Clinical trial results:
Follow-up study to evaluate the long-term immunogenicity and safety of GlaxoSmithKline Biologicals' HPV (580299) vaccine in healthy female subjects

Summary

EudraCT number	2009-011357-41
Trial protocol	DE PL
Global end of trial date	03 February 2015

Results information

Result version number	v1
This version publication date	13 February 2016
First version publication date	13 February 2016

Trial information

Trial identification

Sponsor protocol code	112772

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00947115
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 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	11 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 February 2015
Global end of trial reached?	Yes
Global end of trial date	03 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term immunogenicity of the HPV 16/18 vaccine in serum from all subjects by enzyme-linked immunosorbent assay (ELISA) at Years 5, 6, 7, 8, 9 and 10.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines 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. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 September 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 222
Country: Number of subjects enrolled	Germany: 303
Worldwide total number of subjects	525
EEA total number of subjects	525

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	525
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Some subjects who came for the Year 5 timepoint did not show up for the Year 6, 7, 8 or 9 timepoints, hence the numbers of subjects starting each year do not correspond to the ones of the previous years.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervarix 15-25 years group

Arm description:

Women, aged 15 to 25 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)

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

Dosage and administration details:

All subjects received 3 doses of HPV vaccine administered intramuscularly

Arm title	Cervarix 26-45 years group

Arm description:

Women, aged 26 to 45 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)

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

Dosage and administration details:

All subjects received 3 doses of HPV vaccine administered intramuscularly

Arm title	Cervarix 46-55 years group

Arm description:

Women, aged 46 to 55 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)

Arm type	Experimental

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

Dosage and administration details:

All subjects received 3 doses of HPV vaccine administered intramuscularly

Number of subjects in period 1[1]	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group
Started	159	194	171
Completed	142	172	156
Not completed	17	22	15
Consent withdrawn by subject	1	3	4
Missed reporting interval	3	4	2
Physician decision	-	2	-
Death	-	1	1
Migrated from study area	2	-	-
Lost to follow-up	11	12	8

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: Some subjects participating in study HPV-014 (103514) did not consent or were not selected to take part in the current study, HPV-060 (112772).

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix 15-25 years group
Reporting group description:	
Women, aged 15 to 25 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)	
Reporting group title	Cervarix 26-45 years group
Reporting group description:	
Women, aged 26 to 45 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)	
Reporting group title	Cervarix 46-55 years group
Reporting group description:	
Women, aged 46 to 55 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)	

Reporting group values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group
Number of subjects	159	194	171
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	30.6	46.1	59.6
standard deviation	± 2.8	± 6	± 3.2
Gender categorical Units: Subjects			
Female	159	194	171
Male	0	0	0

Reporting group values	Total		
Number of subjects	524		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		

Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	524		
Male	0		

End points

End points reporting groups

Reporting group title	Cervarix 15-25 years group
Reporting group description:	
Women, aged 15 to 25 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)	
Reporting group title	Cervarix 26-45 years group
Reporting group description:	
Women, aged 26 to 45 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)	
Reporting group title	Cervarix 46-55 years group
Reporting group description:	
Women, aged 46 to 55 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)	

Primary: Anti-Human Papillomavirus (Anti-HPV) 16/18 antibody titers in serum

End point title	Anti-Human Papillomavirus (Anti-HPV) 16/18 antibody titers in serum[1]
End point description:	
Titers were expressed as Geometric Mean Titer (GMT) in Enzyme-Linked Immunosorbent Assay (ELISA) units per milliliter (EL.U/mL).	
End point type	Primary
End point timeframe:	
At Year 5, 6 and 7	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This was a descriptive analysis, hence no statistical methods were required.

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	171	166	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 [Year 5] (N=146; 169; 164)	1473.4 (1246.6 to 1741.5)	620 (512.8 to 749.6)	399.5 (330.8 to 482.4)	
Anti-HPV-18 [Year 5] (N= 145; 168; 166)	439.7 (370.4 to 522.1)	183.6 (155.2 to 217.1)	119.3 (98.8 to 144)	
Anti-HPV-16 [Year 6] (N=145; 171; 159)	1358 (1155.4 to 1596)	591.9 (497.8 to 703.9)	389.8 (320.9 to 473.5)	
Anti-HPV-18 [Year 6] (N= 144; 171; 161)	448.2 (378.1 to 531.2)	182.3 (153 to 217.3)	112.7 (92.3 to 137.6)	
Anti-HPV-16 [Year 7] (N=142; 160; 153)	1011.4 (854.1 to 1197.7)	435.1 (355.9 to 532)	288.5 (235 to 354.2)	
Anti-HPV-18 [Year 7] (N= 141; 159; 155)	317 (265.9 to 377.8)	134.5 (112.1 to 161.4)	92.6 (75.3 to 114)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects.

End point title	Number of seroconverted subjects.[2]

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. anti-HPV-16 and anti-HPV-18 antibody titers respectively greater than or equal to 8 and 7 EL.U/mL) in the serum of subjects seronegative before vaccination in the primary study.

End point type	Primary

End point timeframe:

At Year 5, 6 and 7

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This was a descriptive analysis, hence no statistical methods were required.

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	146	146	
Units: Subjects				
anti-HPV-16 [Year 5] (N= 128; 127; 118)	128	127	118	
anti-HPV-18 [Year 5] (N= 134; 144; 146)	134	144	143	
anti-HPV-16 [Year 6] (N= 128; 130; 116)	128	130	116	
anti-HPV-18 [Year 6] (N= 133; 146; 142)	133	146	138	
anti-HPV-16 [Year 7] (N= 125; 119; 111)	125	119	111	
anti-HPV-18 [Year 7] (N= 130; 136; 137)	130	135	131	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects.

End point title	Number of seroconverted subjects.[3]

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. anti-HPV-16 and anti-HPV-18 antibody titers respectively greater than or equal to 19 and 18 EL.U/mL) in the serum of subjects seronegative before vaccination in the primary study.

End point type	Primary

End point timeframe:

At Years 8, 9 and 10

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This was a descriptive analysis, hence no statistical methods were required.

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	132	148	132	
Units: Subjects				
anti-HPV-16[Year8](N=116;106;99)	116	106	95	
anti-HPV-16[Year9](N=127;132;110)	127	132	106	
anti-HPV-16[Year10](N=123;121;107)	123	120	103	
anti-HPV-18[Year8](N=120;123;120)	120	118	104	
anti-HPV-18[Year9](N=132;148;132)	132	141	113	
anti-HPV-18[Year10](N=127;142;130)	126	133	109	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-Human Papillomavirus (Anti-HPV) 16/18 antibody titers in serum

End point title	Anti-Human Papillomavirus (Anti-HPV) 16/18 antibody titers in serum[4]

End point description:

Titers were expressed as Geometric Mean Titer (GMT) in Enzyme-Linked Immunosorbent Assay (ELISA) units per milliliter (EL.U/mL).

End point type	Primary

End point timeframe:

At Years 8, 9 and 10

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This was a descriptive analysis, hence no statistical methods were required.

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	144	172	153	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
anti-HPV-16[Year8](N=132;143;135)	1114.4 (936.6 to 1325.8)	435.4 (358.1 to 529.3)	279 (224.7 to 346.3)	
anti-HPV-16[Year9](N=144;172;151)	976.1 (832 to 1145.3)	402.5 (340.2 to 476.1)	265.5 (216.4 to 325.8)	
anti-HPV-16[Year10](N=140;162;147)	954.9 (804.2 to 1133.9)	369.4 (306.3 to 445.6)	228.6 (185.8 to 281.4)	

anti-HPV-18[Year8](N=131;143;137)	387.9 (323.7 to 464.8)	146.5 (120 to 178.9)	95.7 (77 to 118.9)	
anti-HPV-18[Year9](N=143;172;153)	330 (277.1 to 392.9)	136.1 (114.1 to 162.4)	87.2 (71 to 107)	
anti-HPV-18[Year10](N=139;162;149)	327.1 (271.8 to 393.7)	128.2 (105.9 to 155.1)	81.6 (66.2 to 100.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Total Immunoglobulin G (IgG) antibody titers in serum

End point title	Total Immunoglobulin G (IgG) antibody titers in serum

End point description:

IgG antibody titers were expressed as GMTs in microgram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Year 5, 6 and 7

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	65	60	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Total IgG serum antibodies [Year 5] (N=68;65;60)	19481.8 (18076.2 to 20996.8)	18388.2 (16844.6 to 20073.3)	17657.2 (16046.7 to 19429.4)	
Total IgG serum antibodies [Year 6] (N=41;38;33)	13376.5 (12498.7 to 14315.9)	12262.7 (11304.8 to 13301.8)	12040.2 (10854.4 to 13355.7)	
Total IgG serum antibodies [Year 7] (N=59;63;57)	13957.2 (13116.6 to 14851.7)	13179.4 (12287.7 to 14135.7)	12992.9 (12096.6 to 13955.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Total Immunoglobulin G (IgG) antibody titers in serum

End point title	Total Immunoglobulin G (IgG) antibody titers in serum

End point description:

IgG antibody titers were expressed as GMTs in microgram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Years 8, 9 and 10

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	61	62	55	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Total IgG serum antibodies[Year8](N=57;58;55)	11059.5 (10547.8 to 11596)	10656.3 (10057.6 to 11290.6)	10605.7 (10061.4 to 11179.5)	
Total IgG serum antibodies[Year9](N=60;56;54)	11212.2 (10661.3 to 11791.6)	10693.8 (10067 to 11359.7)	10427.8 (9871.3 to 11015.6)	
Total IgG serum antibodies[Year10](N=61;62;51)	11071.3 (10546.9 to 11621.8)	10650.8 (10079.2 to 11254.7)	10535 (9979.4 to 11121.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16/18 secretion antibody titers in cervico-vaginal secretion (CVS)

End point title	Anti-HPV-16/18 secretion antibody titers in cervico-vaginal secretion (CVS)

End point description:

Anti-HPV-16/18 titers in CVS were given as GMTs expressed in ELISA units per milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

At Year 5 and Year 6

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	39	29	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 [Year 5] (N=39;39;28)	90.2 (61.9 to 131.3)	47.2 (32.2 to 69.2)	56.8 (28.7 to 112.4)	
Anti-HPV-18 [Year 5] (N=39;39;28)	30.9 (20.9 to 45.6)	24.6 (14.8 to 41)	33.3 (15.8 to 70)	
Anti-HPV-16 [Year 6] (N=29;29;26)	80.3 (46.8 to 137.8)	43.8 (26 to 73.9)	37.1 (20.8 to 66)	

Anti-HPV-18 [Year 6] (N=29;29;26)	22.9 (13.8 to 37.9)	19.9 (11.4 to 34.9)	19.2 (11.7 to 31.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16/18 secretion antibody titers in cervico-vaginal secretion (CVS)

End point title	Anti-HPV-16/18 secretion antibody titers in cervico-vaginal secretion (CVS)

End point description:

Anti-HPV-16/18 titers in CVS were given as GMTs expressed in ELISA units per milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

At Years 7, 8, 9, 10

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	40	32	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 [Year 7] (N=31;30;30)	63 (38.6 to 102.9)	33.3 (21.6 to 51.2)	42.3 (25 to 71.5)	
Anti-HPV-18 [Year 7] (N=31;31;30)	33.5 (19.8 to 56.6)	17.5 (10.2 to 30.1)	49 (22.4 to 107.3)	
Anti-HPV-16 [Year 8] (N=31;34;32)	45.6 (29.6 to 70.1)	43.9 (24.8 to 77.7)	54.6 (34.3 to 86.8)	
Anti-HPV-18 [Year 8] (N=31;34;32)	17.8 (11.2 to 28.4)	26.2 (14.7 to 46.8)	31.9 (14.7 to 69.2)	
Anti-HPV-16 [Year 9] (N=32;35;27)	67.7 (45.4 to 101)	42.6 (23.6 to 76.8)	62.6 (36.7 to 106.5)	
Anti-HPV-18 [Year 9] (N=32;35;27)	28.1 (18.5 to 42.8)	23.9 (15.8 to 36.1)	50.4 (25.1 to 101.3)	
Anti-HPV-16 [Year 10] (N=41;40;26)	43.4 (28.1 to 67.1)	34.3 (24.1 to 48.7)	56 (31.5 to 99.7)	
Anti-HPV-18 [Year 10] (N=41;40;26)	29.4 (17.6 to 49.4)	22.7 (13.8 to 37.3)	45.1 (22.9 to 88.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Total Immunoglobulin G (IgG) secretion antibody titers in CVS

End point title	Total Immunoglobulin G (IgG) secretion antibody titers in CVS
End point description:	
Titers were given as GMTs expressed in microgram per milliliter (µg/mL).	
End point type	Secondary
End point timeframe:	
At Year 5 and Year 6	

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	39	28	
Units: µg/mL				
geometric mean (confidence interval 95%)				
IgG secretion antibodies [Year 5] (N=39;39;28)	577.8 (411.3 to 811.6)	550.5 (373.7 to 811)	990.6 (540.2 to 1816.4)	
IgG secretion antibodies [Year 6] (N=29;29;26)	546.5 (352.2 to 848.2)	499.8 (327.7 to 762.2)	1012.9 (696.7 to 1472.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Total Immunoglobulin G (IgG) secretion antibody titers in CVS

End point title	Total Immunoglobulin G (IgG) secretion antibody titers in CVS
End point description:	
Titers were given as GMTs expressed in microgram per milliliter (µg/mL)	
End point type	Secondary
End point timeframe:	
At Years 7, 8, 9, 10	

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	37	32	
Units: µg/mL				
geometric mean (confidence interval 95%)				
IgG secretion antibodies [Year 7] (N=31;31;30)	517.5 (348.1 to 769.4)	372.2 (236.7 to 585.4)	1263.2 (793.8 to 2010.2)	
IgG secretion antibodies [Year 8] (N=31;34;32)	304.8 (211.1 to 440.1)	457.2 (308.2 to 678.2)	928.2 (578 to 1490.6)	
IgG secretion antibodies [Year 9] (N=32;33;26)	435.1 (293.2 to 645.8)	460.4 (301.7 to 702.4)	925.8 (586.3 to 1461.8)	
IgG secretion antibodies [Year 10] (N=39;37;24)	315.3 (237.9 to 417.8)	373.5 (259.9 to 536.8)	622.9 (405.2 to 957.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Total Immunoglobulin G (IgG) antibody titers in serum

End point title	Total Immunoglobulin G (IgG) antibody titers in serum

End point description:

IgG antibody titers were expressed as GMTs in microgram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Year 5, 6 and 7

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	68	61	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Total IgG serum antibodies [Year 5] (N=69;68;61)	19453 (18068.5 to 20943.6)	18092.4 (16566.3 to 19759.1)	17885 (16224.1 to 19715.9)	
Total IgG serum antibodies [Year 6] (N=42;39;33)	13318.5 (12458.3 to 14238.1)	12173.1 (11231.2 to 13193.9)	12040.2 (10854.4 to 13355.7)	
Total IgG serum antibodies [Year 7] (N=59;66;58)	13957.2 (13116.6 to 14851.7)	13059.5 (12205.2 to 13973.6)	13052.9 (12160.9 to 14010.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Total Immunoglobulin G (IgG) antibody titers in serum

End point title	Total Immunoglobulin G (IgG) antibody titers in serum

End point description:

IgG antibody titers were expressed as GMTs in microgram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Years 8, 9 and 10

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	62	66	57	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Total IgG serum antibodies [Year 8] (N=58;61;57)	11084.4 (10578.2 to 11614.8)	10602.4 (10010.8 to 11229.1)	10725.5 (10151.1 to 11332.4)	
Total IgG serum antibodies [Year 9] (N=60;56;54)	11212.2 (10661.3 to 11791.6)	10693.8 (10067 to 11359.7)	10427.8 (9871.3 to 11015.6)	
Total IgG serum antibodies [Year 10] (N=62;66;55)	11043.6 (10526.3 to 11586.4)	10511.3 (9938.6 to 11117)	10484.8 (9947.5 to 11051.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point title	Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Month 48 in primary study (NCT00196937) up to Month 60 (Year 5)

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	184	170	
Units: Subjects				
SAEs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point title	Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From the Month 60 (Year 5) visit until the Month 72 (Year 6) visit

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	147	177	164	
Units: Subjects				
SAEs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point title	Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Month 72 (Year 6) visit to Month 84 (Year 7) visit

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	149	165	160	
Units: Subjects				
SAEs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point title	Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Month 84 (Year 7) to the Month 96 (Year 8) visit

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	137	147	146	
Units: Subjects				
SAEs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point title	Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Month 96 (Year 8) to the Month 108 (Year 9) visit

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	175	162	
Units: Subjects				
SAEs	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point title	Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication).

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Year 0 up to Year 10

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	194	171	
Units: Subjects				
SAE(s)	0	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline

Biologicals' concomitant medication)

End point title	Number of subjects with any fatal or vaccine-related serious adverse events (SAEs) (including SAEs related to study procedures and GlaxoSmithKline Biologicals' concomitant medication)

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Month 108 (Year 9) to the Month 120 (Year 10) visit

End point values	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	175	162	
Units: Subjects				
SAE(s)	0	1	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

SAEs: throughout the entire study from Day 0 up to the Year 10 visit.

Adverse event reporting additional description:

Other (non-serious) Adverse Events and solicited symptoms were not collected/assessed.
This section displays the safety analysis on the subjects who participated in study NCT00196937, i.e. excluding those who were not selected or not consented for HPV-060.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Cervarix 15-25 years group

Reporting group description:

Women, aged 15 to 25 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)

Reporting group title	Cervarix 26-45 years group

Reporting group description:

Women, aged 26 to 45 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)

Reporting group title	Cervarix 46-55 years group

Reporting group description:

Women, aged 46 to 55 at the time of primary vaccination, who were vaccinated with Cervarix intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6-month schedule in the primary study (NCT00196937)

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No non-serious AEs were reported for this trial.

Serious adverse events	Cervarix 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 159 (0.00%)	2 / 194 (1.03%)	1 / 171 (0.58%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 159 (0.00%)	1 / 194 (0.52%)	0 / 171 (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
Lung neoplasm malignant			

subjects affected / exposed	0 / 159 (0.00%)	0 / 194 (0.00%)	1 / 171 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Reproductive system and breast disorders			
Cervical displasia			
subjects affected / exposed	0 / 159 (0.00%)	1 / 194 (0.52%)	0 / 171 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	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 15-25 years group	Cervarix 26-45 years group	Cervarix 46-55 years group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 159 (0.00%)	0 / 194 (0.00%)	0 / 171 (0.00%)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 December 2013	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. The IgG ELISA assay will be replaced by IgG nephelometry assay to measure total IgG in the serum matrix, because the assay output of nephelometry was proven less variable than that of ELISA.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported