# Clinical trial results:
# A Safety and Immunogenicity Study of Quadrivalent HPV (Types 6, 11, 16, 18) L1 Virus-Like Particle (VLP) Vaccine in Preadolescents and Adolescents (Base Study). A Long Term Immunogenicity, Safety, and Effectiveness Study of GARDASIL™ (Human Papillomavirus [Types 6, 11, 16, 18] Recombinant Vaccine) Among Adolescents Who Received GARDASIL at 9-18 Years of Age (Extension Study)

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

## Summary

| | |
|---|---|
| EudraCT number | 2014-005717-23 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 01 June 2015 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 06 February 2016 |
| First version publication date | 06 February 2016 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | V501-018 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00092547 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., +1 1-800-672-6371, ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., +1 1-800-672-6371, ClinicalTrialsDisclosure@merck.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 | 01 June 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 03 November 2005 |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 June 2015 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

This study is to evaluate the safety, tolerability, and immune response of an investigational vaccine in preadolescent and adolescent boys and girls for the prevention of Human Papilloma Virus (HPV).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

The following additional measure defined for this study was in place for the protection of trial participants: Participants who received placebo vaccine in the base study were offered a complete 3-dose qHPV vaccine regimen in the extension study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 08 October 2003 |
| 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 | Colombia: 171 |
| Country: Number of subjects enrolled | Denmark: 161 |
| Country: Number of subjects enrolled | United States: 740 |
| Country: Number of subjects enrolled | Mexico: 146 |
| Country: Number of subjects enrolled | Norway: 34 |
| Country: Number of subjects enrolled | Portugal: 9 |
| Country: Number of subjects enrolled | Spain: 90 |
| Country: Number of subjects enrolled | Taiwan: 52 |
| Country: Number of subjects enrolled | Thailand: 160 |
| Country: Number of subjects enrolled | United Kingdom: 218 |
| Worldwide total number of subjects | 1781 |
| EEA total number of subjects | 512 |

Notes:

| Subjects enrolled per age group | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 1781 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

1781 participants were randomized to receive qHPV or Placebo in the Base Study. At Month 30, participants who received Placebo in the Base Study were eligible to receive qHPV, and formed the Extension Group. Participants were to be followed for safety and efficacy for up to 10 years. Abbreviations: D=Day; M=Month.

### Pre-assignment

Screening details:

The study enrolled healthy preadolescents and adolescents aged 9 to 15 years of age.

### Period 1

| | |
|---|---|
| Period 1 title | Base Study Vaccine Phase (D1 to M7) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | qHPV Vaccine in Base Study |

Arm description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| | |
|---|---|
| **Arm title** | Placebo in Base Study |

Arm description:

Represents participants who were randomized into the Placebo Group, who received three 0.5 mL intramuscular injections of placebo at Day 1, Month 2, and Month 6.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| Number of subjects in period 1 | qHPV Vaccine in Base Study | Placebo in Base Study |
|---|---|---|
| Started | 1184 | 597 |
| Vaccinated in Base Study | 1179 | 596 |
| Completed | 1121 | 561 |
| Not completed | 63 | 36 |
| Refused Vaccination | 5 | 3 |
| per sponsor request: (noncompliant) | - | 1 |
| Consent withdrawn by subject | 28 | 21 |
| Not Vaccinated | 5 | 1 |
| Adverse event, non-fatal | 4 | 1 |
| Lost to follow-up | 18 | 7 |
| Moved | 3 | 1 |
| Did not meet local regulations | - | 1 |

## Period 2

| | |
|---|---|
| Period 2 title | Base Study Follow-up Phase (M7 to M18) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | qHPV Vaccine in Base Study |

Arm description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered between Month 7 and 18.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| | |
|---|---|
| **Arm title** | Placebo in Base Study |

Arm description:

Represents participants who were randomized into the Placebo Group, who received three 0.5 mL intramuscular injections of placebo at Day 1, Month 2, and Month 6. No study treatment was administered between Month 7 and 18.

| | |
|---|---|
| Arm type | Placebo |

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| **Number of subjects in period 2** | qHPV Vaccine in Base Study | Placebo in Base Study |
|---|---|---|
| Started | 1121 | 561 |
| Completed | 1108 | 551 |
| Not completed | 20 | 14 |
| Physician decision | 1 | - |
| Consent withdrawn by subject | 4 | 2 |
| Subject moved | 1 | 5 |
| Lost to follow-up | 13 | 7 |
| Protocol deviation | 1 | - |
| Joined | 7 | 4 |
| Previously discontinued and re-entered study | 7 | 4 |

## Period 3

| | |
|---|---|
| Period 3 title | Base Study Follow-up Phase (M18 to M30) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | qHPV Vaccine in Base Study |

Arm description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered between Month 18 and 30.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| **Arm title** | Placebo in Base Study |
|---|---|

Arm description:

Represents participants who were randomized into the Placebo Group, who received three 0.5 mL intramuscular injections of placebo at Day 1, Month 2, and Month 6. No study treatment was administered between Month 18 and 30.

| Arm type | Placebo |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| **Number of subjects in period 3[1]** | qHPV Vaccine in Base Study | Placebo in Base Study |
|---|---|---|
| Started | 964 | 490 |
| Completed | 956 | 485 |
| Not completed | 8 | 5 |
| Consent withdrawn by subject | 1 | 3 |
| Subject moved | 4 | 2 |
| Lost to follow-up | 2 | - |
| Protocol deviation | 1 | - |

Notes:

[1] - 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: Includes participants who re-entered the study

## Period 4

| Period 4 title | Ext Study Vaccine Phase (M30 to M37) |
|---|---|
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

## Arms

| Are arms mutually exclusive? | Yes |
|---|---|
| **Arm title** | qHPV Vaccine in Base Study |

Arm description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered between Month 30 and 37.

| Arm type | Experimental |
|---|---|
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| **Arm title** | qHPV Vaccine in Extension Study |
|---|---|

Arm description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| | |
|---|---|
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Month 30, 32, and 36

| **Number of subjects in period 4** | qHPV Vaccine in Base Study | qHPV Vaccine in Extension Study |
|---|---|---|
| Started | 956 | 485 |
| Vaccinated in Extension Study | 0 [2] | 482 |
| Completed | 933 | 469 |
| Not completed | 23 | 16 |
| Consent withdrawn by subject | 6 | 9 |
| Subject moved | 3 | - |
| Lost to follow-up | 14 | 7 |

Notes:

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Includes participants who re-entered the study

## Period 5

| | |
|---|---|
| Period 5 title | Long-term Follow-up (M42 visit) |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |

| **Arm title** | qHPV Vaccine in Base Study |
|---|---|

Arm description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered at the Month 42 visit.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| **Arm title** | qHPV Vaccine in Extension Study |
|---|---|

Arm description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36. No study treatment was administered at the Month 42 visit.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| | |
|---|---|
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Month 30, 32, and 36

| **Number of subjects in period 5[3]** | qHPV Vaccine in Base Study | qHPV Vaccine in Extension Study |
|---|---|---|
| Started | 612 | 308 |
| Completed | 611 | 308 |
| Not completed | 1 | 0 |
| Adverse event, non-fatal | 1 | - |

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: Includes participants who re-entered the study

## Period 6

| | |
|---|---|
| Period 6 title | Long-term Follow-up (M72 visit) |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | qHPV Vaccine in Base Study |

Arm description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered at the Month 72 visit.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| | |
|---|---|
| **Arm title** | qHPV Vaccine in Extension Study |

Arm description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36. No study treatment was administered at the Month 72 visit.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Month 30, 32, and 36

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| Number of subjects in period 6[4] | qHPV Vaccine in Base Study | qHPV Vaccine in Extension Study |
|---|---|---|
| Started | 550 | 276 |
| Completed | 550 | 276 |

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: Includes participants who re-entered the study

## Period 7

| | |
|---|---|
| Period 7 title | Long-term Follow-up (M96 visit) |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | qHPV Vaccine in Base Study |

Arm description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered at the Month 96 visit.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| | |
|---|---|
| **Arm title** | qHPV Vaccine in Extension Study |

Arm description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36. No study treatment was administered at the Month 96 visit.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Month 30, 32, and 36

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| **Number of subjects in period 7[5]** | qHPV Vaccine in Base Study | qHPV Vaccine in Extension Study |
|---|---|---|
| Started | 508 | 267 |
| Completed | 508 | 267 |

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: Includes participants who re-entered the study

## Period 8

| | |
|---|---|
| Period 8 title | Long-term Follow-up (M126 visit) |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | qHPV Vaccine in Base Study |

Arm description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered at the Month 126 visit.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| | |
|---|---|
| **Arm title** | qHPV Vaccine in Extension Study |

Arm description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36. No study treatment was administered at the Month 126 visit.

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

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| | |
|---|---|
| Investigational medicinal product name | qHPV Vaccine |
| Investigational medicinal product code | |
| Other name | Gardasil, Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL intramuscular injection at Month 30, 32, and 36

| **Number of subjects in period 8[6]** | qHPV Vaccine in Base Study | qHPV Vaccine in Extension Study |
|---|---|---|
| Started | 454 | 211 |
| Completed | 454 | 211 |

Notes:

[6] - 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: Includes participants who re-entered the study

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | qHPV Vaccine in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. | |
| Reporting group title | Placebo in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the Placebo Group, who received three 0.5 mL intramuscular injections of placebo at Day 1, Month 2, and Month 6. | |

| Reporting group values | qHPV Vaccine in Base Study | Placebo in Base Study | Total |
|---|---|---|---|
| Number of subjects | 1184 | 597 | 1781 |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 11.9 | 11.8 | |
| standard deviation | ± 1.9 | ± 1.9 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 616 | 322 | 938 |
| Male | 568 | 275 | 843 |
| Race / Ethnicity | | | |
| Units: Subjects | | | |
| Asian | 149 | 70 | 219 |
| Black | 50 | 21 | 71 |
| Hispanic American | 260 | 130 | 390 |
| Native American | 0 | 1 | 1 |
| White | 716 | 369 | 1085 |
| Other | 9 | 6 | 15 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | qHPV Vaccine in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. | |
| Reporting group title | Placebo in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the Placebo Group, who received three 0.5 mL intramuscular injections of placebo at Day 1, Month 2, and Month 6. | |
| Reporting group title | qHPV Vaccine in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered between Month 7 and 18. | |
| Reporting group title | Placebo in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the Placebo Group, who received three 0.5 mL intramuscular injections of placebo at Day 1, Month 2, and Month 6. No study treatment was administered between Month 7 and 18. | |
| Reporting group title | qHPV Vaccine in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered between Month 18 and 30. | |
| Reporting group title | Placebo in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the Placebo Group, who received three 0.5 mL intramuscular injections of placebo at Day 1, Month 2, and Month 6. No study treatment was administered between Month 18 and 30. | |
| Reporting group title | qHPV Vaccine in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered between Month 30 and 37. | |
| Reporting group title | qHPV Vaccine in Extension Study |
| Reporting group description: | |
| Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36. | |
| Reporting group title | qHPV Vaccine in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered at the Month 42 visit. | |
| Reporting group title | qHPV Vaccine in Extension Study |
| Reporting group description: | |
| Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36. No study treatment was administered at the Month 42 visit. | |
| Reporting group title | qHPV Vaccine in Base Study |
| Reporting group description: | |
| Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered at the Month 72 visit. | |
| Reporting group title | qHPV Vaccine in Extension Study |

Reporting group description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36. No study treatment was administered at the Month 72 visit.

| Reporting group title | qHPV Vaccine in Base Study |
|---|---|

Reporting group description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered at the Month 96 visit.

| Reporting group title | qHPV Vaccine in Extension Study |
|---|---|

Reporting group description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36. No study treatment was administered at the Month 96 visit.

| Reporting group title | qHPV Vaccine in Base Study |
|---|---|

Reporting group description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6. No study treatment was administered at the Month 126 visit.

| Reporting group title | qHPV Vaccine in Extension Study |
|---|---|

Reporting group description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36. No study treatment was administered at the Month 126 visit.

| Subject analysis set title | qHPV Vaccine in Base Study: Safety Analysis |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6

| Subject analysis set title | Placebo Vaccine in Base Study: Safety Analysis |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Represents participants who were randomized into the Placebo Group, who received three 0.5 mL intramuscular injections of placebo at Day 1,Month 2, and Month 6

| Subject analysis set title | qHPV Vaccine in Extension Study: Safety Analysis |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36.

| Subject analysis set title | qHPV Vaccine in Base Study: Immunogenicity Analysis |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6 and had immunogenicity follow-up.

| Subject analysis set title | qHPV Vaccine in Extension Study: Immunogenicity Analysis |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36 and had immunogenicity follow-up.

| Subject analysis set title | qHPV in Base Study: Effectiveness Analysis |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Represents participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of V501 (qHPV) at Day 1, Month 2, and Month 6 and had effectiveness follow-up.

| | |
|---|---|
| Subject analysis set title | qHPV Vaccine in Extension Study: Effectiveness Analysis |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Represent participants originally enrolled into the Placebo Group who continued in the study to receive 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36 and had effectiveness follow-up.

## Primary: Number of Participants Reporting Serious Adverse Experiences (SAEs) Through Month 18

| | |
|---|---|
| End point title | Number of Participants Reporting Serious Adverse Experiences (SAEs) Through Month 18[1] |

End point description:

Tolerability as assessed by the number of participants with clinical adverse experiences through Month 18. A serious adverse event is any adverse event that results in death, is life threatening, results in a persistent or significant disability/incapacity, results in hospitalization or prolongs an existing hospitalization, is a congenital anomaly/birth defect, is a cancer, is an overdose, or is considered an "other important medical event" based on medical judgment. The analysis population was all participants who were vaccinated according to actual treatment received (qHPV or placebo) and had safety follow-up during the time frame.

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

End point timeframe:

Up to Month 18

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: No statistical hypothesis was planned for: Number of Participants Reporting Serious Adverse Experiences (SAEs) Through Month 18

| End point values | qHPV Vaccine in Base Study: Safety Analysis | Placebo Vaccine in Base Study: Safety Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 1165 | 584 | | |
| Units: Participants | 6 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Reporting SAEs from Month 18 through Month 37

| | |
|---|---|
| End point title | Number of Participants Reporting SAEs from Month 18 through Month 37[2] |

End point description:

Tolerability as assessed by the number of participants with clinical adverse experiences from Month 18 through Month 37. The analysis population was all participants who were vaccinated according to actual treatment received (qHPV or placebo) and had safety follow-up during the time frame.

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

End point timeframe:

Month 18 to Month 37

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: No statistical hypothesis was planned for: Number of Participants Reporting SAEs from Month 18 through Month 37

| End point values | qHPV Vaccine in Base Study: Safety Analysis | qHPV Vaccine in Extension Study: Safety Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 923 | 477 | | |
| Units: Participants | 0 | 3 | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Reporting Other (non-serious) AEs Through Month 18

| End point title | Number of Participants Reporting Other (non-serious) AEs Through Month 18[3] |
|---|---|

End point description:

Tolerability as assessed by the number of participants with clinical adverse experiences through Month 18. The analysis population was all participants who were vaccinated according to actual treatment received (qHPV or placebo) and had safety follow-up during the time frame.

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

End point timeframe:

Up to Month 18: Injection site AEs were collected from Days 1-5 and other non-serious AEs from Days 1-15 after any vaccination

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: No statistical hypothesis was planned for: Number of Participants Reporting Other (non-serious) AEs Through Month 18

| End point values | qHPV Vaccine in Base Study: Safety Analysis | Placebo Vaccine in Base Study: Safety Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 1165 | 584 | | |
| Units: Participants | 918 | 340 | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants Who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 72

| End point title | Percentage of Participants Who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 72[4] |
|---|---|

End point description:

A participant is considered seropositive for a given HPV type if he or she has a cLIA titer at or above the serostatus cutoff for that HPV type. Serostatus cutoffs are ≥ 20 mMU/mL for HPV 6 and 16, ≥ 16 mMU/mL for HPV 11, and ≥ 24 mMU/mL for HPV 18. Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1 (for the Main Vaccination group), or Month 30 (for the Extension Group), and had a valid

serology result at the specified time for assessment.

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

End point timeframe:

Month 72 (66 Months Post-dose 3 for the Original qHPV Vaccine Cohort and 36 months Post-dose 3 for the Extension Group)

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: No statistical hypothesis was planned for: Percentage of Participants Who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 72

| **End point values** | qHPV Vaccine in Base Study: Immunogenicity Analysis | qHPV Vaccine in Extension Study: Immunogenicity Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 550 | 276 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Type 6: n=475, 151 | 93.3 (90.6 to 95.3) | 91.4 (85.7 to 95.3) | | |
| Type 11: n=475, 151 | 96 (93.8 to 97.6) | 96.7 (92.4 to 98.9) | | |
| Type 16: n=473, 154 | 97.9 (96.1 to 99) | 97.4 (93.5 to 99.3) | | |
| Type 18: n=477, 160 | 74.4 (70.3 to 78.3) | 79.4 (72.3 to 85.4) | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Titers (GMTs) for anti-HPV 6, 11, 16, and 18 at Month 72

| End point title | Geometric Mean Titers (GMTs) for anti-HPV 6, 11, 16, and 18 at Month 72[5] |
|---|---|

End point description:

Per-protocol population: participants without protocol violations who received all 3 vaccinations within appropriate day ranges as defined in the CSR, were seronegative to the
respective HPV type at Day 1 (for the Main Vaccination group), or Month 30 (for the Extension Group), and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 72 (66 Months Post-dose 3 for the Original qHPV Vaccine Cohort and 36 months Post-dose 3 for the Extension Group)

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: No statistical hypothesis was planned for: Geometric Mean Titers (GMTs) for anti-HPV 6, 11, 16, and 18 at Month 72

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | qHPV Vaccine in Extension Study: Immunogenicity Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 550 | 276 | | |
| Units: milliMerck units/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Type 6: n=475, 151 | 118.9 (108.4 to 130.4) | 113.9 (95.7 to 135.6) | | |
| Type 11: n=475, 151 | 135.7 (122.6 to 150.3) | 137.9 (114.9 to 165.5) | | |
| Type 16: n=473, 154 | 521.2 (466.2 to 582.6) | 485.8 (396.4 to 595.3) | | |
| Type 18: n=477, 160 | 70.9 (61.8 to 81.4) | 67.7 (53.1 to 86.3) | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Titers for anti-HPV 6, 11, 16, and 18 at Month 96

| End point title | Geometric Mean Titers for anti-HPV 6, 11, 16, and 18 at Month 96[6] |
|---|---|

End point description:

Per-protocol population: participants without protocol violations who received all 3 vaccinations within appropriate day ranges as defined in the CSR, were seronegative to the respective HPV type at Day 1 (for the Main Vaccination group), or Month 30 (for the Extension Group), and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 96 (90 Months Post-dose 3 for Original qHPV Vaccine Group and 60 Months Post-dose 3 for Extension Group)

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: No statistical hypothesis was planned for: Geometric Mean Titers for anti-HPV 6, 11, 16, and 18 at Month 96

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | qHPV Vaccine in Extension Study: Immunogenicity Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 508 | 267 | | |
| Units: milliMerck units/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Type 6: n=451, 141 | 71.4 (64.6 to 79) | 91 (76.4 to 108.6) | | |
| Type 11: n=451, 141 | 67.5 (60.1 to 75.7) | 90.3 (74 to 110.1) | | |
| Type 16: n=447, 143 | 325.5 (288.6 to 367.1) | 387.4 (314.7 to 476.9) | | |

| | | | | |
|---|---|---|---|---|
| Type 18: n=452, 152 | 41.6 (36.5 to 47.5) | 48.3 (37.6 to 62) | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants Who Are Seropositive for HPV Types 6, 11, 16, and 18 at Month 96

| End point title | Percentage of Participants Who Are Seropositive for HPV Types 6, 11, 16, and 18 at Month 96[7] |
|---|---|

End point description:

A participant is considered seropositive for a given HPV type if he or she has a cLIA titer at or above the serostatus cutoff for that HPV type. Serostatus cutoffs are ≥ 20 mMU/mL for HPV 6 and 16, ≥ 16 mMU/mL for HPV 11, and ≥ 24 mMU/mL for HPV 18. Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1 (for the Main Vaccination group), or Month 30 (for the Extension Group), and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 96 (90 Months Post-dose 3 for Original qHPV Vaccine Cohort and 60 Months Post-dose 3 for Extension Group)

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: No statistical hypothesis was planned for: Percentage of Participants Who Are Seropositive for HPV Types 6, 11, 16, and 18 at Month 96

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | qHPV Vaccine in Extension Study: Immunogenicity Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 508 | 267 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Type 6: n=451, 141 | 88.2 (84.9 to 91.1) | 91.5 (85.6 to 95.5) | | |
| Type 11: n=451, 141 | 89.1 (85.9 to 91.9) | 93.6 (88.2 to 97) | | |
| Type 16: n=447, 143 | 96.9 (94.8 to 98.3) | 97.9 (94 to 99.6) | | |
| Type 18: n=452, 152 | 63.9 (59.3 to 68.4) | 69.1 (61.1 to 76.3) | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Titers for anti-HPV 6, 11, 16, and 18 at Month 126

| End point title | Geometric Mean Titers for anti-HPV 6, 11, 16, and 18 at Month 126[8] |
|---|---|

End point description:

Per-protocol population: participants without protocol violations who received all 3 vaccinations within appropriate day ranges as defined in the CSR, were seronegative to the respective HPV type at Day 1 (for the Main Vaccination group), or Month 30 (for the Extension Group), and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 126 (120 Months Post-dose 3 for Original qHPV Vaccine Cohort and 90 Months Post-dose 3 for Extension Group)

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: No statistical hypothesis was planned for: Geometric Mean Titers for anti-HPV 6, 11, 16, and 18 at Month 126

| **End point values** | qHPV Vaccine in Base Study: Immunogenicity Analysis | qHPV Vaccine in Extension Study: Immunogenicity Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 454 | 211 | | |
| Units: milliMerck units/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Type 6: n=409, 112 | 88 (78.9 to 98.2) | 99.3 (81 to 121.6) | | |
| Type 11: n=409, 112 | 74.6 (66.1 to 84.1) | 96 (76.1 to 121.1) | | |
| Type 16: n=403, 115 | 320.1 (281.2 to 364.4) | 351.6 (277.1 to 446.2) | | |
| Type 18: n=408, 120 | 36.5 (31.7 to 42.1) | 39.6 (30.7 to 51.2) | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants Who Are Seropositive for HPV Types 6, 11, 16, and 18 at Month 126

| End point title | Percentage of Participants Who Are Seropositive for HPV Types 6, 11, 16, and 18 at Month 126[9] |
|---|---|

End point description:

A participant is considered seropositive for a given HPV type if he or she has a cLIA titer at or above the serostatus cutoff for that HPV type. Serostatus cutoffs are ≥ 20 mMU/mL for HPV 6 and 16, ≥ 16 mMU/mL for HPV 11, and ≥ 24 mMU/mL for HPV 18. Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1 (for the Main Vaccination group), or Month 30 (for the Extension Group), and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 126 (120 Months Post-dose 3 for Original qHPV Vaccine Cohort and 90 Months Post-dose 3 for Extension Group)

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: No statistical hypothesis was planned for: Percentage of Participants Who Are Seropositive for HPV Types 6, 11, 16, and 18 at Month 126

| **End point values** | qHPV Vaccine in Base Study: Immunogenicity Analysis | qHPV Vaccine in Extension Study: Immunogenicity Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 454 | 211 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Type 6: n=409, 112 | 89 (85.6 to 91.9) | 91.1 (84.2 to 95.6) | | |
| Type 11: n=409, 112 | 88.8 (85.3 to 91.6) | 92.9 (86.4 to 96.9) | | |
| Type 16: n=403, 115 | 96 (93.6 to 97.7) | 96.5 (91.3 to 99) | | |
| Type 18: n=408, 120 | 60.5 (55.6 to 65.3) | 65 (55.8 to 73.5) | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Reporting SAEs Related to Study Vaccine or to a Study Procedure in the Long-term Follow-up

| End point title | Number of Participants Reporting SAEs Related to Study Vaccine or to a Study Procedure in the Long-term Follow-up[10] |
|---|---|

End point description:

A serious adverse event is any adverse event that results in death, is life threatening, results in a persistent or significant disability/incapacity, results in hospitalization or prolongs an existing hospitalization, is a congenital anomaly/birth defect, is a cancer, is an overdose, or is considered an "other important medical event" based on medical judgment. SAEs considered by the investigator to be possibly, probably, or definitely related to study vaccine or a study procedure were reported. The analysis population was all participants who were vaccinated according to actual treatment received and had safety follow-up.

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

End point timeframe:

Month 37 to Month 126 (31 to 120 months Post-dose 3 for the Original qHPV Vaccine Cohort and 1 to 90 months Post-dose 3 for the Extension Group)

Notes:

[10] - 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: No statistical hypothesis was planned for: Number of Participants Reporting SAEs Related to Study Vaccine or to a Study Procedure in the Long-term Follow-up

| End point values | qHPV Vaccine in Base Study: Safety Analysis | qHPV Vaccine in Extension Study: Safety Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 821 | 424 | | |
| Units: Participants | 0 | 1 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Original qHPV Vaccine Participants who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 1 Postdose 3 (Month 7)

| End point title | Percentage of Original qHPV Vaccine Participants who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 1 Postdose 3 (Month 7) |
|---|---|

End point description:

A participant is considered seropositive for a given HPV type if he or she has a cLIA titer at or above the serostatus cutoff for that HPV type. Serostatus cutoffs are ≥ 20 mMU/mL for HPV 6 and 16, ≥ 16 mMU/mL for HPV 11, and ≥ 24 mMU/mL for HPV 18. Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 7 (1 Month Postdose 3)

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1082 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Type 6: n=953 | 99.8 (99.2 to 100) | | | |
| Type 11: n=954 | 99.8 (99.2 to 100) | | | |
| Type 16: n=949 | 99.7 (99.1 to 99.9) | | | |
| Type 18: n=956 | 99.7 (99.1 to 99.9) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Original qHPV Vaccine Participants who are Seropositive

**for HPV Types 6, 11, 16, and 18 at Month 12 Postdose 3 (Month 18).**

| End point title | Percentage of Original qHPV Vaccine Participants who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 12 Postdose 3 (Month 18). |
|---|---|

End point description:

A participant is considered seropositive for a given HPV type if he or she has a cLIA titer at or above the serostatus cutoff for that HPV type. Serostatus cutoffs are ≥ 20 mMU/mL for HPV 6 and 16, ≥ 16 mMU/mL for HPV 11, and ≥ 24 mMU/mL for HPV 18. Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 18 (12 Months Post-dose 3)

| **End point values** | qHPV Vaccine in Base Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1106 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Type 6: n=937 | 97.8 (96.6 to 98.6) | | | |
| Type 11: n=938 | 99.3 (98.5 to 99.7) | | | |
| Type 16: n=933 | 99.6 (98.9 to 99.9) | | | |
| Type 18: n=940 | 91.6 (89.6 to 93.3) | | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of Original qHPV Vaccine Participants who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 18 Postdose 3 (Month 24)**

| End point title | Percentage of Original qHPV Vaccine Participants who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 18 Postdose 3 (Month 24) |
|---|---|

End point description:

A participant is considered seropositive for a given HPV type if he or she has a cLIA titer at or above the serostatus cutoff for that HPV type. Serostatus cutoffs are ≥ 20 mMU/mL for HPV 6 and 16, ≥ 16 mMU/mL for HPV 11, and ≥ 24 mMU/mL for HPV 18. Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 24 (18 Months Post-dose 3)

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 595 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Type 6: n=446 | 95.1 (92.6 to 96.9) | | | |
| Type 11: n=447 | 98.2 (96.5 to 99.2) | | | |
| Type 16: n=442 | 98.4 (96.8 to 99.4) | | | |
| Type 18: n=447 | 87.5 (84 to 90.4) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Original qHPV Vaccine Participants who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 24 Postdose 3 (Month 30)

| End point title | Percentage of Original qHPV Vaccine Participants who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 24 Postdose 3 (Month 30) |
|---|---|

End point description:

A participant is considered seropositive for a given HPV type if he or she has a cLIA titer at or above the serostatus cutoff for that HPV type. Serostatus cutoffs are ≥ 20 mMU/mL for HPV 6 and 16, ≥ 16 mMU/mL for HPV 11, and ≥ 24 mMU/mL for HPV 18. Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 30 (24 Months Post-dose 3)

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 911 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Type 6: n=799 | 95.6 (94 to 96.9) | | | |
| Type 11: n=800 | 97.5 (96.2 to 98.5) | | | |

| | | | | |
|---|---|---|---|---|
| Type 16: n=795 | 98.6 (97.5 to 99.3) | | | |
| Type 18: n=803 | 84.3 (81.6 to 86.8) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Original qHPV Vaccine Participants who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 31 Postdose 3 (Month 37).

| | |
|---|---|
| End point title | Percentage of Original qHPV Vaccine Participants who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 31 Postdose 3 (Month 37). |

End point description:

A participant is considered seropositive for a given HPV type if he or she has a cLIA titer at or above the serostatus cutoff for that HPV type. Serostatus cutoffs are ≥ 20 mMU/mL for HPV 6 and 16, ≥ 16 mMU/mL for HPV 11, and ≥ 24 mMU/mL for HPV 18. Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 37 (31 Months Post-dose 3)

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 772 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Type 6: n=657 | 94.5 (92.5 to 96.1) | | | |
| Type 11: n=657 | 96 (94.3 to 97.4) | | | |
| Type 16: n=655 | 98.2 (96.8 to 99) | | | |
| Type 18: n=660 | 81.1 (77.9 to 84) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants in the Extension Group who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 1 Postdose 3 of qHPV (Month 37)

| | |
|---|---|
| End point title | Percentage of Participants in the Extension Group who are Seropositive for HPV Types 6, 11, 16, and 18 at Month 1 |

| | |
|---|---|
| | Postdose 3 of qHPV (Month 37) |

End point description:

A participant is considered seropositive for a given HPV type if he or she has a cLIA titer at or above the serostatus cutoff for that HPV type. Serostatus cutoffs are ≥ 20 mMU/mL for HPV 6 and 16, ≥ 16 mMU/mL for HPV 11, and ≥ 24 mMU/mL for HPV 18. Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Month 30, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 37 (1 Month Post-dose 3 of qHPV)

| **End point values** | qHPV Vaccine in Extension Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 440 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Type 6: n=246 | 99.6 (97.8 to 100) | | | |
| Type 11: n=246 | 100 (98.5 to 100) | | | |
| Type 16: n=246 | 100 (98.5 to 100) | | | |
| Type 18: n=255 | 98.8 (96.6 to 99.8) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers of Original qHPV Vaccine Cohort for anti-HPV 6, 11, 16, and 18 at month 1 Postdose 3 of qHPV vaccine (Month 7)

| End point title | Geometric Mean Titers of Original qHPV Vaccine Cohort for anti-HPV 6, 11, 16, and 18 at month 1 Postdose 3 of qHPV vaccine (Month 7) |
|---|---|

End point description:

Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 7 (1 Month Post-dose 3)

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1082 | | | |
| Units: milliMerck units/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Type 6: n=953 | 929.2 (871 to 991.4) | | | |
| Type 11: n=954 | 1362.8 (1279.8 to 1451.3) | | | |
| Type 16: n=949 | 5512.7 (5109.9 to 5947.2) | | | |
| Type 18: n=956 | 1278.9 (1183.2 to 1382.4) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers of Original qHPV Vaccine Cohort for anti-HPV 6, 11, 16, and 18 at month 12 Postdose 3 of qHPV vaccine (Month 18)

| End point title | Geometric Mean Titers of Original qHPV Vaccine Cohort for anti-HPV 6, 11, 16, and 18 at month 12 Postdose 3 of qHPV vaccine (Month 18) |
|---|---|

End point description:

Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 18 (Month 12 Post-dose 3)

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1106 | | | |
| Units: milliMerck units/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Type 6: n=937 | 219.3 (204.9 to 234.7) | | | |
| Type 11: n=938 | 296.9 (276.9 to 318.3) | | | |

| | | | | |
|---|---|---|---|---|
| Type 16: n=933 | 1314.8 (1220.5 to 1416.5) | | | |
| Type 18: n=940 | 203 (184.1 to 223.9) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers of Original qHPV Vaccine Cohort for anti-HPV 6, 11, 16, and 18 at month 18 Postdose 3 of qHPV vaccine (Month 24)

| | |
|---|---|
| End point title | Geometric Mean Titers of Original qHPV Vaccine Cohort for anti-HPV 6, 11, 16, and 18 at month 18 Postdose 3 of qHPV vaccine (Month 24) |

End point description:

Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 24 (18 Months Post-dose 3)

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 595 | | | |
| Units: milliMerck units/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Type 6: n=446 | 143.5 (129.2 to 159.5) | | | |
| Type 11: n=447 | 206.6 (186.9 to 228.3) | | | |
| Type 16: n=442 | 932.1 (833.3 to 1042.7) | | | |
| Type 18: n=447 | 136.2 (118.5 to 156.6) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers of Original qHPV Vaccine Cohort for anti-HPV 6, 11, 16, and 18 at month 24 Postdose 3 of qHPV vaccine (Month 30)

| | |
|---|---|
| End point title | Geometric Mean Titers of Original qHPV Vaccine Cohort for anti-HPV 6, 11, 16, and 18 at month 24 Postdose 3 of qHPV |

| | |
|---|---|
| | vaccine (Month 30) |

End point description:

Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 30 (24 Months Post-dose 3)

| **End point values** | qHPV Vaccine in Base Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 911 | | | |
| Units: milliMerck units/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Type 6: n=799 | 146.5 (135.6 to 158.2) | | | |
| Type 11: n=800 | 177 (163.6 to 191.5) | | | |
| Type 16: n=795 | 826.1 (757.8 to 900.5) | | | |
| Type 18: n=803 | 114.7 (102.8 to 127.9) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers of Original qHPV Vaccine Cohort for anti-HPV 6, 11, 16, and 18 at month 31 Postdose 3 of qHPV vaccine (Month 37)

| End point title | Geometric Mean Titers of Original qHPV Vaccine Cohort for anti-HPV 6, 11, 16, and 18 at month 31 Postdose 3 of qHPV vaccine (Month 37) |
|---|---|

End point description:

Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations, were seronegative to the respective HPV type at Day 1, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 37 (31 Months Post-dose 3)

| End point values | qHPV Vaccine in Base Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 772 | | | |
| Units: milliMerck units/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Type 6: n=657 | 128.6 (118.2 to 139.9) | | | |
| Type 11: n=657 | 149.7 (137 to 163.6) | | | |
| Type 16: n=655 | 680.4 (617.2 to 750.1) | | | |
| Type 18: n=660 | 102.4 (90.9 to 115.3) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers in the Extension Group for anti-HPV 6, 11, 16, and 18 at Month 1 Postdose 3 of qHPV Vaccine (Month 37)

| End point title | Geometric Mean Titers in the Extension Group for anti-HPV 6, 11, 16, and 18 at Month 1 Postdose 3 of qHPV Vaccine (Month 37) |
|---|---|

End point description:

Per-protocol population: participants without protocol violations who received all 3 qHPV vaccinations within appropriate day ranges, were seronegative to the respective HPV type at Month 30, and had a valid serology result at the specified time for assessment.

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

End point timeframe:

Month 37 (1 Month Post-dose 3 of qHPV)

| End point values | qHPV Vaccine in Extension Study: Immunogenicity Analysis | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 440 | | | |
| Units: milliMerck units/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Type 6: n=246 | 768.6 (676.6 to 873) | | | |
| Type 11: n=246 | 1041 (919.8 to 1178.2) | | | |
| Type 16: n=246 | 4312.7 (3715.6 to 5005.7) | | | |

| | | | | |
|---|---|---|---|---|
| Type 18: n=255 | 830.1 (714 to 965.1) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Combined Incidence of HPV 6/11/16/18-related Persistent Infection and HPV 6/11/16/18-related CIN, AIS, VIN, VaIN, Genital Warts, and Cervical/Vaginal/Vulvar Cancer in Females

| End point title | Combined Incidence of HPV 6/11/16/18-related Persistent Infection and HPV 6/11/16/18-related CIN, AIS, VIN, VaIN, Genital Warts, and Cervical/Vaginal/Vulvar Cancer in Females |
|---|---|

End point description:

The HPV types were determined by polymerase chain reaction (PCR) testing. The combined incidence of HPV 6/11/16/18-related persistent infection and HPV 6/11/16/18-related cervical intraepithelial neoplasia (CIN), adenocarcinoma in situ (AIS), vulvar intraepithelial neoplasia (VIN), vaginal intraepithelial neoplasia (VaIN), genital warts, and cervical/Vaginal/vulvar cancer was assessed in female participants. Per-Protocol Effectiveness population: female participants without protocol violations who received at least 1 dose of qHPV vaccine and at least 1 effectiveness follow-up visit.

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

End point timeframe:

Up to Month 126 (up to 120 Months Post-dose 3 for Original qHPV Vaccine Cohort and up to 90 Months Post-dose 3 for Extension Group)

| **End point values** | qHPV in Base Study: Effectiveness Analysis | qHPV Vaccine in Extension Study: Effectiveness Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 259 | 96 | | |
| Units: Incidence per 100 person-years at risk | | | | |
| number (confidence interval 95%) | 0.2 (0.1 to 0.7) | 0.2 (0 to 1.4) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Combined Incidence of HPV 6/11/16/18-related Persistent Infection and HPV 6/11/16/18-related PIN, Genital Warts, and Penile/Perineal/Perianal Cancer in Males

| End point title | Combined Incidence of HPV 6/11/16/18-related Persistent Infection and HPV 6/11/16/18-related PIN, Genital Warts, and Penile/Perineal/Perianal Cancer in Males |
|---|---|

End point description:

The HPV types were determined by PCR testing. Combined incidence of HPV 6/11/16/18-related

persistent infection and HPV 6/11/16/18-related penile/perineal/perianal intraepithelial neoplasia (PIN), genital warts, and penile/perineal/perianal cancer was assessed in male participants. Per-Protocol Effectiveness population: male participants without protocol violations who received at least 1 dose of qHPV vaccine and at least 1 effectiveness follow-up visit.

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

End point timeframe:

Up to Month 126 (up to 120 Months Post-dose 3 for Original qHPV Vaccine Cohort and up to 90 Months Post-dose 3 for Extension Group)

| **End point values** | qHPV in Base Study: Effectiveness Analysis | qHPV Vaccine in Extension Study: Effectiveness Analysis | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179 | 62 | | |
| Units: Incidence per 100 person-years at risk | | | | |
| number (confidence interval 95%) | 0.6 (0.2 to 1.5) | 0.3 (0 to 1.9) | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 1 to Month 30 and Month 30 to Month 126

Adverse event reporting additional description:

Day 1 to Month 30: All adverse events were collected up to Day 15 after any vaccination. Month 30 to Month 126: Nonserious AEs were not collected. Deaths and related SAEs were collected throughout the study. Non-serious AEs were not solicited during the Extension Study; any reported non-serious AEs were unsolicited and not systematically assessed.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 11.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | qHPV Vaccine in Base Study: Day 1 to Month 30 |

Reporting group description:

Participants who were randomized into the qHPV Group, who received three 0.5 mL intramuscular injections of qHPV at Day 1, Month 2, and Month 6, and had safety follow-up. Adverse events are reported for this group from Day 1 to Month 30.

| | |
|---|---|
| Reporting group title | Placebo in Base Study: Day 1 to Month 30 |

Reporting group description:

Participants who were randomized into the Placebo Group, who received three 0.5 mL intramuscular injections of placebo vaccine at Day 1, Month 2, and Month 6, and had safety followup. Adverse events are reported for this group from Day 1 to Month 30.

| | |
|---|---|
| Reporting group title | qHPV Vaccine in Base Stuty: Month 30 to Month 126 |

Reporting group description:

Participants who received qHPV in the Base Study. No study treatment was administered after Month 6 for these participants. Adverse events are reported for this group from Month 30 to Month 126. Non-serious AEs were not solicited.

| | |
|---|---|
| Reporting group title | qHPV Vaccine in Extension Study: Month 30 to Month 126 |

Reporting group description:

Participants who received placebo in the Base Study and three 0.5 mL intramuscular injections of V501 (qHPV) at Month 30, Month 32, and Month 36 in the Extension Study. Adverse events are reported for this group from Month 30 to Month 126. Non-serious AEs were not solicited.

| Serious adverse events | qHPV Vaccine in Base Study: Day 1 to Month 30 | Placebo in Base Study: Day 1 to Month 30 | qHPV Vaccine in Base Stuty: Month 30 to Month 126 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 1165 (0.52%) | 0 / 584 (0.00%) | 2 / 932 (0.21%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Meniscus injury | | | |
| subjects affected / exposed | 0 / 1165 (0.00%) | 0 / 584 (0.00%) | 0 / 932 (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 |

| | | | |
|---|---|---|---|
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 1165 (0.00%) | 0 / 584 (0.00%) | 1 / 932 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Nervous system disorders | | | |
| VIIth nerve paralysis | | | |
| subjects affected / exposed | 0 / 1165 (0.00%) | 0 / 584 (0.00%) | 0 / 932 (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 |
| Tonic clonic movements | | | |
| subjects affected / exposed | 0 / 1165 (0.00%) | 0 / 584 (0.00%) | 1 / 932 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 1 / 1165 (0.09%) | 0 / 584 (0.00%) | 0 / 932 (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 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 1165 (0.00%) | 0 / 584 (0.00%) | 0 / 932 (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 | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 1 / 1165 (0.09%) | 0 / 584 (0.00%) | 0 / 932 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Dysfunctional uterine bleeding | | | |
| subjects affected / exposed | 1 / 1165 (0.09%) | 0 / 584 (0.00%) | 0 / 932 (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 |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 1165 (0.09%) | 0 / 584 (0.00%) | 0 / 932 (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 | 1 / 1165 (0.09%) | 0 / 584 (0.00%) | 0 / 932 (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 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 1165 (0.09%) | 0 / 584 (0.00%) | 0 / 932 (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 |
| Localised infection | | | |
| subjects affected / exposed | 1 / 1165 (0.09%) | 0 / 584 (0.00%) | 0 / 932 (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 |
| Metabolism and nutrition disorders | | | |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 1165 (0.09%) | 0 / 584 (0.00%) | 0 / 932 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | qHPV Vaccine in Extension Study: Month 30 to Month 126 | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 481 (0.62%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Meniscus injury | | | |
| subjects affected / exposed | 1 / 481 (0.21%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| VIIth nerve paralysis | | | |
| subjects affected / exposed | 1 / 481 (0.21%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonic clonic movements | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 481 (0.21%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Dysfunctional uterine bleeding | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Localised infection | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 4 %

| **Non-serious adverse events** | qHPV Vaccine in Base Study: Day 1 to Month 30 | Placebo in Base Study: Day 1 to Month 30 | qHPV Vaccine in Base Stuty: Month 30 to Month 126 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 918 / 1165 (78.80%) | 344 / 584 (58.90%) | 0 / 932 (0.00%) |
| Nervous system disorders | | | |
| Headache | | | |
| alternative dictionary used: MedDRA 7.1 | | | |
| subjects affected / exposed | 221 / 1165 (18.97%) | 111 / 584 (19.01%) | 0 / 932 (0.00%) |
| occurrences (all) | 297 | 163 | 0 |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| Injection site erythema | | | |
| alternative dictionary used: MedDRA 7.1 | | | |
| subjects affected / exposed | 237 / 1165 (20.34%) | 78 / 584 (13.36%) | 0 / 932 (0.00%) |
| occurrences (all) | 323 | 109 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 853 / 1165 (73.22%) | 268 / 584 (45.89%) | 0 / 932 (0.00%) |
| occurrences (all) | 1705 | 434 | 0 |
| Injection site swelling | | | |
| subjects affected / exposed | 241 / 1165 (20.69%) | 45 / 584 (7.71%) | 0 / 932 (0.00%) |
| occurrences (all) | 336 | 63 | 0 |
| Pyrexia | | | |
| alternative dictionary used: MedDRA 7.1 | | | |
| subjects affected / exposed | 100 / 1165 (8.58%) | 44 / 584 (7.53%) | 0 / 932 (0.00%) |
| occurrences (all) | 114 | 60 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| alternative dictionary used: MedDRA 7.1 | | | |
| subjects affected / exposed | 52 / 1165 (4.46%) | 24 / 584 (4.11%) | 0 / 932 (0.00%) |
| occurrences (all) | 56 | 26 | 0 |

| **Non-serious adverse events** | qHPV Vaccine in Extension Study: Month 30 to Month 126 | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 481 (0.62%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| alternative dictionary used: MedDRA 7.1 | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Injection site erythema | | | |
| alternative dictionary used: MedDRA 7.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 481 (0.21%) | | |
| occurrences (all) | 1 | | |
| Injection site pain | | | |
| subjects affected / exposed | 3 / 481 (0.62%) | | |
| occurrences (all) | 3 | | |
| Injection site swelling | | | |
| subjects affected / exposed | 1 / 481 (0.21%) | | |
| occurrences (all) | 1 | | |
| Pyrexia | | | |
| alternative dictionary used: MedDRA 7.1 | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| alternative dictionary used: MedDRA 7.1 | | | |
| subjects affected / exposed | 0 / 481 (0.00%) | | |
| occurrences (all) | 0 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 15 September 2004 | Amendment 3 included changes to an analysis endpoint; language concerning participants who receive placebo; study visits; study assessments; rationale for capturing non-study vaccines throughout the course of the study; and language concerning participants who discontinue from test therapy but continue in the study. |
| 28 November 2005 | Amendment 5 included changes in the duration of the Base Study; placebo participants to be offered vaccination with GARDASIL starting at Month 30; Extension Study visits; details regarding SAE collection for placebo participants who receive GARDASIL; clarification that the Extension Study is open label; statement that participants in the placebo group who do not wish to participate in the Extension Study will be eligible to receive GARDASIL when or if it becomes available in their country; added required pregnancy tests for female participants in the placebo group who receive GARDASIL; added SAE assessment for participants in the placebo group who receive GARDASIL. |
| 27 November 2007 | Amendment 11 included additional clarification on characterization of breakthrough cases and reporting of overdoses. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported