



Clinical trial results:

A Phase III, Randomized, International, Placebo-Controlled, Double-Blind Clinical Trial to Study the Tolerability and Immunogenicity of V503, a Multivalent Human Papillomavirus (HPV) L1 Virus-Like Particle (VLP) Vaccine, Given to Females 12-26 Years of Age Who Have Previously Received GARDASIL™

Summary

EudraCT number	2009-015500-26
Trial protocol	SE DK Outside EU/EEA
Global end of trial date	28 November 2015

Results information

Result version number	v1 (current)
This version publication date	04 June 2016
First version publication date	04 June 2016

Trial information

Trial identification

Sponsor protocol code	V503-006
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01047345
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Registration Number: 2010_504

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., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., 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	28 November 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	28 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate whether V503 (9vHPV vaccine) is well tolerated in girls and women between 12 and 26 years old who have previously been vaccinated with GARDASIL™. Participants will receive vaccination with 9vHPV vaccine or placebo on Day 1, Month 2, and Month 6 of the Base Study. Participants who receive placebo in the Base Study will be eligible to receive vaccination with 9vHPV vaccine on Day 1, Month 2, and Month 6 of the Extension Study.

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 February 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Canada: 70
Country: Number of subjects enrolled	Colombia: 151
Country: Number of subjects enrolled	Denmark: 303
Country: Number of subjects enrolled	Hong Kong: 46
Country: Number of subjects enrolled	Mexico: 20
Country: Number of subjects enrolled	Puerto Rico: 12
Country: Number of subjects enrolled	Sweden: 105
Country: Number of subjects enrolled	United States: 214
Worldwide total number of subjects	924
EEA total number of subjects	408

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	331
Adults (18-64 years)	593
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Healthy female participants Age 12 to 26 who received a 3-dose regimen of marketed GARDASIL™ within a 1 year period and the last dose of GARDASIL™ was at least 1 year from study day 1. Other inclusion and exclusion criteria applied.

Period 1

Period 1 title	Base Study
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	9vHPV Vaccine- Base Study

Arm description:

9vHPV vaccine (V503) 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 of the Base Study. Participants will not continue to the Extension Study

Arm type	Experimental
Investigational medicinal product name	9vHPV Vaccine
Investigational medicinal product code	
Other name	V503
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 of the Base Study

Arm title	Placebo - Base Study
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Arm description:

0.5 mL intramuscular injection of saline placebo at Day 1, Month 2, and Month 6 of the Base Study. After completion of the Base Study, participants will be eligible to receive 9vHPV 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 of the Extension Study.

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

Dosage and administration details:

0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 of the Base Study

Number of subjects in period 1	9vHPV Vaccine- Base Study	Placebo - Base Study
Started	618	306
Vaccination 1	615	306
Vaccination 2	604	304
Vaccination 3	597	300
Completed	596	300
Not completed	22	6
Consent withdrawn by subject	12	4
Adverse event, non-fatal	3	-
Lost to follow-up	4	1
Protocol deviation	3	1

Period 2

Period 2 title	Extension
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	9vHPV Vaccine -Extension
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Arm description:

Participants who received placebo in base study and elected to have 9vHPV vaccination in extension.

Arm type	Experimental
Investigational medicinal product name	9vHPV Vaccine
Investigational medicinal product code	
Other name	V503
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

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

Number of subjects in period 2 ^[1]	9vHPV Vaccine - Extension
Started	102
Vaccination 4	102
Vaccination 5	99
Vaccination 6	95 ^[2]
Completed	96
Not completed	6

Consent withdrawn by subject	1
Lost to follow-up	5

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: Participation in the extension was voluntary. Not all eligible participants elected to enter the extension.

[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: One participant received 3rd 9vHPV vaccination outside the context of the study and therefore was not eligible to receive 3rd dose as part of the study. Participant remained in the study, was followed for safety to study completion.

Baseline characteristics

Reporting groups

Reporting group title	9vHPV Vaccine- Base Study
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Reporting group description:

9vHPV vaccine (V503) 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 of the Base Study. Participants will not continue to the Extension Study

Reporting group title	Placebo - Base Study
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Reporting group description:

0.5 mL intramuscular injection of saline placebo at Day 1, Month 2, and Month 6 of the Base Study. After completion of the Base Study, participants will be eligible to receive 9vHPV 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 of the Extension Study.

Reporting group values	9vHPV Vaccine- Base Study	Placebo - Base Study	Total
Number of subjects	618	306	924
Age Categorical Units: Subjects			
12 to 15 years	122	60	182
16 to 26 years	496	246	742
Gender Categorical Units: Subjects			
Female	618	306	924
Male	0	0	0

End points

End points reporting groups

Reporting group title	9vHPV Vaccine- Base Study
Reporting group description: 9vHPV vaccine (V503) 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 of the Base Study. Participants will not continue to the Extension Study	
Reporting group title	Placebo - Base Study
Reporting group description: 0.5 mL intramuscular injection of saline placebo at Day 1, Month 2, and Month 6 of the Base Study. After completion of the Base Study, participants will be eligible to receive 9vHPV 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 of the Extension Study.	
Reporting group title	9vHPV Vaccine -Extension
Reporting group description: Participants who received placebo in base study and elected to have 9vHPV vaccination in extension.	
Subject analysis set title	9vHPV Vaccine - Efficacy
Subject analysis set type	Per protocol
Subject analysis set description: Participants who received all 3 vaccinations within an acceptable day range, had Month 7 serology sample collected within an acceptable range and had no other protocol violations that could interfere with the immune response to the vaccine.	
Subject analysis set title	Placebo - Efficacy
Subject analysis set type	Per protocol
Subject analysis set description: Participants who received all 3 vaccinations within an acceptable day range, had Month 7 serology sample collected within an acceptable range and had no other protocol violations that could interfere with the immune response to the vaccine.	

Primary: Percentage of Participants Who Experience an Injection-site Adverse Event (AE) – Base Study

End point title	Percentage of Participants Who Experience an Injection-site Adverse Event (AE) – Base Study ^[1]
End point description: An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the vaccine. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE. The percentage of participants who reported an AE that was associated with the injection site such as redness, swelling, and pain/tenderness/soreness was summarized. Analysis population included all participants who received at least 1 vaccination and had follow-up safety data.	
End point type	Primary
End point timeframe: up to 5 days after any vaccination - Base Study	
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 analysis was planned or performed for this endpoint.	

End point values	9vHPV Vaccine- Base Study	Placebo - Base Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	608	305		
Units: Percentage of Participants				
number (not applicable)	91.1	43.9		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Body Temperature $\geq 100.0^{\circ}\text{F}$ ($\geq 37.8^{\circ}\text{C}$) – Base Study

End point title	Percentage of Participants with Body Temperature $\geq 100.0^{\circ}\text{F}$ ($\geq 37.8^{\circ}\text{C}$) – Base Study
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End point description:

Participants collected their oral body temperature in the evening of their vaccination day and at the same time each day thereafter for 4 days. The maximum body temperature obtained within 5 days of any of the 3 vaccinations was recorded. Analysis population included all participants who received at least 1 vaccination and had follow-up safety data.

End point type	Primary
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End point timeframe:

up to 5 days after any vaccination - Base Study

End point values	9vHPV Vaccine- Base Study	Placebo - Base Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	604	304		
Units: Percentage of Participants				
number (not applicable)	6.5	3		

Statistical analyses

Statistical analysis title	Comparison of Difference in Percentages
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Statistical analysis description:

Comparison based on Miettinen & Nurminen method

Comparison groups	9vHPV Vaccine- Base Study v Placebo - Base Study
Number of subjects included in analysis	908
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.026
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentages
Point estimate	3.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	6.2

Primary: Percentage of Participants Who Experience a Systemic AE – Base Study

End point title	Percentage of Participants Who Experience a Systemic AE – Base Study
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End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the vaccine. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE. Systemic AEs were those not categorized as injection-site AEs. Analysis population included all participants who received at least 1 vaccination and had follow-up safety data.

End point type	Primary
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End point timeframe:

up to 14 days after any vaccination - Base Study

End point values	9vHPV Vaccine- Base Study	Placebo - Base Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	608	305		
Units: Percentage of Participants				
number (not applicable)	59.7	55.7		

Statistical analyses

Statistical analysis title	Comparison of Difference in Percentages
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Statistical analysis description:

Analysis was performed based on Miettinen & Nurminen method

Comparison groups	9vHPV Vaccine- Base Study v Placebo - Base Study
Number of subjects included in analysis	913
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	10.8

Primary: Percentage of Participants Who Experience a Serious Adverse Event (SAE) Within 15 Days of any Vaccination – Base Study

End point title	Percentage of Participants Who Experience a Serious Adverse Event (SAE) Within 15 Days of any Vaccination – Base Study
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End point description:

An SAE is one that results in death, disability/incapacity, or hospitalization or is life threatening, a congenital anomaly or birth defect, cancer, an overdose, or otherwise jeopardizes the participant and may require medical intervention. Analysis population included all participants who received at least 1 vaccination and had follow-up safety data.

End point type	Primary
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End point timeframe:

up to 14 days after any vaccination - Base Study

End point values	9vHPV Vaccine- Base Study	Placebo - Base Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	608	305		
Units: Percentage of Participants				
number (not applicable)	0.3	0.3		

Statistical analyses

Statistical analysis title	Comparison of Difference in Percentages
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Statistical analysis description:

Analysis was performed based on Miettinen & Nurminen method

Comparison groups	9vHPV Vaccine- Base Study v Placebo - Base Study
Number of subjects included in analysis	913
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.9

Primary: Percentage of Participants Who Experience a Vaccine-related SAE Any Time During Study– Base Study

End point title	Percentage of Participants Who Experience a Vaccine-related SAE Any Time During Study– Base Study
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End point description:

An SAE is one that results in death, disability/incapacity, or hospitalization or is life threatening, a congenital anomaly or birth defect, cancer, an overdose, or otherwise jeopardizes the participant and may require medical intervention. An SAE that is judged by the Investigator to be "definitely related," "probably related," or "possibly related" is defined as a vaccine-related SAE. Analysis population included all participants who received at least 1 vaccination and had follow-up safety data.

End point type	Primary
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End point timeframe:

up to 7 months - Base Study

End point values	9vHPV Vaccine- Base Study	Placebo - Base Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	608	305		
Units: Percentage of Participants				
number (not applicable)	0.2	0.3		

Statistical analyses

Statistical analysis title	Comparison of Difference in Percentages
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Statistical analysis description:

Analysis was performed based on Miettinen & Nurminen method

Comparison groups	9vHPV Vaccine- Base Study v Placebo - Base Study
Number of subjects included in analysis	913
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.6

Primary: Percentage of Participants Who Experience a Severe Injection-site AE – Base Study

End point title	Percentage of Participants Who Experience a Severe Injection-site AE – Base Study
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End point description:

An AE is any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the vaccine. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE. Participants were instructed to estimate the severity of AEs such as pain at injection site as mild (awareness of symptom, but easily tolerated), moderate (discomfort enough to cause interference with usual activities), or severe (incapacitating with inability to work or do usual activity). Additionally, participants were instructed to measure any swelling and/or erythema at its greatest width. Swelling or erythema with diameter >2 inches (>5 cm) was recorded as severe. All AEs

associated with the injection site and reported as severe were summarized. Analysis population included all participants who received at least 1 vaccination and had follow-up safety data.

End point type	Primary
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End point timeframe:

up to 5 days after any vaccination - Base Study

End point values	9vHPV Vaccine- Base Study	Placebo - Base Study		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	608	305		
Units: Percentage of Participants				
number (not applicable)	11.2	1		

Statistical analyses

Statistical analysis title	Comparison of Difference in Percentages
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Statistical analysis description:

Comparison based on Miettinen & Nurminen method

Comparison groups	9vHPV Vaccine- Base Study v Placebo - Base Study
Number of subjects included in analysis	913
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentages
Point estimate	10.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.5
upper limit	13.1

Secondary: Percentage of Participants who Seroconvert to Each of the HPV Types Contained in the Vaccine - Base Study

End point title	Percentage of Participants who Seroconvert to Each of the HPV Types Contained in the Vaccine - Base Study
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End point description:

Serum antibody titers for HPV virus-like particles (VLPs), Types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined 4 weeks post-vaccination 3 using competitive luminex immunoassay (cLIA). The serostatus cutoffs (milli Merck U/mL) for HPV types were as follows: HPV Type 6: ≥ 30 , HPV Type 11: ≥ 16 ; HPV Type 16: ≥ 20 , HPV Type 18: ≥ 24 , HPV Type 31: ≥ 10 , HPV Type 33: ≥ 8 , HPV Type 45: ≥ 8 , HPV Type 52: ≥ 8 , and HPV Type 58: ≥ 8 . Analysis population included all participants that received all 3 vaccinations within an acceptable day range, had Month 7 serology sample collected within an acceptable range and had no other protocol violations that could interfere with the immune response to the vaccine.

End point type	Secondary
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End point timeframe:

4 weeks post-vaccination 3 (Month 7; End of Base Study)

End point values	9vHPV Vaccine - Efficacy	Placebo - Efficacy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	515	261		
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 (n=511; n=251)	100 (99.3 to 100)	100 (98.5 to 100)		
Anti-HPV 11 (n=515; n=261)	100 (99.3 to 100)	99.6 (97.9 to 100)		
Anti-HPV 16 (n=515; n=261)	100 (99.3 to 100)	100 (98.6 to 100)		
Anti-HPV 18 (n=515; n=261)	100 (99.3 to 100)	85.4 (80.6 to 89.5)		
Anti-HPV 31 (n=515; n=261)	99.8 (98.9 to 100)	23.8 (18.7 to 29.4)		
Anti-HPV 33 (n=515; n=261)	99.8 (98.9 to 100)	8 (5 to 12)		
Anti-HPV 45 (n=515; n=261)	98.3 (96.7 to 99.2)	3.4 (1.6 to 6.4)		
Anti-HPV 52 (n=515; n=261)	99.6 (98.6 to 100)	3.8 (1.9 to 6.9)		
Anti-HPV 58 (n=515; n=261)	99.8 (98.9 to 100)	9.2 (6 to 13.4)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants Who Experience an SAE- Extension Study

End point title	Percentage of Participants Who Experience an SAE- Extension Study
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End point description:

An SAE is one that results in death, disability/incapacity, or hospitalization or is life threatening, a congenital anomaly or birth defect, cancer, an overdose, or otherwise jeopardizes the participant and may require medical intervention.

End point type	Other pre-specified
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End point timeframe:

up to Month 7 - Extension Study

End point values	9vHPV Vaccine -Extension			
Subject group type	Reporting group			
Number of subjects analysed	99			
Units: Percentage of Participants				
number (not applicable)	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 5 days after any vaccination (Non-serious injection site AEs); up to 15 days after any vaccination (Non-serious systemic AEs) and up to 7 months (Serious AEs) - Base Study; up to 7 months-Extension

Adverse event reporting additional description:

Population included all participants who received at least 1 vaccination and had available follow-up data. Only SAEs were collected systematically in the extension. Although some unsolicited non-serious AEs were reported, none exceeded the 5% cut-off.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	9vHPV Vaccine- Base Study
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Reporting group description:

9vHPV vaccine (V503) 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 of the Base Study. Participants will not continue to the Extension Study

Reporting group title	9vHPV Vaccine- Extension
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Reporting group description:

Participants who received placebo in base study and elected to have 9vHPV vaccination in extension.

Reporting group title	Placebo - Base Study
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Reporting group description:

0.5 mL intramuscular injection of saline placebo at Day 1, Month 2, and Month 6 of the Base Study. After completion of the Base Study, participants will be eligible to receive 9vHPV 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 of the Extension Study.

Serious adverse events	9vHPV Vaccine- Base Study	9vHPV Vaccine- Extension	Placebo - Base Study
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 608 (0.49%)	2 / 99 (2.02%)	3 / 305 (0.98%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	0 / 608 (0.00%)	0 / 99 (0.00%)	1 / 305 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 608 (0.00%)	0 / 99 (0.00%)	1 / 305 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 608 (0.00%)	0 / 99 (0.00%)	1 / 305 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 608 (0.00%)	0 / 99 (0.00%)	1 / 305 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 608 (0.16%)	0 / 99 (0.00%)	0 / 305 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 608 (0.00%)	1 / 99 (1.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 608 (0.16%)	0 / 99 (0.00%)	0 / 305 (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
Tonsillitis			
subjects affected / exposed	1 / 608 (0.16%)	0 / 99 (0.00%)	0 / 305 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 608 (0.00%)	1 / 99 (1.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Non-serious adverse events	9vHPV Vaccine- Base Study	9vHPV Vaccine- Extension	Placebo - Base Study
Total subjects affected by non-serious adverse events			
subjects affected / exposed	566 / 608 (93.09%)	0 / 99 (0.00%)	197 / 305 (64.59%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	31 / 608 (5.10%)	0 / 99 (0.00%)	6 / 305 (1.97%)
occurrences (all)	34	0	8
Headache			
subjects affected / exposed	190 / 608 (31.25%)	0 / 99 (0.00%)	81 / 305 (26.56%)
occurrences (all)	318	0	150
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	258 / 608 (42.43%)	0 / 99 (0.00%)	26 / 305 (8.52%)
occurrences (all)	420	0	33
Injection site pain			
subjects affected / exposed	549 / 608 (90.30%)	0 / 99 (0.00%)	117 / 305 (38.36%)
occurrences (all)	1392	0	182
Injection site pruritus			
subjects affected / exposed	48 / 608 (7.89%)	0 / 99 (0.00%)	4 / 305 (1.31%)
occurrences (all)	68	0	5
Injection site swelling			
subjects affected / exposed	298 / 608 (49.01%)	0 / 99 (0.00%)	18 / 305 (5.90%)
occurrences (all)	558	0	27
Pyrexia			
subjects affected / exposed	42 / 608 (6.91%)	0 / 99 (0.00%)	10 / 305 (3.28%)
occurrences (all)	50	0	10
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	52 / 608 (8.55%)	0 / 99 (0.00%)	12 / 305 (3.93%)
occurrences (all)	67	0	13
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	40 / 608 (6.58%)	0 / 99 (0.00%)	12 / 305 (3.93%)
occurrences (all)	46	0	14
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	47 / 608 (7.73%) 55	0 / 99 (0.00%) 0	19 / 305 (6.23%) 20
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 January 2014	Amendment 2: Added extension study. Participants who received placebo in the base study could elect to receive the 9vHPV vaccine in the extension.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported