



Clinical trial results:

Follow-up study to evaluate the long-term immunogenicity and safety of a HPV vaccine (580299) in healthy female subjects

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2008-000369-44 |
| Trial protocol | DE |
| Global end of trial date | 06 January 2015 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 11 May 2016 |
| First version publication date | 19 June 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 111375 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00877877 |
| 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 | Interim |
| Date of interim/final analysis | 21 January 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 06 January 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 January 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term immunogenicity of the HPV-16/18 vaccine by enzyme-linked immunosorbent assay (ELISA).

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 07 May 2008 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 10 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Colombia: 96 |
| Country: Number of subjects enrolled | Germany: 208 |
| Country: Number of subjects enrolled | Panama: 123 |
| Country: Number of subjects enrolled | Taiwan: 103 |
| Country: Number of subjects enrolled | Honduras: 102 |
| Worldwide total number of subjects | 632 |
| EEA total number of subjects | 208 |

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 | 0 |

| | |
|---------------------------|-----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 632 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects who participated in the primary study (NCT00196924) and received 3 doses of Cervarix.

Pre-assignment

Screening details:

Subjects enrolled in this study were primed with Cervarix vaccine as part of study NCT00196924. Subjects not returning for a specific visit were not withdrawn and could participate in the subsequent follow-up phases. Actual enrollment differed depending on the rate of return for the follow-up study, so not all subjects enrolled came to each visit.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Month 60 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|-----------|-------------------------|
| Arm title | Cervarix Month 60 Group |
|-----------|-------------------------|

Arm description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule.

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

Dosage and administration details:

All subjects received 3 doses of HPV vaccine intramuscularly into the deltoid region of the non-dominant arm.

| | |
|---|-------------------------|
| Number of subjects in period 1^[1] | Cervarix Month 60 Group |
| Started | 397 |
| Completed | 397 |

Notes:

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

Justification: Subjects not returning for a specific visit were not withdrawn and could participate in the subsequent follow-up phases. Actual enrolment differed depending on the rate of return for the follow-up study, so not all enrolled subjects came to each visit.

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Month 72 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|-------------------------|
| Arm title | Cervarix Month 72 Group |
|------------------|-------------------------|

Arm description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule.

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

Dosage and administration details:

All subjects received 3 doses of HPV vaccine intramuscularly into the deltoid region of the non-dominant arm.

| | |
|---------------------------------------|-------------------------|
| Number of subjects in period 2 | Cervarix Month 72 Group |
| Started | 397 |
| Completed | 529 |

| | |
|---|-----|
| Joined | 132 |
| Subject inconsistency in coming to study visits | 132 |

Period 3

| | |
|------------------------------|-------------------------|
| Period 3 title | Month 84 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|-------------------------|
| Arm title | Cervarix Month 84 Group |
|------------------|-------------------------|

Arm description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

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

Dosage and administration details:

All subjects received 3 doses of HPV vaccine intramuscularly into the deltoid region of the non-dominant arm.

| | |
|---|-------------------------|
| Number of subjects in period 3^[2] | Cervarix Month 84 Group |
| Started | 523 |
| Completed | 523 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects not returning for a specific visit were not withdrawn and could participate in the subsequent follow-up phases. Actual enrolment differed depending on the rate of return for the follow-up study, so not all enrolled subjects came to each visit.

Period 4

| | |
|------------------------------|-------------------------|
| Period 4 title | Month 96 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|-------------------------|
| Arm title | Cervarix Month 96 Group |
|------------------|-------------------------|

Arm description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule.

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

Dosage and administration details:

All subjects received 3 doses of HPV vaccine intramuscularly into the deltoid region of the non-dominant arm.

| | |
|---|-------------------------|
| Number of subjects in period 4^[3] | Cervarix Month 96 Group |
| Started | 522 |
| Completed | 522 |

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects not returning for a specific visit were not withdrawn and could participate in the subsequent follow-up phases. Actual enrolment differed depending on the rate of return for the follow-up study, so not all enrolled subjects came to each visit.

Period 5

| | |
|------------------------------|-------------------------|
| Period 5 title | Month 108 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|--------------------------|
| Arm title | Cervarix Month 108 Group |
|------------------|--------------------------|

Arm description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule.

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

Dosage and administration details:

All subjects received 3 doses of HPV vaccine intramuscularly into the deltoid region of the non-dominant arm.

| | |
|---|--------------------------|
| Number of subjects in period 5^[4] | Cervarix Month 108 Group |
| Started | 507 |
| Completed | 507 |

Notes:

[4] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects not returning for a specific visit were not withdrawn and could participate in the subsequent follow-up phases. Actual enrolment differed depending on the rate of return for the follow-up study, so not all enrolled subjects came to each visit.

Period 6

| | |
|------------------------------|-------------------------|
| Period 6 title | Month 120 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|--------------------------|
| Arm title | Cervarix Month 120 Group |
|------------------|--------------------------|

Arm description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule.

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

Dosage and administration details:

All subjects received 3 doses of HPV vaccine intramuscularly into the deltoid region of the non-dominant arm.

| | |
|---|--------------------------|
| Number of subjects in period 6^[5] | Cervarix Month 120 Group |
| Started | 495 |
| Completed | 495 |

Notes:

[5] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects not returning for a specific visit were not withdrawn and could participate in the subsequent follow-up phases. Actual enrolment differed depending on the rate of return for the follow-up study, so not all enrolled subjects came to each visit.

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | Month 60 |
|-----------------------|----------|

Reporting group description: -

| Reporting group values | Month 60 | Total | |
|---|----------|-------|--|
| Number of subjects | 397 | 397 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 0 | |
| Newborns (0-27 days) | | 0 | |
| Infants and toddlers (28 days-23 months) | | 0 | |
| Children (2-11 years) | | 0 | |
| Adolescents (12-17 years) | | 0 | |
| Adults (18-64 years) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 17.1 | | |
| standard deviation | ± 1.4 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 397 | 397 | |
| Male | 0 | 0 | |

End points

End points reporting groups

| | |
|--|--------------------------|
| Reporting group title | Cervarix Month 60 Group |
| Reporting group description: Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule. | |
| Reporting group title | Cervarix Month 72 Group |
| Reporting group description: Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule. | |
| Reporting group title | Cervarix Month 84 Group |
| Reporting group description: Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule. | |
| Reporting group title | Cervarix Month 96 Group |
| Reporting group description: Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule. | |
| Reporting group title | Cervarix Month 108 Group |
| Reporting group description: Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule. | |
| Reporting group title | Cervarix Month 120 Group |
| Reporting group description: Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule. | |

Primary: Number of seroconverted subjects with anti-HPV-16 antibody titers equal to or above 8 EL.U/mL

| | |
|---|--|
| End point title | Number of seroconverted subjects with anti-HPV-16 antibody titers equal to or above 8 EL.U/mL ^[1] |
| End point description: Anti-HPV-16 assay cut-off value was defined as 8 ELISA units per milliliter (EL.U/mL). Anti-HPV-18 assay cut-off value was defined as 7 EL.U/mL. Seroconversion was defined as the appearance of antibodies (i.e. titer greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. A seronegative subject is a subject with antibody titer < 8 or 7 EL.U/mL prior to vaccination. A seropositive subject is a subject with antibody titer ≥ 8 or 7 EL.U/mL prior to vaccination. | |
| End point type | Primary |
| End point timeframe: At Months 60, 72, 84, 96 and 108 | |
| Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted. | |

| End point values | Cervarix Month 96 Group | Cervarix Month 84 Group | Cervarix Month 72 Group | Cervarix Month 60 Group |
|-----------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 473 | 475 | 469 | 353 |
| Units: Subjects | | | | |
| anti-HPV-16 | 473 | 475 | 469 | 353 |

| End point values | Cervarix Month 108 Group | | | |
|-----------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 374 | | | |
| Units: Subjects | | | | |
| anti-HPV-16 | 372 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects with anti-HPV-18 antibody titers equal to or above 7 EL.U/mL

| | |
|-----------------|--|
| End point title | Number of seroconverted subjects with anti-HPV-18 antibody titers equal to or above 7 EL.U/mL ^[2] |
|-----------------|--|

End point description:

Anti-HPV-16 assay cut-off value was defined as 8 ELISA units per milliliter (EL.U/mL). Anti-HPV-18 assay cut-off value was defined as 7 EL.U/mL. Seroconversion was defined as the appearance of antibodies (i.e. titer greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. A seronegative subject is a subject with antibody titer < 8 or 7 EL.U/mL prior to vaccination. A seropositive subject is a subject with antibody titer ≥ 8 or 7 EL.U/mL prior to vaccination.

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

End point timeframe:

At Months 60, 72, 84, 96 and 108

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Cervarix Month 96 Group | Cervarix Month 84 Group | Cervarix Month 72 Group | Cervarix Month 60 Group |
|-----------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 477 | 473 | 478 | 358 |
| Units: Subjects | | | | |
| anti-HPV-18 | 477 | 473 | 478 | 358 |

| End point values | Cervarix Month 108 Group | | | |
|-----------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 370 | | | |

| | | | | |
|-----------------|-----|--|--|--|
| Units: Subjects | | | | |
| anti-HPV-18 | 368 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-human papillomavirus-16 (anti-HPV-16) antibody titers

| | |
|-----------------|---|
| End point title | Anti-human papillomavirus-16 (anti-HPV-16) antibody titers ^[3] |
|-----------------|---|

End point description:

Anti-HPV-16 and 18 antibody titers are given in Geometric Mean Titers (GMTs) in Enzyme-linked Immunosorbent Assay (ELISA) Units per milliliter (EL.U/mL).

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

End point timeframe:

At Months 60, 72, 84, 96 and 108

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Cervarix Month 96 Group | Cervarix Month 84 Group | Cervarix Month 72 Group | Cervarix Month 60 Group |
|--|-------------------------|---------------------------|---------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 499 | 494 | 502 | 376 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-HPV-16 | 1671 (1548.1 to 1803.7) | 1756.7 (1622.7 to 1901.7) | 1973.9 (1827.9 to 2131.6) | 2262.9 (2069.1 to 2475) |

| End point values | Cervarix Month 108 Group | | | |
|--|---------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 392 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-HPV-16 | 1946.5 (1779.7 to 2128.9) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-human papillomavirus-18 (anti-HPV-18) antibody titers

| | |
|-----------------|---|
| End point title | Anti-human papillomavirus-18 (anti-HPV-18) antibody titers ^[4] |
|-----------------|---|

End point description:

Anti-HPV-16 and 18 antibody titers are given in Geometric Mean Titers (GMTs) in Enzyme-linked Immunosorbent Assay (ELISA) Units per milliliter (EL.U/mL).

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

End point timeframe:

At months 60, 72, 84, 96 and 108

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Cervarix Month 96 Group | Cervarix Month 84 Group | Cervarix Month 72 Group | Cervarix Month 60 Group |
|--|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 499 | 494 | 502 | 376 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-HPV-18 | 679 (623.5 to 739.4) | 609.7 (559 to 664.9) | 762.8 (701 to 830.1) | 778.6 (703.1 to 862.1) |

| End point values | Cervarix Month 108 Group | | | |
|--|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 391 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-HPV-18 | 754 (685.4 to 829.4) | | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Number of subjects with serious adverse events (SAEs) ^[5] |
|-----------------|--|

End point description:

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

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

End point timeframe:

From Month 48 to 60 (at Month 60), 60 to 72 (at Month 72), 72 to 84 (at Month 84), 84 to 96 (at Month 96), 96 to 108 (at Month 108), 108 to 120 (at Month 120).

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Cervarix Month 96 Group | Cervarix Month 84 Group | Cervarix Month 72 Group | Cervarix Month 60 Group |
|-----------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 522 | 523 | 529 | 397 |
| Units: Subjects | | | | |
| SAEs | 8 | 20 | 20 | 9 |

| End point values | Cervarix Month 108 Group | Cervarix Month 120 Group | | |
|-----------------------------|--------------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 507 | 495 | | |
| Units: Subjects | | | | |
| SAEs | 15 | 6 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-HPV-16 antibody titers

| | |
|---|--|
| End point title | Anti-HPV-16 antibody titers ^[6] |
| End point description: | |
| Anti-HPV-16 assay cut-off value was defined as 8 ELISA units per milliliter (EL.U/mL). Anti-HPV-18 assay cut-off value was defined as 7 EL.U/mL. Seroconversion was defined as the appearance of antibodies (i.e. titer greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. A seronegative subject is a subject with antibody titer < 8 or 7 EL.U/mL prior to vaccination. A seropositive subject is a subject with antibody titer ≥ 8 or 7 EL.U/mL prior to vaccination. | |
| End point type | Primary |
| End point timeframe: | |
| At Month 120 | |

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Cervarix Month 120 Group | | | |
|--|---------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 416 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HPV-16 | 1607.9 (1480.8 to 1746.1) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects with HPV-16 antibody titers ≥ 8 EL.U/mL

| | |
|-----------------|--|
| End point title | Number of seroconverted subjects with HPV-16 antibody titers ≥ 8 EL.U/mL ^[7] |
|-----------------|--|

End point description:

Anti-HPV-16 assay cut-off value was defined as 8 ELISA units per milliliter (EL.U/mL). Anti-HPV-18 assay cut-off value was defined as 7 EL.U/mL. Seroconversion was defined as the appearance of antibodies (i.e. titer greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. A seronegative subject is a subject with antibody titer < 8 or 7 EL.U/mL prior to vaccination. A seropositive subject is a subject with antibody titer ≥ 8 or 7 EL.U/mL prior to vaccination.

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

End point timeframe:

At Month 120

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| | | | | |
|-----------------------------|--------------------------|--|--|--|
| End point values | Cervarix Month 120 Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 393 | | | |
| Units: Subjects | | | | |
| Anti-HPV-16 | 393 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects with HPV-18 antibody titers ≥ 7 EL.U/mL

| | |
|-----------------|--|
| End point title | Number of seroconverted subjects with HPV-18 antibody titers ≥ 7 EL.U/mL ^[8] |
|-----------------|--|

End point description:

Anti-HPV-16 assay cut-off value was defined as 8 ELISA units per milliliter (EL.U/mL). Anti-HPV-18 assay cut-off value was defined as 7 EL.U/mL. Seroconversion was defined as the appearance of antibodies (i.e. titer greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. A seronegative subject is a subject with antibody titer < 8 or 7 EL.U/mL prior to vaccination. A seropositive subject is a subject with antibody titer ≥ 8 or 7 EL.U/mL prior to vaccination.

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

End point timeframe:

At Month 120

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Cervarix Month 120 Group | | | |
|-----------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 395 | | | |
| Units: Subjects | | | | |
| Anti-HPV-18 | 395 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-HPV-18 antibody titers

| | |
|---|--|
| End point title | Anti-HPV-18 antibody titers ^[9] |
| End point description: Anti-HPV-16 assay cut-off value was defined as 8 ELISA units per milliliter (EL.U/mL). Anti-HPV-18 assay cut-off value was defined as 7 EL.U/mL. Seroconversion was defined as the appearance of antibodies (i.e. titer greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. A seronegative subject is a subject with antibody titer < 8 or 7 EL.U/mL prior to vaccination. A seropositive subject is a subject with antibody titer ≥ 8 or 7 EL.U/mL prior to vaccination. | |
| End point type | Primary |
| End point timeframe: At Month 120 | |

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | Cervarix Month 120 Group | | | |
|--|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 415 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HPV-18 | 608 (552.5 to 669.1) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Serious Adverse Events were assessed by time intervals: Months 48-60, Months 60-72, Months 72-84, Months 84-96, Months 96-108 and Months 108-120.

Adverse event reporting additional description:

Other (non-serious) Adverse Events were not collected/assessed during this long-term follow-up study.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Cervarix Group from Month 48 until Month 60 |
|-----------------------|---|

Reporting group description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule and for whom serious adverse events were collected from Month 48 until Month 60.

| | |
|-----------------------|---|
| Reporting group title | Cervarix Group from Month 60 until Month 72 |
|-----------------------|---|

Reporting group description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule and for whom serious adverse events were collected from Month 60 until Month 72.

| | |
|-----------------------|--|
| Reporting group title | Cervarix Group from Month 72 to Month 84 |
|-----------------------|--|

Reporting group description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule and for whom serious adverse events were collected from Month 72 until Month 84.

| | |
|-----------------------|--|
| Reporting group title | Cervarix Group from Month 84 to Month 96 |
|-----------------------|--|

Reporting group description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule and for whom serious adverse events were collected from Month 84 until Month 96.

| | |
|-----------------------|---|
| Reporting group title | Cervarix Group from Month 96 to Month 108 |
|-----------------------|---|

Reporting group description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule and for whom serious adverse events were collected from Month 96 until Month 108.

| | |
|-----------------------|--|
| Reporting group title | Cervarix Group from Month 108 to Month 120 |
|-----------------------|--|

Reporting group description:

Subjects in the Cervarix Group of the primary study (NCT00196924), who had then received 3 doses of Cervarix™ vaccine intramuscularly into the deltoid region of the non-dominant arm according to a 0, 1, 6 month vaccination schedule and for whom serious adverse events were collected from Month 108 to Month 120.

Notes:

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

Justification: Only serious adverse event were collected for this study.

| Serious adverse events | Cervarix Group from Month 48 until Month 60 | Cervarix Group from Month 60 until Month 72 | Cervarix Group from Month 72 to Month 84 |
|---|---|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 397 (2.27%) | 20 / 529 (3.78%) | 20 / 523 (3.82%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Ovarian germ cell teratoma benign | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |
| Fibroadenoma of breast | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian neoplasm | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Hodgkin's disease | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Hypovolaemic shock | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous complete | | | |
| subjects affected / exposed | 1 / 397 (0.25%) | 0 / 529 (0.00%) | 0 / 523 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abortion spontaneous incomplete | | | |
| subjects affected / exposed | 1 / 397 (0.25%) | 3 / 529 (0.57%) | 2 / 523 (0.38%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Threatened labour | | | |
| subjects affected / exposed | 1 / 397 (0.25%) | 1 / 529 (0.19%) | 0 / 523 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pre-eclampsia | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |
| Oligohydramnios | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 2 / 523 (0.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foetal death | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Cervical incompetence | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Gestational diabetes | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Premature baby | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Stillbirth | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 397 (0.25%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Ovarian cyst ruptured | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Neonatal tachypnoea | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 asphyxia | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Neonatal respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Psychiatric disorders | | | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |
| Depression | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Drug abuse | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Injury, poisoning and procedural complications | | | |
| Alcohol poisoning | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |
| Burns third degree | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |
| Multiple injuries | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 2 / 523 (0.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stab wound | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal injury | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Ligament rupture | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Contusion | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Excoriation | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 | | | |
| Skull malformation | | | |
| subjects affected / exposed | 1 / 397 (0.25%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Congenital megaureter | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Talipes | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Heart disease congenital | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Pulmonary malformation | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Nervous system disorders | | | |
| Brain injury | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Cerebral cyst | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Tension headache | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Gastrointestinal disorders | | | |
| Duodenal ulcer | | | |
| subjects affected / exposed | 1 / 397 (0.25%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulum intestinal | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coeliac disease | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Irritable bowel syndrome | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 1 / 397 (0.25%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 397 (0.25%) | 1 / 529 (0.19%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis | | | |
| subjects affected / exposed | 1 / 397 (0.25%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 397 (0.25%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Dengue fever | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 397 (0.00%) | 2 / 529 (0.38%) | 0 / 523 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngeal abscess | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 2 / 529 (0.38%) | 0 / 523 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast abscess | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |
| Chronic sinusitis | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |
| Endometritis | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |
| Endometritis decidual | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 1 / 523 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Pilonidal cyst | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Pneumonia mycoplasmal | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (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 |
| Metabolism and nutrition disorders | | | |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 1 / 529 (0.19%) | 0 / 523 (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 |

| Serious adverse events | Cervarix Group from Month 84 to Month 96 | Cervarix Group from Month 96 to Month 108 | Cervarix Group from Month 108 to Month 120 |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 522 (1.53%) | 15 / 507 (2.96%) | 6 / 495 (1.21%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Ovarian germ cell teratoma benign | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Fibroadenoma of breast | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Ovarian neoplasm | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Hodgkin's disease | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 1 / 495 (0.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 522 (0.19%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 | | | |
| Abortion spontaneous complete | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 incomplete | | | |
| subjects affected / exposed | 1 / 522 (0.19%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Threatened labour | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Pre-eclampsia | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Oligohydramnios | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Foetal death | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Cervical incompetence | | | |
| subjects affected / exposed | 1 / 522 (0.19%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Gestational diabetes | | | |
| subjects affected / exposed | 1 / 522 (0.19%) | 0 / 507 (0.00%) | 0 / 495 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abortion spontaneous | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 1 / 495 (0.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Premature baby | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Stillbirth | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Ovarian cyst ruptured | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Neonatal tachypnoea | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 1 / 495 (0.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Neonatal asphyxia | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Neonatal respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Psychiatric disorders | | | |
| Suicide attempt | | | |
| subjects affected / exposed | 1 / 522 (0.19%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Depression | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Drug abuse | | | |
| subjects affected / exposed | 1 / 522 (0.19%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Injury, poisoning and procedural complications | | | |
| Alcohol poisoning | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Burns third degree | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Multiple injuries | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Stab wound | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Abdominal injury | | | |
| subjects affected / exposed | 1 / 522 (0.19%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Ligament rupture | | | |
| subjects affected / exposed | 1 / 522 (0.19%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Contusion | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Excoriation | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Congenital, familial and genetic disorders | | | |
| Skull malformation | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 megaureter | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Talipes | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Heart disease congenital | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Pulmonary malformation | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Brain injury | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Cerebral cyst | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Syncope | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Tension headache | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Duodenal ulcer | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Diverticulum intestinal | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Coeliac disease | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Irritable bowel syndrome | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 1 / 495 (0.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Pharyngeal abscess | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Breast abscess | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Chronic sinusitis | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Endometritis | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Endometritis decidual | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 522 (0.38%) | 0 / 507 (0.00%) | 1 / 495 (0.20%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 1 / 522 (0.19%) | 0 / 507 (0.00%) | 0 / 495 (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 |
| Pilonidal cyst | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 1 / 507 (0.20%) | 0 / 495 (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 |
| Pneumonia mycoplasmal | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 1 / 495 (0.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (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 |

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

| Non-serious adverse events | Cervarix Group from Month 48 until Month 60 | Cervarix Group from Month 60 until Month 72 | Cervarix Group from Month 72 to Month 84 |
|---|---|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 397 (0.00%) | 0 / 529 (0.00%) | 0 / 523 (0.00%) |

| Non-serious adverse events | Cervarix Group from Month 84 to Month 96 | Cervarix Group from Month 96 to Month 108 | Cervarix Group from Month 108 to Month 120 |
|---|--|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 522 (0.00%) | 0 / 507 (0.00%) | 0 / 495 (0.00%) |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 02 December 2013 | <p>The HPV-025 protocol was amended for the following reasons:</p> <p>The assay used to measure anti-HPV-16/-18 antibody concentrations at the designated laboratory was improved to increase the assay precision by changing the assay cut-off value from 8 EL.U/mL to 19 EL.U/mL for HPV-16 and from 7 EL.U/mL to 18 EL.U/mL for HPV-18. This change in the assay will be implemented for the testing of samples from Month 96 (Year 8) onwards.</p> <p>The number of subjects who were enrolled in the immunogenicity subset of the primary study HPV-013, received three doses of HPV vaccine and participated in the follow-up study Ext HPV-013 was erroneously mentioned as 626 subjects. This has now been corrected to 625 subjects. The total number of subjects in the Ext HPV-013 study was corrected to 1244 subjects.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported