



Clinical trial results:

Immunogenicity and safety study of GSK Biologicals' meningococcal vaccine 134612 with or without co-administration of Cervarix and Boostrix in female adolescents and young adults at 9-25 years of age

Summary

EudraCT number	2012-001876-13
Trial protocol	EE
Global end of trial date	29 April 2014

Results information

Result version number	v1
This version publication date	17 June 2017
First version publication date	17 June 2017

Trial information

Trial identification

Sponsor protocol code	113823
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01755689
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	25 May 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of MenACWY-TT conjugate vaccine co-administered with HPV-16/18 L1 AS04 compared to MenACWY-TT alone with respect to Serum Bactericidal Assay using rabbit complement (rSBA) geometric mean titres (GMTs) for serogroups A, C, W-135 and Y one month after vaccination.

To demonstrate the non-inferiority of HPV-16/18 L1 AS04 co-administered with MenACWY-TT compared to HPV-16/18 L1 AS04 alone in terms of HPV16 and HPV18 GMTs as measured by ELISA one month after the third dose of HPV-16/18 L1 AS04.

To demonstrate the non-inferiority of MenACWY-TT co-administered with HPV-16/18 L1 AS04 and Tdap compared to MenACWY-TT alone with respect to rSBA GMTs for serogroups A, C, W-135 and Y one month after vaccination.

To demonstrate the non-inferiority of HPV-16/18 L1 AS04 co-administered with MenACWY-TT and Tdap compared to HPV-16/18 L1 AS04 co-administered with Tdap in terms of HPV16 and HPV18 GMTs as measured by ELISA one month after the third dose of HPV-16

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	01 November 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Dominican Republic: 435
Country: Number of subjects enrolled	Estonia: 435
Country: Number of subjects enrolled	Thailand: 430
Worldwide total number of subjects	1300
EEA total number of subjects	435

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)	153
Adolescents (12-17 years)	606
Adults (18-64 years)	541
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix+Cervarix (1,2,7-Month) Group

Arm description:

Subjects in this group received 1 dose of Nimenrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 1, Month 2 and Month 7. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.

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

Dosage and administration details:

3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6/7, administered intramuscularly (IM) in the deltoid region of the arm.

Investigational medicinal product name	Nimenrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of Nimenrix vaccine at Month 0, administered intramuscularly (IM) in the deltoid region of the arm.

Arm title	Nimenrix+Cervarix (0,1,6-Month) Group
------------------	---------------------------------------

Arm description:

Subjects in this group received 1 dose of Nimenrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.

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

Dosage and administration details:

3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6/7, administered intramuscularly (IM) in the deltoid region of the arm.

Investigational medicinal product name	Nimenrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
1 dose of Nimenrix vaccine at Month 0, administered intramuscularly (IM) in the deltoid region of the arm.	
Arm title	Cervarix Group
Arm description:	
Subjects in this group received 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6, administered intramuscularly (IM) in the deltoid region of the arm.	
Arm type	Active comparator
Investigational medicinal product name	Cervarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6/7, administered intramuscularly (IM) in the deltoid region of the arm.	
Arm title	Nimenrix+Cervarix+Boostrix Group
Arm description:	
Subjects in this group received 1 dose each of Nimenrix and Boostrix vaccines at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. All vaccines were administered intramuscularly (IM) in the deltoid region of the arm.	
Arm type	Experimental
Investigational medicinal product name	Nimenrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
1 dose of Nimenrix vaccine at Month 0, administered intramuscularly (IM) in the deltoid region of the arm.	
Investigational medicinal product name	Cervarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6/7, administered intramuscularly (IM) in the deltoid region of the arm.	
Investigational medicinal product name	Boostrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
1 dose of Boostrix vaccine at Month 0, administered intramuscularly (IM) in the deltoid region of the arm.	
Arm title	Boostrix+Cervarix Group

Arm description:

Subjects in this group received 1 dose of Boostrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.

Arm type	Active comparator
Investigational medicinal product name	Boostrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of Boostrix vaccine at Month 0, administered intramuscularly (IM) in the deltoid region of the arm.

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

Dosage and administration details:

3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6/7, administered intramuscularly (IM) in the deltoid region of the arm.

Number of subjects in period 1	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group
Started	259	259	261
Completed	256	254	255
Not completed	3	5	6
Consent withdrawn by subject	1	3	2
Migrated/moved from study area	-	1	1
Unspecified	1	1	2
Lost to follow-up	1	-	1

Number of subjects in period 1	Nimenrix+Cervarix+ Boostrix Group	Boostrix+Cervarix Group
Started	260	261
Completed	254	255
Not completed	6	6
Consent withdrawn by subject	1	1
Migrated/moved from study area	1	1
Unspecified	4	2
Lost to follow-up	-	2

Baseline characteristics

Reporting groups

Reporting group title	Nimenrix+Cervarix (1,2,7-Month) Group
Reporting group description:	
Subjects in this group received 1 dose of Nimenrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 1, Month 2 and Month 7. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.	
Reporting group title	Nimenrix+Cervarix (0,1,6-Month) Group
Reporting group description:	
Subjects in this group received 1 dose of Nimenrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.	
Reporting group title	Cervarix Group
Reporting group description:	
Subjects in this group received 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6, administered intramuscularly (IM) in the deltoid region of the arm.	
Reporting group title	Nimenrix+Cervarix+Boostrix Group
Reporting group description:	
Subjects in this group received 1 dose each of Nimenrix and Boostrix vaccines at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. All vaccines were administered intramuscularly (IM) in the deltoid region of the arm.	
Reporting group title	Boostrix+Cervarix Group
Reporting group description:	
Subjects in this group received 1 dose of Boostrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.	

Reporting group values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group
Number of subjects	259	259	261
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	16.3	16.6	16.6
standard deviation	± 4.6	± 4.4	± 4.6
Gender categorical			
Units:			
Male	0	0	0
Female	259	259	261
Race/Ethnicity, Customized			
Units: Subjects			
African Heritage / African American	0	0	0
Asian - South East Asian Heritage	86	86	86
Other	86	87	88
White - Caucasian / European Heritage	87	86	87

Reporting group values	Nimenrix+Cervarix+Boostrix Group	Boostrix+Cervarix Group	Total
------------------------	----------------------------------	-------------------------	-------

Number of subjects	260	261	1300
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	16.6	16.6	
standard deviation	± 4.6	± 4.5	-
Gender categorical			
Units:			
Male	0	0	0
Female	260	261	1300
Race/Ethnicity, Customized			
Units: Subjects			
African Heritage / African American	1	0	1
Asian - South East Asian Heritage	86	86	430
Other	86	87	434
White - Caucasian / European Heritage	87	88	435

End points

End points reporting groups

Reporting group title	Nimenrix+Cervarix (1,2,7-Month) Group
Reporting group description: Subjects in this group received 1 dose of Nimenrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 1, Month 2 and Month 7. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.	
Reporting group title	Nimenrix+Cervarix (0,1,6-Month) Group
Reporting group description: Subjects in this group received 1 dose of Nimenrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.	
Reporting group title	Cervarix Group
Reporting group description: Subjects in this group received 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6, administered intramuscularly (IM) in the deltoid region of the arm.	
Reporting group title	Nimenrix+Cervarix+Boostrix Group
Reporting group description: Subjects in this group received 1 dose each of Nimenrix and Boostrix vaccines at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. All vaccines were administered intramuscularly (IM) in the deltoid region of the arm.	
Reporting group title	Boostrix+Cervarix Group
Reporting group description: Subjects in this group received 1 dose of Boostrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.	

Primary: Anti-Meningitis antibody titers by serum bactericidal assay using rabbit complement (rSBA)

End point title	Anti-Meningitis antibody titers by serum bactericidal assay using rabbit complement (rSBA) ^[1]
End point description: The analysis was performed for the serogroups -MenA, -MenC -MenW-135 and -MenY. Antibody titers, tabulated as geometric mean titers (GMTs), were obtained by serum bactericidal assay using rabbit complement. This analysis was only performed on groups receiving Nimenrix vaccine.	
End point type	Primary
End point timeframe: At one month after vaccination with Nimenrix (Month 1)	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The analysis was performed only on the groups receiving Nimenrix vaccine.

End point values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Nimenrix+Cervarix+Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	256	255	257	
Units: Titers				
geometric mean (confidence interval 95%)				

rSBA-MenA	5517.1 (4791.4 to 6352.6)	5523.5 (4913.2 to 6209.6)	4649.6 (4022.8 to 5374)	
rSBA-MenC	4277.3 (3604.3 to 5076.1)	5091 (4338.6 to 5973.8)	3598.6 (3004.2 to 4310.7)	
rSBA-MenW-135	14782.1 (12254.2 to 17831.5)	18068.3 (15381.6 to 21224.4)	11663.6 (9336.8 to 14570.2)	
rSBA-MenY	11871 (10542.3 to 13367.2)	12758.9 (11569.6 to 14070.5)	11201.2 (9678.7 to 12963.1)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Adjusted GMT ratio of the Nimenrix Group versus Nimenrix+Cervarix+Boostrix Group in terms of rSBA-MenA titers.	
Comparison groups	Nimenrix+Cervarix+Boostrix Group v Nimenrix+Cervarix (1,2,7-Month) Group
Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.43

Notes:

[2] - The non-inferiority criteria: the UL of the 2-sided standardised asymptotic 95% CI for the ratio of rSBA GMTs had to be below the pre-defined limit of 2.

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Adjusted GMT ratio of the Nimenrix Group versus Nimenrix+Cervarix Group in terms of rSBA-MenA titers.	
Comparison groups	Nimenrix+Cervarix (1,2,7-Month) Group v Nimenrix+Cervarix (0,1,6-Month) Group
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.21

Notes:

[3] - The non-inferiority criteria: the UL of the 2-sided standardised asymptotic 95% CI for the ratio of rSBA GMTs had to be below the pre-defined limit of 2.

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Adjusted GMT ratio of the Nimenrix Group versus Nimenrix+Cervarix+Boostrix Group in terms of rSBA-MenC titers.	
Comparison groups	Nimenrix+Cervarix+Boostrix Group v Nimenrix+Cervarix (1,2,7-Month) Group
Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[4]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.51

Notes:

[4] - The non-inferiority criteria: the UL of the 2-sided standardised asymptotic 95% CI for the ratio of rSBA GMTs had to be below the pre-defined limit of 2.

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Adjusted GMT ratio of the Nimenrix Group versus Nimenrix+Cervarix Group in terms of rSBA-MenC titers.	
Comparison groups	Nimenrix+Cervarix (1,2,7-Month) Group v Nimenrix+Cervarix (0,1,6-Month) Group
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[5]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.06

Notes:

[5] - The non-inferiority criteria: the UL of the 2-sided standardised asymptotic 95% CI for the ratio of rSBA GMTs had to be below the pre-defined limit of 2.

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Adjusted GMT ratio of the Nimenrix Group versus Nimenrix+Cervarix+Boostrix Group in terms of rSBA-MenW-135 titers.	
Comparison groups	Nimenrix+Cervarix+Boostrix Group v Nimenrix+Cervarix (1,2,7-Month) Group

Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[6]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.64

Notes:

[6] - The non-inferiority criteria: the UL of the 2-sided standardised asymptotic 95% CI for the ratio of rSBA GMTs had to be below the pre-defined limit of 2.

Statistical analysis title	Statistical analysis 6
-----------------------------------	------------------------

Statistical analysis description:

Adjusted GMT ratio of the Nimenrix Group versus Nimenrix+Cervarix Group in terms of rSBA-MenW-135 titers.

Comparison groups	Nimenrix+Cervarix (1,2,7-Month) Group v Nimenrix+Cervarix (0,1,6-Month) Group
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[7]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.07

Notes:

[7] - The non-inferiority criteria: the UL of the 2-sided standardised asymptotic 95% CI for the ratio of rSBA GMTs had to be below the pre-defined limit of 2.

Statistical analysis title	Statistical analysis 7
-----------------------------------	------------------------

Statistical analysis description:

Adjusted GMT ratio of the Nimenrix Group versus Nimenrix+Cervarix+Boostrix Group in terms of rSBA-MenY titers.

Comparison groups	Nimenrix+Cervarix+Boostrix Group v Nimenrix+Cervarix (1,2,7-Month) Group
Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[8]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.25

Notes:

[8] - The non-inferiority criteria: the UL of the 2-sided standardised asymptotic 95% CI for the ratio of rSBA GMTs had to be below the pre-defined limit of 2.

Statistical analysis title	Statistical analysis 8
Statistical analysis description: Adjusted GMT ratio of the Nimenrix Group versus Nimenrix+Cervarix Group in terms of rSBA-MenY titers.	
Comparison groups	Nimenrix+Cervarix (1,2,7-Month) Group v Nimenrix+Cervarix (0,1,6-Month) Group
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[9]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.12

Notes:

[9] - The non-inferiority criteria: the UL of the 2-sided standardised asymptotic 95% CI for the ratio of rSBA GMTs had to be below the pre-defined limit of 2.

Primary: Anti-HPV-16 and anti-HPV-18 concentrations

End point title	Anti-HPV-16 and anti-HPV-18 concentrations ^[10]
End point description: The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as ELISA units per milliliter (EU/mL).	
End point type	Primary
End point timeframe: At one month after the third dose of Cervarix (Month 7)	

Notes:

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

Justification: The analysis was performed only on the groups receiving Cervarix vaccine.

End point values	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group	Nimenrix+Cervarix+Boostrix Group	Boostrix+Cervarix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	248	249	244	247
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16	12124.9 (10564.5 to 13915.7)	11672.1 (10173.5 to 13391.4)	9563.8 (8262 to 11070.7)	11470.7 (10018.5 to 13133.5)
Anti-HPV-18	5234.1 (4573.9 to 5989.6)	5655 (4978.5 to 6423.4)	4306.2 (3748.3 to 4947.1)	5110 (4487 to 5819.6)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Adjusted GMT ratio of the Cervarix Group versus Nimenrix+Cervarix (0,1,6-Month) Group in terms of HPV-16 titers.	
Comparison groups	Cervarix Group v Nimenrix+Cervarix (0,1,6-Month) Group
Number of subjects included in analysis	497
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[11]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.16

Notes:

[11] - For HPV-16, one month after the third dose, the UL of the two-sided standardized asymptotic 95% CI on the group GMT ratio had to be below the pre-defined limit of 2.

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Adjusted GMT ratio of the Cervarix Group versus Nimenrix+Cervarix (0,1,6-Month) Group in terms of HPV-18 titers.	
Comparison groups	Cervarix Group v Nimenrix+Cervarix (0,1,6-Month) Group
Number of subjects included in analysis	497
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[12]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.29

Notes:

[12] - For HPV-18, one month after the third dose, the UL of the two-sided standardized asymptotic 95% CI on the group GMT ratio had to be below the pre-defined limit of 2.

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Adjusted GMT ratio of the Boostrix+Cervarix Group versus Nimenrix+Cervarix+Boostrix Group in terms of HPV-16 titers.	
Comparison groups	Boostrix+Cervarix Group v Nimenrix+Cervarix+Boostrix Group

Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[13]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.43

Notes:

[13] - For HPV-16, one month after the third dose, the UL of the two-sided standardized asymptotic 95% CI on the group GMT ratio had to be below the pre-defined limit of 2.

Statistical analysis title	Statistical analysis 4
-----------------------------------	------------------------

Statistical analysis description:

Adjusted GMT ratio of the Boostrix+Cervarix Group versus Nimenrix+Cervarix+Boostrix Group in terms of HPV-18 titers.

Comparison groups	Boostrix+Cervarix Group v Nimenrix+Cervarix+Boostrix Group
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[14]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.41

Notes:

[14] - For HPV-18, one month after the third dose, the UL of the two-sided standardized asymptotic 95% CI on the group GMT ratio had to be below the pre-defined limit of 2.

Primary: Number of subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) concentrations equal to or above (\geq) 1.0 IU/mL

End point title	Number of subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) concentrations equal to or above (\geq) 1.0 IU/mL ^[15]
-----------------	--

End point description:

The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as International Units per milliliter (IU/mL). This analysis was only performed in the groups receiving Boostrix vaccine.

End point type	Primary
----------------	---------

End point timeframe:

At one month after Boostrix vaccination (Month 1)

Notes:

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

Justification: The analysis was performed only on the groups receiving Boostrix vaccine.

End point values	Nimenrix+Cervarix+Boostrix Group	Boostrix+Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	250	256		
Units: Participants				
Anti-D	235	248		
Anti-T	249	256		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Adjusted GMC ratio of the Cervarix+Boostrix Group versus Nimenrix+Cervarix+Boostrix Group in terms of Anti-D titers	
Comparison groups	Boostrix+Cervarix Group v Nimenrix+Cervarix+Boostrix Group
Number of subjects included in analysis	506
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[16]
Parameter estimate	Adjusted GMT Ratio
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	1.6

Notes:

[16] - For anti-D the LL of the 2-sided standardised asymptotic 95% CI for the group difference (Co-ad group minus Boostrix group) had to be greater than or equal to the pre-defined limit of -10%.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Adjusted GMC ratio of the Cervarix+Boostrix Group versus Nimenrix+Cervarix+Boostrix Group in terms of Anti-D titers	
Comparison groups	Boostrix+Cervarix Group v Nimenrix+Cervarix+Boostrix Group
Number of subjects included in analysis	506
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[17]
Parameter estimate	Adjusted GMT ratio
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.23
upper limit	1.08

Notes:

[17] - For anti-T the LL of the 2-sided standardised asymptotic 95% CI for the group difference (Co-ad group minus Boostrix group) had to be greater than or equal to the pre-defined limit of -10%.

Primary: Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations ^[18]
-----------------	--

End point description:

The antibody concentrations were tabulated as geometric mean concentrations (GMCs) and expressed as international units per milliliter (IU/mL). GMCs were only analyzed in subjects receiving Boostrix vaccination.

End point type	Primary
----------------	---------

End point timeframe:

At one month after Boostrix vaccination (Month 1)

Notes:

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

Justification: The analysis was performed only on the groups receiving Boostrix vaccine.

End point values	Nimenrix+Cervarix+Boostrix Group	Boostrix+Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	247	256		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-PT	52.9 (46.4 to 60.4)	73.2 (65 to 82.5)		
Anti-FHA	278.7 (249.5 to 311.2)	472.4 (419.7 to 531.8)		
Anti-PRN	193.4 (159 to 235.1)	318.6 (262.4 to 386.8)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
----------------------------	------------------------

Statistical analysis description:

Adjusted GMT ratio of the Nimenrix+Cervarix+Boostrix Group versus Boostrix+ Cervarix Group in terms of anti-PRN titers

Comparison groups	Boostrix+Cervarix Group v Nimenrix+Cervarix+Boostrix Group
Number of subjects included in analysis	503
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[19]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	1.9

Notes:

[19] - For anti-PRN the UL of the 2-sided standardised asymptotic 95% CI for the adjusted group ratio of GMCs (Boostrix group/Co-ad group) had to be less than or equal to the pre-defined limit of 1.5

Statistical analysis title	Statistical analysis 2
----------------------------	------------------------

Statistical analysis description:

Adjusted GMT ratio of the Nimenrix+Cervarix Group versus Boostrix+ Cervarix Group in terms of anti-

FHA titers	
Comparison groups	Boostrix+Cervarix Group v Nimenrix+Cervarix+Boostrix Group
Number of subjects included in analysis	503
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[20]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	1.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.42
upper limit	1.93

Notes:

[20] - For anti-FHA the UL of the 2-sided standardised asymptotic 95% CI for the adjusted group ratio of GMCs (Boostrix group/Co-ad group) had to be less than or equal to the pre-defined limit of 1.5

Statistical analysis title	Statistical analysis 3
-----------------------------------	------------------------

Statistical analysis description:

Adjusted GMT ratio of the Nimenrix+Cervarix Group versus Boostrix+ Cervarix Group in terms of anti-PT titers

Comparison groups	Boostrix+Cervarix Group v Nimenrix+Cervarix+Boostrix Group
Number of subjects included in analysis	503
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[21]
Method	ANCOVA
Parameter estimate	Adjusted GMT Ratio
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	1.6

Notes:

[21] - For anti-PT the UL of the 2-sided standardised asymptotic 95% CI for the adjusted group ratio of GMCs (Boostrix group/Co-ad group) had to be less than or equal to the pre-defined limit of 1.5

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titres $\geq 1:8$ and $\geq 1:128$

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titres $\geq 1:8$ and $\geq 1:128$ ^[22]
-----------------	---

End point description:

The number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers $\geq 1:8$ and $\geq 1:128$ prior to and one month after vaccination with Nimenrix vaccine.

End point type	Secondary
----------------	-----------

End point timeframe:

Prior to and one month after vaccination with Nimenrix (Months 0 and 1)

Notes:

[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: The analysis was performed only on the groups receiving Nimenrix vaccine.

End point values	Nimenrix+Cerv arix (1,2,7- Month) Group	Nimenrix+Cerv arix (0,1,6- Month) Group	Nimenrix+Cerv arix+Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	256	255	257	
Units: Participants				
rSBA-MenA $\geq 1:8$, Month 0	112	118	129	
rSBA-MenC $\geq 1:8$, Month 0	34	29	40	
rSBA-MenW-135 $\geq 1:8$, Month 0	23	24	22	
rSBA-MenY $\geq 1:8$, Month 0	86	102	80	
rSBA-MenA $\geq 1:128$, Month 0	78	86	82	
rSBA-MenC $\geq 1:128$, Month 0	20	10	23	
rSBA-MenW-135 $\geq 1:128$, Month 0	22	23	20	
rSBA-MenY $\geq 1:128$, Month 0	84	99	74	
rSBA-MenA $\geq 1:8$, Month 1	255	255	255	
rSBA-MenC $\geq 1:8$, Month 1	254	253	253	
rSBA-MenW-135 $\geq 1:8$, Month 1	253	255	250	
rSBA-MenY $\geq 1:8$, Month 1	256	255	255	
rSBA-MenA $\geq 1:128$, Month 1	255	255	255	
rSBA-MenC $\geq 1:128$, Month 1	254	252	252	
rSBA-MenW-135 $\geq 1:128$, Month 1	253	255	250	
rSBA-MenY $\geq 1:128$, Month 1	256	255	255	

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY vaccine response

End point title	rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY vaccine response ^[23]
-----------------	--

End point description:

rSBA vaccine response for serogroups A, C, W-135 and Y was defined as: • For initially seronegative subjects (pre-vaccination titre below the cut-off of 1:8): number of subjects with rSBA antibody titres $\geq 1:32$ one month after vaccination. • For initially seropositive subjects (pre-vaccination titre $\geq 1:8$): number of subjects with rSBA antibody titres at least four times the pre-vaccination antibody titres, one month after vaccination.

End point type	Secondary
----------------	-----------

End point timeframe:

At one month after Nimenrix vaccination (Month 1)

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: The analysis was performed only on the groups receiving Nimenrix vaccine.

End point values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Nimenrix+Cervarix+Boostrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	256	255	256	
Units: Participants				
rSBA-MenA	240	235	230	
rSBA-MenC	250	251	246	
rSBA-MenW-135	252	255	248	
rSBA-MenY	245	253	251	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-T antibody concentrations ≥ 0.1 IU/mL and ≥ 1.0 IU/mL

End point title	Number of subjects with anti-T antibody concentrations ≥ 0.1 IU/mL and ≥ 1.0 IU/mL ^[24]
-----------------	--

End point description:

The antibody concentrations were tabulated as geometric mean concentrations (GMCs) and expressed as international units per milliliter (IU/mL), only for the Nimenrix+Cervarix (1,2,7-Month) Group.

End point type	Secondary
----------------	-----------

End point timeframe:

Prior to and one month after vaccination with Nimenrix (Months 0 and 1)

Notes:

[24] - 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: The analysis was performed only on the groups receiving Boostrix vaccine.

End point values	Nimenrix+Cervarix (1,2,7-Month) Group			
Subject group type	Reporting group			
Number of subjects analysed	255			
Units: Participants				
Anti-T ≥ 0.1 IU/mL, Month 0	236			
Anti-T ≥ 0.1 IU/mL, Month 1	255			
Anti-T ≥ 1 IU/mL, Month 0	151			
Anti-T ≥ 1 IU/mL, Month 1	253			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-T antibody concentrations

End point title	Anti-T antibody concentrations ^[25]
-----------------	--

End point description:

The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as international units per milliliter (IU/mL). This analysis was only performed for the Nimenrix+Cervarix (1,2,7-Month) Group.

End point type	Secondary
----------------	-----------

End point timeframe:

Prior to and one month after vaccination with Nimenrix (Months 0 and 1)

Notes:

[25] - 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: The analysis was performed only on the groups receiving Boostrix vaccine.

End point values	Nimenrix+Cervarix (1,2,7-Month) Group			
Subject group type	Reporting group			
Number of subjects analysed	255			
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-T, Month 0	1.2 (1 to 1.4)			
Anti-T, Month 1	25.4 (22.8 to 28.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-HPV-16 concentrations ≥ 19 EU/mL and anti-HPV-18 concentrations ≥ 18 EU/mL

End point title	Number of subjects with anti-HPV-16 concentrations ≥ 19 EU/mL and anti-HPV-18 concentrations ≥ 18 EU/mL ^[26]
-----------------	---

End point description:

The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as ELISA units per milliliter (EU/mL).

End point type	Secondary
----------------	-----------

End point timeframe:

Prior to the first dose and one month after the third dose of Cervarix [Month 0 and Month 7/Month 8 in Nimenrix+Cervarix (1,2,7-Month) Group]

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: The analysis was performed only on the groups receiving Cervarix vaccine.

End point values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group	Boostrix+Cervarix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	246	248	249	247
Units: Participants				
Anti-HPV-16, Month 0	17	29	32	22
Anti-HPV-16, Month 7/Month 8	245	248	249	247

Anti-HPV-18, Month 0	11	12	17	14
Anti-HPV-18, Month 7/Month 8	245	248	249	247

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for anti-HPV-16 and anti-HPV-18 antibodies

End point title	Number of subjects seroconverted for anti-HPV-16 and anti-HPV-18 antibodies
-----------------	---

End point description:

Seroconversion rate is defined as the appearance of antibodies (i.e. titers greater than or equal to the cut-off value) in the serum of subjects who are seronegative before vaccination. The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as ELISA units per milliliter (EU/mL).

End point type	Secondary
----------------	-----------

End point timeframe:

Prior to and one month after the third dose of Cervarix (Month 0 and Month 7/Month 8)

End point values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group	Nimenrix+Cervarix+Boostrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	235	236	232	230
Units: Participants				
Anti-HPV-16, Month 0	0	0	0	0
Anti-HPV-16, Month 7/Month 8	228	219	217	215
Anti-HPV-18, Month 0	0	0	0	0
Anti-HPV-18, Month 7/Month 8	234	236	232	230

End point values	Boostrix+Cervarix Group			
Subject group type	Reporting group			
Number of subjects analysed	233			
Units: Participants				
Anti-HPV-16, Month 0	0			
Anti-HPV-16, Month 7/Month 8	225			
Anti-HPV-18, Month 0	0			
Anti-HPV-18, Month 7/Month 8	233			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16 and anti-HPV-18 concentrations in Nimenrix+Cervarix (1,2,7-Month) Group

End point title	Anti-HPV-16 and anti-HPV-18 concentrations in Nimenrix+Cervarix (1,2,7-Month) Group ^[27]
-----------------	---

End point description:

The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as ELISA units per milliliter (EU/mL).

End point type	Secondary
----------------	-----------

End point timeframe:

Prior to and one month after the third dose of Cervarix (Months 0 and 8)

Notes:

[27] - 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: The analysis was performed only on the Nimenrix+Cervarix (1,2,7-Month) Group.

End point values	Nimenrix+Cervarix (1,2,7-Month) Group			
Subject group type	Reporting group			
Number of subjects analysed	246			
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16, Month 0	10.9 (10.2 to 11.6)			
Anti-HPV-16, Month 8	11128.2 (9471.8 to 13074.4)			
Anti-HPV-18, Month 0	9.8 (9.3 to 10.4)			
Anti-HPV-18, Month 8	5357 (4550.2 to 6306.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Booster responses for anti-PT, anti-FHA and anti-PRN antibodies

End point title	Booster responses for anti-PT, anti-FHA and anti-PRN antibodies ^[28]
-----------------	---

End point description:

Booster responses to the PT, FHA and PRN antigens were defined as: -For initially seronegative subjects (antibody concentrations: < 2.046 IU/ml for anti-FHA, < 2.187 IU/ml for anti-PRN, < 2.693 IU/ml for anti-PT), antibody concentration $\geq 4 \times \text{cut_off}$ IU/ml at Month 1 post-vaccination; -For initially seropositive subjects (antibody concentrations: ≥ 2.046 IU/ml for anti-FHA, ≥ 2.187 IU/ml for anti-PRN, ≥ 2.693 IU/ml for anti-PT) with pre-vaccination antibody concentration < $4 \times \text{cut_off}$ IU/ml : antibody concentration at Month 1 ≥ 4 fold the pre-vaccination antibody concentration; -For initially seropositive subjects (antibody concentrations: ≥ 2.046 IU/ml for anti-FHA, ≥ 2.187 IU/ml for anti-PRN, ≥ 2.693 IU/ml for anti-PT) with pre-vaccination antibody concentration $\geq 4 \times \text{cut_off}$ IU/ml : antibody concentration at Month 1 ≥ 2 fold the pre-vaccination antibody concentration.

End point type	Secondary
----------------	-----------

End point timeframe:

At one month after Boostrix vaccination (Month 1)

Notes:

[28] - 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: The analysis was performed only on the groups receiving Boostrix vaccine.

End point values	Boostrix+Cervarix Group			
Subject group type	Reporting group			
Number of subjects analysed	256			
Units: Participants				
Anti-PT	235			
Anti-FHA	247			
Anti-PRN	248			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-D and anti-T antibody concentrations ≥ 0.1 IU/mL

End point title	Number of subjects with anti-D and anti-T antibody concentrations ≥ 0.1 IU/mL ^[29]
-----------------	--

End point description:

The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as international units per milliliter (IU/mL).

End point type	Secondary
----------------	-----------

End point timeframe:

Prior to and one month after Boostrix vaccination (Month 0 and Month 1)

Notes:

[29] - 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: The analysis was performed only on the groups receiving Boostrix vaccine.

End point values	Nimenrix+Cervarix+Boostrix Group	Boostrix+Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	251	256		
Units: Participants				
Anti-D, Month 0	214	223		
Anti-D, Month 1	250	256		
Anti-T, Month 0	239	248		
Anti-T, Month 1	250	256		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D and anti-T antibody concentrations

End point title	Anti-D and anti-T antibody concentrations ^[30]
End point description: The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as international units per milliliter (IU/mL).	
End point type	Secondary
End point timeframe: Prior to and one month after Boostrix vaccination (Months 0 and 1)	

Notes:

[30] - 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: The analysis was performed only on the groups receiving Boostrix vaccine.

End point values	Nimenrix+Cervarix+Boostrix Group	Boostrix+Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	251	256		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D, Month 0	0.5 (0.4 to 0.5)	0.5 (0.4 to 0.6)		
Anti-D, Month 1	4.7 (4.2 to 5.2)	6.6 (5.9 to 7.4)		
Anti-T, Month 0	1.3 (1.1 to 1.5)	1.3 (1.1 to 1.5)		
Anti-T, Month 1	25.9 (23.4 to 28.8)	15.4 (14.1 to 16.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PT, anti-FHA and anti-PRN antibody concentrations equal to or above the cut-off value

End point title	Number of subjects with anti-PT, anti-FHA and anti-PRN antibody concentrations equal to or above the cut-off value ^[31]
End point description: The antibody concentrations were calculated as geometric mean concentrations (GMCs) and expressed as international units per milliliter (IU/mL). Anti-PT assay cut-off=2.693 IU/mL, anti-FHA assay cut-off=2.046 IU/mL, anti-PRN assay cut-off=2.187 IU/mL.	
End point type	Secondary
End point timeframe: Prior to and one month after Boostrix vaccination (Months 0 and 1)	

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: The analysis was performed only on the groups receiving Boostrix vaccine.

End point values	Nimenrix+Cervarix+Boostrix Group	Boostrix+Cervarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	251	256		
Units: Participants				
Anti-PT, Month 0	156	153		
Anti-PT, Month 1	240	252		
Anti-FHA, Month 0	235	256		
Anti-FHA, Month 1	247	256		
Anti-PRN, Month 0	218	229		
Anti-PRN, Month 1	246	256		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms

End point title	Number of subjects reporting solicited local symptoms
End point description:	
Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 50 millimeters (mm) of injection site. Symptoms were presented by vaccination site. Some groups do not have results for "Dose 2" because solicited local symptoms were not collected for these subjects at the Dose 2 timepoint.	
End point type	Secondary
End point timeframe:	
Days 0-6 following each vaccination	

End point values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group	Nimenrix+Cervarix+Boostrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	259	259	261	260
Units: Participants				
Any Pain (Nimenrix), Dose 1	152	140	0	156
Grade 3 Pain (Nimenrix), Dose 1	4	3	0	7
Any Pain (Boostrix), Dose 1	0	0	0	189
Grade 3 Pain (Boostrix), Dose 1	0	0	0	21
Any Pain (Cervarix), Dose 1	0	213	205	217
Grade 3 Pain (Cervarix), Dose 1	0	8	11	23
Any Redness (Nimenrix), Dose 1	57	42	0	54
Grade 3 Redness (Nimenrix), Dose 1	4	2	0	0
Any Redness (Boostrix), Dose 1	0	0	0	73
Grade 3 Redness (Boostrix), Dose 1	0	0	0	2
Any Redness (Cervarix), Dose 1	0	56	54	62
Grade 3 Redness (Cervarix), Dose 1	0	0	0	1
Any Swelling (Nimenrix), Dose 1	40	34	0	58
Grade 3 Swelling (Nimenrix), Dose 1	1	1	0	5

Any Swelling (Boostrix), Dose 1	0	0	0	79
Grade 3 Swelling (Boostrix), Dose 1	0	0	0	5
Any Swelling (Cervarix), Dose 1	0	42	37	64
Grade 3 Swelling (Cervarix), Dose 1	0	1	1	1
Any Pain (Cervarix), Dose 2	193	0	0	0
Grade 3 Pain (Cervarix), Dose 2	15	0	0	0
Any Redness (Cervarix), Dose 2	43	0	0	0
Grade 3 Redness (Cervarix), Dose 2	0	0	0	0
Any Swelling (Cervarix), Dose 2	41	0	0	0
Grade 3 Swelling (Cervarix), Dose 2	1	0	0	0
Any Pain (Nimenrix), Across doses	152	140	0	156
Grade 3 Pain (Nimenrix), Across doses	4	3	0	7
Any Pain (Boostrix), Across doses	0	0	0	189
Grade 3 Pain (Boostrix), Across doses	0	0	0	21
Any Pain (Cervarix), Across doses	193	213	205	217
Grade 3 Pain (Cervarix), Across doses	15	8	11	23
Any Redness (Nimenrix), Across doses	57	42	0	54
Grade 3 Redness (Nimenrix), Across doses	4	2	0	0
Any Redness (Boostrix), Across doses	0	0	0	73
Grade 3 Redness (Boostrix), Across doses	0	0	0	2
Any Redness (Cervarix), Across doses	43	56	54	62
Grade 3 Redness (Cervarix), Across doses	0	0	0	1
Any Swelling (Nimenrix), Across doses	40	34	0	58
Grade 3 Swelling (Nimenrix), Across doses	1	1	0	5
Any Swelling (Boostrix), Across doses	0	0	0	79
Grade 3 Swelling (Boostrix), Across doses	0	0	0	5
Any Swelling (Cervarix), Across doses	41	42	37	64
Grade 3 Swelling (Cervarix), Across doses	1	1	1	1

End point values	Boostrix+Cervarix Group			
Subject group type	Reporting group			
Number of subjects analysed	261			
Units: Participants				
Any Pain (Nimenrix), Dose 1	0			
Grade 3 Pain (Nimenrix), Dose 1	0			
Any Pain (Boostrix), Dose 1	200			
Grade 3 Pain (Boostrix), Dose 1	15			
Any Pain (Cervarix), Dose 1	221			
Grade 3 Pain (Cervarix), Dose 1	18			
Any Redness (Nimenrix), Dose 1	0			
Grade 3 Redness (Nimenrix), Dose 1	0			
Any Redness (Boostrix), Dose 1	53			
Grade 3 Redness (Boostrix), Dose 1	4			
Any Redness (Cervarix), Dose 1	48			

Grade 3 Redness (Cervarix), Dose 1	0			
Any Swelling (Nimenrix), Dose 1	0			
Grade 3 Swelling (Nimenrix), Dose 1	0			
Any Swelling (Boostrix), Dose 1	58			
Grade 3 Swelling (Boostrix), Dose 1	7			
Any Swelling (Cervarix), Dose 1	55			
Grade 3 Swelling (Cervarix), Dose 1	5			
Any Pain (Cervarix), Dose 2	0			
Grade 3 Pain (Cervarix), Dose 2	0			
Any Redness (Cervarix), Dose 2	0			
Grade 3 Redness (Cervarix), Dose 2	0			
Any Swelling (Cervarix), Dose 2	0			
Grade 3 Swelling (Cervarix), Dose 2	0			
Any Pain (Nimenrix), Across doses	0			
Grade 3 Pain (Nimenrix), Across doses	0			
Any Pain (Boostrix), Across doses	200			
Grade 3 Pain (Boostrix), Across doses	15			
Any Pain (Cervarix), Across doses	221			
Grade 3 Pain (Cervarix), Across doses	18			
Any Redness (Nimenrix), Across doses	0			
Grade 3 Redness (Nimenrix), Across doses	0			
Any Redness (Boostrix), Across doses	53			
Grade 3 Redness (Boostrix), Across doses	4			
Any Redness (Cervarix), Across doses	48			
Grade 3 Redness (Cervarix), Across doses	0			
Any Swelling (Nimenrix), Across doses	0			
Grade 3 Swelling (Nimenrix), Across doses	0			
Any Swelling (Boostrix), Across doses	58			
Grade 3 Swelling (Boostrix), Across doses	7			
Any Swelling (Cervarix), Across doses	55			
Grade 3 Swelling (Cervarix), Across doses	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general symptoms

End point title	Number of subjects reporting solicited general symptoms
End point description:	
Assessed solicited general symptoms were arthralgia, fatigue, gastrointestinal symptoms, headache, myalgia, rash, fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)] and urticaria. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.5 °C. Related = symptom assessed by the investigator as related to the vaccination. Some groups do not have results for "Dose 2" because solicited local symptoms were not collected for these subjects at the Dose 2 timepoint.	
End point type	Secondary

End point timeframe:

Days 0-6 following each vaccination

End point values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group	Nimenrix+Cervarix+Boostrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	259	257	259	260
Units: Participants				
Any Arthralgia, Dose 1	23	18	13	36
Grade 3 Arthralgia, Dose 1	0	1	1	1
Related Arthralgia, Dose 1	23	18	13	34
Any Fatigue, Dose 1	87	95	85	110
Grade 3 Fatigue, Dose 1	2	4	2	8
Related Fatigue, Dose 1	82	92	79	103
Any Gastrointestinal, Dose 1	21	27	23	29
Grade 3 Gastrointestinal, Dose 1	1	1	0	2
Related Gastrointestinal, Dose 1	19	27	21	26
Any Headache, Dose 1	82	94	78	99
Grade 3 Headache, Dose 1	5	3	5	5
Related Headache, Dose 1	81	89	73	92
Any Myalgia, Dose 1	65	83	85	96
Grade 3 Myalgia, Dose 1	0	4	6	9
Related Myalgia, Dose 1	60	81	82	92
Any Rash, Dose 1	4	8	8	6
Grade 3 Rash, Dose 1	0	0	0	0
Related Rash, Dose 1	1	6	7	6
Any Fever, Dose 1	24	32	15	38
Grade 3 Fever, Dose 1	0	0	0	0
Related Fever, Dose 1	21	31	14	37
Any Urticaria, Dose 1	0	4	4	5
Grade 3 Urticaria, Dose 1	0	0	0	0
Related Urticaria, Dose 1	0	3	4	5
Any Arthralgia, Dose 2	18	0	0	0
Grade 3 Arthralgia, Dose 2	0	0	0	0
Related Arthralgia, Dose 2	18	0	0	0
Any Fatigue, Dose 2	61	0	0	0
Grade 3 Fatigue, Dose 2	2	0	0	0
Related Fatigue, Dose 2	58	0	0	0
Any Gastrointestinal, Dose 2	10	0	0	0
Grade 3 Gastrointestinal, Dose 2	1	0	0	0
Related Gastrointestinal, Dose 2	8	0	0	0
Any Headache, Dose 2	58	0	0	0
Grade 3 Headache, Dose 2	3	0	0	0
Related Headache, Dose 2	55	0	0	0
Any Myalgia, Dose 2	73	0	0	0
Grade 3 Myalgia, Dose 2	4	0	0	0
Related Myalgia, Dose 2	72	0	0	0
Any Rash, Dose 2	3	0	0	0

Grade 3 Rash, Dose 2	0	0	0	0
Related Rash, Dose 2	3	0	0	0
Any Fever, Dose 2	11	0	0	0
Grade 3 Fever, Dose 2	0	0	0	0
Related Fever, Dose 2	10	0	0	0
Any Urticaria, Dose 2	2	0	0	0
Grade 3 Urticaria, Dose 2	0	0	0	0
Related Urticaria, Dose 2	2	0	0	0
Any Arthralgia, Across doses	34	18	13	36
Grade 3 Arthralgia, Across doses	0	1	1	1
Related Arthralgia, Across doses	34	18	13	34
Any Fatigue, Across doses	105	95	85	110
Grade 3 Fatigue, Across doses	4	4	2	8
Related Fatigue, Across doses	98	92	79	103
Any Gastrointestinal, Across doses	26	27	23	29
Grade 3 Gastrointestinal, Across doses	2	1	0	2
Related Gastrointestinal, Across doses	23	27	21	26
Any Headache, Across doses	101	94	78	99
Grade 3 Headache, Across doses	8	3	5	5
Related Headache, Across doses	99	89	73	92
Any Myalgia, Across doses	95	83	85	96
Grade 3 Myalgia, Across doses	4	4	6	9
Related Myalgia, Across doses	91	81	82	92
Any Rash, Across doses	7	8	8	6
Grade 3 Rash, Across doses	0	0	0	0
Related Rash, Across doses	4	6	7	6
Any Fever, Across doses	34	32	15	38
Grade 3 Fever, Across doses	0	0	0	0
Related Fever, Across doses	30	31	14	37
Any Urticaria, Across doses	2	4	4	5
Grade 3 Urticaria, Across doses	0	0	0	0
Related Urticaria, Across doses	2	3	4	5

End point values	Boostrix+Cervarix Group			
Subject group type	Reporting group			
Number of subjects analysed	261			
Units: Participants				
Any Arthralgia, Dose 1	23			
Grade 3 Arthralgia, Dose 1	4			
Related Arthralgia, Dose 1	23			
Any Fatigue, Dose 1	101			
Grade 3 Fatigue, Dose 1	5			
Related Fatigue, Dose 1	99			
Any Gastrointestinal, Dose 1	22			
Grade 3 Gastrointestinal, Dose 1	0			
Related Gastrointestinal, Dose 1	20			
Any Headache, Dose 1	95			
Grade 3 Headache, Dose 1	4			

Related Headache, Dose 1	85			
Any Myalgia, Dose 1	101			
Grade 3 Myalgia, Dose 1	9			
Related Myalgia, Dose 1	100			
Any Rash, Dose 1	6			
Grade 3 Rash, Dose 1	0			
Related Rash, Dose 1	4			
Any Fever, Dose 1	27			
Grade 3 Fever, Dose 1	0			
Related Fever, Dose 1	25			
Any Urticaria, Dose 1	5			
Grade 3 Urticaria, Dose 1	0			
Related Urticaria, Dose 1	3			
Any Arthralgia, Dose 2	0			
Grade 3 Arthralgia, Dose 2	0			
Related Arthralgia, Dose 2	0			
Any Fatigue, Dose 2	0			
Grade 3 Fatigue, Dose 2	0			
Related Fatigue, Dose 2	0			
Any Gastrointestinal, Dose 2	0			
Grade 3 Gastrointestinal, Dose 2	0			
Related Gastrointestinal, Dose 2	0			
Any Headache, Dose 2	0			
Grade 3 Headache, Dose 2	0			
Related Headache, Dose 2	0			
Any Myalgia, Dose 2	0			
Grade 3 Myalgia, Dose 2	0			
Related Myalgia, Dose 2	0			
Any Rash, Dose 2	0			
Grade 3 Rash, Dose 2	0			
Related Rash, Dose 2	0			
Any Fever, Dose 2	0			
Grade 3 Fever, Dose 2	0			
Related Fever, Dose 2	0			
Any Urticaria, Dose 2	0			
Grade 3 Urticaria, Dose 2	0			
Related Urticaria, Dose 2	0			
Any Arthralgia, Across doses	23			
Grade 3 Arthralgia, Across doses	4			
Related Arthralgia, Across doses	23			
Any Fatigue, Across doses	101			
Grade 3 Fatigue, Across doses	5			
Related Fatigue, Across doses	99			
Any Gastrointestinal, Across doses	22			
Grade 3 Gastrointestinal, Across doses	0			
Related Gastrointestinal, Across doses	20			
Any Headache, Across doses	95			
Grade 3 Headache, Across doses	4			
Related Headache, Across doses	85			
Any Myalgia, Across doses	101			
Grade 3 Myalgia, Across doses	9			
Related Myalgia, Across doses	100			

Any Rash, Across doses	6			
Grade 3 Rash, Across doses	0			
Related Rash, Across doses	4			
Any Fever, Across doses	27			
Grade 3 Fever, Across doses	0			
Related Fever, Across doses	25			
Any Urticaria, Across doses	5			
Grade 3 Urticaria, Across doses	0			
Related Urticaria, Across doses	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events AE(s)

End point title	Number of subjects with unsolicited adverse events AE(s)
-----------------	--

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

End point type	Secondary
----------------	-----------

End point timeframe:

During Days 0-30 following vaccination with Nimenrix, Boostrix or the first dose of Cervarix

End point values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group	Nimenrix+Cervarix+Boostrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	259	259	261	260
Units: Participants				
Participants	37	35	35	42

End point values	Boostrix+Cervarix Group			
Subject group type	Reporting group			
Number of subjects analysed	261			
Units: Participants				
Participants	39			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events SAE(s)

End point title	Number of subjects with serious adverse events SAE(s)
End point description: Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.	
End point type	Secondary
End point timeframe: During the entire study period (from Month 0 to Month 8)	

End point values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group	Nimenrix+Cervarix+Boostrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	259	259	261	260
Units: Participants				
Participants	3	2	5	7

End point values	Boostrix+Cervarix Group			
Subject group type	Reporting group			
Number of subjects analysed	261			
Units: Participants				
Participants	6			

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: pIMDs 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: During the entire study period (from Month 0 to Month 8)	

End point values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group	Nimenrix+Cervarix+Boostrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	259	259	261	260
Units: Participants				
Participants	0	0	0	0

End point values	Boostrix+Cervarix Group			
Subject group type	Reporting group			
Number of subjects analysed	261			
Units: Participants				
Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with new onset chronic illnesses (NOCIs)

End point title Number of subjects with new onset chronic illnesses (NOCIs)

End point description:

NOCIs include autoimmune disorders, asthma, type I diabetes, allergies.

End point type Secondary

End point timeframe:

During the entire study period (from Month 0 to Month 8)

End point values	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group	Nimenrix+Cervarix+Boostrix Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	259	259	261	260
Units: Participants				
Participants	3	0	1	0

End point values	Boostrix+Cervarix Group			
Subject group type	Reporting group			
Number of subjects analysed	261			
Units: Participants				
Participants	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: Days 0-6 following each vaccination, Unsolicited AEs: Days 0-30 following each vaccination; SAEs: throughout the whole study period (from Month 0 up to Month 8).

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	17.0
--------------------	------

Reporting groups

Reporting group title	Nimenrix+Cervarix (1,2,7-Month) Group
-----------------------	---------------------------------------

Reporting group description:

Subjects in this group received 1 dose of Nimenrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 1, Month 2 and Month 7. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.

Reporting group title	Nimenrix+Cervarix (0,1,6-Month) Group
-----------------------	---------------------------------------

Reporting group description:

Subjects in this group received 1 dose of Nimenrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.

Reporting group title	Cervarix Group
-----------------------	----------------

Reporting group description:

Subjects in this group received 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6, administered intramuscularly (IM) in the deltoid region of the arm.

Reporting group title	Nimenrix+Cervarix+Boostrix Group
-----------------------	----------------------------------

Reporting group description:

Subjects in this group received 1 dose each of Nimenrix and Boostrix vaccines at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. All vaccines were administered intramuscularly (IM) in the deltoid region of the arm.

Reporting group title	Boostrix+Cervarix Group
-----------------------	-------------------------

Reporting group description:

Subjects in this group received 1 dose of Boostrix vaccine at Month 0 and 3 doses of Cervarix vaccine at Month 0, Month 1 and Month 6. Both vaccines were administered intramuscularly (IM) in the deltoid region of the arm.

Serious adverse events	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 259 (1.16%)	2 / 259 (0.77%)	5 / 261 (1.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Stab wound			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Premature baby			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion incomplete			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion spontaneous			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 259 (0.39%)	0 / 259 (0.00%)	0 / 261 (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			
Pain in extremity			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 259 (0.77%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	0 / 259 (0.00%)	1 / 259 (0.39%)	2 / 261 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic inflammatory disease			

subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	1 / 261 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 259 (0.00%)	1 / 259 (0.39%)	0 / 261 (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
Metabolism and nutrition disorders			
Underweight			
subjects affected / exposed	0 / 259 (0.00%)	0 / 259 (0.00%)	0 / 261 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Nimenrix+Cervarix+Boostrix Group	Boostrix+Cervarix Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 260 (2.69%)	6 / 261 (2.30%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Stab wound			
subjects affected / exposed	0 / 260 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	1 / 260 (0.38%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Premature baby			
subjects affected / exposed	0 / 260 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Abortion incomplete			

subjects affected / exposed	1 / 260 (0.38%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous			
subjects affected / exposed	0 / 260 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 260 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 260 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic pain			
subjects affected / exposed	0 / 260 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 260 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			

subjects affected / exposed	1 / 260 (0.38%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 260 (0.38%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	2 / 260 (0.77%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 260 (0.38%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 260 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic inflammatory disease			
subjects affected / exposed	0 / 260 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 260 (0.00%)	0 / 261 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Underweight			
subjects affected / exposed	0 / 260 (0.00%)	1 / 261 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	Nimenrix+Cervarix (1,2,7-Month) Group	Nimenrix+Cervarix (0,1,6-Month) Group	Cervarix Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	232 / 259 (89.58%)	228 / 259 (88.03%)	222 / 261 (85.06%)
Nervous system disorders			
Headache			
subjects affected / exposed	103 / 259 (39.77%)	98 / 259 (37.84%)	78 / 261 (29.89%)
occurrences (all)	147	99	78
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	105 / 259 (40.54%)	95 / 259 (36.68%)	85 / 261 (32.57%)
occurrences (all)	148	95	85
Pain			
subjects affected / exposed	217 / 259 (83.78%)	220 / 259 (84.94%)	205 / 261 (78.54%)
occurrences (all)	345	220	205
Pyrexia			
subjects affected / exposed	35 / 259 (13.51%)	33 / 259 (12.74%)	16 / 261 (6.13%)
occurrences (all)	36	34	16
Swelling			
subjects affected / exposed	62 / 259 (23.94%)	54 / 259 (20.85%)	37 / 261 (14.18%)
occurrences (all)	81	54	37
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	26 / 259 (10.04%)	27 / 259 (10.42%)	23 / 261 (8.81%)
occurrences (all)	31	27	23
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	78 / 259 (30.12%)	68 / 259 (26.25%)	54 / 261 (20.69%)
occurrences (all)	100	68	54
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	34 / 259 (13.13%)	18 / 259 (6.95%)	13 / 261 (4.98%)
occurrences (all)	41	18	13
Myalgia			

subjects affected / exposed	95 / 259 (36.68%)	83 / 259 (32.05%)	85 / 261 (32.57%)
occurrences (all)	139	83	85

Non-serious adverse events	Nimenrix+Cervarix+Boostrix Group	Boostrix+Cervarix Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	236 / 260 (90.77%)	243 / 261 (93.10%)	
Nervous system disorders			
Headache			
subjects affected / exposed	102 / 260 (39.23%)	98 / 261 (37.55%)	
occurrences (all)	107	101	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	110 / 260 (42.31%)	101 / 261 (38.70%)	
occurrences (all)	110	101	
Pain			
subjects affected / exposed	228 / 260 (87.69%)	233 / 261 (89.27%)	
occurrences (all)	228	233	
Pyrexia			
subjects affected / exposed	39 / 260 (15.00%)	28 / 261 (10.73%)	
occurrences (all)	39	28	
Swelling			
subjects affected / exposed	98 / 260 (37.69%)	70 / 261 (26.82%)	
occurrences (all)	98	70	
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	29 / 260 (11.15%)	22 / 261 (8.43%)	
occurrences (all)	29	22	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	90 / 260 (34.62%)	64 / 261 (24.52%)	
occurrences (all)	90	64	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	36 / 260 (13.85%)	23 / 261 (8.81%)	
occurrences (all)	36	23	
Myalgia			

subjects affected / exposed	96 / 260 (36.92%)	101 / 261 (38.70%)	
occurrences (all)	96	101	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported