anti-HPV-16, Month 7 (N=63, 58, 62)	1357 (537 to 2660)	712.5 (378 to 1037)	866 (561 to 1420)	
CD4-d-IL-2, Anti-HPV-18, Month 7 (N=63, 58, 63)	737 (420 to 2185)	304 (206 to 573)	486 (281 to 959)	

CD4-d-IL-2, Anti-HPV-16, Month 12 (N=67, 58, 66)	832 (493 to 2050)	479 (283 to 946)	674.5 (450 to 1316)	
CD4-d-IL-2, Anti-HPV-18, Month 12 (N=67, 59, 66)	620 (304 to 1157)	259 (144 to 547)	354 (155 to 622)	
CD4-d-IL-2, Anti-HPV-16, Month 24 (N=66, 60, 74)	855 (390 to 1711)	579.5 (270.5 to 934.5)	700 (479 to 1459)	
CD4-d-IL-2, Anti-HPV-18, Month 24 (N=65, 60, 73)	494 (252 to 994)	240 (125.5 to 387.5)	426 (216 to 695)	
CD4-d-IL-2, Anti-HPV-16, Month 36 (N=58,55, 64)	784 (331 to 1673)	517 (295 to 1014)	680 (308 to 1245.5)	
CD4-d-IL-2, Anti-HPV-18, Month 36 (N=57, 55, 63)	507 (213 to 1069)	274 (137 to 467)	341 (168 to 798)	
CD4-d-TNFα, Anti-HPV-16, Day 0 (N=53, 42, 53)	6 (1 to 50)	33 (1 to 82)	16 (1 to 69)	
CD4-d-TNFα, Anti-HPV-18, Day 0 (N=53, 42, 54)	27 (1 to 75)	22.5 (1 to 82)	23 (1 to 60)	
CD4-d-TNFα, Anti-HPV-16, Month 7 (N=63, 58, 62)	1111 (430 to 2386)	625 (292 to 899)	796 (458 to 1448)	
CD4-d-TNFα, Anti-HPV-18, Month 7 (N=63, 58, 63)	647 (336 to 1415)	283.5 (168 to 594)	457 (266 to 978)	
CD4-d-TNFα, Anti-HPV-16, Month 12 (N=67, 58, 66)	790 (488 to 1924)	482 (210 to 932)	716 (457 to 1445)	
CD4-d-TNFα, Anti-HPV-18, Month 12 (N=67, 59, 66)	674 (288 to 1272)	266 (133 to 588)	384.5 (175 to 714)	
CD4-d-TNFα, Anti-HPV-16, Month 24 (N=66, 60, 74)	795.5 (343 to 1668)	563.5 (241.5 to 895)	760.5 (443 to 1494)	
CD4-d-TNFα, Anti-HPV-18, Month 24 (N=65, 60, 73)	510 (183 to 1164)	239 (127.5 to 440.5)	522 (228 to 710)	
CD4-d-TNFα, Anti-HPV-16, Month 36 (N=58, 55, 64)	786.5 (343 to 1930)	547 (282 to 1005)	724.5 (368 to 1338)	
CD4-d-TNFα, Anti-HPV-18, Month 36 (N=57, 55, 63)	588 (250 to 1138)	301 (120 to 453)	479 (200 to 808)	
CD8-All Doubles, Anti-HPV-16, Day 0 (N=53, 42, 53)	1 (1 to 14)	4 (1 to 49)	1 (1 to 25)	
CD8-All Doubles, Anti-HPV-18, Day 0 (N=53, 42, 54)	1 (1 to 16)	1 (1 to 29)	1 (1 to 22)	
CD8-All Doubles,Anti-HPV-16,Month 7(N=63, 58, 62)	1 (1 to 34)	1 (1 to 41)	1 (1 to 30)	
CD8-All Doubles,Anti-HPV-18,Month 7(N=63, 58, 63)	1 (1 to 19)	1 (1 to 40)	1 (1 to 40)	
CD8-All Doubles,Anti-HPV-16,Month 12(N=67, 58, 66)	1 (1 to 31)	1 (1 to 29)	1 (1 to 29)	
CD8-All Doubles,Anti-HPV-18,Month 12(N=67, 59, 66)	1 (1 to 27)	1 (1 to 27)	1 (1 to 20)	
CD8-All Doubles,Anti-HPV-16,Month 24(N=66, 60, 74)	1 (1 to 25)	1 (1 to 1)	1 (1 to 1)	
CD8-All Doubles,Anti-HPV-18,Month 24(N=65, 60, 73)	1 (1 to 32)	1 (1 to 23)	1 (1 to 28)	
CD8-All doubles,Anti-HPV-16,Month 36(N=58, 55, 64)	1 (1 to 48)	1 (1 to 28)	1 (1 to 38.5)	
CD8-All doubles,Anti-HPV-18,Month 36(N=57, 55, 63)	4 (1 to 40)	2 (1 to 41)	1 (1 to 28)	
CD8-d-CD40L, Anti-HPV-16, Day 0 (N=53, 42, 53)	1 (1 to 1)	1 (1 to 26)	1 (1 to 1)	
CD8-d-CD40L, Anti-HPV-18, Day 0 (N=53, 42, 54)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-CD40L, Anti-HPV-16, Month 7 (N=63, 58, 62)	1 (1 to 1)	1 (1 to 29)	1 (1 to 24)	
CD8-d-CD40L, Anti-HPV-18, Month 7 (N=63, 58, 63)	1 (1 to 1)	1 (1 to 24)	1 (1 to 23)	
CD8-d-CD40L, Anti-HPV-16, Month 12 (N=67, 58, 66)	1 (1 to 1)	1 (1 to 1)	1 (1 to 3)	

CD8-d-CD40L, Anti-HPV-18, Month 12 (N=67, 59, 66)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-CD40L, Anti-HPV-16, Month 24 (N=66, 60, 74)	1 (1 to 16)	1 (1 to 1)	1 (1 to 1)	
CD8-d-CD40L, Anti-HPV-18, Month 24 (N=65, 60, 73)	1 (1 to 1)	1 (1 to 1)	1 (1 to 18)	
CD8-d-CD40L, Anti-HPV-16, Month 36 (N=58, 55, 64)	1 (1 to 31)	1 (1 to 24)	1 (1 to 29)	
CD8-d-CD40L, Anti-HPV-18, Month 36 (N=57, 55, 63)	1 (1 to 6)	1 (1 to 27)	1 (1 to 28)	
CD8-d-IFNγ, Anti-HPV-16, Day 0 (N=53, 42, 53)	1 (1 to 1)	1 (1 to 39)	1 (1 to 26)	
CD8-d-IFNγ, Anti-HPV-18, Day 0 (N=53, 42, 54)	1 (1 to 2)	1 (1 to 23)	1 (1 to 18)	
CD8-d-IFNγ, Anti-HPV-16, Month 7 (N=63, 58, 62)	1 (1 to 32)	1 (1 to 40)	1 (1 to 30)	
CD8-d-IFNγ, Anti-HPV-18, Month 7 (N=63, 58, 63)	1 (1 to 1)	1 (1 to 28)	1 (1 to 28)	
CD8-d-IFNγ, Anti-HPV-16, Month 12 (N=67, 58, 66)	1 (1 to 28)	1 (1 to 26)	1 (1 to 27)	
CD8-d-IFNγ, Anti-HPV-18, Month 12 (N=67, 59, 66)	1 (1 to 22)	1 (1 to 26)	1 (1 to 10)	
CD8-d-IFNγ, Anti-HPV-16, Month 24 (N=66, 60, 74)	1 (1 to 16)	1 (1 to 1)	1 (1 to 1)	
CD8-d-IFNγ, Anti-HPV-18, Month 24 (N=65, 60, 73)	1 (1 to 18)	1 (1 to 23)	1 (1 to 1)	
CD8-d-IFNγ, Anti-HPV-16, Month 36 (N=58, 55, 64)	1 (1 to 47)	1 (1 to 25)	1 (1 to 33)	
CD8-d-IFNγ, Anti-HPV-18, Month 36 (N=57, 55, 63)	1 (1 to 31)	2 (1 to 40)	1 (1 to 25)	
CD8-d-IL-2, Anti-HPV-16, Day 0 (N=53, 42, 53)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-IL-2, Anti-HPV-18, Day 0 (N=53, 42, 54)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-IL-2, Anti-HPV-16, Month 7 (N=63, 58, 62)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-IL-2, Anti-HPV-18, Month 7 (N=63, 58, 63)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-IL-2, Anti-HPV-16, Month 12 (N=67, 58, 66)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-IL-2, Anti-HPV-18, Month 12 (N=67, 59, 66)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-IL-2, Anti-HPV-16, Month 24 (N=66, 60, 74)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-IL-2, Anti-HPV-18, Month 24 (N=65, 60, 73)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-IL-2, Anti-HPV-16, Month 36 (N=58, 55, 64)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-IL-2, Anti-HPV-18, Month 36 (N=57, 55, 63)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
CD8-d-TNFα, Anti-HPV-16, Day 0 (N=53, 42, 53)	1 (1 to 1)	1 (1 to 36)	1 (1 to 16)	
CD8-d-TNFα, Anti-HPV-18, Day 0 (N=53, 42, 54)	1 (1 to 27)	1 (1 to 29)	1 (1 to 26)	
CD8-d-TNFα, Anti-HPV-16, Month 7 (N=63, 58, 62)	1 (1 to 28)	1 (1 to 26)	1 (1 to 18)	
CD8-d-TNFα, Anti-HPV-18, Month 7 (N=63, 58, 63)	1 (1 to 1)	1 (1 to 2)	1 (1 to 24)	
CD8-d-TNFα, Anti-HPV-16, Month 12 (N=67, 58, 66)	1 (1 to 1)	1 (1 to 25)	1 (1 to 28)	
CD8-d-TNFα, Anti-HPV-18, Month 12 (N=67, 59, 66)	1 (1 to 8)	1 (1 to 21)	1 (1 to 24)	

CD8-d-TNFα, Anti-HPV-16, Month 24 (N=66, 60, 74)	1 (1 to 20)	1 (1 to 1)	1 (1 to 1)	
CD8-d-TNFα, Anti-HPV-18, Month 24 (N=65, 60, 73)	1 (1 to 28)	1 (1 to 7)	1 (1 to 18)	
CD8-d-TNFα, Anti-HPV-16, Month 36 (N=58, 55, 64)	1 (1 to 24)	1 (1 to 1)	1 (1 to 26)	
CD8-d-TNFα, Anti-HPV-18, Month 36 (N=57, 55, 63)	1 (1 to 31)	1 (1 to 21)	1 (1 to 12)	

Statistical analyses

No statistical analyses for this end point

Secondary: B-cell-mediated immune responses in the sub-cohort for CMI

End point title	B-cell-mediated immune responses in the sub-cohort for CMI

End point description:

The frequency of B-cell Elispot response to HPV-16/18 by overall status was presented. The assay was performed on a sub-cohort of 100 subjects per study group.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	65	76	
Units: B-cells/million cells				
median (inter-quartile range (Q1-Q3))				
HPV-16, Day 0 (N=69, 55, 70)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
HPV-18, Day 0 (N=69, 55, 70)	1 (1 to 1)	1 (1 to 1)	1 (1 to 1)	
HPV-16, Month 7 (N=71, 65, 76)	1733 (577 to 3733)	1254 (495 to 2173)	733 (106.5 to 1966.5)	
HPV-18, Month 7 (N=71, 65, 76)	558 (106 to 1847)	155 (1 to 379)	111 (1 to 343.5)	
HPV-16, Month 12 (N=51, 51, 53)	408 (90 to 1186)	278 (66 to 794)	289 (66 to 982)	
HPV-18, Month 12 (N=51, 51, 53)	249 (73 to 658)	69 (1 to 184)	69 (1 to 250)	
HPV-16, Month 24 (N=54, 46, 63)	270 (49 to 724)	218.5 (28 to 651)	249 (37 to 601)	
HPV-18, Month 24 (N=54, 46, 63)	128.5 (35 to 402)	57.5 (1 to 203)	111 (1 to 317)	
HPV-16, Month 36 (N=59, 54, 53)	353 (91 to 927)	382.5 (166 to 614)	246 (21 to 565)	
HPV-18, Month 36 (N=59, 54, 53)	116 (1 to 329)	25 (1 to 228)	63 (1 to 150)	

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 the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 50 millimetres (mm) of injection site.

End point type	Secondary

End point timeframe:

During the 7-day period (from the day of vaccination up to 6 subsequent days) following vaccination after each dose and across doses

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	357	356	
Units: Subjects				
Any Pain - Dose 1 (N=359, 357, 356)	311	235	231	
Any Pain - Dose 2 (N=357, 353, 354)	193	183	215	
Any Pain - Dose 3 (N=356, 348, 350)	280	194	222	
Any Pain - Across doses (N=359, 357, 356)	329	276	295	
Grade 3 Pain - Dose 1 (N=359, 357, 356)	22	4	6	
Grade 3 Pain - Dose 2 (N=357, 353, 354)	8	8	8	
Grade 3 Pain - Dose 3 (N=356, 348, 350)	23	11	10	
Grade 3 Pain - Across doses (N=359, 357, 356)	42	17	18	
Any Redness - Dose 1 (N=359, 357, 356)	137	84	87	
Any Redness - Dose 2 (N=357, 353, 354)	100	84	99	
Any Redness - Dose 3 (N=356, 348, 350)	133	92	102	
Any Redness - Across doses (N=359, 357, 356)	191	134	157	
Grade 3 Redness - Dose 1 (N=359, 357, 356)	0	0	1	
Grade 3 Redness - Dose 2 (N=357, 353, 354)	0	0	0	
Grade 3 Redness - Dose 3 (N=356, 348, 350)	0	0	1	
Grade 3 Redness - Across doses (N=359, 357, 356)	0	0	2	
Any Swelling - Dose 1 (N=359, 357, 356)	112	44	39	
Any Swelling - Dose 2 (N=357, 353, 354)	63	35	76	
Any Swelling - Dose 3 (N=356, 348, 350)	113	67	85	

Any Swelling - Across doses (N=359, 357, 356)	163	98	118	
Grade 3 Swelling - Dose 1 (N=359, 357, 356)	3	0	0	
Grade 3 Swelling - Dose 2 (N=357, 353, 354)	0	0	0	
Grade 3 Swelling - Dose 3 (N=356, 348, 350)	2	0	2	
Grade 3 Swelling - Across doses (N=359, 357, 356)	5	0	2	

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, temperature [defined as oral temperature equal to or above (≥) 37.5 degrees Celsius (°C)] and urticaria. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever above (>) 39.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

During the 7-day period (from the day of vaccination up to 6 subsequent days) following vaccination after each dose and across doses

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	357	356	
Units: Subjects				
Any Arthralgia - Dose 1 (N=359, 357, 355)	44	50	39	
Any Arthralgia - Dose 2 (N=357, 353, 354)	23	30	34	
Any Arthralgia - Dose 3 (N=354, 347, 351)	31	38	35	
Any Arthralgia - Across doses (N=359, 357, 356)	68	81	67	
Grade 3 Arthralgia - Dose 1 (N=359, 357, 355)	5	1	1	
Grade 3 Arthralgia - Dose 2 (N=357, 353, 354)	1	2	1	
Grade 3 Arthralgia - Dose 3 (N=354, 347, 351)	2	3	1	
Grade 3 Arthralgia -Across doses (N=359, 357, 356)	6	4	1	
Related Arthralgia - Dose 1 (N=359, 357, 355)	29	32	28	

Related Arthralgia - Dose 2 (N=357, 353, 354)	17	17	18	
Related Arthralgia - Dose 3 (N=354, 347, 351)	20	27	27	
Related Arthralgia -Across doses (N=359, 357, 356)	51	55	51	
Any Fatigue - Dose 1 (N=359, 357, 355)	163	157	168	
Any Fatigue - Dose 2 (N=357, 353, 354)	103	104	119	
Any Fatigue - Dose 3 (N=354, 347, 351)	108	97	103	
Any Fatigue - Across doses (N=359, 357, 356)	192	199	193	
Grade 3 Fatigue - Dose 1 (N=359, 357, 355)	7	10	5	
Grade 3 Fatigue - Dose 2 (N=357, 353, 354)	12	3	2	
Grade 3 Fatigue - Dose 3 (N=354, 347, 351)	7	3	3	
Grade 3 Fatigue - Across doses (N=359, 357, 356)	18	15	7	
Related Fatigue - Dose 1 (N=359, 357, 355)	103	102	98	
Related Fatigue - Dose 2 (N=357, 353, 354)	68	66	67	
Related Fatigue - Dose 3 (N=354, 347, 351)	70	67	67	
Related Fatigue -Across doses (N=359, 357, 356)	152	151	143	
Any Gastrointestinal - Dose 1 (N=359, 357, 355)	34	52	44	
Any Gastrointestinal - Dose 2 (N=357, 353, 354)	19	22	23	
Any Gastrointestinal - Dose 3 (N=354, 347, 351)	16	29	24	
Any Gastrointestinal -Across doses (N=359,357,356)	55	74	70	
Grade 3 Gastrointestinal -Dose 1 (N=359, 357, 355)	3	2	2	
Grade 3 Gastrointestinal -Dose 2 (N=357, 353, 354)	2	1	0	
Grade 3 Gastrointestinal -Dose 3 (N=354, 347, 351)	1	4	2	
Grade 3 Gastro -Across doses (N=359, 357, 356)	5	6	3	
Related Gastrointestinal -Dose 1 (N=359, 357, 355)	21	26	22	
Related Gastrointestinal -Dose 2 (N=357, 353, 354)	8	17	6	
Related Gastrointestinal -Dose 3 (N=354, 347, 351)	10	20	17	
Related Gastro - Across doses (N=359, 357, 356)	32	49	40	
Any Headache - Dose 1 (N=359, 357, 355)	102	87	90	
Any Headache - Dose 2 (N=357, 353, 354)	62	64	73	
Any Headache - Dose 3 (N=354, 347, 351)	63	54	65	
Any Headache -Across doses (N=359, 357, 356)	147	133	151	

Grade 3 Headache - Dose 1 (N=359, 357, 355)	7	6	1	
Grade 3 Headache - Dose 2 (N=357, 353, 354)	6	2	4	
Grade 3 Headache - Dose 3 (N=354, 347, 351)	7	1	1	
Grade 3 Headache -Across doses (N=359, 357, 356)	17	7	4	
Related Headache - Dose 1 (N=359, 357, 355)	61	51	48	
Related Headache - Dose 2 (N=357, 353, 354)	39	37	41	
Related Headache - Dose 3 (N=354, 347, 351)	45	33	42	
Related Headache -Across doses (N=359, 357, 356)	107	88	100	
Any Myalgia - Dose 1 (N=359, 357, 355)	131	101	101	
Any Myalgia - Dose 2 (N=357, 353, 354)	59	60	80	
Any Myalgia - Dose 3 (N=354, 347, 351)	77	68	72	
Any Myalgia - Across doses (N=359, 357, 356)	166	143	136	
Grade 3 Myalgia - Dose 1 (N=359, 357, 355)	5	3	2	
Grade 3 Myalgia - Dose 2 (N=357, 353, 354)	2	3	2	
Grade 3 Myalgia - Dose 3 (N=354, 347, 351)	3	4	5	
Grade 3 Myalgia -Across doses (N=359, 357, 356)	8	8	6	
Related Myalgia - Dose 1 (N=359, 357, 355)	91	70	67	
Related Myalgia - Dose 2 (N=357, 353, 354)	36	40	51	
Related Myalgia - Dose 3 (N=354, 347, 351)	50	49	46	
Related Myalgia -Across doses (N=359, 357, 356)	128	111	100	
Any Rash - Dose 1 (N=359, 357, 355)	14	7	10	
Any Rash - Dose 2 (N=357, 353, 354)	10	5	8	
Any Rash - Dose 3 (N=354, 347, 351)	7	5	4	
Any Rash - Across doses (N=359, 357, 356)	25	16	18	
Grade 3 Rash - Dose 1 (N=359, 357, 356)	0	0	0	
Grade 3 Rash - Dose 2 (N=357, 353, 354)	0	0	0	
Grade 3 Rash - Dose 3 (N=354, 347, 351)	0	0	0	
Grade 3 Rash -Across doses (N=359, 357, 356)	0	0	0	
Related Rash - Dose 1 (N=359, 357, 355)	6	5	6	
Related Rash - Dose 2 (N=357, 353, 354)	6	3	4	
Related Rash - Dose 3 (N=354, 347, 351)	6	3	3	
Related Rash - Across doses (N=359, 357, 356)	16	10	12	

Any Temperature(≥ 37.5°C) -Dose 1(N=359, 357, 355)	19	23	18	
Any Temperature(≥ 37.5°C) -Dose 2(N=357, 353, 354)	13	21	19	
Any Temperature(≥ 37.5°C) -Dose 3(N=354, 347, 351)	32	22	22	
Any Temp (≥ 37.5°C) -Across doses(N=359, 357, 356)	53	59	47	
Grade 3 Temp (> 39.0°C) - Dose 1 (N=359, 357, 355)	2	2	2	
Grade 3 Temp (> 39.0°C) - Dose 2 (N=357, 353, 354)	0	0	2	
Grade 3 Temp (> 39.0°C) - Dose 3 (N=354, 347, 351)	6	0	0	
Grade 3 Temp(>39.0°C) -Across doses(N=359,357,356)	7	2	4	
Related Temperature - Dose 1 (N=359, 357, 355)	13	11	7	
Related Temperature - Dose 2 (N=357, 353, 354)	8	9	11	
Related Temperature - Dose 3 (N=354, 347, 351)	19	12	15	
Related Temperature -Across doses(N=359, 357, 356)	35	31	30	
Any Urticaria - Dose 1 (N=359, 357, 355)	15	7	12	
Any Urticaria - Dose 2 (N=357, 353, 354)	8	5	12	
Any Urticaria - Dose 3 (N=354, 347, 351)	11	4	9	
Any Urticaria - Across doses (N=359, 357, 356)	28	13	25	
Grade 3 Urticaria - Dose 1 (N=359, 357, 355)	2	0	0	
Grade 3 Urticaria - Dose 2 (N=357, 353, 354)	0	1	0	
Grade 3 Urticaria - Dose 3 (N=354, 347, 351)	2	0	0	
Grade 3 Urticaria -Across doses (N=359, 357, 356)	4	1	0	
Related Urticaria - Dose 1 (N=359, 357, 355)	7	6	7	
Related Urticaria - Dose 2 (N=357, 353, 354)	5	4	4	
Related Urticaria - Dose 3 (N=354, 347, 351)	6	4	2	
Related Urticaria -Across doses (N=359, 357, 356)	15	11	9	

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 was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

During the 30-day (from the day of vaccination up to 29 subsequent days) post-vaccination period

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	358	358	
Units: Subjects				
Subjects with any AE(s) (N=359, 358, 358)	91	96	101	
Subjects with any Grade 3 AE(s) (N=359, 358, 358)	18	8	20	
Subjects with any Related AE(s) (N=359, 358, 358)	8	14	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potentially immune mediated diseases (pIMDs)

End point title	Number of subjects with potentially immune mediated diseases (pIMDs)

End point description:

pIMDs are defined as a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 12

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	358	358	
Units: Subjects				
pIMD(s)	3	3	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with medically significant conditions (MSCs)

End point title	Number of subjects with medically significant conditions (MSCs)

End point description:

MSCs are defined as AEs prompting emergency room (ER) or physician visits that were not (1) related to common diseases or (2) routine visits for physical examination or vaccination, or SAEs not related to common diseases. Common diseases include: upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervicovaginal 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 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	358	358	
Units: Subjects	77	79	63	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

SAEs assessed include medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	358	358	
Units: Subjects	21	11	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAEs related to the investigational product, to study participation, to GSK concomitant products or any fatal SAE

End point title	Number of subjects with SAEs related to the investigational product, to study participation, to GSK concomitant products or any fatal SAE

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. Related = an event assessed by the investigator as causally related to the investigational product, to study participation or to GSK concomitant products.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	358	358	
Units: Subjects				
Related SAE(s) (N=359, 358, 358)	0	0	0	
Fatal SAE(s) (N=359, 358, 358)	0	0	1	

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 pregnancies were: Live infant NO apparent congenital anomaly (ACA), Live infant congenital anomaly (CA), Elective termination NO ACA, Elective termination CA, Ectopic pregnancy, Spontaneous abortion NO ACA, Stillbirth NO ACA, Stillbirth CA, Lost to follow up and Pregnancy ongoing.

End point type	Secondary

End point timeframe:

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

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[7]	0[8]	1	
Units: Subjects				
Live infant NO ACA			0	
Live infant CA			0	
Elective termination NO ACA			1	
Elective termination CA			0	
Ectopic pregnancy			0	
Spontaneous abortion NO ACA			0	
Stillbirth NO ACA			0	
Stillbirth CA			0	
Lost to follow up			0	
Pregnancy ongoing			0	
Missing			0	

Notes:

[7] - No pregnancies were reported for this group.

[8] - No pregnancies were reported for this group.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects using a concomitant medication throughout the study period

End point title	Number of subjects using a concomitant medication throughout the study period

End point description:

The number of subjects who have used any concomitant medication, as well as any antipyretic, any prophylactic antipyretic and any antibiotic.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 36 (throughout the study period) following vaccination after each dose and across doses

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	358	358	
Units: Subjects				
Any, Dose 1 (N=359, 358, 358)	85	87	93	
Any antipyretic, Dose 1 (N=359, 358, 358)	51	53	47	
Prophylactic antipyretic, Dose 1 (N=359, 358, 358)	4	0	0	
Any antibiotic, Dose 1 (N=359, 358, 358)	15	13	23	
Prophylactic antibiotic, Dose 1 (N=359, 358, 358)	0	0	0	
Any, Dose 2 (N=358, 356, 356)	52	55	47	

Any antipyretic, Dose 2 (N=358, 356, 356)	32	26	29	
Prophylactic antipyretic, Dose 2 (N=358, 356, 356)	0	1	2	
Any antibiotic, Dose 2 (N=358, 356, 356)	8	13	12	
Prophylactic antibiotic, Dose 2 (N=358, 356, 356)	0	0	0	
Any, Dose 3 (N=357, 352, 354)	90	83	81	
Any antipyretic, Dose 3 (N=357, 352, 354)	48	45	38	
Prophylactic antipyretic, Dose 3 (N=357, 352, 354)	3	1	0	
Any antibiotic, Dose 3 (N=357, 352, 354)	28	21	24	
Prophylactic antibiotic, Dose 3 (N=357, 352, 354)	0	0	0	
Any, Across doses (N=359, 358, 358)	171	157	161	
Any antipyretic, Across doses (N=359, 358, 358)	110	102	95	
Prophylactic antipyretic,Across doses N359,358,358	5	2	2	
Any antibiotic, Across doses (N=359, 358, 358)	48	42	50	
Prophylactic antibiotic,Across doses N=359,358,358	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects completing the vaccination schedule

End point title	Number of subjects completing the vaccination schedule
End point description:	
The number of subjects who have completed the three-dose vaccination schedule in all groups.	
End point type	Secondary
End point timeframe:	
From Day 0 up to Month 36 (throughout the study period)	

End point values	Cervarix 2 dose Group	Gardasil 2 dose Group	Gardasil 3 dose Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	358	358	
Units: Subjects	351	339	346	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: during the 7-day period after vaccination. Unsolicited AEs: during the 30-day period after vaccination. SAEs: throughout the study period (from Day 0 up to Month 36).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Cervarix 2 dose Group

Reporting group description:

Subjects who received 2 doses of Cervarix vaccine at Day 0 and Month 6 and 1 dose of placebo at Month 2. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.

Reporting group title	Gardasil 3 dose Group

Reporting group description:

Subjects who received 3 doses of Gardasil vaccine at Day 0 and at Months 2 and 6. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.

Reporting group title	Gardasil 2 dose Group

Reporting group description:

Subjects who received 2 doses of Gardasil vaccine at Day 0 and Month 6 and 1 dose of placebo at Month 2. The vaccines were administered intramuscularly, in the deltoid muscle of the non-dominant upper arm.

Serious adverse events	Cervarix 2 dose Group	Gardasil 3 dose Group	Gardasil 2 dose Group
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 359 (5.85%)	14 / 358 (3.91%)	11 / 358 (3.07%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Teratoma			
subjects affected / exposed	0 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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
Pregnancy, puerperium and perinatal conditions			

Abortion spontaneous incomplete			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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			
Anaphylactic reaction			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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
Anaphylactic shock			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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
Vulval ulceration			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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			
Asthma			
subjects affected / exposed	2 / 359 (0.56%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Depression			

subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	2 / 359 (0.56%)	0 / 358 (0.00%)	0 / 358 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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
Foreign body			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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
Joint dislocation			
subjects affected / exposed	0 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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
Tendon injury			

subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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
Seizure			
subjects affected / exposed	0 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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
Tension headache			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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
Abdominal pain lower			
subjects affected / exposed	0 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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
Mouth cyst			
subjects affected / exposed	0 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema nodosum			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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			
Juvenile idiopathic arthritis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	3 / 359 (0.84%)	0 / 358 (0.00%)	0 / 358 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	2 / 359 (0.56%)	1 / 358 (0.28%)	0 / 358 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 359 (0.28%)	1 / 358 (0.28%)	0 / 358 (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
Epstein-Barr virus infection			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 359 (0.00%)	1 / 358 (0.28%)	0 / 358 (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
Lung abscess			

subjects affected / exposed	0 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	1 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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 / 359 (0.28%)	0 / 358 (0.00%)	0 / 358 (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 / 359 (0.00%)	0 / 358 (0.00%)	1 / 358 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 2 dose Group	Gardasil 3 dose Group	Gardasil 2 dose Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	343 / 359 (95.54%)	324 / 358 (90.50%)	321 / 358 (89.66%)
Nervous system disorders			
Headache			
subjects affected / exposed	149 / 359 (41.50%)	152 / 358 (42.46%)	134 / 358 (37.43%)
occurrences (all)	241	232	213
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	192 / 359 (53.48%)	193 / 358 (53.91%)	199 / 358 (55.59%)
occurrences (all)	374	390	359
Pain			

subjects affected / exposed	329 / 359 (91.64%)	295 / 358 (82.40%)	277 / 358 (77.37%)
occurrences (all)	784	669	613
Pyrexia			
subjects affected / exposed	59 / 359 (16.43%)	53 / 358 (14.80%)	64 / 358 (17.88%)
occurrences (all)	70	65	71
Swelling			
subjects affected / exposed	163 / 359 (45.40%)	118 / 358 (32.96%)	98 / 358 (27.37%)
occurrences (all)	288	200	146
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	55 / 359 (15.32%)	70 / 358 (19.55%)	74 / 358 (20.67%)
occurrences (all)	69	91	103
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	191 / 359 (53.20%)	157 / 358 (43.85%)	135 / 358 (37.71%)
occurrences (all)	370	288	261
Rash			
subjects affected / exposed	26 / 359 (7.24%)	18 / 358 (5.03%)	16 / 358 (4.47%)
occurrences (all)	32	23	17
Urticaria			
subjects affected / exposed	28 / 359 (7.80%)	25 / 358 (6.98%)	13 / 358 (3.63%)
occurrences (all)	36	33	16
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	68 / 359 (18.94%)	67 / 358 (18.72%)	82 / 358 (22.91%)
occurrences (all)	98	108	119
Myalgia			
subjects affected / exposed	166 / 359 (46.24%)	136 / 358 (37.99%)	144 / 358 (40.22%)
occurrences (all)	267	254	230
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	8 / 359 (2.23%)	20 / 358 (5.59%)	11 / 358 (3.07%)
occurrences (all)	10	22	12
Upper respiratory tract infection			
subjects affected / exposed	27 / 359 (7.52%)	31 / 358 (8.66%)	29 / 358 (8.10%)
occurrences (all)	31	34	33

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 July 2012	Amendment 1: At the European Medicines Agency's (EMA) request, GSK Biologicals has updated its procedure for emergency unblinding during the conduct of a clinical study. According to the revised procedure, the responsibility and the decision to break the treatment code in emergency situations resides solely with the investigator and consequently, the investigator had full authority to break the treatment code.
28 November 2013	Amendment 2: 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 at all time points.
24 June 2014	Amendment 3: At the time of study initiation, Cervarix was approved to be administered according to a 3-dose vaccination course. Subjects belonging to the Cervarix 2 dose Group and Gardasil 2 dose Group received two doses of either Cervarix or Gardasil during the primary study epoch. These subjects were to be offered a third dose of the vaccine that they received at the end of the study, at Month 36. Recently, the 2-dose schedule of Cervarix and Gardasil has been approved in some countries, and hence the protocol is being amended to reflect that a third dose of the vaccine that they received was offered to the subjects in the two 2-dose groups (Cervarix 2 dose Group and Gardasil 2 dose Group) only if required based on local prescribing recommendations. In addition, the indication for Cervarix and the list of contributing authors have been updated. The number of countries in which Cervarix and Gardasil are licensed has been updated. Minor changes have been made in a few sections to correct typographical errors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported