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: 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[3]

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:

[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: 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: 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[4]

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:

[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: 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: 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
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
Injection site swelling			
subjects affected / exposed	241 / 1165 (20.69%)	45 / 584 (7.71%)	0 / 932 (0.00%)
occurrences (all)	336	63	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		
Pyrexia			
alternative dictionary used: MedDRA 7.1			
subjects affected / exposed	0 / 481 (0.00%)		
occurrences (all)	0		
Injection site swelling			
subjects affected / exposed	1 / 481 (0.21%)		
occurrences (all)	1		
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