



## Clinical trial results:

### Evaluation of Safety, Tolerability and Immunogenicity of Quadrivalent HPV Vaccine in healthy females 9 to 15 years of age in India

#### Summary

EudraCT number	2017-000111-16
Trial protocol	Outside EU/EEA
Global end of trial date	04 February 2008

#### Results information

Result version number	v1 (current)
This version publication date	25 February 2017
First version publication date	25 February 2017

#### Trial information

##### Trial identification

Sponsor protocol code	V501-029
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00380367
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., 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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	04 February 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 February 2008
Global end of trial reached?	Yes
Global end of trial date	04 February 2008
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

The purpose of this study is to evaluate the safety and tolerability of the Quadrivalent Human Papilloma Virus (HPV) vaccine in healthy females 9 to 15 years of age in India. Quadrivalent HPV Vaccine is composed of L1 virus-like particles (VLPs) from HPV types 6, 11, 16, and 18.

mMU/mL = milli-Merck units/milliliter

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	03 May 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	India: 110
Worldwide total number of subjects	110
EEA total number of subjects	0

Notes:

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**Subjects enrolled per age group**

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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)	44
Adolescents (12-17 years)	66
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0
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## Subject disposition

### Recruitment

Recruitment details:

First Patient In (FPI): 03 May 2007

Last Patient Out (LPO): 04 Feb 2008

Multi-center study. Seven sites participated in the study. All sites were medical centers located in Bangalore, Mumbai and Pune.

### Pre-assignment

Screening details:

Open-label, single-arm, nonrandomized study. Females >9 to 15 years of age who at first vaccination had not had coitarche, did not plan on becoming sexually active through the course of the study, and who did not have a feverish feeling within 24 hours prior to the first injection, were included in the study.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

<b>Arm title</b>	Quadrivalent HPV VLP Vaccine (Types 6, 11, 16, 18)
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Arm description:

Participants who were enrolled received a total of 3 intramuscular injections of Quadrivalent HPV VLP vaccine (types 6, 11, 16, 18) given on Day 1, Month 2 and Month 6.

Arm type	Experimental
Investigational medicinal product name	Quadrivalent HPV VLP Recombinant Vaccine (Types 6, 11, 16, 18)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Quadrivalent HPV vaccine (6, 11, 16, 18) given intramuscularly on Day 1, Month 2, and Month 6.

<b>Number of subjects in period 1</b>	Quadrivalent HPV VLP Vaccine (Types 6, 11, 16, 18)
Started	110
Completed	108
Not completed	2
Consent withdrawn by subject	1
Lost to follow-up	1

## Baseline characteristics

### Reporting groups

Reporting group title	Quadrivalent HPV VLP Vaccine (Types 6, 11, 16, 18)
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Reporting group description:

Participants who were enrolled received a total of 3 intramuscular injections of Quadrivalent HPV VLP vaccine (types 6, 11, 16, 18) given on Day 1, Month 2 and Month 6.

Reporting group values	Quadrivalent HPV VLP Vaccine (Types 6, 11, 16, 18)	Total	
Number of subjects	110	110	
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	11.54 ± 1.67	-	
Gender, Male/Female Units: Subjects			
Female	110	110	
Male	0	0	
Study Specific Characteristic   Body Mass Index (BMI) Units: Kg/m2 arithmetic mean standard deviation	16.76 ± 2.79	-	
Study Specific Characteristic   Height Units: Cm arithmetic mean standard deviation	143.32 ± 9.58	-	
Study Specific Characteristic   Weight Units: Kg median standard deviation	34.9 ± 8.81	-	

## End points

### End points reporting groups

Reporting group title	Quadrivalent HPV VLP Vaccine (Types 6, 11, 16, 18)
Reporting group description:	
Participants who were enrolled received a total of 3 intramuscular injections of Quadrivalent HPV VLP vaccine (types 6, 11, 16, 18) given on Day 1, Month 2 and Month 6.	

### Primary: Percentage of Participants Who Seroconvert to Each HPV Serotype (Types 6, 11, 16, 18) at Month 7

End point title	Percentage of Participants Who Seroconvert to Each HPV Serotype (Types 6, 11, 16, 18) at Month 7 <sup>[1]</sup>
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#### End point description:

Month 7 HPV competitive Luminex Immunoassay (cLIA) seroconversion rates among participants who received Quadrivalent HPV (Types 6, 11, 16, 18) Late 1 (L1) capsid protein VLP vaccine reported. Quadrivalent HPV competitive cLIA (v2.0) used to detect antibody to HPV VLPs serotypes 6, 11, 16, 18 before and after vaccination. Seropositivity cutoffs of HPV cLIAs assessed using a panel of sera from participants highly likely to be HPV naïve (children), and from participants highly likely to be seropositive. Samples with value < cutoffs = serostatus negative. Samples with values ≥ cutoff = serostatus positive. Cutoffs for HPV 6, 11, 16, and 18 cLIAs were 20 mMU/mL, 16 mMU/mL, 20 mMU/mL, and 24 mMU/mL, respectively.

Analysis performed in all participants who were not general protocol violators, received all 3 vaccinations within acceptable day ranges, were sero-negative at Day 1 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

End point type	Primary
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#### End point timeframe:

One month post-dose 3 (Month 7)

#### 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: There was no formal efficacy hypothesis testing planned for this endpoint, and there were no between-group statistical comparisons performed.

End point values	Quadrivalent HPV VLP Vaccine (Types 6, 11, 16, 18)			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: percentage of participants				
number (confidence interval 95%)				
Anti-HPV 6 (n=99)	96.97 (93.59 to 100.35)			
Anti-HPV 11 (n=105)	99.05 (97.19 to 100.91)			
Anti-HPV 16 (n=105)	99.05 (97.19 to 100.91)			
Anti-HPV 18 (n=105)	99.05 (97.19 to 100.91)			

## Statistical analyses

**Primary: Number of Participants With Any Adverse Events (AEs), Injection-site AEs, Systemic AEs, or Vaccine-related AEs During the Study**

End point title	Number of Participants With Any Adverse Events (AEs), Injection-site AEs, Systemic AEs, or Vaccine-related AEs During the Study <sup>[2]</sup>
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## End point description:

AE defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with use of SPONSOR's product, whether or not considered related to the use of the product. Any worsening of a preexisting condition temporally associated with the use of the SPONSOR's product, was also an AE. Pre-specified injection site AEs included pain, tenderness, erythema, and swelling. A vaccine-related AE was an AE considered by the investigator to be possibly, probably, or definitely related to the vaccine. All AEs collected on participant's Vaccination Report Card daily for 14 days after each vaccination (Days 1-15).

Number of participants experiencing  $\geq 1$  AE, number of participants experiencing  $\geq 1$  injection site AE, number of participants experiencing  $\geq 1$  systemic AE, and number of participants experiencing  $\geq 1$  vaccine-related AE were reported for the Safety Cohort (all enrolled participants who received  $\geq 1$  injection and had safety follow-up data).

End point type	Primary
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## End point timeframe:

Up to 7 months

## 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: There was no formal efficacy hypothesis testing planned for this endpoint, and there were no between-group statistical comparisons performed.

<b>End point values</b>	Quadrivalent HPV VLP Vaccine (Types 6, 11, 16, 18)			
Subject group type	Reporting group			
Number of subjects analysed	108 <sup>[3]</sup>			
Units: participants				
Any AE	63			
Injection site AE	50			
Systemic AE	35			
Vaccine-related AE	45			

## Notes:

[3] - 2 participants did not have safety follow-up data and were excluded from safety analyses.

**Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 7 months

Adverse event reporting additional description:

Safety Cohort: All enrolled participants who received  $\geq 1$  injection and had safety follow-up data. Two participants did not have safety follow-up data and were excluded from safety analyses.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.1
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### Reporting groups

Reporting group title	Quadrivalent HPV VLP Vaccine (Types 6, 11, 16, 18)
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Reporting group description:

Participants who were enrolled received a total of 3 intramuscular injections of Quadrivalent HPV VLP vaccine (types 6, 11, 16, 18) given on Day 1, Month 2 and Month 6.

Serious adverse events	Quadrivalent HPV VLP Vaccine (Types 6, 11, 16, 18)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 108 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Quadrivalent HPV VLP Vaccine (Types 6, 11, 16, 18)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 108 (58.33%)		
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Somnolence			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
General disorders and administration site conditions			



Asthenia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	25 / 108 (23.15%)		
occurrences (all)	25		
Injection site pain			
subjects affected / exposed	46 / 108 (42.59%)		
occurrences (all)	83		
Injection site tenderness			
subjects affected / exposed	25 / 108 (23.15%)		
occurrences (all)	41		
Injection site erythema			
subjects affected / exposed	13 / 108 (12.04%)		
occurrences (all)	20		
Injection site swelling			
subjects affected / exposed	10 / 108 (9.26%)		
occurrences (all)	16		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	4 / 108 (3.70%) 4		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)  Pharyngitis subjects affected / exposed occurrences (all)	8 / 108 (7.41%) 8  1 / 108 (0.93%) 1		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported