Clinical trial results:
A Randomized, Double-Blinded, Tolerability and Immunogenicity Study of a Multivalent Human Papillomavirus (HPV) L1 Virus-Like Particle (VLP) Vaccine (V504) Administered Concomitantly with GARDASIL™ to 16- to 26-Year-Old Women

Summary

EudraCT number	2007-003852-13
Trial protocol	SE AT DK
Global end of trial date	20 May 2009

Results information

Result version number	v1
This version publication date	16 February 2016
First version publication date	01 April 2015

Trial information

Trial identification

Sponsor protocol code	V504-001-00

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00551187
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, New Jersey, 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	20 May 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 May 2009
Global end of trial reached?	Yes
Global end of trial date	20 May 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To evaluate the tolerability of the 5-valent HPV L1 VLP vaccine when administered concomitantly with GARDASIL™ to 16- to 26-year-old women.
2. To demonstrate that administration of the 5-valent HPV L1 VLP vaccine concomitantly with GARDASIL™ (different injection sites in separate limbs) induces non-inferior Geometric Mean Titers (GMTs) for anti-HPV 6, 11, 16, and 18 compared to GARDASIL™ administered concomitantly with placebo.

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	20 October 2007
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	Canada: 156
Country: Number of subjects enrolled	United States: 146
Country: Number of subjects enrolled	Puerto Rico: 39
Country: Number of subjects enrolled	Sweden: 115
Country: Number of subjects enrolled	Austria: 40
Country: Number of subjects enrolled	Denmark: 127
Worldwide total number of subjects	623
EEA total number of subjects	282

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)	72
Adults (18-64 years)	551
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study enrolled healthy female participants 16 to 26 years old with <=4 lifetime sexual partners, no history of an abnormal Papanicolaou (Pap) test, no positive test for HPV or abnormal cervical biopsy, and no history of or baseline clinical evidence of HPV-related lesions or cancer. Other inclusion and exclusion criteria applied.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	V504 + Gardasil™

Arm description:

Participants received 0.5 mL intramuscular injections of V504 and Gardasil™ in separate limbs on Day 1, Month 2, and Month 6

Arm type	Experimental
Investigational medicinal product name	V504
Investigational medicinal product code	
Other name	5-Valent Human Papillomavirus (HPV) L1 Virus-like Particle (VLP) Vaccine (HPV Types 31, 33, 45, 52, 58)
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received 0.5 mL intramuscular injections (deltoid muscle of the non-dominant limb preferred) on Day 1, Month 2, and Month 6

Investigational medicinal product name	Gardasil™
Investigational medicinal product code	
Other name	4-Valent Human Papillomavirus (HPV) L1 Virus-like Particle (VLP) Vaccine (HPV Types 6, 11, 16, 18); Gardasil™, Silgard™
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received 0.5 mL intramuscular injections (deltoid muscle of the dominant limb preferred) on Day 1, Month 2, and Month 6

Arm title	Placebo + Gardasil™

Arm description:

Participants received 0.5 mL intramuscular injections of placebo and Gardasil™ in separate limbs on Day 1, Month 2, and Month 6

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo for V504
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:	
Participants received 0.5 mL intramuscular injections (deltoid muscle of the non-dominant limb preferred) on Day 1, Month 2, and Month 6	
Investigational medicinal product name	Gardasil™
Investigational medicinal product code	
Other name	4-Valent Human Papillomavirus (HPV) L1 Virus-like Particle (VLP) Vaccine (HPV Types 6, 11, 16, 18); Gardasil™, Silgard™
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Participants received 0.5 mL intramuscular injections (deltoid muscle of the dominant limb preferred) on Day 1, Month 2, and Month 6	

Number of subjects in period 1	V504 + Gardasil™	Placebo + Gardasil™
Started	310	313
Vaccination 1	308	313
Vaccination 2	301	307
Vaccination 3	298	303
Completed	297	296
Not completed	13	17
Consent withdrawn by subject	7	8
Pregnancy	1	-
Lost to follow-up	4	9
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	V504 + Gardasil™
Reporting group description:	
Participants received 0.5 mL intramuscular injections of V504 and Gardasil™ in separate limbs on Day 1, Month 2, and Month 6	
Reporting group title	Placebo + Gardasil™
Reporting group description:	
Participants received 0.5 mL intramuscular injections of placebo and Gardasil™ in separate limbs on Day 1, Month 2, and Month 6	

Reporting group values	V504 + Gardasil™	Placebo + Gardasil™	Total
Number of subjects	310	313	623
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	21.1	21	
standard deviation	± 2.9	± 2.7	-
Gender categorical			
Units: Subjects			
Female	310	313	623
Male	0	0	0

End points

End points reporting groups

Reporting group title	V504 + Gardasil™
Reporting group description:	
Participants received 0.5 mL intramuscular injections of V504 and Gardasil™ in separate limbs on Day 1, Month 2, and Month 6	
Reporting group title	Placebo + Gardasil™
Reporting group description:	
Participants received 0.5 mL intramuscular injections of placebo and Gardasil™ in separate limbs on Day 1, Month 2, and Month 6	
Subject analysis set title	V504 + Gardasil™ - Safety Analysis
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received 0.5 mL intramuscular injections of V504 and Gardasil™ in separate limbs on Day 1, Month 2, and Month 6. The analysis set includes participants who received >=1 vaccination and had safety follow-up.	
Subject analysis set title	Placebo + Gardasil™ - Safety Analysis
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received 0.5 mL intramuscular injections of Placebo and Gardasil™ in separate limbs on Day 1, Month 2, and Month 6. The analysis set includes participants who received >=1 vaccination and had safety follow-up.	

Primary: Geometric Mean Titers (GMTs) to the HPV Types Contained in the Study Vaccines

End point title	Geometric Mean Titers (GMTs) to the HPV Types Contained in the Study Vaccines
End point description:	
Serum antibodies to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 were measured using a Competitive Luminex Immunoassay. Titers are reported in milli Merck Units/mL. Titers given as zero (0) were reported as 'less than' values; these were <4 milli Merck Units/mL for Type 33 and Type 45, <2 milli Merck Units/mL for Type 52, and <3 milli Merck Units/mL for Type 58. Statistical analysis includes only HPV types contained in the Gardasil™ vaccine.	
End point type	Primary
End point timeframe:	
Four weeks post vaccination 3 (Month 7)	

End point values	V504 + Gardasil™	Placebo + Gardasil™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239[1]	258[2]		
Units: milli Merck Units/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=216, 234)	734 (655.1 to 822.4)	844.8 (757.4 to 942.2)		
Anti-HPV Type 11 (n=216, 234)	687 (609.1 to 774.7)	801.1 (713.7 to 899.3)		
Anti-HPV Type 16 (n=203, 214)	2743.6 (2469.2 to 3048.4)	3153.9 (2846.3 to 3494.8)		

Anti-HPV Type 18 (n=221, 240)	664.9 (570.3 to 775.1)	680.9 (587.7 to 789)		
Anti-HPV Type 31 (n=226, 242)	633.4 (547.9 to 732.3)	9.4 (8.2 to 10.8)		
Anti-HPV Type 33 (n=236, 249)	337 (301.6 to 376.7)	0 (0 to 0)		
Anti-HPV Type 45 (n=233, 253)	269.1 (238.8 to 303.2)	0 (0 to 0)		
Anti-HPV Type 52 (n=224, 244)	372.1 (334.9 to 413.6)	0 (0 to 0)		
Anti-HPV Type 58 (n=225, 245)	437.6 (386.7 to 495.3)	3.1 (0 to 3.5)		

Notes:

[1] - Had 3 doses, Month 7 results, and negative results to ≥1 HPV type by PCR and serology up to Month 7

[2] - Had 3 doses, Month 7 results, and negative results to ≥1 HPV type by PCR and serology up to Month 7

Statistical analyses

Statistical analysis title	Non-inferiority Anti-HPV Type 6

Statistical analysis description:

Primary analysis evaluated non-inferiority of the GMT for anti-HPV Type 6 in participants who received V504 + Gardasil™ compared with those who received placebo + Gardasil™

Comparison groups	Placebo + Gardasil™ v V504 + Gardasil™
Number of subjects included in analysis	497
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.02

Notes:

[3] - Criterion for non-inferiority with respect to the GMT ratio (V504 + Gardasil™ / placebo + Gardasil™) requires that the lower bound of the 95% confidence interval be >0.5 to rule out a decrease of 2-fold or more. An analysis of variance model with a response of log individual titers and a fixed effect for group was used.

Statistical analysis title	Non-inferiority Anti-HPV Type 11

Statistical analysis description:

Primary analysis evaluated non-inferiority of the GMT for anti-HPV Type 11 in participants who received V504 + Gardasil™ compared with those who received placebo + Gardasil™

Comparison groups	V504 + Gardasil™ v Placebo + Gardasil™
Number of subjects included in analysis	497
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.86

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.01

Notes:

[4] - Criterion for non-inferiority with respect to the GMT ratio (V504 + Gardasil™ / placebo + Gardasil™) requires that the lower bound of the 95% confidence interval be >0.5 to rule out a decrease of 2-fold or more. An analysis of variance model with a response of log individual titers and a fixed effect for group was used.

Statistical analysis title	Non-inferiority Anti-HPV Type 16

Statistical analysis description:

Primary analysis evaluated non-inferiority of the GMT for anti-HPV Type 16 in participants who received V504 + Gardasil™ compared with those who received placebo + Gardasil™

Comparison groups	V504 + Gardasil™ v Placebo + Gardasil™
Number of subjects included in analysis	497
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.01

Notes:

[5] - Criterion for non-inferiority with respect to the GMT ratio (V504 + Gardasil™ / placebo + Gardasil™) requires that the lower bound of the 95% confidence interval be >0.5 to rule out a decrease of 2-fold or more. An analysis of variance model with a response of log individual titers and a fixed effect for group was used.

Statistical analysis title	Non-inferiority Anti-HPV Type 18

Statistical analysis description:

Primary analysis evaluated non-inferiority of the GMT for anti-HPV Type 18 in participants who received V504 + Gardasil™ compared with those who received placebo + Gardasil™

Comparison groups	V504 + Gardasil™ v Placebo + Gardasil™
Number of subjects included in analysis	497
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.21

Notes:

[6] - Criterion for non-inferiority with respect to the GMT ratio (V504 + Gardasil™ / placebo + Gardasil™) requires that the lower bound of the 95% confidence interval be >0.5 to rule out a decrease of 2-fold or more. An analysis of variance model with a response of log individual titers and a fixed

effect for group was used.

Primary: Number of Participants with an Adverse Event

End point title	Number of Participants with an Adverse Event[7]

End point description:

An adverse event (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 product. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE.

End point type	Primary

End point timeframe:

Up to 7 weeks after vaccination 3 (up to 31 weeks)

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 analysis was conducted for Number of Participants with an Adverse Event

End point values	V504 + Gardasil™ - Safety Analysis	Placebo + Gardasil™ - Safety Analysis		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	307	309		
Units: Participants	289	291		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Discontinued from Study Vaccine Due to an Adverse Event

End point title	Number of Participants Discontinued from Study Vaccine Due to an Adverse Event[8]

End point description:

An adverse event (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 product. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE.

End point type	Primary

End point timeframe:

Up to Month 6

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 analysis was conducted for Number of Participants Discontinued from Study Vaccine Due to an Adverse Event

End point values	V504 + Gardasil™ - Safety Analysis	Placebo + Gardasil™ - Safety Analysis		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	307	309		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with a Vaccine-Related Adverse Event

End point title	Number of Participants with a Vaccine-Related Adverse Event[9]

End point description:

An adverse event (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 product. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE. An AE that is judged by the Investigator to be "definitely related," "probably related," or "possibly related" is defined as a vaccine-related.

End point type	Primary

End point timeframe:

Up to 7 weeks after vaccination 3 (up to 31 weeks)

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 analysis was performed for Number of Participants with a Vaccine-Related Adverse Event

End point values	V504 + Gardasil™ - Safety Analysis	Placebo + Gardasil™ - Safety Analysis		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	307	309		
Units: Participants	278	282		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with one or more Injection-site Adverse Events Prompted on the Vaccination Report Card

End point title	Number of Participants with one or more Injection-site Adverse Events Prompted on the Vaccination Report Card

End point description:

An adverse event (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 product. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE. Specific injection-site AEs, such as erythema, pain, and swelling, were prompted for on the Vaccination Report Card.

End point type	Primary

End point timeframe:

Up to 5 days after any vaccination

End point values	V504 + Gardasil™ - Safety Analysis	Placebo + Gardasil™ - Safety Analysis		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	306[10]	303[11]		
Units: Participants				
Injection-site erythema	109	88		
Injection-site pain	276	265		
Injection-site swelling	109	85		

Notes:

[10] - Participants in the Safety Analysis who had Vaccination Report Card results

[11] - Participants in the Safety Analysis who had Vaccination Report Card results

Statistical analyses

Statistical analysis title	Injection-site Erythema AEs

Statistical analysis description:

The incidence of VRC-prompted injection-site erythema was compared between the treatment groups. Injection-site erythema AEs on both injection sites were included in the analysis.

Comparison groups	V504 + Gardasil™ - Safety Analysis v Placebo + Gardasil™ - Safety Analysis
Number of subjects included in analysis	609
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.083
Method	Miettinen & Nurminen
Parameter estimate	Risk difference (RD)
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	14

Statistical analysis title	Injection-site Pain AEs

Statistical analysis description:

The incidence of VRC-prompted injection-site pain was compared between the treatment groups. Injection-site pain AEs on both injection sites were included in the analysis.

Comparison groups	V504 + Gardasil™ - Safety Analysis v Placebo + Gardasil™ - Safety Analysis

Number of subjects included in analysis	609
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.284
Method	Miettinen & Nurminen
Parameter estimate	Risk difference (RD)
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	7.9

Statistical analysis title	Injection-site Swelling AEs

Statistical analysis description:

The incidence of VRC-prompted injection-site swelling was compared between the treatment groups. Injection-site swelling AEs on both injection sites were included in the analysis.

Comparison groups	V504 + Gardasil™ - Safety Analysis v Placebo + Gardasil™ - Safety Analysis
Number of subjects included in analysis	609
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.045
Method	Miettinen & Nurminen
Parameter estimate	Risk difference (RD)
Point estimate	7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	14.9

Primary: Number of Participants with Elevated Body Temperature (>=37.8° C, >=100° F)

End point title	Number of Participants with Elevated Body Temperature (>=37.8° C, >=100° F)

End point description:

Participants were instructed by the investigator to use the Vaccine Report Card to document evening oral temperature daily after each study vaccination

End point type	Primary

End point timeframe:

Up to 5 days after any vaccination

End point values	V504 + Gardasil™ - Safety Analysis	Placebo + Gardasil™ - Safety Analysis		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	305[12]	309[13]		
Units: Participants	14	8		

Notes:

[12] - Participants in the Safety Analysis who had temperature results

[13] - Participants in the Safety Analysis who had temperature results

Statistical analyses

Statistical analysis title	Elevated Body Temperature

Statistical analysis description:

The incidence of maximum body temperature >=37.8° C reported on the Vaccine Report Card was compared between the treatment groups

Comparison groups	V504 + Gardasil™ - Safety Analysis v Placebo + Gardasil™ - Safety Analysis
Number of subjects included in analysis	614
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.183
Method	Miettinen & Nurminen
Parameter estimate	Risk difference (RD)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	5.3

Secondary: Percentage of Participants with Seroconversion to the HPV Types Contained in the Study Vaccines

End point title	Percentage of Participants with Seroconversion to the HPV Types Contained in the Study Vaccines

End point description:

Serum antibodies to HPV types were measured with a Competitive Luminex Immunoassay. The serostatus cutoffs (milli Merck U/mL) for HPV types were as follows: HPV Type 6: ≥20; HPV Type 11: ≥16; HPV Type 16: ≥20; HPV Type 18: ≥24; HPV Type 31: ≥10; HPV Types 33, 45, 52, and 58: ≥8. For the V504 + Gardasil™ arm, the criterion for acceptability of the seroconversion percentage for HPV Types 31, 33, 45, 52, and 58 required that the lower bound of the 2-sided 95% confidence interval be >90%.

End point type	Secondary

End point timeframe:

Four weeks post vaccination 3 (Month 7)

End point values	V504 + Gardasil™	Placebo + Gardasil™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239[14]	258[15]		
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV Type 6 (n=216, 234)	100 (98.3 to 100)	99.6 (97.6 to 100)		
Anti-HPV Type 11 (n=216, 234)	100 (98.3 to 100)	99.6 (97.6 to 100)		
Anti-HPV Type 16 (n=203, 214)	100 (98.2 to 100)	100 (98.3 to 100)		
Anti-HPV Type 18 (n=221, 240)	100 (98.3 to 100)	99.6 (97.7 to 100)		
Anti-HPV Type 31 (n=226, 242)	99.6 (97.6 to 100)	45.5 (39.1 to 52)		
Anti-HPV Type 33 (n=236, 249)	99.6 (97.7 to 100)	15.7 (11.4 to 20.8)		
Anti-HPV Type 45 (n=233, 253)	100 (98.4 to 100)	7.1 (4.3 to 11)		
Anti-HPV Type 52 (n=224, 244)	100 (98.4 to 100)	1.2 (0.3 to 3.6)		
Anti-HPV Type 58 (n=225, 245)	100 (98.4 to 100)	17.1 (12.6 to 22.5)		

Notes:

[14] - Had 3 doses, Month 7 results, and negative results to ≥1 HPV type by PCR and serology up to Month 7

[15] - Had 3 doses, Month 7 results, and negative results to ≥1 HPV type by PCR and serology up to Month 7

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Serious adverse events: up to Month 7; Non-serious adverse events: up to 15 days after any vaccination.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups	
Reporting group title	V504 + Gardasil™
Reporting group description: Participants received 0.5 mL intramuscular injections of V504 and Gardasil™ in separate limbs on Day 1, Month 2, and Month 6	
Reporting group title	Placebo + Gardasil™
Reporting group description: Participants received 0.5 mL intramuscular injections of placebo and Gardasil™ in separate limbs on Day 1, Month 2, and Month 6	

Serious adverse events	V504 + Gardasil™	Placebo + Gardasil™	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 307 (0.00%)	0 / 309 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	V504 + Gardasil™	Placebo + Gardasil™	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	286 / 307 (93.16%)	283 / 309 (91.59%)	
Nervous system disorders			
Headache			
subjects affected / exposed	93 / 307 (30.29%)	96 / 309 (31.07%)	
occurrences (all)	158	141	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	110 / 307 (35.83%)	90 / 309 (29.13%)	
occurrences (all)	237	211	
Injection site haematoma			

subjects affected / exposed	26 / 307 (8.47%)	17 / 309 (5.50%)	
occurrences (all)	34	24	
Injection site pain			
subjects affected / exposed	277 / 307 (90.23%)	270 / 309 (87.38%)	
occurrences (all)	1153	1064	
Injection site pruritus			
subjects affected / exposed	18 / 307 (5.86%)	19 / 309 (6.15%)	
occurrences (all)	33	33	
Injection site swelling			
subjects affected / exposed	112 / 307 (36.48%)	87 / 309 (28.16%)	
occurrences (all)	278	214	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	34 / 307 (11.07%)	35 / 309 (11.33%)	
occurrences (all)	39	40	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	17 / 307 (5.54%)	13 / 309 (4.21%)	
occurrences (all)	19	14	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	18 / 307 (5.86%)	19 / 309 (6.15%)	
occurrences (all)	21	19	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	31 / 307 (10.10%)	34 / 309 (11.00%)	
occurrences (all)	37	40	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported