



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 | v3 (current) |
| This version publication date | 25 January 2018 |
| First version publication date | 17 June 2017 |
| Version creation reason | |

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 | 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.

| | |
|------------------|---------------------------------------|
| 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 |
| Pregnancy | 1 | 1 | 2 |
| Migrated/moved from study area | - | 1 | 1 |
| 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 |
| Pregnancy | 4 | 2 |
| Migrated/moved from study area | 1 | 1 |
| 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 |
| White - Caucasian / European Heritage | 87 | 86 | 87 |
| Other | 86 | 87 | 88 |

| 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 |
| White - Caucasian / European Heritage | 87 | 88 | 435 |
| Other | 86 | 87 | 434 |

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 5374.0) | |
| rSBA-MenC | 4277.3 (3604.3 to 5076.1) | 5091.0 (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 | 11871.0 (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 upper limit (UL) of the 2-sided standardised asymptotic 95% confidence interval (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 | 0.84 |
| 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 | 1.24 |

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 Enzyme-linked Immunosorbent Assay (ELISA) units per milliliter (EU/mL). | |
| End point type | Primary |
| End point timeframe: At one month after vaccination with 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 (8262.0 to 11070.7) | 11470.7 (10018.5 to 13133.5) |
| Anti-HPV-18 | 5234.1 (4573.9 to 5989.6) | 5655.0 (4978.5 to 6423.4) | 4306.2 (3748.3 to 4947.1) | 5110.0 (4487.0 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 | 1.15 |

Notes:

[11] - For HPV-16, one month after the third dose of Cervarix, 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 | 0.92 |
| upper limit | 1.29 |

Notes:

[12] - For HPV-18, one month after the third dose of Cervarix, 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 | 1.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.01 |
| upper limit | 1.43 |

Notes:

[13] - For HPV-16, one month after the third dose of Cervarix, 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 | 1.19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1 |
| upper limit | 1.41 |

Notes:

[14] - For HPV-18, one month after the third dose of Cervarix, 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: | |
| The group difference of the Nimenrix+Cervarix+Boostrix Group and Boostrix +Cervarix 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 | Difference between groups |
| Point estimate | -2.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.9 |
| upper limit | 0.81 |

Notes:

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

| Statistical analysis title | Statistical analysis 2 |
|---|--|
| Statistical analysis description: | |
| The group difference of the Nimenrix+Cervarix+Boostrix Group and Boostrix+Cervarix Group in terms of Anti-T 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 | Difference between groups |
| 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 (Nimenrix+Cervarix+Boostrix Group minus Boostrix +Cervarix Group) had to be greater than or equal to the pre-defined limit of -10%.

Primary: Anti-Pertussis Toxoid(anti-PT), anti-filamentous haemagglutinin (anti-

FHA) and anti-pertactin (anti-PRN) antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-Pertussis Toxoid(anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations ^[18] |
|-----------------|--|

End point description:

The antibody concentrations were tabulated as GMCs and expressed as 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, (N=245;254) | 52.9 (46.4 to 60.4) | 73.2 (65.0 to 82.5) | | |
| Anti-FHA, (N=247;256) | 278.7 (249.5 to 311.2) | 472.4 (419.7 to 531.8) | | |
| Anti-PRN, (N=246;256) | 193.4 (159.0 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 | 1.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.25 |
| upper limit | 1.87 |

Notes:

[19] - For anti-PRN the UL of the 2-sided standardised asymptotic 95% CI for the adjusted group ratio of GMCs (Nimenrix+Cervarix+Boostrix Group/Boostrix+Cervarix 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 (Nimenrix+Cervarix+Boostrix Group/Boostrix+Cervarix 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 | 1.61 |

Notes:

[21] - For anti-PT the UL of the 2-sided standardised asymptotic 95% CI for the adjusted group ratio of GMCs (Nimenrix+Cervarix+Boostrix Group/Boostrix+Cervarix 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+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: Participants | | | | |
| rSBA-MenA $\geq 1:8$, Month 0 (N=256;255;255) | 112 | 118 | 129 | |
| rSBA-MenC $\geq 1:8$, Month 0 (N=255;255;255) | 34 | 29 | 40 | |
| rSBA-MenW-135 $\geq 1:8$, Month 0 (N=256;255;256) | 23 | 24 | 22 | |
| rSBA-MenY $\geq 1:8$, Month 0 (N=255;255;256) | 86 | 102 | 80 | |
| rSBA-MenA $\geq 1:128$, Month 0 (N=256;255;255) | 78 | 86 | 82 | |
| rSBA-MenC $\geq 1:128$, Month 0 (N=255;255;255) | 20 | 10 | 23 | |
| rSBA-MenW-135 $\geq 1:128$, Month 0 (N=256;255;256) | 22 | 23 | 20 | |
| rSBA-MenY $\geq 1:128$, Month 0 (N=255;255;256) | 84 | 99 | 74 | |
| rSBA-MenA $\geq 1:8$, Month 1 (N=256;255;257) | 255 | 255 | 255 | |
| rSBA-MenC $\geq 1:8$, Month 1 (N=256;255;257) | 254 | 253 | 253 | |
| rSBA-MenW-135 $\geq 1:8$, Month 1 (N=256;255;257) | 253 | 255 | 250 | |
| rSBA-MenY $\geq 1:8$, Month 1 (N=256;255;257) | 256 | 255 | 255 | |
| rSBA-MenA $\geq 1:128$, Month 1 (N=256;255;257) | 255 | 255 | 255 | |
| rSBA-MenC $\geq 1:128$, Month 1 (N=256;255;257) | 254 | 252 | 252 | |
| rSBA-MenW-135 $\geq 1:128$, Month 1 (N=256;255;257) | 253 | 255 | 250 | |
| rSBA-MenY $\geq 1:128$, Month 1 (N=256;255;257) | 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, (N=256;255;255) | 240 | 235 | 230 | |
| rSBA-MenC, (N=255;255;255) | 250 | 251 | 246 | |
| rSBA-MenW-135, (N=256;255;256) | 252 | 255 | 248 | |
| rSBA-MenY, (N=255;255;256) | 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 GMCs and expressed as 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 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 | 255 | | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-T, Month 0 | 1.2 (1.0 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 GMCs and expressed as 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, (N=229;219;217;215;225) | 0 | 0 | 0 | 0 |
| Anti-HPV-16, Month 7/8, (N=229;219;217;215;225) | 228 | 219 | 217 | 215 |
| Anti-HPV-18, Month 0, (N=235;236;232;230;233) | 0 | 0 | 0 | 0 |
| Anti-HPV-18, Month 7/8. (N=235;236;232;230;233) | 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, (N=229;219;217;215;225) | 0 | | | |
| Anti-HPV-16, Month 7/8, (N=229;219;217;215;225) | 225 | | | |
| Anti-HPV-18, Month 0, (N=235;236;232;230;233) | 0 | | | |
| Anti-HPV-18, Month 7/8. (N=235;236;232;230;233) | 233 | | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|---|--|
| End point title | Anti-HPV-16 and anti-HPV-18 concentrations ^[27] |
| End point description: The antibody concentrations were calculated as GMCs and expressed as EU/mL, only for the Nimenrix+Cervarix (1,2,7-Month) Group. | |
| 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 | 5357.0 (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, (N=245;254) | 235 | | | |
| Anti-FHA, (N=247;256) | 247 | | | |
| Anti-PRN, (N=246;256) | 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, (N=249;254) | 214 | 223 | | |
| Anti-D, Month 1, (N=250;256) | 250 | 256 | | |
| Anti-T, Month 0, (N=251;256) | 239 | 248 | | |
| Anti-T, Month 1, (N=250;256) | 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, (N=249;254) | 0.5 (0.4 to 0.5) | 0.5 (0.4 to 0.6) | | |
| Anti-D, Month 1, (N=250;256) | 4.7 (4.2 to 5.2) | 6.6 (5.9 to 7.4) | | |
| Anti-T, Month 0, (N=251;256) | 1.3 (1.1 to 1.5) | 1.3 (1.1 to 1.5) | | |
| Anti-T, Month 1, (N=250;256) | 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 |
|-----------------|--|

End point description:

The antibody concentrations were calculated as GMCs and expressed as 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, (N=249;254) | 156 | 153 | | |
| Anti-PT, Month 1, (N=245;254) | 240 | 252 | | |
| Anti-FHA, Month 0, (N=251;256) | 235 | 244 | | |
| Anti-FHA, Month 1, (N=247;256) | 247 | 256 | | |
| Anti-PRN, Month 0, (N=250;256) | 218 | 229 | | |
| Anti-PRN, Month 1, (N=246;256) | 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 (Gr. 3) pain = significant pain at rest, pain that prevented normal every day activities. 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:

During the 7-day (Days 0-6) post-vaccination period following each dose and across doses

| 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, (N=259;257;0;260;0) | 152 | 140 | 0 | 156 |
| Gr.3 Pain (Nimenrix),Dose 1, (N=259;257;0;260;0) | 4 | 3 | 0 | 7 |
| Any Pain (Boostrix), Dose 1, (N=0;0;0;260;261) | 0 | 0 | 0 | 189 |
| Gr. 3 Pain (Boostrix), Dose 1, (N=0;0;0;260;261) | 0 | 0 | 0 | 21 |
| Any Pain (Cervarix), Dose 1, (N=0;257;259;260;261) | 0 | 213 | 205 | 217 |
| Gr.3 Pain (Cervarix), Dose 1,(N=0;257;259;260;261) | 0 | 8 | 11 | 23 |
| Any Redness (Nimenrix), Dose 1,(N=259;257;0;260;0) | 57 | 42 | 0 | 54 |
| Gr.3 Redness (Nimenrix),Dose 1,(N=259;257;0;260;0) | 4 | 2 | 0 | 0 |
| Any Redness (Boostrix), Dose 1, (N=0;0;0;260;261) | 0 | 0 | 0 | 73 |
| Gr. 3 Redness (Boostrix),Dose 1, (N=0;0;0;260;261) | 0 | 0 | 0 | 2 |
| Any Redness(Cervarix),Dose 1,(N=0;257;259;260;261) | 0 | 56 | 54 | 62 |
| Gr.3 Redness(Cervarix),Dose1,(N=0;257;259;260;261) | 0 | 0 | 0 | 1 |
| Any Swelling (Nimenrix),Dose 1,(N=259;257;0;260;0) | 40 | 34 | 0 | 58 |
| Gr.3 Swelling(Nimenrix),Dose 1,(N=259;257;0;260;0) | 1 | 1 | 0 | 5 |
| Any Swelling (Boostrix), Dose 1, (N=0;0;0;260;261) | 0 | 0 | 0 | 79 |
| Gr.3 Swelling (Boostrix),Dose 1,(N=0;0;0;260;261) | 0 | 0 | 0 | 5 |
| Any Swelling (Cerv.),Dose 1,(N=0;257;259;260;261) | 0 | 42 | 37 | 64 |
| Gr.3 Swelling (Cerv.),Dose 1,(N=0;257;259;260;261) | 0 | 1 | 1 | 1 |
| Any Pain (Cervarix), Dose 2, (N=258;0;0;0;0) | 193 | 0 | 0 | 0 |
| Gr. 3 Pain (Cervarix), Dose 2, (N=258;0;0;0;0) | 15 | 0 | 0 | 0 |
| Any Redness (Cervarix), Dose 2, (N=258;0;0;0;0) | 43 | 0 | 0 | 0 |
| Gr. 3 Redness (Cervarix), Dose 2,(N=258;0;0;0;0) | 0 | 0 | 0 | 0 |
| Any Swelling (Cervarix), Dose 2, (N=258;0;0;0;0) | 41 | 0 | 0 | 0 |
| Gr. 3 Swelling (Cervarix), Dose 2, (N=258;0;0;0;0) | 1 | 0 | 0 | 0 |
| Any Pain (Nimenrix), Across, (N=259;257;0;260;0) | 152 | 140 | 0 | 156 |
| Gr. 3 Pain (Nimenrix), Across, (N=259;257;0;260;0) | 4 | 3 | 0 | 7 |
| Any Pain (Boostrix), Across, (N=0;0;0;260;261) | 0 | 0 | 0 | 189 |
| Gr. 3 Pain (Boostrix), Across, (N=0;0;0;260;261) | 0 | 0 | 0 | 21 |

| | | | | |
|---|-----|-----|-----|-----|
| Any Pain (Cervarix),Across,(N=258;257;259;260 | 193 | 213 | 205 | 217 |
| Gr.3 Pain (Cervarix),Across,(N=258;257;259;260 | 15 | 8 | 11 | 23 |
| Any Redness (Nimenrix), Across,(N=259;257;0;260;0) | 57 | 42 | 0 | 54 |
| Gr.3 Redness (Nimenrix),Across,(N=259;257;0;260;0 | 4 | 2 | 0 | 0 |
| Any Redness (Boostrix), Across, (N=0;0;0;260;261) | 0 | 0 | 0 | 73 |
| Gr. 3 Redness (Boostrix), Across,(N=0;0;0;260;261) | 0 | 0 | 0 | 2 |
| Any Redness(Cerv.),Across,(N=258;257;259 | 43 | 56 | 54 | 62 |
| Gr.3 Redness(Cerv.),Across,(N=258;257;259 | 0 | 0 | 0 | 1 |
| Any Swelling (Nimenrix),Across,(N=259;257;0;260;0 | 40 | 34 | 0 | 58 |
| Gr.3 Swelling(Nimenrix),Across,(N=259;257; | 1 | 1 | 0 | 5 |
| Any Swelling (Boostrix), Across, (N=0;0;0;260;261) | 0 | 0 | 0 | 79 |
| Gr.3 Swelling (Boostrix),Across,(N=0;0;0;260;261) | 0 | 0 | 0 | 5 |
| Any Swelling(Cerv.),Across,(N=258;257;259 | 41 | 42 | 37 | 64 |
| Gr.3 Swelling(Cerv.),Across,(N=258;257;259 | 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, (N=259;257;0;260;0) | 0 | | | |
| Gr.3 Pain (Nimenrix),Dose 1, (N=259;257;0;260;0) | 0 | | | |
| Any Pain (Boostrix), Dose 1, (N=0;0;0;260;261) | 200 | | | |
| Gr. 3 Pain (Boostrix), Dose 1, (N=0;0;0;260;261) | 15 | | | |
| Any Pain (Cervarix), Dose 1, (N=0;257;259;260;261) | 221 | | | |
| Gr.3 Pain (Cervarix), Dose 1,(N=0;257;259;260;261) | 18 | | | |
| Any Redness (Nimenrix), Dose 1,(N=259;257;0;260;0) | 0 | | | |
| Gr.3 Redness (Nimenrix),Dose 1,(N=259;257;0;260;0) | 0 | | | |
| Any Redness (Boostrix), Dose 1, (N=0;0;0;260;261) | 53 | | | |
| Gr. 3 Redness (Boostrix),Dose 1, (N=0;0;0;260;261) | 4 | | | |
| Any Redness(Cervarix),Dose 1,(N=0;257;259;260;261) | 48 | | | |
| Gr.3 Redness(Cervarix),Dose1,(N=0;257;259 | 0 | | | |

| | | | | |
|--|-----|--|--|--|
| Any Swelling (Nimenrix),Dose 1,(N=259;257;0;260;0) | 0 | | | |
| Gr.3 Swelling(Nimenrix),Dose 1,(N=259;257;0;260;0) | 0 | | | |
| Any Swelling (Boostrix), Dose 1, (N=0;0;0;260;261) | 58 | | | |
| Gr.3 Swelling (Boostrix),Dose 1,(N=0;0;0;260;261) | 7 | | | |
| Any Swelling (Cerv.),Dose 1,(N=0;257;259;260;261) | 55 | | | |
| Gr.3 Swelling (Cerv.),Dose 1,(N=0;257;259;260;261) | 5 | | | |
| Any Pain (Cervarix), Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Gr. 3 Pain (Cervarix), Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Any Redness (Cervarix), Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Gr. 3 Redness (Cervarix), Dose 2,(N=258;0;0;0;0) | 0 | | | |
| Any Swelling (Cervarix), Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Gr. 3 Swelling (Cervarix), Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Any Pain (Nimenrix), Across, (N=259;257;0;260;0) | 0 | | | |
| Gr. 3 Pain (Nimenrix), Across, (N=259;257;0;260;0) | 0 | | | |
| Any Pain (Boostrix), Across, (N=0;0;0;260;261) | 200 | | | |
| Gr. 3 Pain (Boostrix), Across, (N=0;0;0;260;261) | 15 | | | |
| Any Pain (Cervarix),Across,(N=258;257;259;260) | 221 | | | |
| Gr.3 Pain (Cervarix),Across,(N=258;257;259;260) | 18 | | | |
| Any Redness (Nimenrix), Across,(N=259;257;0;260;0) | 0 | | | |
| Gr.3 Redness (Nimenrix),Across,(N=259;257;0;260;0) | 0 | | | |
| Any Redness (Boostrix), Across, (N=0;0;0;260;261) | 53 | | | |
| Gr. 3 Redness (Boostrix), Across,(N=0;0;0;260;261) | 4 | | | |
| Any Redness(Cerv.),Across,(N=258;257;259) | 48 | | | |
| Gr.3 Redness(Cerv.),Across,(N=258;257;259) | 0 | | | |
| Any Swelling (Nimenrix),Across,(N=259;257;0;260;0) | 0 | | | |
| Gr.3 Swelling(Nimenrix),Across,(N=259;257;0;260;0) | 0 | | | |
| Any Swelling (Boostrix), Across, (N=0;0;0;260;261) | 58 | | | |
| Gr.3 Swelling (Boostrix),Across,(N=0;0;0;260;261) | 7 | | | |
| Any Swelling(Cerv.),Across,(N=258;257;259) | 55 | | | |
| Gr.3 Swelling(Cerv.),Across,(N=258;257;259) | 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 (gastro.), 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 (Gr. 3) = 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:

During the 7-day (Days 0-6) post-vaccination period following each dose and across doses

| 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, (N=259;257;259;260;261) | 23 | 18 | 13 | 36 |
| Grade 3 Arthralgia, Dose 1, (N=259;257;259;260;261) | 0 | 1 | 1 | 1 |
| Related Arthralgia, Dose 1, (N=259;257;259;260;261) | 23 | 18 | 13 | 34 |
| Any Fatigue, Dose 1, (N=259;257;259;260;261) | 87 | 95 | 85 | 110 |
| Grade 3 Fatigue, Dose 1, (N=259;257;259;260;261) | 2 | 4 | 2 | 8 |
| Related Fatigue, Dose 1, (N=259;257;259;260;261) | 82 | 92 | 79 | 103 |
| Any Gastro., Dose 1, (N=259;257;259;260;261) | 21 | 27 | 23 | 29 |
| Grade 3 Gastro., Dose 1, (N=259;257;259;260;261) | 1 | 1 | 0 | 2 |
| Related Gastro., Dose 1, (N=259;257;259;260;261) | 19 | 27 | 21 | 26 |
| Any Headache, Dose 1, (N=259;257;259;260;261) | 82 | 94 | 78 | 99 |
| Grade 3 Headache, Dose 1, (N=259;257;259;260;261) | 5 | 3 | 5 | 5 |
| Related Headache, Dose 1, (N=259;257;259;260;261) | 81 | 89 | 73 | 92 |

| | | | | |
|---|----|----|----|----|
| Any Myalgia, Dose 1, (N=259;257;259;260;261) | 65 | 83 | 85 | 96 |
| Grade 3 Myalgia, Dose 1, (N=259;257;259;260;261) | 0 | 4 | 6 | 9 |
| Related Myalgia, Dose 1, (N=259;257;259;260;261) | 60 | 81 | 82 | 92 |
| Any Rash, Dose 1, (N=259;257;259;260;261) | 4 | 8 | 8 | 6 |
| Grade 3 Rash, Dose 1, (N=259;257;259;260;261) | 0 | 0 | 0 | 0 |
| Related Rash, Dose 1, (N=259;257;259;260;261) | 1 | 6 | 7 | 6 |
| Any Fever, Dose 1, (N=259;257;259;260;261) | 24 | 32 | 15 | 38 |
| Grade 3 Fever, Dose 1, (N=259;257;259;260;261) | 0 | 0 | 0 | 0 |
| Related Fever, Dose 1, (N=259;257;259;260;261) | 21 | 31 | 14 | 37 |
| Any Urticaria, Dose 1, (N=259;257;259;260;261) | 0 | 4 | 4 | 5 |
| Grade 3 Urticaria, Dose 1, (N=259;257;259;260;261) | 0 | 0 | 0 | 0 |
| Related Urticaria, Dose 1, (N=259;257;259;260;261) | 0 | 3 | 4 | 5 |
| Any Arthralgia, Dose 2, (N=258;0;0;0;0) | 18 | 0 | 0 | 0 |
| Grade 3 Arthralgia, Dose 2, (N=258;0;0;0;0) | 0 | 0 | 0 | 0 |
| Related Arthralgia, Dose 2, (N=258;0;0;0;0) | 18 | 0 | 0 | 0 |
| Any Fatigue, Dose 2, (N=258;0;0;0;0) | 61 | 0 | 0 | 0 |
| Grade 3 Fatigue, Dose 2, (N=258;0;0;0;0) | 2 | 0 | 0 | 0 |
| Related Fatigue, Dose 2, (N=258;0;0;0;0) | 58 | 0 | 0 | 0 |
| Any Gastro., Dose 2, (N=258;0;0;0;0) | 10 | 0 | 0 | 0 |
| Grade 3 Gastro., Dose 2, (N=258;0;0;0;0) | 1 | 0 | 0 | 0 |
| Related Gastro., Dose 2, (N=258;0;0;0;0) | 8 | 0 | 0 | 0 |
| Any Headache, Dose 2, (N=258;0;0;0;0) | 58 | 0 | 0 | 0 |
| Grade 3 Headache, Dose 2, (N=258;0;0;0;0) | 3 | 0 | 0 | 0 |
| Related Headache, Dose 2, (N=258;0;0;0;0) | 55 | 0 | 0 | 0 |
| Any Myalgia, Dose 2, (N=258;0;0;0;0) | 73 | 0 | 0 | 0 |
| Grade 3 Myalgia, Dose 2, (N=258;0;0;0;0) | 4 | 0 | 0 | 0 |
| Related Myalgia, Dose 2, (N=258;0;0;0;0) | 72 | 0 | 0 | 0 |
| Any Rash, Dose 2, (N=258;0;0;0;0) | 3 | 0 | 0 | 0 |
| Grade 3 Rash, Dose 2, (N=258;0;0;0;0) | 0 | 0 | 0 | 0 |
| Related Rash, Dose 2, (N=258;0;0;0;0) | 3 | 0 | 0 | 0 |
| Any Fever, Dose 2, (N=258;0;0;0;0) | 11 | 0 | 0 | 0 |
| Grade 3 Fever, Dose 2, (N=258;0;0;0;0) | 0 | 0 | 0 | 0 |
| Related Fever, Dose 2, (N=258;0;0;0;0) | 10 | 0 | 0 | 0 |
| Any Urticaria, Dose 2, (N=258;0;0;0;0) | 2 | 0 | 0 | 0 |

| | | | | |
|---|-----|----|----|-----|
| Grade 3 Urticaria, Dose 2, (N=258;0;0;0;0) | 0 | 0 | 0 | 0 |
| Related Urticaria, Dose 2, (N=258;0;0;0;0) | 2 | 0 | 0 | 0 |
| Any Arthralgia, Across, (N=259;257;259;260;261) | 34 | 18 | 13 | 36 |
| Grade 3 Arthralgia, Across,(N=259;257;259;260;261) | 0 | 1 | 1 | 1 |
| Related Arthralgia, Across,(N=259;257;259;260;261) | 34 | 18 | 13 | 34 |
| Any Fatigue, Across, (N=259;257;259;260;261) | 105 | 95 | 85 | 110 |
| Grade 3 Fatigue, Across, (N=259;257;259;260;261) | 4 | 4 | 2 | 8 |
| Related Fatigue, Across, (N=259;257;259;260;261) | 98 | 92 | 79 | 103 |
| Any Gastro., Across, (N=259;257;259;260;261) | 26 | 27 | 23 | 29 |
| Grade 3 Gastro., Across, (N=259;257;259;260;261) | 2 | 1 | 0 | 2 |
| Related Gastro., Across, (N=259;257;259;260;261) | 23 | 27 | 21 | 26 |
| Any Headache, Across, (N=259;257;259;260;261) | 101 | 94 | 78 | 99 |
| Grade 3 Headache, Across, (N=259;257;259;260;261) | 8 | 3 | 5 | 5 |
| Related Headache, Across, (N=259;257;259;260;261) | 99 | 89 | 73 | 92 |
| Any Myalgia, Across, (N=259;257;259;260;261) | 95 | 83 | 85 | 96 |
| Grade 3 Myalgia, Across, (N=259;257;259;260;261) | 4 | 4 | 6 | 9 |
| Related Myalgia, Across, (N=259;257;259;260;261) | 91 | 81 | 82 | 92 |
| Any Rash, Across, (N=259;257;259;260;261) | 7 | 8 | 8 | 6 |
| Grade 3 Rash, Across, (N=259;257;259;260;261) | 0 | 0 | 0 | 0 |
| Related Rash, Across, (N=259;257;259;260;261) | 4 | 6 | 7 | 6 |
| Any Fever, Across, (N=259;257;259;260;261) | 34 | 32 | 15 | 38 |
| Grade 3 Fever, Across, (N=259;257;259;260;261) | 0 | 0 | 0 | 0 |
| Related Fever, Across, (N=259;257;259;260;261) | 30 | 31 | 14 | 37 |
| Any Urticaria, Across, (N=259;257;259;260;261) | 2 | 4 | 4 | 5 |
| Grade 3 Urticaria, Across, (N=259;257;259;260;261) | 0 | 0 | 0 | 0 |
| Related Urticaria, Across, (N=259;257;259;260;261) | 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, (N=259;257;259;260;261) | 23 | | | |
| Grade 3 Arthralgia, Dose 1,(N=259;257;259;260;261) | 4 | | | |
| Related Arthralgia, Dose 1,(N=259;257;259;260;261) | 23 | | | |
| Any Fatigue, Dose 1, (N=259;257;259;260;261) | 101 | | | |
| Grade 3 Fatigue, Dose 1, (N=259;257;259;260;261) | 5 | | | |
| Related Fatigue, Dose 1, (N=259;257;259;260;261) | 99 | | | |
| Any Gastro., Dose 1, (N=259;257;259;260;261) | 22 | | | |
| Grade 3 Gastro., Dose 1, (N=259;257;259;260;261) | 0 | | | |
| Related Gastro., Dose 1, (N=259;257;259;260;261) | 20 | | | |
| Any Headache, Dose 1, (N=259;257;259;260;261) | 95 | | | |
| Grade 3 Headache, Dose 1, (N=259;257;259;260;261) | 4 | | | |
| Related Headache, Dose 1, (N=259;257;259;260;261) | 85 | | | |
| Any Myalgia, Dose 1, (N=259;257;259;260;261) | 101 | | | |
| Grade 3 Myalgia, Dose 1, (N=259;257;259;260;261) | 9 | | | |
| Related Myalgia, Dose 1, (N=259;257;259;260;261) | 100 | | | |
| Any Rash, Dose 1, (N=259;257;259;260;261) | 6 | | | |
| Grade 3 Rash, Dose 1, (N=259;257;259;260;261) | 0 | | | |
| Related Rash, Dose 1, (N=259;257;259;260;261) | 4 | | | |
| Any Fever, Dose 1, (N=259;257;259;260;261) | 27 | | | |
| Grade 3 Fever, Dose 1, (N=259;257;259;260;261) | 0 | | | |
| Related Fever, Dose 1, (N=259;257;259;260;261) | 25 | | | |
| Any Urticaria, Dose 1, (N=259;257;259;260;261) | 5 | | | |
| Grade 3 Urticaria, Dose 1, (N=259;257;259;260;261) | 0 | | | |
| Related Urticaria, Dose 1, (N=259;257;259;260;261) | 3 | | | |
| Any Arthralgia, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Grade 3 Arthralgia, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Related Arthralgia, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Any Fatigue, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Grade 3 Fatigue, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Related Fatigue, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Any Gastro., Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Grade 3 Gastro., Dose 2, (N=258;0;0;0;0) | 0 | | | |

| | | | | |
|---|-----|--|--|--|
| Related Gastro., Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Any Headache, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Grade 3 Headache, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Related Headache, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Any Myalgia, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Grade 3 Myalgia, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Related Myalgia, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Any Rash, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Grade 3 Rash, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Related Rash, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Any Fever, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Grade 3 Fever, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Related Fever, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Any Urticaria, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Grade 3 Urticaria, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Related Urticaria, Dose 2, (N=258;0;0;0;0) | 0 | | | |
| Any Arthralgia, Across, (N=259;257;259;260;261) | 23 | | | |
| Grade 3 Arthralgia, Across,(N=259;257;259;260;261) | 4 | | | |
| Related Arthralgia, Across,(N=259;257;259;260;261) | 23 | | | |
| Any Fatigue, Across, (N=259;257;259;260;261) | 101 | | | |
| Grade 3 Fatigue, Across, (N=259;257;259;260;261) | 5 | | | |
| Related Fatigue, Across, (N=259;257;259;260;261) | 99 | | | |
| Any Gastro., Across, (N=259;257;259;260;261) | 22 | | | |
| Grade 3 Gastro., Across, (N=259;257;259;260;261) | 0 | | | |
| Related Gastro., Across, (N=259;257;259;260;261) | 20 | | | |
| Any Headache, Across, (N=259;257;259;260;261) | 95 | | | |
| Grade 3 Headache, Across, (N=259;257;259;260;261) | 4 | | | |
| Related Headache, Across, (N=259;257;259;260;261) | 85 | | | |
| Any Myalgia, Across, (N=259;257;259;260;261) | 101 | | | |
| Grade 3 Myalgia, Across, (N=259;257;259;260;261) | 9 | | | |
| Related Myalgia, Across, (N=259;257;259;260;261) | 100 | | | |
| Any Rash, Across, (N=259;257;259;260;261) | 6 | | | |
| Grade 3 Rash, Across, (N=259;257;259;260;261) | 0 | | | |

| | | | | |
|---|----|--|--|--|
| Related Rash, Across, (N=259;257;259;260;261) | 4 | | | |
| Any Fever, Across, (N=259;257;259;260;261) | 27 | | | |
| Grade 3 Fever, Across, (N=259;257;259;260;261) | 0 | | | |
| Related Fever, Across, (N=259;257;259;260;261) | 25 | | | |
| Any Urticaria, Across, (N=259;257;259;260;261) | 5 | | | |
| Grade 3 Urticaria, Across, (N=259;257;259;260;261) | 0 | | | |
| Related Urticaria, Across, (N=259;257;259;260;261) | 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 the 31-day (Days 0-30) period 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:

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: during the 7-day (Days 0-6) period following each vaccination, Unsolicited AEs: during the 31-day (Days 0-30) period 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