Clinical trial results:
A phase IV, observer-blind, randomized, controlled, multicentric study to assess the safety and immunogenicity of GSK Biologicals' HPV-16/18 L1 VLP AS04 vaccine (Cervarix) administered intramuscularly according to a three-dose schedule (Day 0, Week 6, Month 6) in human immunodeficiency virus-infected (HIV+) female subjects aged 15 - 25 years, as compared to Merck's HPV-6/11/16/18 vaccine (Gardasil)

Summary

EudraCT number	2013-003429-28
Trial protocol	EE
Global end of trial date	19 April 2017

Results information

Result version number	v3 (current)
This version publication date	05 June 2019
First version publication date	30 April 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	109823

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01031069
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	19 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 January 2016
Global end of trial reached?	Yes
Global end of trial date	19 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of both vaccines in HIV+ subjects for up to 1 month after the third dose of vaccine. To demonstrate non-inferiority of Cervarix versus (vs.) Gardasil in terms of geometric mean titres (GMTs) against HPV-16 and HPV-18 measured by Pseudovirion-based neutralization assay (PBNA) 1 month after administration of the third dose of vaccine in HIV+ subjects. If the first primary objective for immunogenicity was demonstrated, superiority of Cervarix over Gardasil in terms of GMTs against HPV-16 and HPV-18 measured by PBNA in HIV+ subjects was assessed following a sequential approach.

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 October 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 431
Country: Number of subjects enrolled	Estonia: 37
Country: Number of subjects enrolled	India: 224
Country: Number of subjects enrolled	Thailand: 181
Worldwide total number of subjects	873
EEA total number of subjects	37

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)	265
Adults (18-64 years)	608
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A number of 873 subjects were enrolled, out of which 173 subjects were excluded from all statistical analyses.
154 subjects were not administered any vaccine dose (146 screen failures subjects and 8 subjects that did not participate from Visit 1).

Pre-assignment

Screening details:

Screening involved: checking of inclusion/exclusion criteria, demographic data, history and physical examination, AF B sputum test and/or chest X-ray, blood sampling for HIV testing and safety, urine pregnancy testing, birth control and HIV, STI, STD counselling, checking records for concomitant medication/vaccination, subject card distribution.

Pre-assignment period milestones

Number of subjects started	873
Number of subjects completed	546

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Excluded from all statistical analyses: 173
Reason: Number of subjects	No vaccination received: 154

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 collected in an observer-blind manner. The vaccine recipient and those responsible for the evaluation of any study endpoint were unaware of which vaccine was administered during the entire study period.

Arms

Are arms mutually exclusive?	Yes
Arm title	HIV+/Cervarix Group

Arm description:

HIV seropositive female subjects, between and including 15 and 25 years of age, who received 3 doses of Cervarix vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.

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

Dosage and administration details:

Subjects received three doses of the study vaccine administered intramuscularly according to a Day 0, Week 6, and Month 6 vaccination schedule.

Arm title	HIV+/Gardasil Group

Arm description:

HIV seropositive female subjects, between and including 15 and 25 years of age, who received 3 doses of Gardasil vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.

Arm type	Active comparator
Investigational medicinal product name	Gardasil
Investigational medicinal product code	
Other name	Merck's Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received three doses of the study vaccine administered intramuscularly according to a Day 0, Week 6, and Month 6 vaccination schedule.

Arm title	HIV-/Cervarix Group

Arm description:

HIV seronegative female subjects, between and including 15 and 25 years of age, who received 3 doses of Cervarix vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.

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

Dosage and administration details:

Subjects received three doses of the study vaccine administered intramuscularly according to a Day 0, Week 6, and Month 6 vaccination schedule.

Arm title	HIV-/Gardasil Group

Arm description:

HIV seronegative female subjects, between and including 15 and 25 years of age, who received 3 doses of Gardasil vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.

Arm type	Active comparator
Investigational medicinal product name	Gardasil
Investigational medicinal product code	
Other name	Merck's Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received three doses of the study vaccine administered intramuscularly according to a Day 0, Week 6, and Month 6 vaccination schedule.

Number of subjects in period 1[1]	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group
Started	129	128	144
Completed	117	117	103
Not completed	12	11	41
Consent withdrawn by subject	2	3	18

Migrated/moved from study area	1	2	1
Unspecified	-	-	1
Lost to follow-up	9	5	21
Serious Adverse Event	-	1	-

Number of subjects in period 1[1]	HIV-/Gardasil Group
Started	145
Completed	111
Not completed	34
Consent withdrawn by subject	18
Migrated/moved from study area	1
Unspecified	-
Lost to follow-up	15
Serious Adverse Event	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A number of 873 subjects were enrolled, out of which 173 subjects were excluded because of data integrity issues at one center and 154 subjects were not administered any vaccine dose (146 screen failures subjects and 8 subjects that did not participate from Visit 1).

Baseline characteristics

Reporting groups	
Reporting group title	HIV+/Cervarix Group
Reporting group description:	
HIV seropositive female subjects, between and including 15 and 25 years of age, who received 3 doses of Cervarix vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.	
Reporting group title	HIV+/Gardasil Group
Reporting group description:	
HIV seropositive female subjects, between and including 15 and 25 years of age, who received 3 doses of Gardasil vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.	
Reporting group title	HIV-/Cervarix Group
Reporting group description:	
HIV seronegative female subjects, between and including 15 and 25 years of age, who received 3 doses of Cervarix vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.	
Reporting group title	HIV-/Gardasil Group
Reporting group description:	
HIV seronegative female subjects, between and including 15 and 25 years of age, who received 3 doses of Gardasil vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.	

Reporting group values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group
Number of subjects	129	128	144
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	37	36	47
Adults (18-64 years)	92	92	97
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	20.4	20.1	19.3
standard deviation	± 3.4	± 3.5	± 3.0
Gender categorical Units: Subjects			
Female	129	128	144
Male	0	0	0
Race/Ethnicity, Customized Units: Subjects			
African Heritage/African American	10	6	4
Asian - Central/South Asian Heritage	20	18	67

Asian - East Asian Heritage	3	2	1
Asian - Japanese Heritage	0	0	1
Asian - South East Asian Heritage	40	44	39
White - Arabic/North African Heritage	17	12	7
White - Caucasian/European Heritage	33	37	24
Unspecified	6	9	1

Reporting group values	HIV-/Gardasil Group	Total	
Number of subjects	145	546	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	47	167	
Adults (18-64 years)	98	379	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	19.6		
standard deviation	± 3.0	-	
Gender categorical Units: Subjects			
Female	145	546	
Male	0	0	
Race/Ethnicity, Customized Units: Subjects			
African Heritage/African American	4	24	
Asian - Central/South Asian Heritage	68	173	
Asian - East Asian Heritage	0	6	
Asian - Japanese Heritage	2	3	
Asian - South East Asian Heritage	42	165	
White - Arabic/North African Heritage	6	42	
White - Caucasian/European Heritage	19	113	
Unspecified	4	20	

End points

End points reporting groups

Reporting group title	HIV+/Cervarix Group
Reporting group description:	
HIV seropositive female subjects, between and including 15 and 25 years of age, who received 3 doses of Cervarix vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.	
Reporting group title	HIV+/Gardasil Group
Reporting group description:	
HIV seropositive female subjects, between and including 15 and 25 years of age, who received 3 doses of Gardasil vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.	
Reporting group title	HIV-/Cervarix Group
Reporting group description:	
HIV seronegative female subjects, between and including 15 and 25 years of age, who received 3 doses of Cervarix vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.	
Reporting group title	HIV-/Gardasil Group
Reporting group description:	
HIV seronegative female subjects, between and including 15 and 25 years of age, who received 3 doses of Gardasil vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.	

Primary: Number of human immunodeficiency virus positive subjects (HIV+) with any and Grade 3 solicited local symptoms

End point title	Number of human immunodeficiency virus positive subjects (HIV+) with any and Grade 3 solicited local symptoms[1][2]
End point description:	
Assessed solicited local symptoms were pain, redness, swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = significant pain at rest, pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling with a maximum diameter greater than 50 millimeters (mm).	
End point type	Primary
End point timeframe:	
During the 7-day follow-up period (from the day of vaccination up to 6 subsequent days) after each vaccine dose and across doses	

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 endpoint was descriptive, hence no statistical analyses were available.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Participants				
Any Pain, Dose 1 (N=128;125)	115	58		
Grade 3 Pain, Dose 1 (N=128;125)	4	0		
Any Redness, Dose 1 (N=128;125)	24	19		
Grade 3 Redness, Dose 1 (N=128;125)	0	0		

Any Swelling, Dose 1 (N=128;125)	25	6		
Grade 3 Swelling, Dose 1 (N=128;125)	2	0		
Any Pain, Dose 2 (N=127;125)	98	56		
Grade 3 Pain, Dose 2 (N=127;125)	5	6		
Any Redness, Dose 2 (N=127;125)	18	13		
Grade 3 Redness, Dose 2 (N=127;125)	1	0		
Any Swelling, Dose 2 (N=127;125)	16	11		
Grade 3 Swelling, Dose 2 (N=127;125)	0	0		
Any Pain, Dose 3 (N=117;117)	87	60		
Grade 3 Pain, Dose 3 (N=117;117)	5	2		
Any Redness, Dose 3 (N=117;117)	17	18		
Grade 3 Redness, Dose 3 (N=117;117)	0	0		
Any Swelling, Dose 3 (N=117;117)	19	10		
Grade 3 Swelling, Dose 3 (N=117;117)	1	0		
Any Pain, Across Doses (N=128;127)	120	85		
Grade 3 Pain, Across Doses (N=128;127)	11	6		
Any Redness, Across Doses (N=128;127)	41	34		
Grade 3 Redness, Across Doses (N=128;127)	1	0		
Any Swelling, Across Doses (N=128;127)	38	20		
Grade 3 Swelling, Across Doses (N=128;127)	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of HIV+ subjects with any, Grade 3 and related solicited general symptoms

End point title	Number of HIV+ subjects with any, Grade 3 and related solicited general symptoms[3][4]

End point description:

Assessed solicited general symptoms were arthralgia, fatigue, gastrointestinal [nausea, vomiting, diarrhoea and/or abdominal pain], headache, myalgia, rash, temperature [defined as axillary temperature higher than (>) 37.5 degrees Celsius (°C)] and urticaria. Any = occurrence of the symptom regardless of intensity grade and relationship. Grade 3 symptom = symptom that prevented normal activity. Grade 3 temperature = temperature > 39.0 °C. Grade 3 urticaria = urticaria distributed on at least 4 body areas. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Primary

End point timeframe:

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

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 endpoint was descriptive, hence no statistical analyses were available.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	127		
Units: Participants				
Any Arthralgia, Dose 1 (N=128;125)	29	20		
Grade 3 Arthralgia, Dose 1 (N=128;125)	1	1		
Related Arthralgia, Dose 1 (N=128;125)	19	13		
Any Fatigue, Dose 1 (N=128;125)	50	47		
Grade 3 Fatigue, Dose 1 (N=128;125)	4	0		
Related Fatigue, Dose 1 (N=128;125)	30	29		
Any Gastrointestinal, Dose 1 (N=128;125)	30	21		
Grade 3 Gastrointestinal, Dose 1 (N=128;125)	2	0		
Related Gastrointestinal, Dose 1 (N=128;125)	19	15		
Any Headache, Dose 1 (N=128;125)	61	48		
Grade 3 Headache, Dose 1 (N=128;125)	4	1		
Related Headache, Dose 1 (N=128;125)	39	27		
Any Myalgia, Dose 1 (N=128;125)	49	34		
Grade 3 Myalgia, Dose 1 (N=128;125)	2	1		
Related Myalgia, Dose 1 (N=128;125)	35	25		
Any Rash, Dose 1 (N=128;125)	7	4		
Grade 3 Rash, Dose 1 (N=128;125)	1	0		
Related Rash, Dose 1 (N=128;125)	4	0		
Any Temperature, Dose 1 (N=128;125)	9	5		
Grade 3 Temperature, Dose 1 (N=128;125)	0	0		
Related Temperature, Dose 1 (N=128;125)	7	4		
Any Urticaria, Dose 1 (N=128;125)	8	3		
Grade 3 Urticaria, Dose 1 (N=128;125)	0	0		
Related Urticaria, Dose 1 (N=128;125)	6	3		
Any Arthralgia, Dose 2 (N=127;125)	18	21		
Grade 3 Arthralgia, Dose 2 (N=127;125)	0	3		
Related Arthralgia, Dose 2 (N=127;125)	11	14		
Any Fatigue, Dose 2 (N=127;125)	38	40		
Grade 3 Fatigue, Dose 2 (N=127;125)	2	1		
Related Fatigue, Dose 2 (N=127;125)	20	25		
Any Gastrointestinal, Dose 2 (N=127;125)	15	17		
Grade 3 Gastrointestinal, Dose 2 (N=127;125)	0	0		
Related Gastrointestinal, Dose 2 (N=127;125)	11	11		
Any Headache, Dose 2 (N=127;125)	48	37		
Grade 3 Headache, Dose 2 (N=127;125)	5	3		
Related Headache, Dose 2 (N=127;125)	30	20		
Any Myalgia, Dose 2 (N=127;125)	36	26		
Grade 3 Myalgia, Dose 2 (N=127;125)	2	4		
Related Myalgia, Dose 2 (N=127;125)	25	19		

Any Rash, Dose 2 (N=127;125)	2	1		
Grade 3 Rash, Dose 2 (N=127;125)	0	0		
Related Rash, Dose 2 (N=127;125)	0	0		
Any Temperature, Dose 2 (N=127;125)	11	4		
Grade 3 Temperature, Dose 2 (N=127;125)	0	0		
Related Temperature, Dose 2 (N=127;125)	9	2		
Any Urticaria, Dose 2 (N=127;125)	5	4		
Grade 3 Urticaria, Dose 2 (N=127;125)	1	0		
Related Urticaria, Dose 2 (N=127;125)	4	4		
Any Arthralgia, Dose 3 (N=117;117)	17	15		
Grade 3 Arthralgia, Dose 3 (N=117;117)	2	1		
Related Arthralgia, Dose 3 (N=117;117)	13	12		
Any Fatigue, Dose 3 (N=117;117)	40	31		
Grade 3 Fatigue, Dose 3 (N=117;117)	1	1		
Related Fatigue, Dose 3 (N=117;117)	30	22		
Any Gastrointestinal, Dose 3 (N=117;117)	13	17		
Grade 3 Gastrointestinal, Dose 3 (N=117;117)	1	1		
Related Gastrointestinal, Dose 3 (N=117;117)	9	13		
Any Headache, Dose 3 (N=117;117)	48	27		
Grade 3 Headache, Dose 3 (N=117;117)	2	2		
Related Headache, Dose 3 (N=117;117)	39	16		
Any Myalgia, Dose 3 (N=117;117)	30	21		
Grade 3 Myalgia, Dose 3 (N=117;117)	4	1		
Related Myalgia, Dose 3 (N=117;117)	26	17		
Any Rash, Dose 3 (N=117;117)	2	1		
Grade 3 Rash, Dose 3 (N=117;117)	0	0		
Related Rash, Dose 3 (N=117;117)	1	0		
Any Temperature, Dose 3 (N=117;117)	10	12		
Grade 3 Temperature, Dose 3 (N=117;117)	1	1		
Related Temperature, Dose 3 (N=117;117)	7	6		
Any Urticaria, Dose 3 (N=117;117)	2	4		
Grade 3 Urticaria, Dose 3 (N=117;117)	0	0		
Related Urticaria, Dose 3 (N=117;117)	2	2		
Any Arthralgia, Across Doses (N=128;127)	41	38		
Grade 3 Arthralgia, Across Doses (N=128;127)	3	4		
Related Arthralgia, Across Doses (N=128;127)	31	28		
Any Fatigue, Across Doses (N=128;127)	73	59		
Grade 3 Fatigue, Across Doses (N=128;127)	6	2		
Related Fatigue, Across Doses (N=128;127)	50	39		
Any Gastrointestinal, Across Doses (N=128;127)	41	35		
Grade 3 Gastrointestinal, Across Doses (N=128;127)	3	1		

Related Gastrointestinal, Across Doses (N=128;127)	27	23		
Any Headache, Across Doses (N=128;127)	88	63		
Grade 3 Headache, Across Doses (N=128;127)	11	4		
Related Headache, Across Doses (N=128;127)	65	39		
Any Myalgia, Across Doses (N=128;127)	68	51		
Grade 3 Myalgia, Across Doses (N=128;127)	7	4		
Related Myalgia, Across Doses (N=128;127)	52	37		
Any Rash, Across Doses (N=128;127)	11	5		
Grade 3 Rash, Across Doses (N=128;127)	1	0		
Related Rash, Across Doses (N=128;127)	5	0		
Any Temperature, Across Doses (N=128;127)	23	19		
Grade 3 Temperature, Across Doses (N=128;127)	1	1		
Related Temperature, Across Doses (N=128;127)	18	10		
Any Urticaria, Across Doses (N=128;127)	13	9		
Grade 3 Urticaria, Across Doses (N=128;127)	1	0		
Related Urticaria, Across Doses (N=128;127)	10	8		

Statistical analyses

No statistical analyses for this end point

Primary: Number of HIV+ subjects with any, Grade 3 and related unsolicited adverse events (AEs)

End point title	Number of HIV+ subjects with any, Grade 3 and related unsolicited adverse events (AEs)[5][6]

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 symptom = symptom that prevented normal activity. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Primary

End point timeframe:

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

Notes:

[5] - 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 endpoint was descriptive, hence no statistical analyses were available.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the

baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	128		
Units: Participants				
Any AE(s)	41	41		
Grade 3 AE(s)	7	4		
Related AE(s)	9	8		

Statistical analyses

No statistical analyses for this end point

Primary: Number of HIV+ subjects with serious adverse events (SAEs)

End point title	Number of HIV+ subjects with serious adverse events

End point description:

SAEs assessed include any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or represented a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Primary

End point timeframe:

From Day 0 up to Month 7 (from Day 0 up to 30 days after the last vaccination dose at Month 6)

Notes:

[7] - 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 endpoint was descriptive, hence no statistical analyses were available.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	128		
Units: Participants				
SAE(s)	6	6		

Statistical analyses

No statistical analyses for this end point

Primary: Number of HIV+ subjects with medically significant conditions (MSCs)

End point title	Number of HIV+ subjects with medically significant conditions (MSCs)[9][10]

End point description:

Medically significant conditions (MSCs) are defined as AEs prompting emergency room or physician visits that were not related to common diseases, or not related to routine visits for physical examination or vaccination, SAEs that were not related to common diseases.

End point type	Primary

End point timeframe:

From Day 0 up to Month 7 (from Day 0 up to 30 days after the last vaccination dose at Month 6)

Notes:

[9] - 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 endpoint was descriptive, hence no statistical analyses were available.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	128		
Units: Participants				
MSC(s)	17	27		

Statistical analyses

No statistical analyses for this end point

Primary: Number of HIV+ subjects with potential immune-mediated diseases (pIMDs)

End point title	Number of HIV+ subjects with potential immune-mediated diseases (pIMDs)[11][12]

End point description:

Potential immune-mediated diseases are 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	Primary

End point timeframe:

From Day 0 up to Month 7 (from Day 0 up to 30 days after the last vaccination dose at Month 6)

Notes:

[11] - 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 endpoint was descriptive, hence no statistical analyses were available.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	128		
Units: Participants				
pIMD(s)	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of HIV+ subjects reporting pregnancies and outcomes of reported pregnancies

End point title	Number of HIV+ subjects reporting pregnancies and outcomes of reported pregnancies[13][14]

End point description:

Pregnancy related outcomes were: live infant no apparent congenital anomaly, live infant congenital anomaly, elective termination (termin.) no apparent congenital anomaly, elective termination (termin.) congenital anomaly, ectopic pregnancy, spontaneous abortion no apparent congenital (congen.) anomaly, stillbirth no apparent congenital anomaly, stillbirth congenital anomaly, lost to follow-up, pregnancy ongoing, missing.

End point type	Primary

End point timeframe:

From Day 0 up to Month 7 (from Day 0 up to 30 days after the last vaccination dose at Month 6)

Notes:

[13] - 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 endpoint was descriptive, hence no statistical analyses were available.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: Participants				
Live infant NO apparent congenital anomaly	3	1		
Live infant congenital anomaly	0	0		
Elective termin. NO apparent congenital anomaly	0	0		
Elective termin. congenital anomaly	0	0		
Ectopic pregnancy	0	0		
Spontaneous abortion NO apparent congen. anomaly	1	1		
Stillbirth NO apparent congenital anomaly	0	0		
Stillbirth congenital anomaly	0	0		
Lost to follow-up	0	0		
Pregnancy ongoing	0	0		
Missing	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of HIV+ subjects with haematological and biochemical parameter abnormalities

End point title	Number of HIV+ subjects with haematological and biochemical parameter abnormalities[15][16]

End point description:

Among assessed haematological and biochemical parameters were: alanine aminotransferase [ALAT], basophilis [BSPH], creatinine [CRT], eosinophils [ESPH], haematocrit [HTCR], haemoglobin [HGB], lymphocytes [LYMP], monocytes [MONO], neutrophils [NTPH], platelets [PLAT], red blood cells [RBC] and white blood cells [WBC]. Unknown = value unknown for the specified visit and laboratory parameter; Below = value below the laboratory reference range defined for the specified visit and laboratory parameter; Within = value within the laboratory reference range defined for the specified visit and laboratory parameter; Above = value above the laboratory reference range defined for the specified visit and laboratory parameter.

End point type	Primary

End point timeframe:

At Month 7 (30 days after the last vaccination dose at Month 6)

Notes:

[15] - 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 endpoint was descriptive, hence no statistical analyses were available.

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	121		
Units: Participants				
ALAT, Unknown (N=121;121)	0	0		
ALAT, Below (N=121;121)	4	3		
ALAT, Within (N=121;121)	110	105		
ALAT, Above (N=121;121)	7	13		
BSPH, Unknown (N=121;121)	0	0		
BSPH, Below (N=121;121)	0	0		
BSPH, Within (N=121;121)	120	121		
BSPH, Above (N=121;121)	1	0		
CRT, Unknown (N=121;120)	0	0		
CRT, Below (N=121;120)	29	36		
CRT, Within (N=121;120)	91	84		
CRT, Above (N=121;120)	1	0		
ESPH, Unknown (N=121;121)	0	0		
ESPH, Below (N=121;121)	9	10		
ESPH, Within (N=121;121)	108	106		
ESPH, Above (N=121;121)	4	5		
HTCR, Unknown (N=121;121)	0	0		
HTCR, Below (N=121;121)	19	27		
HTCR, Within (N=121;121)	101	92		
HTCR, Above (N=121;121)	1	2		
HGB, Unknown (N=121;121)	0	0		
HGB, Below (N=121;121)	28	37		

HGB, Within (N=121;121)	92	83		
HGB, Above (N=121;121)	1	1		
LYMP, Unknown (N=121;121)	0	0		
LYMP, Below (N=121;121)	12	11		
LYMP, Within (N=121;121)	96	97		
LYMP, Above (N=121;121)	13	13		
MONO, Unknown (N=121;121)	0	0		
MONO, Below (N=121;121)	4	7		
MONO, Within (N=121;121)	106	97		
MONO, Above (N=121;121)	11	17		
NTPH, Unknown (N=121;121)	0	0		
NTPH, Below (N=121;121)	16	17		
NTPH, Within (N=121;121)	97	93		
NTPH, Above (N=121;121)	8	11		
PLAT, Unknown (N=121;121)	0	0		
PLAT, Below (N=121;121)	1	3		
PLAT, Within (N=121;121)	118	114		
PLAT, Above (N=121;121)	2	4		
RBC, Unknown (N=121;121)	0	0		
RBC, Below (N=121;121)	36	34		
RBC, Within (N=121;121)	82	84		
RBC, Above (N=121;121)	3	3		
WBC, Unknown (N=121;121)	0	0		
WBC, Below (N=121;121)	10	9		
WBC, Within (N=121;121)	106	108		
WBC, Above (N=121;121)	5	4		

Statistical analyses

No statistical analyses for this end point

Primary: Cluster of differentiation 4 (CD4+) cell count in HIV+ subjects at Month 7

End point title	Cluster of differentiation 4 (CD4+) cell count in HIV+ subjects at Month 7[17][18]

End point description:

CD4+ cell count, expressed in cells/cubic millimeter (mm3), was assessed for HIV+ subjects.

End point type	Primary

End point timeframe:

At Month 7 (30 days after the last vaccination dose at Month 6)

Notes:

[17] - 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 endpoint is only reporting values for HIV positive subjects.

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	121		
Units: cells/mm3				
median (inter-quartile range (Q1-Q3))				
CD4+ cell count	554.0 (440.0 to 799.0)	568.0 (457.0 to 773.4)		

Statistical analyses

No statistical analyses for this end point

Primary: HIV viral load (VL) in HIV+ subjects at Month 7

End point title	HIV viral load (VL) in HIV+ subjects at Month 7[19][20]

End point description:

HIV VL, expressed in HIV copies/milliliter (mL), was assessed for HIV+ subjects.

End point type	Primary

End point timeframe:

At Month 7 (30 days after the last vaccination dose at Month 6)

Notes:

[19] - 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 endpoint was descriptive, hence no statistical analyses were available.

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	95		
Units: HIV copies/mL				
median (inter-quartile range (Q1-Q3))				
HIV viral load	1.9 (1.3 to 3.8)	2.5 (1.3 to 3.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of HIV+ subjects by World Health Organization (WHO) HIV clinical staging

End point title	Number of HIV+ subjects by World Health Organization (WHO) HIV clinical staging[21][22]

End point description:

HIV+ subjects were categorised into clinical stages 1 through 4, as per the WHO classification [WHO, 2009].

End point type	Primary

End point timeframe:

At Month 7 (30 days after the last vaccination dose at Month 6)

Notes:

[21] - 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 endpoint was descriptive, hence no statistical analyses were available.

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	128		
Units: Participants				
Clinical Stage 1	113	114		
Clinical Stage 2	6	2		
Clinical Stage 3	1	1		
Clinical Stage 4	1	4		

Statistical analyses

No statistical analyses for this end point

Primary: Pseudovirion-Based Neutralization Assay (PBNA) Titers of anti-HPV-16/18 antibodies in HIV+ subjects, based on Adapted According-to-Protocol (ATP) cohort for immunogenicity

End point title	Pseudovirion-Based Neutralization Assay (PBNA) Titers of anti-HPV-16/18 antibodies in HIV+ subjects, based on Adapted According-to-Protocol (ATP) cohort for immunogenicity[23]

End point description:

Titers of anti-HPV-16/18 antibodies, expressed as Geometric Mean Titers (GMTs), with cut-offs greater than or equal to (≥) 40 estimated dose giving 50% signal reduction when compared to a control without serum (ED50), as assessed by the Pseudovirion-Based Neutralization Assay [PBNA], in HIV+ subjects. Between-group comparisons to assess non-inferiority were performed on the ATP cohort for immunogenicity (by PBNA, regardless of HPV serostatus at baseline).

End point type	Primary

End point timeframe:

At Month 7 (30 days after the last vaccination dose at Month 6)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	83		
Units: Titers				
geometric mean (confidence interval 95%)				

Anti-HPV-16 (N=79;83)	23436.1 (18186.4 to 30201.1)	7507.0 (5378.1 to 10478.6)		
Anti-HPV-18 (N=79;82)	12490.9 (9681.7 to 16115.2)	1459.6 (965.4 to 2206.7)		

Statistical analyses

Statistical analysis title	Anti-HPV-16 Adjusted GMT ratios - non-inferiority

Statistical analysis description:

Adjusted GMT ratios for anti-HPV-16 neutra antibody (ED50): To demonstrate that the immunogenicity of Cervarix vaccine (HIV+/Cervarix Group) was non-inferior to that of Gardasil vaccine (HIV+/Gardasil Group), in terms of geometric mean titers (GMTs) against HPV-16, measured by Pseudovirion-based neutralization assay (PBNA) one month after the administration of the third dose of vaccine in HIV+ subjects.

Comparison groups	HIV+/Gardasil Group v HIV+/Cervarix Group
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
Parameter estimate	Adjusted GMT ratio
Point estimate	2.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.92
upper limit	4.52

Notes:

[24] - Non-inferiority was defined as the lower limit of the 95% confidence interval (CI) for the ratio of GMTs (Cervarix over Gardasil) being above (>) 0.5 for HPV-16 type. Note: Primary objectives were to be assessed sequentially: firstly, non-inferiority for both HPV-16 and HPV-18, and then, superiority for HPV-18 followed by superiority for HPV-16.

Statistical analysis title	Anti-HPV-18 Adjusted GMT ratios - non-inferiority

Statistical analysis description:

Adjusted GMT ratios for anti-HPV-18 neutra antibody (ED50): To demonstrate that the immunogenicity of Cervarix vaccine (HIV+/Cervarix Group) was non-inferior to that of Gardasil vaccine (HIV+/Gardasil Group), in terms of geometric mean titers (GMTs) against HPV-18, measured by Pseudovirion-based neutralization assay (PBNA) one month after the administration of the third dose of vaccine in HIV+ subjects.

Comparison groups	HIV+/Gardasil Group v HIV+/Cervarix Group
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
Parameter estimate	Adjusted GMT ratio
Point estimate	7.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.84
upper limit	12.66

Notes:

[25] - Non-inferiority was defined as the lower limit of the 95% confidence interval (CI) for the ratio of GMTs (Cervarix over Gardasil) being above (>) 0.5 for HPV-18 type. Note: Primary objectives were to be assessed sequentially: firstly, non-inferiority for both HPV-16 and HPV-18, and then, superiority for

HPV-18 followed by superiority for HPV-16.

Primary: Pseudovirion-Based Neutralization Assay (PBNA) Titers of anti-HPV-16/18 antibodies in HIV+ subjects, based on Total Vaccinated Cohort (TVC)

End point title	Pseudovirion-Based Neutralization Assay (PBNA) Titers of anti-HPV-16/18 antibodies in HIV+ subjects, based on Total Vaccinated Cohort (TVC)[26]

End point description:

Titers of anti-HPV-16/18 antibodies, expressed as Geometric Mean Titers (GMTs), with cut-offs greater than or equal to (≥) 40 estimated dose giving 50% signal reduction when compared to a control without serum (ED50), as assessed by the Pseudovirion-Based Neutralization Assay [PBNA], in HIV+ subjects. Between-group comparisons to assess superiority were performed on the TVC (by PBNA, regardless of HPV serostatus at baseline).

End point type	Primary

End point timeframe:

At Month 7 (30 days after the last vaccination dose at Month 6)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	109		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-HPV-16	21106.6 (15961.3 to 27910.6)	7533.7 (5616.7 to 10105.0)		
Anti-HPV-18	11580.5 (8851.5 to 15150.9)	1451.9 (1009.0 to 2089.2)		

Statistical analyses

Statistical analysis title	Anti-HPV-18 Adjusted GMT ratios - superiority

Statistical analysis description:

Adjusted GMT ratios for anti-HPV-18 neutra antibody (ED50): To demonstrate that the immunogenicity of Cervarix vaccine (HIV+/Cervarix Group) was superior to that of Gardasil vaccine (HIV+/Gardasil Group), in terms of geometric mean titers (GMTs) against HPV-18, measured by Pseudovirion-based neutralization assay (PBNA) in HIV+ subjects, assessed following a sequential approach.

Comparison groups	HIV+/Cervarix Group v HIV+/Gardasil Group
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	< 0.0001 [28]
Method	ANOVA
Parameter estimate	Adjusted GMT ratio
Point estimate	7.44

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.79
upper limit	11.54

Notes:

[27] - Superiority was defined as the lower limit of the 95% CI for the ratio of GMTs (Cervarix over Gardasil) being above 1 for HPV-18 type, with a statistically significant p-value.
Note: Primary objectives were to be assessed sequentially: firstly, non-inferiority for both HPV-16 and HPV-18, and then, superiority for HPV-18 followed by superiority for HPV-16.
[28] - ANOVA model on the log10 transformation of the titers for HIV+ subjects and including the vaccine group as fixed effect.

Statistical analysis title	Anti-HPV-16 Adjusted GMT ratio - superiority

Statistical analysis description:

Adjusted GMT ratios for anti-HPV-16 neutra antibody (ED50): To demonstrate that the immunogenicity of Cervarix vaccine (HIV+/Cervarix Group) was superior to that of Gardasil vaccine (HIV+/Gardasil Group), in terms of geometric mean titers (GMTs) against HPV-16, measured by Pseudovirion-based neutralization assay (PBNA) in HIV+ subjects, following a sequential approach.

Comparison groups	HIV+/Cervarix Group v HIV+/Gardasil Group
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	< 0.0001 [30]
Method	ANOVA
Parameter estimate	Adjusted GMT ratio
Point estimate	2.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.83
upper limit	4.11

Notes:

[29] - Superiority was defined as the lower limit of the 95% CI for the ratio of GMTs (Cervarix over Gardasil) being above 1 for HPV-16 type, with a statistically significant p-value.
Note: Primary objectives were to be assessed sequentially: firstly, non-inferiority for both HPV-16 and HPV-18, and then, superiority for HPV-18 followed by superiority for HPV-16.
[30] - ANOVA model on the log10 transformation of the titers for HIV+ subjects and including the vaccine group as fixed effect.

Secondary: Number of HIV- subjects with any and Grade 3 solicited local symptoms

End point title	Number of HIV- subjects with any and Grade 3 solicited local symptoms[31]

End point description:

Assessed solicited local symptoms were pain, redness, swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = significant pain at rest, pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling with a maximum diameter greater than 50 millimeters (mm).

End point type	Secondary

End point timeframe:

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

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV negative subjects.

End point values	HIV-/Cervarix Group	HIV-/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	144		
Units: Participants				
Any Pain, Dose 1 (N=141;144)	127	91		
Grade 3 Pain, Dose 1 (N=141;144)	10	1		
Any Redness, Dose 1 (N=141;144)	32	21		
Grade 3 Redness, Dose 1 (N=141;144)	0	0		
Any Swelling, Dose 1 (N=141;144)	23	14		
Grade 3 Swelling, Dose 1 (N=141;144)	0	0		
Any Pain, Dose 2 (N=136;139)	108	92		
Grade 3 Pain, Dose 2 (N=136;139)	6	2		
Any Redness, Dose 2 (N=136;139)	29	29		
Grade 3 Redness, Dose 2 (N=136;139)	0	0		
Any Swelling, Dose 2 (N=136;139)	24	27		
Grade 3 Swelling, Dose 2 (N=136;139)	0	0		
Any Pain, Dose 3 (N=125;129)	94	82		
Grade 3 Pain, Dose 3 (N=125;129)	10	6		
Any Redness, Dose 3 (N=125;129)	28	19		
Grade 3 Redness, Dose 3 (N=125;129)	0	0		
Any Swelling, Dose 3 (N=125;129)	29	19		
Grade 3 Swelling, Dose 3 (N=125;129)	0	0		
Any Pain, Across Doses (N=141;144)	133	119		
Grade 3 Pain, Across Doses (N=141;144)	22	8		
Any Redness, Across Doses (N=141;144)	52	42		
Grade 3 Redness, Across Doses (N=141;144)	0	0		
Any Swelling, Across Doses (N=141;144)	47	39		
Grade 3 Swelling, Across Doses (N=141;144)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of HIV- subjects with any, Grade 3 and related solicited general symptoms

End point title	Number of HIV- subjects with any, Grade 3 and related solicited general symptoms[32]

End point description:

Assessed solicited general symptoms were arthralgia, fatigue, gastrointestinal [nausea, vomiting, diarrhoea and/or abdominal pain], headache, myalgia, rash, temperature [defined as axillary temperature higher than (>) 37.5 degrees Celsius (°C)] and urticaria. Any = occurrence of the symptom regardless of intensity grade and relationship. Grade 3 symptom = symptom that prevented normal activity. Grade 3 temperature = temperature > 39.0 °C. Grade 3 urticaria = urticaria distributed on at least 4 body areas. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

During the 7-day follow-up period (from the day of vaccination up to 6 subsequent days) after each

vaccine dose and across doses

Notes:

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

Justification: This endpoint is only reporting values for HIV negative subjects.

End point values	HIV-/Cervarix Group	HIV-/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	144		
Units: Participants				
Any Arthralgia, Dose 1 (N=141;144)	17	21		
Grade 3 Arthralgia, Dose 1 (N=141;144)	0	0		
Related Arthralgia, Dose 1 (N=141;144)	9	11		
Any Fatigue, Dose 1 (N=141;144)	45	34		
Grade 3 Fatigue, Dose 1 (N=141;144)	3	2		
Related Fatigue, Dose 1 (N=141;144)	29	17		
Any Gastrointestinal, Dose 1 (N=141;144)	19	14		
Grade 3 Gastrointestinal, Dose 1 (N=141;144)	1	1		
Related Gastrointestinal, Dose 1 (N=141;144)	8	11		
Any Headache, Dose 1 (N=141;144)	45	45		
Grade 3 Headache, Dose 1 (N=141;144)	0	2		
Related Headache, Dose 1 (N=141;144)	29	22		
Any Myalgia, Dose 1 (N=141;144)	44	36		
Grade 3 Myalgia, Dose 1 (N=141;144)	1	2		
Related Myalgia, Dose 1 (N=141;144)	28	21		
Any Rash, Dose 1 (N=141;144)	2	6		
Grade 3 Rash, Dose 1 (N=141;144)	0	0		
Related Rash, Dose 1 (N=141;144)	2	2		
Any Temperature, Dose 1 (N=141;144)	11	8		
Grade 3 Temperature, Dose 1 (N=141;144)	0	0		
Related Temperature, Dose 1 (N=141;144)	7	5		
Any Urticaria, Dose 1 (N=141;144)	3	3		
Grade 3 Urticaria, Dose 1 (N=141;144)	0	0		
Related Urticaria, Dose 1 (N=141;144)	3	3		
Any Arthralgia, Dose 2 (N=136;139)	14	12		
Grade 3 Arthralgia, Dose 2 (N=136;139)	0	0		
Related Arthralgia, Dose 2 (N=136;139)	9	5		
Any Fatigue, Dose 2 (N=136;139)	34	34		
Grade 3 Fatigue, Dose 2 (N=136;139)	2	0		
Related Fatigue, Dose 2 (N=136;139)	19	19		
Any Gastrointestinal, Dose 2 (N=136;139)	9	15		
Grade 3 Gastrointestinal, Dose 2 (N=136;139)	1	1		
Related Gastrointestinal, Dose 2 (N=136;139)	7	6		

Any Headache, Dose 2 (N=136;139)	35	31		
Grade 3 Headache, Dose 2 (N=136;139)	5	2		
Related Headache, Dose 2 (N=136;139)	23	19		
Any Myalgia, Dose 2 (N=136;139)	36	26		
Grade 3 Myalgia, Dose 2 (N=136;139)	1	0		
Related Myalgia, Dose 2 (N=136;139)	28	19		
Any Rash, Dose 2 (N=136;139)	2	4		
Grade 3 Rash, Dose 2 (N=136;139)	0	0		
Related Rash, Dose 2 (N=136;139)	1	1		
Any Temperature, Dose 2 (N=136;139)	10	10		
Grade 3 Temperature, Dose 2 (N=136;139)	1	0		
Related Temperature, Dose 2 (N=136;139)	5	8		
Any Urticaria, Dose 2 (N=136;139)	1	1		
Grade 3 Urticaria, Dose 2 (N=136;139)	0	0		
Related Urticaria, Dose 2 (N=136;139)	1	1		
Any Arthralgia, Dose 3 (N=125;129)	9	14		
Grade 3 Arthralgia, Dose 3 (N=125;129)	0	2		
Related Arthralgia, Dose 3 (N=125;129)	9	11		
Any Fatigue, Dose 3 (N=125;129)	32	20		
Grade 3 Fatigue, Dose 3 (N=125;129)	1	2		
Related Fatigue, Dose 3 (N=125;129)	29	15		
Any Gastrointestinal, Dose 3 (N=125;129)	7	9		
Grade 3 Gastrointestinal, Dose 3 (N=125;129)	1	0		
Related Gastrointestinal, Dose 3 (N=125;129)	6	6		
Any Headache, Dose 3 (N=125;129)	33	25		
Grade 3 Headache, Dose 3 (N=125;129)	3	2		
Related Headache, Dose 3 (N=125;129)	26	17		
Any Myalgia, Dose 3 (N=125;129)	26	28		
Grade 3 Myalgia, Dose 3 (N=125;129)	2	2		
Related Myalgia, Dose 3 (N=125;129)	22	21		
Any Rash, Dose 3 (N=125;129)	2	0		
Grade 3 Rash, Dose 3 (N=125;129)	0	0		
Related Rash, Dose 3 (N=125;129)	2	0		
Any Temperature, Dose 3 (N=125;129)	9	10		
Grade 3 Temperature, Dose 3 (N=125;129)	2	1		
Related Temperature, Dose 3 (N=125;129)	7	6		
Any Urticaria, Dose 3 (N=125;129)	2	3		
Grade 3 Urticaria, Dose 3 (N=125;129)	0	0		
Related Urticaria, Dose 3 (N=125;129)	2	3		
Any Arthralgia, Across Doses (N=141;144)	31	34		
Grade 3 Arthralgia, Across Doses (N=141;144)	0	2		
Related Arthralgia, Across Doses (N=141;144)	20	18		
Any Fatigue, Across Doses (N=141;144)	65	56		

Grade 3 Fatigue, Across Doses (N=141;144)	5	4		
Related Fatigue, Across Doses (N=141;144)	45	33		
Any Gastrointestinal, Across Doses (N=141;144)	28	26		
Grade 3 Gastrointestinal, Across Doses (N=141;144)	2	1		
Related Gastrointestinal, Across Doses (N=141;144)	17	17		
Any Headache, Across Doses (N=141;144)	69	67		
Grade 3 Headache, Across Doses (N=141;144)	7	5		
Related Headache, Across Doses (N=141;144)	51	40		
Any Myalgia, Across Doses (N=141;144)	64	53		
Grade 3 Myalgia, Across Doses (N=141;144)	3	4		
Related Myalgia, Across Doses (N=141;144)	44	40		
Any Rash, Across Doses (N=141;144)	5	8		
Grade 3 Rash, Across Doses (N=141;144)	0	0		
Related Rash, Across Doses (N=141;144)	5	3		
Any Temperature, Across Doses (N=141;144)	22	24		
Grade 3 Temperature, Across Doses (N=141;144)	3	1		
Related Temperature, Across Doses (N=141;144)	16	16		
Any Urticaria, Across Doses (N=141;144)	4	6		
Grade 3 Urticaria, Across Doses (N=141;144)	0	0		
Related Urticaria, Across Doses (N=141;144)	4	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of HIV- subjects with unsolicited adverse events (AEs)

End point title	Number of HIV- subjects with unsolicited adverse events

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 symptom = symptom that prevented normal activity. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

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

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV negative subjects.

End point values	HIV-/Cervarix Group	HIV-/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	145		
Units: Participants				
Any AE(s)	26	32		
Grade 3 AE(s)	1	3		
Related AE(s)	4	2		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of HIV- subjects with serious adverse events (SAEs)[34]

End point description:

SAEs assessed include any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or represented a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 7 (from Day 0 up to 30 days after the last vaccination dose at Month 6)

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV negative subjects.

End point values	HIV-/Cervarix Group	HIV-/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	145		
Units: Participants				
SAE(s)	1	0		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of HIV- subjects with medically significant conditions (MSCs)[35]

End point description:

Medically significant conditions (MSCs) are defined as AEs prompting emergency room or physician visits that were not related to common diseases, or not related to routine visits for physical examination or vaccination, SAEs that were not related to common diseases.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 7 (from Day 0 up to 30 days after the last vaccination dose at Month 6)

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV negative subjects.

End point values	HIV-/Cervarix Group	HIV-/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	145		
Units: Participants				
MSC(s)	7	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of HIV- subjects with potential immune-mediated disease (pIMDs)

End point title	Number of HIV- subjects with potential immune-mediated disease (pIMDs)[36]

End point description:

Potential immune-mediated diseases are 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 7 (from Day 0 up to 30 days after the last vaccination dose at Month 6)

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV negative subjects.

End point values	HIV-/Cervarix Group	HIV-/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	145		
Units: Participants				
pIMD(s)	0	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Pregnancy related outcomes were: live infant no apparent congenital anomaly, live infant congenital anomaly, elective termination (termin.) no apparent congenital anomaly, elective termination (termin.) congenital anomaly, ectopic pregnancy, spontaneous abortion no apparent congenital (congen.) anomaly, stillbirth no apparent congenital anomaly, stillbirth congenital anomaly, lost to follow-up, pregnancy ongoing, missing.

End point type	Secondary

End point timeframe:

During the entire study period (from Day 0 up to Month 24)

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	8	3	7
Units: Participants				
Live infant NO apparent congenital anomaly	8	7	3	7
Live infant congenital anomaly	0	0	0	0
Elective termin. NO apparent congenital anomaly	1	0	0	0
Elective termin. congenital anomaly	0	0	0	0
Ectopic pregnancy	0	0	0	0
Spontaneous abortion NO apparent congen. anomaly	1	1	0	0
Stillbirth NO apparent congenital anomaly	0	0	0	0
Stillbirth congenital anomaly	0	0	0	0
Lost to follow-up	0	0	0	0
Pregnancy ongoing	0	0	0	0
Missing	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with relevant abnormalities in alanine aminotransferase, basophils, creatinine and eosinophils parameters

End point title	Number of subjects with relevant abnormalities in alanine aminotransferase, basophils, creatinine and eosinophils parameters

End point description:

Among assessed haematological and biochemical parameters were: alanine aminotransferase [ALAT], basophils [BSPH], creatinine [CRT], eosinophils [ESPH]. Unknown = value unknown for the specified visit and laboratory parameter; Below = value below the laboratory reference range defined for the specified visit and laboratory parameter; Within = value within the laboratory reference range defined

for the specified visit and laboratory parameter; Above = value above the laboratory reference range defined for the specified visit and laboratory parameter. Note: Month 7 data for HIV+/Cervarix and HIV+/Gardasil groups are also reported in the Primary outcome measure.

End point type	Secondary

End point timeframe:

At Day 0, Week 6, Week 10, Month 6, Month 7, Month 12, Month 18 and Month 24

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	128	144	145
Units: Participants				
ALAT, Day 0, Unknown (N=129;128;144;145)	0	0	0	0
ALAT, Week 6, Unknown (N=128;126;137;142)	0	0	0	0
ALAT, Week 10, Unknown (N=128;127;135;136)	1	0	0	0
ALAT, Month 6, Unknown (N=123;123;128;134)	0	0	0	0
ALAT, Month 7, Unknown (N=121;121;115;125)	0	0	0	0
ALAT, Month 12, Unknown (N=122;119;108;118)	0	0	0	1
ALAT, Month 18, Unknown (N=121;117;110;117)	0	0	0	0
ALAT, Month 24, Unknown (N=116;117;103;111)	0	0	0	0
ALAT, Day 0, Below (N=129;128;144;145)	9	4	33	35
ALAT, Week 6, Below (N=128;126;137;142)	4	5	35	32
ALAT, Week 10, Below (N=128;127;135;136)	2	8	27	26
ALAT, Month 6, Below (N=123;123;128;134)	3	4	25	27
ALAT, Month 7, Below (N=121;121;115;125)	4	3	20	23
ALAT, Month 12, Below (N=122;119;108;118)	6	1	20	22
ALAT, Month 18, Below (N=121;117;110;117)	2	2	23	17
ALAT, Month 24, Below (N=116;117;103;111)	0	1	14	14
ALAT, Day 0, Within (N=129;128;144;145)	109	118	109	106
ALAT, Week 6, Within (N=128;126;137;142)	119	115	97	106
ALAT, Week 10, Within (N=128;127;135;136)	117	110	104	109
ALAT, Month 6, Within (N=123;123;128;134)	112	110	101	102
ALAT, Month 7, Within (N=121;121;115;125)	110	105	94	98
ALAT, Month 12, Within (N=122;119;108;118)	104	112	86	95

ALAT, Month 18, Within (N=121;117;110;117)	115	109	85	98
ALAT, Month 24, Within (N=116;117;103;111)	112	110	87	95
ALAT, Day 0, Above (N=129;128;144;145)	11	6	2	4
ALAT, Week 6, Above (N=128;126;137;142)	5	6	5	4
ALAT, Week 10, Above (N=128;127;135;136)	8	9	4	1
ALAT, Month 6, Above (N=123;123;128;134)	8	9	2	5
ALAT, Month 7, Above (N=121;121;115;125)	7	13	1	4
ALAT, Month 12, Above (N=122;119;108;118)	12	6	2	0
ALAT, Month 18, Above (N=121;117;110;117)	4	6	2	2
ALAT, Month 24, Above (N=116;117;103;111)	4	6	2	2
BSPH, Day 0, Unknown (N=129;128;144;145)	0	0	0	0
BSPH, Week 6, Unknown (N=128;126;137;142)	0	0	2	3
BSPH, Week 10, Unknown (N=128;127;135;136)	0	0	0	0
BSPH, Month 6, Unknown (N=123;123;128;134)	0	0	0	0
BSPH, Month 7, Unknown (N=121;121;115;125)	0	0	0	0
BSPH, Month 12, Unknown (N=122;119;108;118)	1	0	0	0
BSPH, Month 18, Unknown (N=121;117;110;117)	0	0	0	0
BSPH, Month 24, Unknown (N=116;117;103;111)	1	0	0	0
BSPH, Day 0, Below (N=129;128;144;145)	0	1	21	20
BSPH, Week 6, Below (N=128;126;137;142)	0	1	8	7
BSPH, Week 10, Below (N=128;127;135;136)	0	0	15	17
BSPH, Month 6, Below (N=123;123;128;134)	0	0	12	13
BSPH, Month 7, Below (N=121;121;115;125)	0	0	6	8
BSPH, Month 12, Below (N=122;119;108;118)	0	0	6	7
BSPH, Month 18, Below (N=121;117;110;117)	0	0	10	12
BSPH, Month 24, Below (N=116;117;103;111)	0	0	7	8
BSPH, Day 0, Within (N=129;128;144;145)	129	127	123	125
BSPH, Week 6, Within (N=128;126;137;142)	128	125	127	131
BSPH, Week 10, Within (N=128;127;135;136)	127	124	119	119
BSPH, Month 6, Within (N=123;123;128;134)	123	122	116	120
BSPH, Month 7, Within (N=121;121;115;125)	120	121	109	116

BSPH, Month 12, Within (N=122;119;108;118)	121	119	102	111
BSPH, Month 18, Within (N=121;117;110;117)	120	117	99	104
BSPH, Month 24, Within (N=116;117;103;111)	115	117	96	102
BSPH, Day 0, Above (N=129;128;144;145)	0	0	0	0
BSPH, Week 6, Above (N=128;126;137;142)	0	0	0	1
BSPH, Week 10, Above (N=128;127;135;136)	1	3	1	0
BSPH, Month 6, Above (N=123;123;128;134)	0	1	0	1
BSPH, Month 7, Above (N=121;121;115;125)	1	0	0	1
BSPH, Month 12, Above (N=122;119;108;118)	0	0	0	0
BSPH, Month 18, Above (N=121;117;110;117)	1	0	1	1
BSPH, Month 24, Above (N=116;117;103;111)	0	0	0	1
CRT, Day 0, Unknown (N=129;127;144;145)	0	0	0	0
CRT, Week 6, Unknown (N=128;125;137;142)	0	0	0	0
CRT, Week 10, Unknown (N=128;126;135;136)	0	0	0	0
CRT, Month 6, Unknown (N=123;122;128;134)	0	0	0	0
CRT, Month 7, Unknown (N=121;120;115;125)	0	0	0	0
CRT, Month 12, Unknown (N=122;118;108;118)	0	0	0	0
CRT, Month 18, Unknown (N=121;116;110;117)	0	0	0	0
CRT, Month 24, Unknown (N=116;116;103;111)	0	0	0	0
CRT, Day 0, Below (N=129;127;144;145)	31	26	27	21
CRT, Week 6, Below (N=128;125;137;142)	35	28	36	28
CRT, Week 10, Below (N=128;126;135;136)	33	30	27	29
CRT, Month 6, Below (N=123;122;128;134)	33	32	25	26
CRT, Month 7, Below (N=121;120;115;125)	29	36	22	17
CRT, Month 12, Below (N=122;118;108;118)	25	23	24	22
CRT, Month 18, Below (N=121;116;110;117)	25	17	11	12
CRT, Month 24, Below (N=116;116;103;111)	27	30	17	17
CRT, Day 0, Within (N=129;127;144;145)	97	100	115	123
CRT, Week 6, Within (N=128;125;137;142)	93	97	101	113
CRT, Week 10, Within (N=128;126;135;136)	95	96	108	107
CRT, Month 6, Within (N=123;122;128;134)	89	89	103	107

CRT, Month 7, Within (N=121;120;115;125)	91	84	93	107
CRT, Month 12, Within (N=122;118;108;118)	94	91	83	95
CRT, Month 18, Within (N=121;116;110;117)	93	98	98	102
CRT, Month 24, Within (N=116;116;103;111)	88	85	86	93
CRT, Day 0, Above (N=129;127;144;145)	1	1	2	1
CRT, Week 6, Above (N=128;125;137;142)	0	0	0	1
CRT, Week 10, Above (N=128;126;135;136)	0	0	0	0
CRT, Month 6, Above (N=123;122;128;134)	1	1	0	1
CRT, Month 7, Above (N=121;120;115;125)	1	0	0	1
CRT, Month 12, Above (N=122;118;108;118)	3	4	1	1
CRT, Month 18, Above (N=121;116;110;117)	3	1	1	3
CRT, Month 24, Above (N=116;116;103;111)	1	1	0	1
ESPH, Day 0, Unknown (N=129;128;144;145)	0	0	0	0
ESPH, Week 6, Unknown (N=128;126;137;142)	0	0	2	3
ESPH, Week 10, Unknown (N=128;127;135;136)	0	0	0	0
ESPH, Month 6, Unknown (N=123;123;128;134)	0	0	0	0
ESPH, Month 7, Unknown (N=121;121;115;125)	0	0	0	0
ESPH, Month 12, Unknown (N=122;119;108;118)	1	0	0	0
ESPH, Month 18, Unknown (N=121;117;110;117)	0	0	0	0
ESPH, Month 24, Unknown (N=116;117;103;111)	1	0	0	0
ESPH, Day 0, Below (N=129;128;144;145)	15	18	3	4
ESPH, Week 6, Below (N=128;126;137;142)	10	13	7	6
ESPH, Week 10, Below (N=128;127;135;136)	11	12	3	1
ESPH, Month 6, Below (N=123;123;128;134)	9	13	4	4
ESPH, Month 7, Below (N=121;121;115;125)	9	10	6	6
ESPH, Month 12, Below (N=122;119;108;118)	9	10	3	6
ESPH, Month 18, Below (N=121;117;110;117)	4	9	6	4
ESPH, Month 24, Below (N=116;117;103;111)	7	15	3	6
ESPH, Day 0, Within (N=129;128;144;145)	108	102	130	133
ESPH, Week 6, Within (N=128;126;137;142)	109	102	115	126
ESPH, Week 10, Within (N=128;127;135;136)	112	108	125	130

ESPH, Month 6, Within (N=123;123;128;134)	103	108	118	124
ESPH, Month 7, Within (N=121;121;115;125)	108	106	103	112
ESPH, Month 12, Within (N=122;119;108;118)	105	104	98	107
ESPH, Month 18, Within (N=121;117;110;117)	111	106	96	105
ESPH, Month 24, Within (N=116;117;103;111)	103	99	99	99
ESPH, Day 0, Above (N=129;128;144;145)	6	8	11	8
ESPH, Week 6, Above (N=128;126;137;142)	9	11	13	7
ESPH, Week 10, Above (N=128;127;135;136)	5	7	7	5
ESPH, Month 6, Above (N=123;123;128;134)	11	2	6	6
ESPH, Month 7, Above (N=121;121;115;125)	4	5	6	7
ESPH, Month 12, Above (N=122;119;108;118)	7	5	7	5
ESPH, Month 18, Above (N=121;117;110;117)	6	2	8	8
ESPH, Month 24, Above (N=116;117;103;111)	5	3	1	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with relevant abnormalities in haematocrit, haemoglobin, lymphocytes and monocytes parameters

End point title	Number of subjects with relevant abnormalities in haematocrit, haemoglobin, lymphocytes and monocytes parameters

End point description:

Among assessed haematological parameters were: haematocrit [HTCR], haemoglobin [HGB], lymphocytes [LYMP] and monocytes [MONO]. Unknown = value unknown for the specified visit and laboratory parameter; Below = value below the laboratory reference range defined for the specified visit and laboratory parameter; Within = value within the laboratory reference range defined for the specified visit and laboratory parameter; Above = value above the laboratory reference range defined for the specified visit and laboratory parameter. Note: Month 7 data for HIV+/Cervarix and HIV+/Gardasil groups are also reported in the Primary outcome measure.

End point type	Secondary

End point timeframe:

At Day 0, Week 6, Week 10, Month 6, Month 7, Month 12, Month 18 and Month 24

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	128	144	145
Units: Participants				
HTCR, Day 0, Unknown (N=129;128;144;145)	0	0	0	0
HTCR, Week 6, Unknown (N=128;126;137;142)	0	1	0	0
HTCR, Week 10, Unknown (N=128;127;135;136)	0	0	0	0
HTCR, Month 6, Unknown (N=123;123;128;134)	0	0	0	0
HTCR, Month 7, Unknown (N=121;121;115;125)	0	0	0	1
HTCR, Month 12, Unknown (N=122;119;108;118)	1	0	0	0
HTCR, Month 18, Unknown (N=121;117;110;117)	0	0	0	0
HTCR, Month 24, Unknown (N=116;117;103;111)	1	0	0	0
HTCR, Day 0, Below (N=129;128;144;145)	32	23	24	24
HTCR, Week 6, Below (N=128;126;137;142)	22	17	18	13
HTCR, Week 10, Below (N=128;127;135;136)	30	22	11	7
HTCR, Month 6, Below (N=123;123;128;134)	26	27	13	17
HTCR, Month 7, Below (N=121;121;115;125)	19	27	13	14
HTCR, Month 12, Below (N=122;119;108;118)	24	25	15	17
HTCR, Month 18, Below (N=121;117;110;117)	30	22	17	16
HTCR, Month 24, Below (N=116;117;103;111)	24	24	21	17
HTCR, Day 0, Within (N=129;128;144;145)	96	102	120	118
HTCR, Week 6, Within (N=128;126;137;142)	106	105	119	125
HTCR, Week 10, Within (N=128;127;135;136)	97	103	123	126
HTCR, Month 6, Within (N=123;123;128;134)	97	95	115	117
HTCR, Month 7, Within (N=121;121;115;125)	101	92	102	108
HTCR, Month 12, Within (N=122;119;108;118)	95	94	93	100
HTCR, Month 18, Within (N=121;117;110;117)	91	92	90	101
HTCR, Month 24, Within (N=116;117;103;111)	91	92	82	93
HTCR, Day 0, Above (N=129;128;144;145)	1	3	0	3
HTCR, Week 6, Above (N=128;126;137;142)	0	3	0	4
HTCR, Week 10, Above (N=128;127;135;136)	1	2	1	3
HTCR, Month 6, Above (N=123;123;128;134)	0	1	0	0

HTCR, Month 7, Above (N=121;121;115;125)	1	2	0	2
HTCR, Month 12, Above (N=122;119;108;118)	2	0	0	1
HTCR, Month 18, Above (N=121;117;110;117)	0	3	3	0
HTCR, Month 24, Above (N=116;117;103;111)	0	1	0	1
HGB, Day 0, Unknown (N=129;128;144;145)	0	0	0	0
HGB, Week 6, Unknown (N=128;126;137;142)	0	0	0	0
HGB, Week 10, Unknown (N=128;127;135;136)	0	0	0	0
HGB, Month 6, Unknown (N=123;123;128;134)	0	0	0	0
HGB, Month 7, Unknown (N=121;121;115;125)	0	0	0	0
HGB, Month 12, Unknown (N=122;119;108;118)	1	0	0	0
HGB, Month 18, Unknown (N=121;117;110;117)	0	0	0	0
HGB, Month 24, Unknown (N=116;117;103;111)	1	0	0	0
HGB, Day 0, Below (N=129;128;144;145)	38	37	40	45
HGB, Week 6, Below (N=128;126;137;142)	38	35	40	50
HGB, Week 10, Below (N=128;127;135;136)	38	35	37	38
HGB, Month 6, Below (N=123;123;128;134)	38	36	45	38
HGB, Month 7, Below (N=121;121;115;125)	28	37	36	38
HGB, Month 12, Below (N=122;119;108;118)	29	35	39	39
HGB, Month 18, Below (N=121;117;110;117)	34	32	32	35
HGB, Month 24, Below (N=116;117;103;111)	27	27	28	26
HGB, Day 0, Within (N=129;128;144;145)	88	89	104	98
HGB, Week 6, Within (N=128;126;137;142)	88	88	97	88
HGB, Week 10, Within (N=128;127;135;136)	89	90	98	97
HGB, Month 6, Within (N=123;123;128;134)	85	86	83	96
HGB, Month 7, Within (N=121;121;115;125)	92	83	79	86
HGB, Month 12, Within (N=122;119;108;118)	91	83	69	79
HGB, Month 18, Within (N=121;117;110;117)	84	82	77	82
HGB, Month 24, Within (N=116;117;103;111)	88	89	75	84
HGB, Day 0, Above (N=129;128;144;145)	3	2	0	2
HGB, Week 6, Above (N=128;126;137;142)	2	3	0	4
HGB, Week 10, Above (N=128;127;135;136)	1	2	0	1

HGB, Month 6, Above (N=123;123;128;134)	0	1	0	0
HGB, Month 7, Above (N=121;121;115;125)	1	1	0	1
HGB, Month 12, Above (N=122;119;108;118)	1	1	0	0
HGB, Month 18, Above (N=121;117;110;117)	3	3	1	0
HGB, Month 24, Above (N=116;117;103;111)	0	1	0	1
LYMP, Day 0, Unknown (N=129;128;144;145)	0	0	0	0
LYMP, Week 6, Unknown (N=128;126;137;142)	0	0	2	3
LYMP, Week 10, Unknown (N=128;127;135;136)	0	0	0	0
LYMP, Month 6, Unknown (N=123;123;128;134)	0	0	0	0
LYMP, Month 7, Unknown (N=121;121;115;125)	0	0	0	0
LYMP, Month 12, Unknown (N=122;119;108;118)	1	0	0	0
LYMP, Month 18, Unknown (N=121;117;110;117)	0	0	0	0
LYMP, Month 24, Unknown (N=116;117;103;111)	1	0	0	0
LYMP, Day 0, Below (N=129;128;144;145)	7	9	11	6
LYMP, Week 6, Below (N=128;126;137;142)	6	11	12	6
LYMP, Week 10, Below (N=128;127;135;136)	11	9	13	6
LYMP, Month 6, Below (N=123;123;128;134)	6	8	9	11
LYMP, Month 7, Below (N=121;121;115;125)	12	11	6	6
LYMP, Month 12, Below (N=122;119;108;118)	6	10	6	8
LYMP, Month 18, Below (N=121;117;110;117)	4	4	6	4
LYMP, Month 24, Below (N=116;117;103;111)	8	9	6	7
LYMP, Day 0, Within (N=129;128;144;145)	105	105	120	132
LYMP, Week 6, Within (N=128;126;137;142)	109	109	113	121
LYMP, Week 10, Within (N=128;127;135;136)	101	102	110	124
LYMP, Month 6, Within (N=123;123;128;134)	98	104	106	115
LYMP, Month 7, Within (N=121;121;115;125)	96	97	103	111
LYMP, Month 12, Within (N=122;119;108;118)	104	95	92	98
LYMP, Month 18, Within (N=121;117;110;117)	105	103	94	106
LYMP, Month 24, Within (N=116;117;103;111)	98	97	88	101
LYMP, Day 0, Above (N=129;128;144;145)	17	14	13	7
LYMP, Week 6, Above (N=128;126;137;142)	13	6	10	12

LYMP, Week 10, Above (N=128;127;135;136)	16	16	12	6
LYMP, Month 6, Above (N=123;123;128;134)	19	11	13	8
LYMP, Month 7, Above (N=121;121;115;125)	13	13	6	8
LYMP, Month 12, Above (N=122;119;108;118)	11	14	10	12
LYMP, Month 18, Above (N=121;117;110;117)	12	10	10	7
LYMP, Month 24, Above (N=116;117;103;111)	9	11	9	3
MONO, Day 0, Unknown (N=129;128;144;145)	0	0	0	0
MONO, Week 6, Unknown (N=128;126;137;142)	0	0	2	3
MONO, Week 10, Unknown (N=128;127;135;136)	0	0	0	0
MONO, Month 6, Unknown (N=123;123;128;134)	0	0	0	0
MONO, Month 7, Unknown (N=121;121;115;125)	0	0	0	0
MONO, Month 12, Unknown (N=122;119;108;118)	1	0	0	0
MONO, Month 18, Unknown (N=121;117;110;117)	0	0	0	0
MONO, Month 24, Unknown (N=116;117;103;111)	1	0	0	0
MONO, Day 0, Below (N=129;128;144;145)	7	4	10	17
MONO, Week 6, Below (N=128;126;137;142)	4	4	3	4
MONO, Week 10, Below (N=128;127;135;136)	4	4	2	6
MONO, Month 6, Below (N=123;123;128;134)	3	5	0	7
MONO, Month 7, Below (N=121;121;115;125)	4	7	5	2
MONO, Month 12, Below (N=122;119;108;118)	2	5	5	2
MONO, Month 18, Below (N=121;117;110;117)	3	6	5	4
MONO, Month 24, Below (N=116;117;103;111)	5	5	7	10
MONO, Day 0, Within (N=129;128;144;145)	111	117	133	126
MONO, Week 6, Within (N=128;126;137;142)	117	112	129	133
MONO, Week 10, Within (N=128;127;135;136)	116	108	129	127
MONO, Month 6, Within (N=123;123;128;134)	107	104	113	121
MONO, Month 7, Within (N=121;121;115;125)	106	97	107	118
MONO, Month 12, Within (N=122;119;108;118)	104	101	101	113
MONO, Month 18, Within (N=121;117;110;117)	108	99	101	109
MONO, Month 24, Within (N=116;117;103;111)	98	99	95	99
MONO, Day 0, Above (N=129;128;144;145)	11	7	1	2

MONO, Week 6, Above (N=128;126;137;142)	7	10	3	2
MONO, Week 10, Above (N=128;127;135;136)	8	15	4	3
MONO, Month 6, Above (N=123;123;128;134)	13	14	6	6
MONO, Month 7, Above (N=121;121;115;125)	11	17	3	5
MONO, Month 12, Above (N=122;119;108;118)	15	13	2	3
MONO, Month 18, Above (N=121;117;110;117)	10	12	4	4
MONO, Month 24, Above (N=116;117;103;111)	12	13	1	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with relevant abnormalities in neutrophils, platelets, red blood cells and white blood cells parameters

End point title	Number of subjects with relevant abnormalities in neutrophils, platelets, red blood cells and white blood cells parameters

End point description:

Among assessed haematological parameters were: neutrophils [NTPH], platelets [PLAT], red blood cells [RBC] and white blood cells [WBC]. Unknown = value unknown for the specified visit and laboratory parameter; Below = value below the laboratory reference range defined for the specified visit and laboratory parameter; Within = value within the laboratory reference range defined for the specified visit and laboratory parameter; Above = value above the laboratory reference range defined for the specified visit and laboratory parameter. Note: Month 7 data for HIV+/Cervarix and HIV+/Gardasil groups are also reported in the Primary outcome measure.

End point type	Secondary

End point timeframe:

At Day 0, Week 6, Week 10, Month 6, Month 7, Month 12, Month 18 and Month 24

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	128	144	145
Units: Participants				
NTPH, Day 0, Unknown (N=129;128;144;145)	0	0	0	0
NTPH, Week 6, Unknown (N=128;126;137;142)	0	0	2	3
NTPH, Week 10, Unknown (N=128;127;135;136)	0	0	0	0
NTPH, Month 6, Unknown (N=123;123;128;134)	0	0	0	0
NTPH, Month 7, Unknown (N=121;121;115;125)	0	0	0	0
NTPH, Month 12, Unknown (N=122;119;108;118)	1	0	0	0

NTPH, Month 18, Unknown (N=121;117;110;117)	0	0	0	0
NTPH, Month 24, Unknown (N=116;117;103;111)	1	0	0	0
NTPH, Day 0, Below (N=129;128;144;145)	14	12	11	7
NTPH, Week 6, Below (N=128;126;137;142)	16	13	8	13
NTPH, Week 10, Below (N=128;127;135;136)	18	17	12	10
NTPH, Month 6, Below (N=123;123;128;134)	18	14	15	14
NTPH, Month 7, Below (N=121;121;115;125)	16	17	10	9
NTPH, Month 12, Below (N=122;119;108;118)	19	16	12	11
NTPH, Month 18, Below (N=121;117;110;117)	15	15	9	14
NTPH, Month 24, Below (N=116;117;103;111)	14	11	9	10
NTPH, Day 0, Within (N=129;128;144;145)	106	99	117	122
NTPH, Week 6, Within (N=128;126;137;142)	101	95	107	116
NTPH, Week 10, Within (N=128;127;135;136)	103	100	104	113
NTPH, Month 6, Within (N=123;123;128;134)	100	98	98	104
NTPH, Month 7, Within (N=121;121;115;125)	97	93	92	106
NTPH, Month 12, Within (N=122;119;108;118)	92	93	84	94
NTPH, Month 18, Within (N=121;117;110;117)	98	89	86	92
NTPH, Month 24, Within (N=116;117;103;111)	92	95	83	89
NTPH, Day 0, Above (N=129;128;144;145)	9	17	16	16
NTPH, Week 6, Above (N=128;126;137;142)	11	18	20	10
NTPH, Week 10, Above (N=128;127;135;136)	7	10	19	13
NTPH, Month 6, Above (N=123;123;128;134)	5	11	15	16
NTPH, Month 7, Above (N=121;121;115;125)	8	11	13	10
NTPH, Month 12, Above (N=122;119;108;118)	10	10	12	13
NTPH, Month 18, Above (N=121;117;110;117)	8	13	15	11
NTPH, Month 24, Above (N=116;117;103;111)	9	11	11	12
PLAT, Day 0, Unknown (N=129;128;144;145)	0	0	0	0
PLAT, Week 6, Unknown (N=128;126;137;142)	0	0	1	1
PLAT, Week 10, Unknown (N=128;127;135;136)	0	0	1	0
PLAT, Month 6, Unknown (N=123;123;128;134)	0	0	0	0
PLAT, Month 7, Unknown (N=121;121;115;125)	0	0	1	0

PLAT, Month 12, Unknown (N=122;119;108;118)	1	0	1	0
PLAT, Month 18, Unknown (N=121;117;110;117)	0	0	0	0
PLAT, Month 24, Unknown (N=116;117;103;111)	1	0	0	0
PLAT, Day 0, Below (N=129;128;144;145)	0	0	3	0
PLAT, Week 6, Below (N=128;126;137;142)	1	0	1	0
PLAT, Week 10, Below (N=128;127;135;136)	1	1	0	0
PLAT, Month 6, Below (N=123;123;128;134)	2	2	0	0
PLAT, Month 7, Below (N=121;121;115;125)	1	3	1	1
PLAT, Month 12, Below (N=122;119;108;118)	3	1	0	2
PLAT, Month 18, Below (N=121;117;110;117)	3	4	1	2
PLAT, Month 24, Below (N=116;117;103;111)	1	2	2	3
PLAT, Day 0, Within (N=129;128;144;145)	123	122	133	138
PLAT, Week 6, Within (N=128;126;137;142)	124	119	130	137
PLAT, Week 10, Within (N=128;127;135;136)	122	124	131	132
PLAT, Month 6, Within (N=123;123;128;134)	116	118	127	131
PLAT, Month 7, Within (N=121;121;115;125)	118	114	110	121
PLAT, Month 12, Within (N=122;119;108;118)	113	114	103	111
PLAT, Month 18, Within (N=121;117;110;117)	117	110	106	111
PLAT, Month 24, Within (N=116;117;103;111)	109	110	97	103
PLAT, Day 0, Above (N=129;128;144;145)	6	6	8	7
PLAT, Week 6, Above (N=128;126;137;142)	3	7	5	4
PLAT, Week 10, Above (N=128;127;135;136)	5	2	3	4
PLAT, Month 6, Above (N=123;123;128;134)	5	3	1	3
PLAT, Month 7, Above (N=121;121;115;125)	2	4	3	3
PLAT, Month 12, Above (N=122;119;108;118)	5	4	4	5
PLAT, Month 18, Above (N=121;117;110;117)	1	3	3	4
PLAT, Month 24, Above (N=116;117;103;111)	5	5	4	5
RBC, Day 0, Unknown (N=129;128;141;141)	0	0	0	0
RBC, Week 6, Unknown (N=128;126;136;139)	0	0	0	1
RBC, Week 10, Unknown (N=128;127;134;135)	0	0	0	0
RBC, Month 6, Unknown (N=123;123;127;134)	0	0	0	1

RBC, Month 7, Unknown (N=121;121;115;125)	0	0	0	0
RBC, Month 12, Unknown (N=122;119;108;118)	1	0	0	1
RBC, Month 18, Unknown (N=121;117;110;116)	0	0	2	3
RBC, Month 24, Unknown (N=116;117;103;111)	1	0	0	0
RBC, Day 0, Below (N=129;128;141;141)	43	38	18	13
RBC, Week 6, Below (N=128;126;136;139)	44	36	14	12
RBC, Week 10, Below (N=128;127;134;135)	48	37	11	8
RBC, Month 6, Below (N=123;123;127;134)	40	39	14	12
RBC, Month 7, Below (N=121;121;115;125)	36	34	15	19
RBC, Month 12, Below (N=122;119;108;118)	39	31	19	14
RBC, Month 18, Below (N=121;117;110;116)	38	31	9	13
RBC, Month 24, Below (N=116;117;103;111)	38	34	10	9
RBC, Day 0, Within (N=129;128;141;141)	83	87	118	123
RBC, Week 6, Within (N=128;126;136;139)	81	85	118	120
RBC, Week 10, Within (N=128;127;134;135)	78	87	120	122
RBC, Month 6, Within (N=123;123;127;134)	79	81	111	117
RBC, Month 7, Within (N=121;121;115;125)	82	84	100	100
RBC, Month 12, Within (N=122;119;108;118)	79	86	88	100
RBC, Month 18, Within (N=121;117;110;116)	81	80	97	96
RBC, Month 24, Within (N=116;117;103;111)	74	83	91	98
RBC, Day 0, Above (N=129;128;141;141)	3	3	5	5
RBC, Week 6, Above (N=128;126;136;139)	3	5	4	6
RBC, Week 10, Above (N=128;127;134;135)	2	3	3	5
RBC, Month 6, Above (N=123;123;127;134)	4	3	2	4
RBC, Month 7, Above (N=121;121;115;125)	3	3	0	6
RBC, Month 12, Above (N=122;119;108;118)	3	2	1	3
RBC, Month 18, Above (N=121;117;110;116)	2	6	2	4
RBC, Month 24, Above (N=116;117;103;111)	3	0	2	4
WBC, Day 0, Unknown (N=129;128;143;145)	0	0	0	0
WBC, Week 6, Unknown (N=128;126;136;142)	0	0	0	0
WBC, Week 10, Unknown (N=128;127;134;136)	0	0	0	0

WBC, Month 6, Unknown (N=123;123;127;134)	0	0	0	0
WBC, Month 7, Unknown (N=121;121;114;125)	0	0	0	0
WBC, Month 12, Unknown (N=122;119;107;118)	1	0	0	0
WBC, Month 18, Unknown (N=121;117;109;117)	0	0	0	0
WBC, Month 24, Unknown (N=116;117;102;111)	1	0	0	0
WBC, Day 0, Below (N=129;128;143;145)	8	7	5	2
WBC, Week 6, Below (N=128;126;136;142)	9	11	5	4
WBC, Week 10, Below (N=128;127;134;136)	9	9	2	3
WBC, Month 6, Below (N=123;123;127;134)	12	6	2	2
WBC, Month 7, Below (N=121;121;114;125)	10	9	5	1
WBC, Month 12, Below (N=122;119;107;118)	14	13	3	2
WBC, Month 18, Below (N=121;117;109;117)	12	10	4	5
WBC, Month 24, Below (N=116;117;102;111)	11	5	3	4
WBC, Day 0, Within (N=129;128;143;145)	118	116	135	140
WBC, Week 6, Within (N=128;126;136;142)	118	111	124	135
WBC, Week 10, Within (N=128;127;134;136)	116	113	131	129
WBC, Month 6, Within (N=123;123;127;134)	106	116	122	128
WBC, Month 7, Within (N=121;121;114;125)	106	108	106	120
WBC, Month 12, Within (N=122;119;107;118)	103	103	100	115
WBC, Month 18, Within (N=121;117;109;117)	106	107	100	107
WBC, Month 24, Within (N=116;117;102;111)	102	107	94	101
WBC, Day 0, Above (N=129;128;143;145)	3	5	3	3
WBC, Week 6, Above (N=128;126;136;142)	1	4	7	3
WBC, Week 10, Above (N=128;127;134;136)	3	5	1	4
WBC, Month 6, Above (N=123;123;127;134)	5	1	3	4
WBC, Month 7, Above (N=121;121;114;125)	5	4	3	4
WBC, Month 12, Above (N=122;119;107;118)	4	3	4	1
WBC, Month 18, Above (N=121;117;109;117)	3	0	5	5
WBC, Month 24, Above (N=116;117;102;111)	2	5	5	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAEs

End point title	Number of subjects with SAEs

End point description:

SAEs assessed include any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or represented a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

During the entire study period (from Day 0 up to Month 24)

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	128	144	145
Units: Participants				
SAE(s)	9	9	4	1

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:

Medically significant conditions (MSCs) are defined as AEs prompting emergency room or physician visits that were not related to common diseases, or not related to routine visits for physical examination or vaccination, SAEs that were not related to common diseases.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 18 (from Day 0 up to 12 months after the last vaccination dose at Month 6)

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	128	144	145
Units: Participants				
MSC(s)	25	37	10	17

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Potential immune-mediated diseases are 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 18 (from Day 0 up to 12 months after the last vaccination dose at Month 6)

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	128	144	145
Units: Participants				
pIMD(s)	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cluster of differentiation 4 (CD4+) cell count in HIV+ subjects at Months 12, 18 and 24

End point title	Cluster of differentiation 4 (CD4+) cell count in HIV+ subjects at Months 12, 18 and 24[37]

End point description:

CD4+ cell count, expressed in cells/cubic millimeter (mm3), was assessed for HIV+ subjects.

End point type	Secondary

End point timeframe:

At Months 12, 18 and 24

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	119		
Units: cells/mm3				
median (inter-quartile range (Q1-Q3))				
CD4+ cell counts, Month 12 (N=122;119)	584.5 (498.0 to 832.0)	602.0 (445.0 to 835.0)		

CD4+ cell counts, Month 18 (N=121;117)	621.0 (472.0 to 789.0)	572.0 (443.0 to 770.0)		
CD4+ cell counts, Month 24 (N=115;117)	568.0 (447.0 to 738.0)	598.0 (441.0 to 834.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: HIV viral load (VL) in HIV+ subjects at Months 12, 18 and 24

End point title	HIV viral load (VL) in HIV+ subjects at Months 12, 18 and

End point description:

HIV VL, expressed in HIV copies/milliliter (mL), was assessed for HIV+ subjects.

End point type	Secondary

End point timeframe:

At Months 12, 18 and 24

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	96		
Units: HIV copies/mL				
median (inter-quartile range (Q1-Q3))				
HIV viral load, Month 12 (N=94;96)	1.6 (1.3 to 3.2)	2.3 (1.3 to 3.7)		
HIV viral load, Month 18 (N=94;91)	1.7 (1.3 to 3.2)	2.2 (1.3 to 3.8)		
HIV viral load, Month 24 (N=93;87)	1.6 (1.3 to 2.8)	2.1 (1.3 to 3.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of HIV+ subjects by WHO HIV clinical staging

End point title	Number of HIV+ subjects by WHO HIV clinical staging[39]

End point description:

HIV+ subjects were categorised into clinical stages 1 through 4, as per the WHO classification [WHO, 2009].

End point type	Secondary

End point timeframe:

At Months 12, 18 and 24

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV positive subjects.

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	128		
Units: Participants				
Clinical stage 1, Month 12	113	112		
Clinical stage 2, Month 12	7	1		
Clinical stage 3, Month 12	1	2		
Clinical stage 4, Month 12	2	4		
Clinical stage 1, Month 18	112	110		
Clinical stage 2, Month 18	7	1		
Clinical stage 3, Month 18	1	2		
Clinical stage 4, Month 18	2	4		
Clinical stage 1, Month 24	107	110		
Clinical stage 2, Month 24	7	1		
Clinical stage 3, Month 24	1	2		
Clinical stage 4, Month 24	2	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Pseudovirion-Based Neutralization Assay (PBNA) Titers of anti-HPV-16/18 antibodies in HIV- subjects, based on TVC

End point title	Pseudovirion-Based Neutralization Assay (PBNA) Titers of anti-HPV-16/18 antibodies in HIV- subjects, based on TVC[40]

End point description:

Titers of anti-HPV-16/18 antibodies, expressed as Geometric Mean Titers (GMTs), with cut-offs greater than or equal to (≥) 40 estimated dose giving 50% signal reduction when compared to a control without serum (ED50), as assessed by the Pseudovirion-Based Neutralization Assay [PBNA], for HIV- subjects. Between-group comparisons to assess superiority were performed on the TVC (by PBNA, regardless of HPV serostatus at baseline).

End point type	Secondary

End point timeframe:

At Month 7 (30 days after the last vaccination dose at Month 6)

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for HIV negative subjects.

End point values	HIV-/Cervarix Group	HIV-/Gardasil Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	112		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (N=105;112)	60550.6 (44040.1 to 83250.9)	19634.8 (14410.8 to 26752.4)		
Anti-HPV-18 (N=105;111)	32118.1 (23195.8 to 44472.3)	5773.4 (4205.2 to 7926.4)		

Statistical analyses

Statistical analysis title	Anti-HPV-18 Adjusted GMT ratio - superiority

Statistical analysis description:

Adjusted GMT ratio for anti-HPV-18 neutra antibody (ED50): To demonstrate that the immunogenicity of Cervarix vaccine (HIV-/Cervarix Group) was superior to that of Gardasil vaccine (HIV-/Gardasil Group), in terms of geometric mean titers (GMTs) against HPV-18, measured by Pseudovirion-based neutralization assay (PBNA) in HIV- subjects.

Comparison groups	HIV-/Gardasil Group v HIV-/Cervarix Group
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority[41]
P-value	< 0.0001 [42]
Method	ANOVA
Parameter estimate	Adjusted GMT ratio
Point estimate	5.38
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	3.2
upper limit	9.06

Notes:

[41] - Superiority was defined as the lower limit of the 97.5% CI for the ratio of GMTs (Cervarix over Gardasil) for HPV-18 type being above 1, with a statistically significant p-value.
[42] - ANOVA model on the log10 transformation of the titers for HIV- subjects and including the vaccine group as fixed effect.

Statistical analysis title	Anti-HPV-16 Adjusted GMT ratio - superiority

Statistical analysis description:

Adjusted GMT ratio for anti-HPV-16 neutra antibody (ED50): To demonstrate that the immunogenicity of Cervarix vaccine (HIV-/Cervarix Group) was superior to that of Gardasil vaccine (HIV-/Gardasil Group), in terms of geometric mean titers (GMTs) against HPV-16, measured by Pseudovirion-based neutralization assay (PBNA) in HIV- subjects.

Comparison groups	HIV-/Gardasil Group v HIV-/Cervarix Group
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	superiority[43]
P-value	< 0.0001 [44]
Method	ANOVA
Parameter estimate	Adjusted GMT ratio
Point estimate	3.05
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.84
upper limit	5.06

Notes:

[43] - Superiority was defined as the lower limit of the 97.5% CI for the ratio of GMTs (Cervarix over Gardasil) for HPV-16 type being above 1, with a statistically significant p-value.
[44] - ANOVA model on the log10 transformation of the titers for HIV- subjects and including the vaccine group as fixed effect.

Secondary: Anti-HPV-16 and Anti-HPV-18 antibody concentrations by Enzyme-linked immunosorbent assay (ELISA) in serum

End point title	Anti-HPV-16 and Anti-HPV-18 antibody concentrations by Enzyme-linked immunosorbent assay (ELISA) in serum

End point description:

Anti-HPV-16 and anti-HPV-18 antibody concentrations in serum, are presented as Geometric Mean Concentrations (GMCs), with cut-offs greater than or equal to (≥) 19 ELISA units per milliliter (EU/mL) and 18 EU/mL respectively, as assessed by Enzyme-linked immunosorbent assay (ELISA), in all (HIV+ and HIV-) subjects.

End point type	Secondary

End point timeframe:

At Day 0, Week 6, Week 10, Month 7, Month 12, Month 18 and Month 24

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81	84	77	80
Units: EU/mL				
geometric mean (confidence interval 95%)				
anti-HPV-16, Day 0 (N=81;84;77;80)	17.2 (13.3 to 22.2)	15.0 (12.0 to 18.9)	10.2 (9.4 to 11.0)	10.9 (9.5 to 12.5)
anti-HPV-16, Week 6 (N=81;84;77;80)	452.9 (302.3 to 678.5)	280.2 (182.5 to 430.1)	390.6 (298.3 to 511.6)	303.2 (228.0 to 403.3)
anti-HPV-16, Week 10 (N=81;84;77;80)	2191.2 (1775.7 to 2704.0)	1565.5 (1197.5 to 2046.6)	4512.7 (3771.5 to 5399.7)	2993.2 (2459.1 to 3643.3)
anti-HPV-16, Month 7 (N=81;84;77;80)	4896.0 (4002.2 to 5989.3)	2145.2 (1647.8 to 2792.7)	15493.0 (12537.0 to 19146.0)	5960.9 (5028.9 to 7065.7)
anti-HPV-16, Month 12 (N=81;81;73;76)	1392.3 (1077.5 to 1799.0)	608.8 (445.4 to 832.1)	4389.3 (3400.5 to 5665.7)	1772.2 (1473.3 to 2131.7)
anti-HPV-16, Month 18 (N=77;76;70;72)	861.3 (662.3 to 1119.9)	311.4 (226.3 to 428.4)	2294.1 (1785.0 to 2948.4)	798.0 (646.6 to 984.8)
anti-HPV-16, Month 24 (N=71;74;64;69)	664.6 (499.9 to 883.7)	243.5 (173.9 to 341.0)	1893.6 (1443.8 to 2483.7)	601.9 (481.8 to 752.1)
anti-HPV-18, Day 0 (N=81;84;77;80)	13.4 (11.2 to 16.0)	10.7 (9.3 to 12.3)	9.3 (8.9 to 9.8)	9.2 (8.9 to 9.5)
anti-HPV-18, Week 6 (N=81;84;77;80)	205.6 (146.3 to 288.7)	53.2 (36.4 to 77.6)	277.3 (217.5 to 353.5)	60.4 (47.5 to 76.8)
anti-HPV-18, Week 10 (N=81;84;77;80)	1432.4 (1136.9 to 1804.6)	277.2 (200.8 to 382.8)	3174.4 (2596.2 to 3881.4)	666.1 (549.8 to 806.9)
anti-HPV-18, Month 7 (N=81;84;77;80)	2540.8 (2085.9 to 3094.9)	493.8 (356.6 to 683.8)	6779.3 (5382.6 to 8538.5)	1516.5 (1232.9 to 1865.2)
anti-HPV-18, Month 12 (N=81;81;73;76)	676.9 (520.1 to 880.9)	116.2 (82.2 to 164.2)	1747.7 (1329.4 to 2297.6)	338.3 (261.2 to 438.1)

anti-HPV-18, Month 18 (N=77;76;70;72)	408.7 (310.4 to 538.2)	55.6 (39.6 to 78.0)	895.5 (679.6 to 1179.9)	160.1 (123.7 to 207.1)
anti-HPV-18, Month 24 (N=71;74;64;69)	295.2 (216.9 to 401.7)	52.4 (37.2 to 73.8)	761.9 (576.6 to 1006.7)	116.2 (88.8 to 151.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16 and anti-HPV-18 antibody concentrations by ELISA in cervicovaginal secretion (CVS)

End point title	Anti-HPV-16 and anti-HPV-18 antibody concentrations by ELISA in cervicovaginal secretion (CVS)

End point description:

Anti-HPV-16 and anti-HPV-18 antibody concentrations in CVS, are presented as Geometric Mean Concentrations (GMCs), with cut-offs greater than or equal to (≥) 0 EU/mL, as assessed by ELISA, in postmenarcheal subjects who volunteered for this procedure. Note: When only 1 subject is analyzed, the lower limit (LL) and the upper limit (UL) are entered equal to the geometric mean concentration (GMC) value as the confidence interval could not be calculated with only 1 subject analyzed.

End point type	Secondary

End point timeframe:

At Day 0, Week 6, Week 10, Month 7, Month 12, Month 18 and Month 24

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	18	3	5
Units: EU/mL				
geometric mean (confidence interval 95%)				
anti-HPV-16, Day 0 (N=12;18;3;5)	1.5 (0.8 to 2.6)	1.4 (0.7 to 2.8)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)
anti-HPV-16, Week 6 (N=7;11;3;5)	31.5 (4.7 to 211.5)	3.1 (0.8 to 11.6)	27.1 (8.7 to 84.2)	2.7 (0.4 to 16.5)
anti-HPV-16, Week 10 (N=9;11;0;1)	38.8 (6.1 to 245.0)	15.7 (5.4 to 45.2)	0 (0.0 to 0.0)	159.8 (159.8 to 159.8)
anti-HPV-16, Month 7 (N=8;14;3;3)	23.6 (3.4 to 163.0)	5.4 (1.6 to 17.6)	104.2 (40.3 to 269.4)	53.5 (3.0 to 945.1)
anti-HPV-16, Month 12 (N=9;15;2;1)	18.7 (3.2 to 109.0)	6.8 (2.1 to 22.3)	107.6 (29.1 to 398.1)	34.7 (34.7 to 34.7)
anti-HPV-16, Month 24 (N=7;10;3;1)	8.1 (1.3 to 50.3)	4.3 (1.4 to 12.9)	49.0 (4.5 to 534.2)	1.0 (1.0 to 1.0)
anti-HPV-18, Day 0 (N=12;18;3;5)	1.2 (0.8 to 1.9)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)
anti-HPV-18, Week 6 (N=7;11;3;5)	16.8 (2.5 to 113.1)	1.7 (0.5 to 5.2)	3.0 (0.0 to 312.7)	1.0 (1.0 to 1.0)
anti-HPV-18, Week 10 (N=9;11;0;1)	22.9 (3.4 to 152.2)	2.3 (0.9 to 5.8)	0 (0.0 to 0.0)	21.6 (21.6 to 21.6)
anti-HPV-18, Month 7 (N=8;14;3;3)	10.1 (1.8 to 58.2)	2.2 (1.0 to 4.8)	44.2 (14.3 to 136.9)	16.3 (1.0 to 265.0)
anti-HPV-18, Month 12 (N=9;15;2;1)	23.9 (8.0 to 72.0)	2.4 (0.9 to 6.8)	32.7 (17.2 to 62.1)	16.3 (16.3 to 16.3)
anti-HPV-18, Month 24 (N=7;10;3;1)	8.8 (1.6 to 48.5)	1.5 (0.8 to 3.0)	13.8 (1.3 to 149.2)	1.0 (1.0 to 1.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of specific B-cells for HPV-16/18 antigens

End point title	Frequency of specific B-cells for HPV-16/18 antigens

End point description:

B cell memory was assessed by Enzyme Linked Immuno Spot (ELISPOT) assay. The assay was performed in a subset of approximately 100 subjects (50 HIV+ and 50 HIV-).

End point type	Secondary

End point timeframe:

At Day 0, Week 6, Week 10, Month 7 and Month 12

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	12	20	20
Units: B-cells/million cells				
median (inter-quartile range (Q1-Q3))				
HPV-16, Day 0 (N=12;11;18;20)	1.0 (1.0 to 1.0)	1.0 (1.0 to 61.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)
HPV-18, Day 0 (N=12;11;18;20)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)
HPV-16, Week 6 (N=10;12;15;15)	91.0 (1.0 to 154.0)	1.0 (1.0 to 1.0)	22.0 (1.0 to 154.0)	1.0 (1.0 to 204.0)
HPV-18, Week 6 (N=10;12;15;15)	39.5 (1.0 to 693.0)	1.0 (1.0 to 45.5)	155.0 (1.0 to 345.0)	33.0 (1.0 to 80.0)
HPV-16, Week 10 (N=12;9;20;20)	558.0 (95.5 to 989.5)	198.0 (1.0 to 391.0)	494.0 (90.5 to 834.0)	150.5 (33.5 to 726.5)
HPV-18, Week 10 (N=12;9;20;20)	150.0 (31.0 to 471.0)	1.0 (1.0 to 42.0)	211.0 (84.0 to 656.0)	29.5 (1.0 to 222.0)
HPV-16, Month 7 (N=13;9;20;17)	624.0 (457.0 to 1196.0)	213.0 (165.0 to 632.0)	1504.0 (481.0 to 3026.0)	448.0 (257.0 to 890.0)
HPV-18, Month 7 (N=13;9;20;17)	332.0 (153.0 to 494.0)	1.0 (1.0 to 392.0)	513.5 (111.5 to 1292.0)	65.0 (1.0 to 158.0)
HPV-16, Month 12 (N=16;8;20;17)	256.5 (75.5 to 891.5)	121.0 (64.5 to 315.0)	414.5 (94.5 to 640.5)	256.0 (218.0 to 449.0)
HPV-18, Month 12 (N=16;8;20;17)	101.0 (1.0 to 525.0)	1.0 (1.0 to 159.0)	250.5 (1.0 to 481.5)	58.0 (1.0 to 101.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of cluster of differentiation 4/8 [CD4+/CD8+] T-cell response

End point title	Frequency of cluster of differentiation 4/8 [CD4+/CD8+] T-cell response

End point description:

The combinations of cytokines expressed were CD4/8-all doubles, CD4/8-d-cluster of differentiation 40 Ligand (CD40L), CD4/8-d-interferon gamma (IFNG), CD4/8-interleukin-2 (IL-2), CD4/8-d-tumour necrosis alpha (TNFA), as assessed by Intracellular cytokine staining (ICS). The assay was performed in a subset of approximately 100 subjects (50 HIV+ and 50 HIV-).

End point type	Secondary

End point timeframe:

At Day 0, Week 6, Week 10, Month 7 and Month 12

End point values	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group	HIV-/Gardasil Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	15	21	19
Units: CD4 cells/million T-cells				
median (inter-quartile range (Q1-Q3))				
CD4-All doubles,Anti-HPV-16,Day 0 (N=17;15;17;18)	41.0 (1.0 to 118.0)	101.0 (43.0 to 215.0)	1.0 (1.0 to 28.0)	54.5 (1.0 to 88.0)
CD4-All doubles,Anti-HPV-18,Day 0 (N=17;15;17;18)	7.0 (1.0 to 116.0)	87.0 (18.0 to 184.0)	1.0 (1.0 to 82.0)	1.0 (1.0 to 98.0)
CD4-All doubles,Anti-HPV-16,Week 6 (N=16;14;16;18)	445.5 (262.0 to 1028.0)	345.5 (227.0 to 1034.0)	298.0 (173.0 to 540.5)	661.0 (234.0 to 982.0)
CD4-All doubles,Anti-HPV-18,Week 6 (N=16;14;16;18)	396.0 (163.0 to 832.0)	309.5 (203.0 to 852.0)	237.0 (81.0 to 421.5)	320.5 (117.0 to 524.0)
CD4-All doubles,Anti-HPV-16,Week 10(N=14;14;19;18)	2955.5 (1075.0 to 5200.0)	1449.0 (922.0 to 1778.0)	1767.0 (916.0 to 4428.0)	1268.5 (648.0 to 2453.0)
CD4-All doubles,Anti-HPV-18,Week 10(N=14;14;19;18)	2036.5 (951.0 to 3123.0)	602.0 (498.0 to 2079.0)	1243.0 (587.0 to 3400.0)	515.5 (414.0 to 1178.0)
CD4-All doubles,Anti-HPV-16,Month 7(N=13;14;16;17)	3693.0 (1870.0 to 5153.0)	1679.5 (1052.0 to 2734.0)	3414.5 (1424.5 to 4520.0)	1505.0 (995.0 to 2205.0)
CD4-All doubles,Anti-HPV-18,Month 7(N=13;14;16;17)	1866.0 (1267.0 to 2875.0)	840.5 (518.0 to 1641.0)	2084.5 (911.0 to 4110.0)	669.0 (470.0 to 1035.0)
CD4-All doubles,Anti-HPV-16,Month 12(N=15;14;21;19	2328.0 (1225.0 to 4614.0)	1288.0 (976.0 to 2485.0)	2543.0 (1232.0 to 4264.0)	830.0 (367.0 to 1386.0)
CD4-All doubles,Anti-HPV-18,Month 12(N=15;14;21;19	1654.0 (836.0 to 2634.0)	808.5 (295.0 to 1932.0)	1641.0 (985.0 to 2939.0)	428.0 (162.0 to 938.0)
CD4-d-CD40L, Anti-HPV-16, Day 0 (N=17;15;17;18)	22.0 (1.0 to 118.0)	99.0 (60.0 to 215.0)	1.0 (1.0 to 58.0)	46.0 (1.0 to 81.0)
CD4-d-CD40L, Anti-HPV-18, Day 0 (N=17;15;17;18)	36.0 (1.0 to 81.0)	89.0 (1.0 to 176.0)	1.0 (1.0 to 54.0)	13.5 (1.0 to 100.0)
CD4-d-CD40L, Anti-HPV-16, Week 6 (N=16;14;16;18)	426.0 (258.5 to 999.5)	326.5 (196.0 to 1034.0)	298.0 (209.5 to 540.0)	582.0 (223.0 to 967.0)
CD4-d-CD40L, Anti-HPV-18, Week 6 (N=16;14;16;18)	403.5 (144.0 to 835.0)	296.0 (216.0 to 840.0)	242.5 (36.5 to 393.0)	310.0 (95.0 to 521.0)
CD4-d-CD40L, Anti-HPV-16, Week 10 (N=14;14;19;18)	2893.5 (988.0 to 5006.0)	1440.0 (882.0 to 1814.0)	1678.0 (917.0 to 4306.0)	1239.0 (562.0 to 2362.0)
CD4-d-CD40L, Anti-HPV-18, Week 10 (N=14;14;19;18)	2015.0 (944.0 to 3021.0)	564.5 (507.0 to 2045.0)	1051.0 (631.0 to 3317.0)	474.5 (385.0 to 811.0)

CD4-d-CD40L, Anti-HPV-16, Month 7 (N=13;14;16;17)	3658.0 (1804.0 to 5070.0)	1619.5 (1071.0 to 2600.0)	3290.0 (1464.5 to 4387.5)	1389.0 (949.0 to 2133.0)
CD4-d-CD40L, Anti-HPV-18, Month 7 (N=13;14;16;17)	1839.0 (1066.0 to 2893.0)	833.5 (518.0 to 1605.0)	2014.0 (979.0 to 3878.5)	647.0 (442.0 to 981.0)
CD4-d-CD40L, Anti-HPV-16, Month 12 (N=15;14;21;19)	2266.0 (1178.0 to 4558.0)	1278.0 (955.0 to 2478.0)	2519.0 (1232.0 to 4190.0)	862.0 (353.0 to 1197.0)
CD4-d-CD40L, Anti-HPV-18, Month 12 (N=15;14;21;19)	1668.0 (807.0 to 2427.0)	808.5 (295.0 to 1914.0)	1641.0 (984.0 to 2767.0)	394.0 (155.0 to 913.0)
CD4-d-IFNG, Anti-HPV-16, Day 0 (N=17;15;17;18)	27.0 (1.0 to 63.0)	30.0 (1.0 to 51.0)	1.0 (1.0 to 45.0)	39.0 (1.0 to 61.0)
CD4-d-IFNG, Anti-HPV-18, Day 0 (N=17;15;17;18)	4.0 (1.0 to 42.0)	51.0 (1.0 to 59.0)	1.0 (1.0 to 54.0)	21.0 (1.0 to 46.0)
CD4-d-IFNG, Anti-HPV-16, Week 6 (N=16;14;16;18)	222.5 (117.0 to 393.0)	116.0 (75.0 to 222.0)	42.5 (1.0 to 127.5)	241.5 (71.0 to 404.0)
CD4-d-IFNG, Anti-HPV-18, Week 6 (N=16;14;16;18)	98.0 (25.0 to 361.0)	104.5 (35.0 to 211.0)	1.0 (1.0 to 44.0)	129.5 (1.0 to 182.0)
CD4-d-IFNG, Anti-HPV-16, Week 10 (N=14;14;19;18)	1220.0 (554.0 to 1478.0)	450.0 (245.0 to 527.0)	332.0 (282.0 to 1251.0)	442.0 (160.0 to 935.0)
CD4-d-IFNG, Anti-HPV-18, Week 10 (N=14;14;19;18)	694.0 (342.0 to 1207.0)	326.5 (121.0 to 455.0)	222.0 (124.0 to 569.0)	202.0 (122.0 to 279.0)
CD4-d-IFNG, Anti-HPV-16, Month 7 (N=13;14;16;17)	1513.0 (891.0 to 1993.0)	585.5 (190.0 to 846.0)	731.0 (267.5 to 1245.0)	495.0 (319.0 to 859.0)
CD4-d-IFNG, Anti-HPV-18, Month 7 (N=13;14;16;17)	694.0 (409.0 to 868.0)	306.0 (171.0 to 382.0)	414.5 (245.5 to 616.5)	198.0 (126.0 to 435.0)
CD4-d-IFNG, Anti-HPV-16, Month 12 (N=15;14;21;19)	452.0 (368.0 to 1097.0)	432.0 (202.0 to 835.0)	621.0 (239.0 to 1042.0)	302.0 (129.0 to 555.0)
CD4-d-IFNG, Anti-HPV-18, Month 12 (N=15;14;21;19)	402.0 (191.0 to 585.0)	253.5 (92.0 to 415.0)	273.0 (88.0 to 406.0)	98.0 (1.0 to 154.0)
CD4-d-IL-2, Anti-HPV-16, Day 0 (N=17;15;17;18)	43.0 (1.0 to 81.0)	30.0 (7.0 to 121.0)	1.0 (1.0 to 58.0)	1.0 (1.0 to 21.0)
CD4-d-IL-2, Anti-HPV-18, Day 0 (N=17;15;17;18)	46.0 (1.0 to 115.0)	37.0 (1.0 to 102.0)	1.0 (1.0 to 31.0)	13.5 (1.0 to 57.0)
CD4-d-IL-2, Anti-HPV-16, Week 6 (N=16;14;16;18)	361.0 (235.5 to 966.0)	300.0 (234.0 to 827.0)	245.5 (137.0 to 468.0)	454.5 (228.0 to 816.0)
CD4-d-IL-2, Anti-HPV-18, Week 6 (N=16;14;16;18)	364.5 (161.0 to 858.0)	193.5 (94.0 to 687.0)	227.5 (131.5 to 379.5)	286.0 (129.0 to 413.0)
CD4-d-IL-2, Anti-HPV-16, Week 10 (N=14;14;19;18)	2503.0 (938.0 to 4606.0)	1221.0 (678.0 to 1584.0)	1542.0 (776.0 to 3499.0)	929.5 (435.0 to 2128.0)
CD4-d-IL-2, Anti-HPV-18, Week 10 (N=14;14;19;18)	1668.5 (635.0 to 2183.0)	555.5 (349.0 to 1687.0)	1183.0 (456.0 to 2311.0)	411.0 (245.0 to 891.0)
CD4-d-IL-2, Anti-HPV-16, Month 7 (N=13;14;16;17)	2847.0 (1557.0 to 4064.0)	1318.5 (672.0 to 2141.0)	2608.5 (1147.5 to 3875.0)	1128.0 (697.0 to 1574.0)
CD4-d-IL-2, Anti-HPV-18, Month 7 (N=13;14;16;17)	1522.0 (914.0 to 2285.0)	615.0 (472.0 to 1234.0)	1442.0 (811.0 to 3471.0)	537.0 (341.0 to 643.0)
CD4-d-IL-2, Anti-HPV-16, Month 12 (N=15;14;21;19)	1792.0 (1076.0 to 4087.0)	1040.5 (804.0 to 1972.0)	1861.0 (1861.0 to 3754.0)	723.0 (330.0 to 1255.0)
CD4-d-IL-2, Anti-HPV-18, Month 12 (N=15;14;21;19)	1170.0 (683.0 to 2375.0)	601.5 (230.0 to 1568.0)	1342.0 (825.0 to 2794.0)	337.0 (243.0 to 636.0)
CD4-d-TNFA, Anti-HPV-16, Day 0 (N=17;15;17;18)	1.0 (1.0 to 58.0)	71.0 (1.0 to 252.0)	32.0 (1.0 to 74.0)	34.0 (1.0 to 76.0)
CD4-d-TNFA, Anti-HPV-18, Day 0 (N=17;15;17;18)	1.0 (1.0 to 52.0)	35.0 (1.0 to 131.0)	25.0 (1.0 to 39.0)	15.5 (1.0 to 83.0)
CD4-d-TNFA, Anti-HPV-16, Week 6 (N=16;14;16;18)	326.5 (49.5 to 714.0)	171.0 (133.0 to 701.0)	237.0 (89.5 to 325.0)	337.5 (183.0 to 648.0)
CD4-d-TNFA, Anti-HPV-18, Week 6 (N=16;14;16;18)	234.0 (66.0 to 579.0)	204.0 (94.0 to 539.0)	162.5 (75.5 to 247.0)	156.5 (72.0 to 398.0)
CD4-d-TNFA, Anti-HPV-16, Week 10 (N=14;14;19;18)	2086.0 (519.0 to 4016.0)	903.5 (606.0 to 1355.0)	1260.0 (764.0 to 3094.0)	865.5 (453.0 to 2100.0)

CD4-d-TNFA, Anti-HPV-18, Week 10 (N=14;14;19;18)	1493.5 (592.0 to 2341.0)	443.0 (248.0 to 1432.0)	899.0 (415.0 to 2310.0)	334.5 (203.0 to 958.0)
CD4-d-TNFA, Anti-HPV-16, Month 7 (N=13;14;16;17)	2688.0 (1399.0 to 3994.0)	1109.0 (670.0 to 2066.0)	2621.0 (1062.0 to 3652.5)	1215.0 (792.0 to 1665.0)
CD4-d-TNFA, Anti-HPV-18, Month 7 (N=13;14;16;17)	1366.0 (1126.0 to 2449.0)	598.0 (362.0 to 1522.0)	1614.0 (760.5 to 3463.5)	505.0 (330.0 to 683.0)
CD4-d-TNFA, Anti-HPV-16, Month 12 (N=15;14;21;19)	1937.0 (883.0 to 3961.0)	1011.5 (681.0 to 2066.0)	2344.0 (1053.0 to 3741.0)	646.0 (344.0 to 1219.0)
CD4-d-TNFA, Anti-HPV-18, Month 12 (N=15;14;21;19)	1264.0 (707.0 to 2500.0)	527.0 (174.0 to 1684.0)	1480.0 (703.0 to 2619.0)	358.0 (186.0 to 617.0)
CD8-All doubles,Anti-HPV-16, Day 0 (N=17;15;17;18)	1.0 (1.0 to 40.0)	1.0 (1.0 to 43.0)	1.0 (1.0 to 28.0)	1.0 (1.0 to 29.0)
CD8-All doubles,Anti-HPV-18, Day 0 (N=17;15;17;18)	6.0 (1.0 to 50.0)	23.0 (1.0 to 60.0)	21.0 (1.0 to 54.0)	1.0 (1.0 to 35.0)
CD8-All doubles,Anti-HPV-16,Week 6 (N=16;14;16;18)	2.0 (1.0 to 34.5)	13.0 (1.0 to 70.0)	1.0 (1.0 to 14.5)	1.0 (1.0 to 3.0)
CD8-All doubles,Anti-HPV-18,Week 6 (N=16;14;16;18)	37.5 (9.0 to 66.5)	2.0 (1.0 to 42.0)	1.0 (1.0 to 42.5)	30.5 (1.0 to 74.0)
CD8-All doubles,Anti-HPV-16,Week 10(N=14;14;19;18)	41.0 (1.0 to 75.0)	3.5 (1.0 to 36.0)	1.0 (1.0 to 54.0)	1.0 (1.0 to 29.0)
CD8-All doubles,Anti-HPV-18,Week 10(N=14;14;19;18)	11.0 (1.0 to 60.0)	1.0 (1.0 to 60.0)	5.0 (1.0 to 84.0)	1.0 (1.0 to 41.0)
CD8-All doubles,Anti-HPV-16,Month 7(N=13;14;16;17)	51.0 (18.0 to 69.0)	9.5 (1.0 to 33.0)	1.0 (1.0 to 74.5)	2.0 (1.0 to 54.0)
CD8-All doubles,Anti-HPV-18,Month 7(N=13;14;16;17)	41.0 (1.0 to 159.0)	30.0 (3.0 to 49.0)	15.5 (1.0 to 106.5)	24.0 (1.0 to 54.0)
CD8-All doubles,Anti-HPV-16,Month 12(N=15;14;21;19	1.0 (1.0 to 23.0)	34.0 (1.0 to 79.0)	23.0 (1.0 to 49.0)	1.0 (1.0 to 24.0)
CD8-All doubles,Anti-HPV-18,Month 12(N=15;14;21;19	25.0 (1.0 to 92.0)	1.0 (1.0 to 29.0)	1.0 (1.0 to 37.0)	1.0 (1.0 to 24.0)
CD8-d-CD40L, Anti-HPV-16, Day 0 (N=17;15;17;18)	1.0 (1.0 to 29.0)	1.0 (1.0 to 6.0)	1.0 (1.0 to 10.0)	1.0 (1.0 to 7.0)
CD8-d-CD40L, Anti-HPV-18, Day 0 (N=17;15;17;18)	1.0 (1.0 to 29.0)	1.0 (1.0 to 19.0)	1.0 (1.0 to 33.0)	1.0 (1.0 to 16.0)
CD8-d-CD40L, Anti-HPV-16, Week 6 (N=16;14;16;18)	1.0 (1.0 to 24.5)	1.0 (1.0 to 32.0)	1.0 (1.0 to 18.0)	1.0 (1.0 to 1.0)
CD8-d-CD40L, Anti-HPV-18, Week 6 (N=16;14;16;18)	9.5 (1.0 to 27.5)	1.0 (1.0 to 17.0)	1.0 (1.0 to 23.0)	1.0 (1.0 to 36.0)
CD8-d-CD40L, Anti-HPV-16, Week 10 (N=14;14;19;18)	18.5 (1.0 to 73.0)	1.0 (1.0 to 29.0)	1.0 (1.0 to 41.0)	1.0 (1.0 to 27.0)
CD8-d-CD40L, Anti-HPV-18, Week 10 (N=14;14;19;18)	10.5 (1.0 to 34.0)	2.5 (1.0 to 34.0)	26.0 (1.0 to 72.0)	1.0 (1.0 to 30.0)
CD8-d-CD40L, Anti-HPV-16, Month 7 (N=13;14;16;17)	26.0 (1.0 to 63.0)	3.0 (1.0 to 20.0)	2.0 (1.0 to 52.0)	1.0 (1.0 to 36.0)
CD8-d-CD40L, Anti-HPV-18, Month 7 (N=13;14;16;17)	4.0 (1.0 to 42.0)	15.0 (1.0 to 31.0)	38.0 (1.0 to 92.0)	4.0 (1.0 to 33.0)
CD8-d-CD40L, Anti-HPV-16, Month 12 (N=15;14;21;19)	1.0 (1.0 to 73.0)	31.0 (7.0 to 39.0)	3.0 (1.0 to 30.0)	1.0 (1.0 to 24.0)
CD8-d-CD40L, Anti-HPV-18, Month 12 (N=15;14;21;19)	23.0 (1.0 to 59.0)	1.0 (1.0 to 8.0)	1.0 (1.0 to 39.0)	1.0 (1.0 to 24.0)
CD8-d-IFNG, Anti-HPV-16, Day 0 (N=17;15;17;18)	1.0 (1.0 to 29.0)	1.0 (1.0 to 43.0)	1.0 (1.0 to 28.0)	1.0 (1.0 to 2.0)
CD8-d-IFNG, Anti-HPV-18, Day 0 (N=17;15;17;18)	6.0 (1.0 to 33.0)	19.0 (1.0 to 47.0)	21.0 (1.0 to 54.0)	4.0 (1.0 to 35.0)
CD8-d-IFNG, Anti-HPV-16, Week 6 (N=16;14;16;18)	2.5 (1.0 to 39.5)	17.5 (1.0 to 78.0)	1.0 (1.0 to 14.5)	1.0 (1.0 to 11.0)
CD8-d-IFNG, Anti-HPV-18, Week 6 (N=16;14;16;18)	27.5 (1.0 to 55.5)	1.0 (1.0 to 47.0)	1.0 (1.0 to 42.5)	35.5 (1.0 to 84.0)

CD8-d-IFNG, Anti-HPV-16, Week 10 (N=14;14;19;18)	34.0 (1.0 to 99.0)	25.0 (1.0 to 30.0)	1.0 (1.0 to 38.0)	1.0 (1.0 to 29.0)
CD8-d-IFNG, Anti-HPV-18, Week 10 (N=14;14;19;18)	3.0 (1.0 to 68.0)	7.5 (1.0 to 34.0)	24.0 (1.0 to 76.0)	1.0 (1.0 to 1.0)
CD8-d-IFNG, Anti-HPV-16, Month 7 (N=13;14;16;17)	46.0 (1.0 to 68.0)	1.0 (1.0 to 26.0)	1.0 (1.0 to 74.5)	1.0 (1.0 to 50.0)
CD8-d-IFNG, Anti-HPV-18, Month 7 (N=13;14;16;17)	41.0 (1.0 to 68.0)	21.0 (1.0 to 41.0)	4.0 (1.0 to 90.5)	3.0 (1.0 to 52.0)
CD8-d-IFNG, Anti-HPV-16, Month 12 (N=15;14;21;19)	1.0 (1.0 to 31.0)	25.0 (1.0 to 57.0)	1.0 (1.0 to 39.0)	1.0 (1.0 to 24.0)
CD8-d-IFNG, Anti-HPV-18, Month 12 (N=15;14;21;19)	23.0 (1.0 to 92.0)	1.0 (1.0 to 31.0)	1.0 (1.0 to 7.0)	1.0 (1.0 to 4.0)
CD8-d-IL-2, Anti-HPV-16, Day 0 (N=17;15;17;18)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 16.0)
CD8-d-IL-2, Anti-HPV-18, Day 0 (N=17;15;17;18)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)
CD8-d-IL-2, Anti-HPV-16, Week 6 (N=16;14;16;18)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)
CD8-d-IL-2, Anti-HPV-18, Week 6 (N=16;14;16;18)	1.0 (1.0 to 23.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)
CD8-d-IL-2, Anti-HPV-16, Week 10 (N=14;14;19;18)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 32.0)	1.0 (1.0 to 1.0)
CD8-d-IL-2, Anti-HPV-18, Week 10 (N=14;14;19;18)	1.0 (1.0 to 26.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 25.0)	1.0 (1.0 to 1.0)
CD8-d-IL-2, Anti-HPV-16, Month 7 (N=13;14;16;17)	1.0 (1.0 to 23.0)	1.0 (1.0 to 17.0)	1.0 (1.0 to 37.5)	1.0 (1.0 to 1.0)
CD8-d-IL-2, Anti-HPV-18, Month 7 (N=13;14;16;17)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 29.0)	1.0 (1.0 to 1.0)
CD8-d-IL-2, Anti-HPV-16, Month 12 (N=15;14;21;19)	1.0 (1.0 to 27.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)
CD8-d-IL-2, Anti-HPV-18, Month 12 (N=15;14;21;19)	1.0 (1.0 to 48.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 19.0)	1.0 (1.0 to 1.0)
CD8-d-TNFA, Anti-HPV-16, Day 0 (N=17;15;17;18)	1.0 (1.0 to 10.0)	1.0 (1.0 to 35.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 29.0)
CD8-d-TNFA, Anti-HPV-18, Day 0 (N=17;15;17;18)	6.0 (1.0 to 50.0)	7.0 (1.0 to 54.0)	1.0 (1.0 to 33.0)	1.0 (1.0 to 34.0)
CD8-d-TNFA, Anti-HPV-16, Week 6 (N=16;14;16;18)	1.0 (1.0 to 46.0)	1.0 (1.0 to 35.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 31.0)
CD8-d-TNFA, Anti-HPV-18, Week 6 (N=16;14;16;18)	19.0 (1.0 to 50.0)	1.0 (1.0 to 57.0)	1.0 (1.0 to 28.0)	1.0 (1.0 to 26.0)
CD8-d-TNFA, Anti-HPV-16, Week 10 (N=14;14;19;18)	1.5 (1.0 to 32.0)	1.0 (1.0 to 24.0)	1.0 (1.0 to 31.0)	1.0 (1.0 to 26.0)
CD8-d-TNFA, Anti-HPV-18, Week 10 (N=14;14;19;18)	17.5 (1.0 to 34.0)	14.0 (1.0 to 61.0)	5.0 (1.0 to 42.0)	1.0 (1.0 to 34.0)
CD8-d-TNFA, Anti-HPV-16, Month 7 (N=13;14;16;17)	34.0 (1.0 to 41.0)	13.0 (1.0 to 33.0)	1.0 (1.0 to 49.0)	2.0 (1.0 to 33.0)
CD8-d-TNFA, Anti-HPV-18, Month 7 (N=13;14;16;17)	41.0 (1.0 to 111.0)	26.5 (15.0 to 58.0)	1.0 (1.0 to 58.0)	1.0 (1.0 to 32.0)
CD8-d-TNFA, Anti-HPV-16, Month 12 (N=15;14;21;19)	1.0 (1.0 to 26.0)	1.0 (1.0 to 54.0)	28.0 (1.0 to 49.0)	1.0 (1.0 to 42.0)
CD8-d-TNFA, Anti-HPV-18, Month 12 (N=15;14;21;19)	30.0 (24.0 to 62.0)	1.0 (1.0 to 28.0)	1.0 (1.0 to 48.0)	1.0 (1.0 to 40.0)

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 follow-up period after vaccination; Unsolicited AEs: During the 30-day follow-up period after vaccination; SAEs: during the whole study period (from Day 0 up to Month 24).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	HIV+/Cervarix Group

Reporting group description:

HIV seropositive female subjects, between and including 15 and 25 years of age, who received 3 doses of Cervarix vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.

Reporting group title	HIV+/Gardasil Group

Reporting group description:

HIV seropositive female subjects, between and including 15 and 25 years of age, who received 3 doses of Gardasil vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.

Reporting group title	HIV-/Cervarix Group

Reporting group description:

HIV seronegative female subjects, between and including 15 and 25 years of age, who received 3 doses of Cervarix vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.

Reporting group title	HIV-/Gardasil Group

Reporting group description:

HIV seronegative female subjects, between and including 15 and 25 years of age, who received 3 doses of Gardasil vaccine, administered intramuscularly in the deltoid muscle of the non-dominant arm, according to a three-dose schedule: at Day 0, Week 6, Month 6.

Serious adverse events	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 129 (6.98%)	9 / 128 (7.03%)	4 / 144 (2.78%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			

subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (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
Spinal compression fracture			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (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
Vaccination complication			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion spontaneous complete			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (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			
Immune thrombocytopenic purpura			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			

subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (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			
Cervical dysplasia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Dissociative disorder			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (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
Suicide attempt			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (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
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (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			
Arthritis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 129 (0.00%)	2 / 128 (1.56%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			

subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis tuberculous			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (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
Pneumonia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (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
Pneumonia bacterial			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (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
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (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
Pulmonary tuberculosis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (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
Tonsillitis			
subjects affected / exposed	1 / 129 (0.78%)	1 / 128 (0.78%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (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
Vaginitis gardnerella			

subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	HIV-/Gardasil Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 145 (0.69%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vaccination complication			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abortion spontaneous complete			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Dissociative disorder			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			

subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dengue fever			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis tuberculous			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pneumonia mycoplasmal			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary tuberculosis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vaginitis gardnerella			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	HIV+/Cervarix Group	HIV+/Gardasil Group	HIV-/Cervarix Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	123 / 129 (95.35%)	109 / 128 (85.16%)	136 / 144 (94.44%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenoma benign			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0

Anogenital warts			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Uterine leiomyoma			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Administration site pruritus			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Administration site swelling			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Discomfort			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	73 / 129 (56.59%)	59 / 128 (46.09%)	65 / 144 (45.14%)
occurrences (all)	128	118	111
Injection site erythema			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Injection site haematoma			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Injection site pain			

subjects affected / exposed	1 / 129 (0.78%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	1	1	0
Injection site rash			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	121 / 129 (93.80%)	85 / 128 (66.41%)	133 / 144 (92.36%)
occurrences (all)	303	174	329
Peripheral swelling			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	24 / 129 (18.60%)	20 / 128 (15.63%)	23 / 144 (15.97%)
occurrences (all)	32	22	31
Swelling			
subjects affected / exposed	38 / 129 (29.46%)	21 / 128 (16.41%)	47 / 144 (32.64%)
occurrences (all)	60	28	76
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Dysmenorrhoea			
subjects affected / exposed	3 / 129 (2.33%)	1 / 128 (0.78%)	4 / 144 (2.78%)
occurrences (all)	3	1	5
Metrorrhagia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Vaginal discharge			

subjects affected / exposed	1 / 129 (0.78%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	1	1	0
Vulvovaginal pruritus			
subjects affected / exposed	2 / 129 (1.55%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	3	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 129 (0.00%)	2 / 128 (1.56%)	0 / 144 (0.00%)
occurrences (all)	0	2	0
Cough			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	1 / 144 (0.69%)
occurrences (all)	0	1	1
Epistaxis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 129 (0.78%)	2 / 128 (1.56%)	2 / 144 (1.39%)
occurrences (all)	1	2	2
Productive cough			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	3 / 129 (2.33%)	1 / 128 (0.78%)	1 / 144 (0.69%)
occurrences (all)	3	1	1
Sneezing			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	1 / 144 (0.69%)
occurrences (all)	0	1	1
Psychiatric disorders			

Anxiety			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Cd4 lymphocytes decreased			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Viral load increased			
subjects affected / exposed	1 / 129 (0.78%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	1	1	0
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	1 / 129 (0.78%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	1	1	0
Muscle strain			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Nail injury			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1

Tachycardia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 129 (1.55%)	2 / 128 (1.56%)	0 / 144 (0.00%)
occurrences (all)	2	2	0
Formication			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	88 / 129 (68.22%)	63 / 128 (49.22%)	70 / 144 (48.61%)
occurrences (all)	165	116	115
Hypoaesthesia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 129 (1.55%)	3 / 128 (2.34%)	0 / 144 (0.00%)
occurrences (all)	2	3	0
Lymphadenopathy			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Polycythaemia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			

Cerumen impaction			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	1 / 129 (0.78%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Blindness			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 129 (0.78%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	1	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Dental caries			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	1 / 144 (0.69%)
occurrences (all)	0	1	1
Dyspepsia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Food poisoning			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			

subjects affected / exposed	41 / 129 (31.78%)	35 / 128 (27.34%)	28 / 144 (19.44%)
occurrences (all)	58	55	35
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Tooth impacted			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 129 (0.00%)	2 / 128 (1.56%)	0 / 144 (0.00%)
occurrences (all)	0	2	0
Eczema			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	41 / 129 (31.78%)	34 / 128 (26.56%)	52 / 144 (36.11%)
occurrences (all)	59	50	89
Miliaria			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	2 / 129 (1.55%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	11 / 129 (8.53%)	5 / 128 (3.91%)	5 / 144 (3.47%)
occurrences (all)	11	6	6
Rash papular			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Skin discolouration			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0

Skin hyperpigmentation			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	14 / 129 (10.85%)	9 / 128 (7.03%)	4 / 144 (2.78%)
occurrences (all)	17	11	6
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	2	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Ureterolithiasis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	41 / 129 (31.78%)	38 / 128 (29.69%)	31 / 144 (21.53%)
occurrences (all)	64	56	40
Musculoskeletal pain			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	68 / 129 (52.71%)	51 / 128 (39.84%)	64 / 144 (44.44%)
occurrences (all)	115	81	106
Neck pain			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 129 (0.00%)	2 / 128 (1.56%)	0 / 144 (0.00%)
occurrences (all)	0	2	0

Tendonitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Torticollis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Acarodermatitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Bacterial vaginosis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Bartholinitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Body tinea			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Cervicitis gonococcal			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	1 / 129 (0.78%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	1	1	0
Cystitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Dermatophytosis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Furuncle			

subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Hepatitis c			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	2 / 129 (1.55%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	2	1	0
Nasopharyngitis			
subjects affected / exposed	2 / 129 (1.55%)	4 / 128 (3.13%)	2 / 144 (1.39%)
occurrences (all)	4	5	3
Oral herpes			
subjects affected / exposed	2 / 129 (1.55%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	3	0	0
Otitis media acute			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	1 / 129 (0.78%)	2 / 128 (1.56%)	1 / 144 (0.69%)
occurrences (all)	1	3	1
Sinusitis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	1	0	1
Skin infection			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	2 / 129 (1.55%)	0 / 128 (0.00%)	2 / 144 (1.39%)
occurrences (all)	2	0	2
Tooth abscess			

subjects affected / exposed	0 / 129 (0.00%)	0 / 128 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 129 (2.33%)	3 / 128 (2.34%)	2 / 144 (1.39%)
occurrences (all)	3	3	2
Urethritis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Varicella			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	1 / 144 (0.69%)
occurrences (all)	0	1	1
Viral pharyngitis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 128 (0.78%)	1 / 144 (0.69%)
occurrences (all)	0	1	1
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 128 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	HIV-/Gardasil Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	127 / 145 (87.59%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenoma benign			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Anogenital warts			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Uterine leiomyoma			

subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Administration site pruritus			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Administration site swelling			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Discomfort			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	56 / 145 (38.62%)		
occurrences (all)	88		
Injection site erythema			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Injection site haematoma			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Injection site rash			

subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	119 / 145 (82.07%)		
occurrences (all)	265		
Peripheral swelling			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	25 / 145 (17.24%)		
occurrences (all)	29		
Swelling			
subjects affected / exposed	39 / 145 (26.90%)		
occurrences (all)	60		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Dysmenorrhoea			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences (all)	3		
Metrorrhagia			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Vaginal discharge			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Vulvovaginal pruritus			

subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Sneezing			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Depression			

subjects affected / exposed occurrences (all)	1 / 145 (0.69%) 1		
Investigations Blood pressure increased subjects affected / exposed occurrences (all) Cd4 lymphocytes decreased subjects affected / exposed occurrences (all) Viral load increased subjects affected / exposed occurrences (all)	 0 / 145 (0.00%) 0 0 / 145 (0.00%) 0 0 / 145 (0.00%) 0		
Injury, poisoning and procedural complications Burns second degree subjects affected / exposed occurrences (all) Ligament sprain subjects affected / exposed occurrences (all) Muscle strain subjects affected / exposed occurrences (all) Nail injury subjects affected / exposed occurrences (all) Skin abrasion subjects affected / exposed occurrences (all)	 1 / 145 (0.69%) 1 0 / 145 (0.00%) 0 1 / 145 (0.69%) 1 1 / 145 (0.69%) 1 1 / 145 (0.69%) 1		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all)	 0 / 145 (0.00%) 0 0 / 145 (0.00%) 0		
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Formication			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	67 / 145 (46.21%)		
occurrences (all)	104		
Hypoaesthesia			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Lymphadenopathy			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Polycythaemia			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Ear pain			

subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Eye disorders			
Blindness			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Dental caries			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Food poisoning			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Gastrointestinal disorder			
subjects affected / exposed	26 / 145 (17.93%)		
occurrences (all)	38		
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Tooth impacted			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	42 / 145 (28.97%)		
occurrences (all)	69		
Miliaria			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	8 / 145 (5.52%)		
occurrences (all)	10		
Rash papular			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Skin discolouration			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Skin hyperpigmentation			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		

Urticaria subjects affected / exposed occurrences (all)	6 / 145 (4.14%) 7		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) Nephrolithiasis subjects affected / exposed occurrences (all) Ureterolithiasis subjects affected / exposed occurrences (all)	 1 / 145 (0.69%) 1 1 / 145 (0.69%) 1 0 / 145 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	 0 / 145 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Tendonitis subjects affected / exposed occurrences (all)	 34 / 145 (23.45%) 47 0 / 145 (0.00%) 0 54 / 145 (37.24%) 91 0 / 145 (0.00%) 0 0 / 145 (0.00%) 0 1 / 145 (0.69%) 1		

Torticollis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Acarodermatitis			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Bacterial vaginosis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Bartholinitis			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Body tinea			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Cervicitis gonococcal			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Cystitis			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Dermatophytosis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Furuncle			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Hepatitis c			

subjects affected / exposed	0 / 145 (0.00%)			
occurrences (all)	0			
Herpes zoster				
subjects affected / exposed	0 / 145 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	2 / 145 (1.38%)			
occurrences (all)	3			
Nasopharyngitis				
subjects affected / exposed	6 / 145 (4.14%)			
occurrences (all)	7			
Oral herpes				
subjects affected / exposed	0 / 145 (0.00%)			
occurrences (all)	0			
Otitis media acute				
subjects affected / exposed	1 / 145 (0.69%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	2 / 145 (1.38%)			
occurrences (all)	2			
Sinusitis				
subjects affected / exposed	2 / 145 (1.38%)			
occurrences (all)	3			
Skin infection				
subjects affected / exposed	0 / 145 (0.00%)			
occurrences (all)	0			
Tonsillitis				
subjects affected / exposed	0 / 145 (0.00%)			
occurrences (all)	0			
Tooth abscess				
subjects affected / exposed	0 / 145 (0.00%)			
occurrences (all)	0			
Upper respiratory tract infection				

subjects affected / exposed	4 / 145 (2.76%)		
occurrences (all)	5		
Urethritis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Vaginal infection			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Varicella			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences (all)	1		
Viral pharyngitis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 145 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2010	The main reason for amending this protocol was that, since the last revision of the WHO guidelines in 2006, new and compelling evidence has become available concerning the start of antiretroviral therapy (ART) in HIV-infected adults and adolescents. Subjects who have a CD4 count ≤ 350 cells/mm3 should be treated irrespective of their clinical stage [WHO, 2009]. - Some clarifications have been made to the flowchart, weight and ARV therapy (if applicable) would be recorded at each visit. Also, a history-directed physical examination will be performed at each visit. - Section 6.2 (Storage and handling of study vaccines) has been modified in order to align the wording with the new version of SOP-BIO-CLIN-7055 v04 entitled "Management of the Cold Chain for GlaxoSmithKline Biologicals investigational human subject research" effective since 31 March 2010. - Facsimile numbers for prompting SAEs to GSK Biologicals have been updated as well as the phone numbers in case of emergency unblinding. - Minor corrections such as inconsistencies, formatting and typos have been made.
23 December 2010	Protocol Amendment 2 was developed to: - Implement reporting of potential immune-mediated diseases (pIMDs). Due to their potent immune stimulating effect, there are theoretical concerns that modern adjuvants like GSK Biologicals' novel adjuvant systems might result in undesirable effects on the body's immune system, which could include onset of new or exacerbation of underlying autoimmune diseases in particular. Accordingly, a heightened surveillance on the occurrence of any such conditions in recipients of novel adjuvant containing vaccines in clinical trials has been put in place by GSK. - Add two additional HIV tests at Month 7 and Month 24 for HIV negative subjects. - Update the formulation of the HPV-16/18 L1 VLP AS04 vaccine. - Update the list of contributing authors. - Make minor modifications/ clarifications to the protocol.
23 May 2011	This amendment was issued to clarify that for HIV+ subjects whose HIV status is documented, the HIV Rapid test does not need to be repeated. - As recommended by the study IDMC, exploratory analyses have been included to evaluate the immunogenicity of the study vaccines in HIV+ subjects stratified by HIV mode of transmission and by nadir CD4 cell count category. - The introduction has been updated with the current licensure status and indication of Cervarix and Gardasil. - Minor corrections such as formatting and typos have been made.
04 October 2011	Per protocol, assessment of primary objectives for non-inferiority/superiority were planned to be performed on the ATP cohort for immunogenicity in initially seronegative (S-) subjects. In the HPV-020 study, there was a high baseline seropositivity (S+) rate in both HIV + and HIV – subjects (50-80%). As this can also be expected in the HPV-019 study, many subjects will be eliminated from the primary endpoint analysis and this objective might not be met due to a low sample size. Therefore, the HPV-019 protocol was amended to analyse the primary endpoints regardless of initial HPV serostatus. The text in Section 10.3 (sample size estimation) was reworded accordingly.
20 March 2012	Amendment 5 for the HPV-019 PRI protocol was developed in order to: - Revise the length of interval between the study visits 4 and 5, by allowing subjects to be considered for ATP analyses even if the first four visits occur at the maximum permissible interval for each visit. - Furthermore, since the primary endpoint is evaluated 1 month after administration of the third dose of vaccine, the recommended interval between Visit 4 and Visit 5 has been modified to 30 days. - Update the list of contributing authors.

06 June 2012	The protocol was amended for the following reason: 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 would have full authority to break the treatment code.
19 December 2013	The HPV-019 protocol was amended for the following reasons: - Due to high rate of non evaluable subjects, (data integrity issue at one site; protocol non compliance; high drop out rate) additional subjects would be enrolled in this study, in order to maintain the statistical power for analysis. - 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. This change in the assay will be implemented for the testing of serum samples for all time points. - 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 would be implemented for the testing of samples for all time points. - Other small changes were made in order to accommodate the recruitment of subjects from another country, to clarify that some activities in the protocol are mandatory only for HIV+ subjects (this reflects what is actually done in the study procedures and is in line with the study procedures manual) and to clarify the blinding strategy for analysis.
26 April 2016	The protocol was amended to align the section of the protocol on management of HIV+ subjects with the recently revised WHO guidelines on when to start antiretroviral therapy (ART) in HIV+ subjects. The revision of the WHO guidelines presented evidence that earlier use of ART results in better long-term clinical outcomes for people living with HIV compared with delayed treatment, including pregnant and breastfeeding women. This guideline advises to start ART in all adults with HIV regardless of their clinical stage and at any CD4 cell count. At the time of implementation of the protocol amendment, the vaccination phase had already completed, and therefore the exclusion criterion for subsequent vaccination after initiation of ART during the course of the study was not revised.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported