Clinical trial results:
A Phase IIa Randomized, Double-Blinded, Controlled With GARDASIL™ Clinical Trial to Study the Tolerability and Immunogenicity of V505 (a Multivalent Human Papillomavirus [HPV] L1 Virus-Like Particle [VLP] Vaccine) in Healthy 16- to 26-Year-Old Women

Summary

EudraCT number	2017-000108-42
Trial protocol	Outside EU/EEA
Global end of trial date	16 May 2011

Results information

Result version number	v1 (current)
This version publication date	10 March 2017
First version publication date	10 March 2017

Trial information

Trial identification

Sponsor protocol code	v505-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00520598
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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 May 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 May 2011
Global end of trial reached?	Yes
Global end of trial date	16 May 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the safety and immunogenicity of V505 in comparison with GARDASIL™. The primary hypothesis of the study is that administration of a 3-dose regimen of at least 1 of 2 formulations of V505 generates anti-HPV 6, 11, 16, and 18 geometric mean antibody titers 4 weeks post dose 3 that are noninferior to those generated by GARDASIL™ in 16- to 26-year old adolescent and young adult women who are seronegative at Day 1 and polymerase chain reaction (PCR) negative Day 1 through Month 7 to the relevant HPV type(s) and the vaccines are well-tolerated.

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	18 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	Australia: 212
Country: Number of subjects enrolled	New Zealand: 299
Worldwide total number of subjects	511
EEA total number of subjects	0

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)	65
Adults (18-64 years)	446

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Twelve clinical sites participated in this study in Australia and New Zealand.

Pre-assignment

Screening details:

A total of 529 participants were screened for inclusion in this study and 511 participants were randomized. A total of 17 non-randomized participants did not meet inclusion/exclusion criteria.

Period 1

Period 1 title	Day 1 Through Month 7
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	V505 Formulation 1 Vaccine [3 doses]

Arm description:

V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)

Arm type	Experimental
Investigational medicinal product name	V505 Formulation 1 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)

Arm title	V505 Formulation 2 Vaccine [3 doses]

Arm description:

V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)

Arm type	Experimental
Investigational medicinal product name	V505 Formulation 2 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)

Arm title	V505 Formulation 2 Vaccine [2 doses]

Arm description:

V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)

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

Dosage and administration details: Placebo vaccine [1 dose] intramuscular (Month 2)	
Investigational medicinal product name	V505 Formulation 2 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)	
Arm title	V505 Formulation 3 Vaccine [2 doses]
Arm description: V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)	
Arm type	Experimental
Investigational medicinal product name	Placebo to vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: Placebo vaccine [1 dose] intramuscular (Month 2)	
Investigational medicinal product name	V505 Formulation 3 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)	
Arm title	qHPV Vaccine [3 doses]
Arm description: HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6)	
Arm type	Active comparator
Investigational medicinal product name	qHPV Vaccine
Investigational medicinal product code	
Other name	GARDASIL™
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™) [3 doses] (Day 1, Month 2, and Month 6)	

Number of subjects in period 1	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 Vaccine [3 doses]	V505 Formulation 2 Vaccine [2 doses]
Started	101	105	103
Vaccination 1	101	105	103
Vaccination 2	99	102	102
Vaccination 3	98	101	99
Completed	97	101	97
Not completed	4	4	6

Consent withdrawn by subject	-	3	2
Lost to follow-up	4	1	4

Number of subjects in period 1	V505 Formulation 3 Vaccine [2 doses]	qHPV Vaccine [3 doses]
Started	101	101
Vaccination 1	101	101
Vaccination 2	101	99
Vaccination 3	100	96
Completed	100	96
Not completed	1	5
Consent withdrawn by subject	1	1
Lost to follow-up	-	4

Period 2

Period 2 title	Month 7 to Month 36
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	V505 Formulation 1 Vaccine [3 doses]

Arm description:

V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)

Arm type	Experimental
Investigational medicinal product name	V505 Formulation 1 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)

Arm title	V505 Formulation 2 Vaccine [3 doses]

Arm description:

V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)

Arm type	Experimental
Investigational medicinal product name	V505 Formulation 2 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)

Arm title	V505 Formulation 2 Vaccine [2 doses]
Arm description:	
V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)	
Arm type	Experimental
Investigational medicinal product name	Placebo to vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Placebo vaccine [1 dose] intramuscular (Month 2)	
Investigational medicinal product name	V505 Formulation 2 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)	
Arm title	V505 Formulation 3 Vaccine [2 doses]
Arm description:	
V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)	
Arm type	Experimental
Investigational medicinal product name	V505 Formulation 3 vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)	
Investigational medicinal product name	Placebo to vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Placebo vaccine [1 dose] intramuscular (Month 2)	
Arm title	qHPV Vaccine [3 doses]
Arm description:	
HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6)	
Arm type	Active comparator
Investigational medicinal product name	qHPV Vaccine
Investigational medicinal product code	
Other name	GARDASIL™
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6)	

Number of subjects in period 2	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 Vaccine [3 doses]	V505 Formulation 2 Vaccine [2 doses]
Started	97	101	97
Completed	92	95	91
Not completed	5	6	6
Consent withdrawn by subject	3	1	-
Study Terminated By Sponsor	-	-	-
Lost to follow-up	2	5	6

Number of subjects in period 2	V505 Formulation 3 Vaccine [2 doses]	qHPV Vaccine [3 doses]
Started	100	96
Completed	92	82
Not completed	8	14
Consent withdrawn by subject	1	6
Study Terminated By Sponsor	1	-
Lost to follow-up	6	8

Baseline characteristics

Reporting groups	
Reporting group title	V505 Formulation 1 Vaccine [3 doses]
Reporting group description: V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)	
Reporting group title	V505 Formulation 2 Vaccine [3 doses]
Reporting group description: V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)	
Reporting group title	V505 Formulation 2 Vaccine [2 doses]
Reporting group description: V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)	
Reporting group title	V505 Formulation 3 Vaccine [2 doses]
Reporting group description: V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)	
Reporting group title	qHPV Vaccine [3 doses]
Reporting group description: HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6)	

Reporting group values	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 Vaccine [3 doses]	V505 Formulation 2 Vaccine [2 doses]
Number of subjects	101	105	103
Age Categorical Units: Subjects			
Adolescents (12-17 years)	17	15	10
Adults (18-64 years)	84	90	93
Age Continuous Units: years			
arithmetic mean	20.6	20.6	20.5
standard deviation	± 2.8	± 2.6	± 2.5
Gender Categorical Units: Subjects			
Female	101	105	103
Male	0	0	0

Reporting group values	V505 Formulation 3 Vaccine [2 doses]	qHPV Vaccine [3 doses]	Total
Number of subjects	101	101	511
Age Categorical Units: Subjects			
Adolescents (12-17 years)	10	13	65
Adults (18-64 years)	91	88	446
Age Continuous Units: years			
arithmetic mean	21	20.4	
standard deviation	± 2.5	± 2.6	-
Gender Categorical Units: Subjects			
Female	101	101	511
Male	0	0	0

End points

End points reporting groups

Reporting group title	V505 Formulation 1 Vaccine [3 doses]
Reporting group description: V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)	
Reporting group title	V505 Formulation 2 Vaccine [3 doses]
Reporting group description: V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)	
Reporting group title	V505 Formulation 2 Vaccine [2 doses]
Reporting group description: V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)	
Reporting group title	V505 Formulation 3 Vaccine [2 doses]
Reporting group description: V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)	
Reporting group title	qHPV Vaccine [3 doses]
Reporting group description: HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6)	
Reporting group title	V505 Formulation 1 Vaccine [3 doses]
Reporting group description: V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)	
Reporting group title	V505 Formulation 2 Vaccine [3 doses]
Reporting group description: V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)	
Reporting group title	V505 Formulation 2 Vaccine [2 doses]
Reporting group description: V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)	
Reporting group title	V505 Formulation 3 Vaccine [2 doses]
Reporting group description: V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)	
Reporting group title	qHPV Vaccine [3 doses]
Reporting group description: HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6)	
Subject analysis set title	V505 Formulation 1 Vaccine [3 doses]
Subject analysis set type	Full analysis
Subject analysis set description: V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)	
Subject analysis set title	V505 Formulation 2 Vaccine [3 doses]
Subject analysis set type	Full analysis
Subject analysis set description: V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)	
Subject analysis set title	V505 Formulation 2 Vaccine [2 doses]
Subject analysis set type	Full analysis
Subject analysis set description: V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)	
Subject analysis set title	V505 Formulation 3 Vaccine [2 doses]
Subject analysis set type	Full analysis
Subject analysis set description: V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)	
Subject analysis set title	qHPV Vaccine [3 doses]

Subject analysis set type	Full analysis

Subject analysis set description:

HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™) [3 doses] (Day 1, Month 2, and Month 6)

Primary: Percentage of participants with injection-site adverse events

End point title	Percentage of participants with injection-site adverse events[1]

End point description:

An adverse event (AE) is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. Vaccination Report Cards were used to collect these AEs. The safety population included all participants who received at least 1 study vaccination and had follow-up data. Participants were summarized according to the clinical material received.

End point type	Primary

End point timeframe:

Day 1 to Day 5 following any vaccination

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 end point.

End point values	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 Vaccine [3 doses]	V505 Formulation 2 Vaccine [2 doses]	V505 Formulation 3 Vaccine [2 doses]
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	101	105	102	100
Units: Percentage of participants				
number (not applicable)	97	100	98	100

End point values	qHPV Vaccine [3 doses]			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: Percentage of participants				
number (not applicable)	88.9			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with maximum temperatures (oral or oral equivalent ≥ 37.8 °C [100.0 °F])

End point title	Percentage of participants with maximum temperatures (oral or oral equivalent ≥ 37.8 °C [100.0 °F])

End point description:

Multiple occurrences of maximum temperature were counted only once. Non-oral temperatures were converted to oral equivalent. Vaccination Report Cards were used to collect these AEs. The safety population included all participants who received at least 1 study vaccination and had follow-up data. Participants were summarized according to the clinical material received.

End point type	Primary

End point timeframe:

Day 1 to Day 5 following any vaccination.

End point values	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 Vaccine [3 doses]	V505 Formulation 2 Vaccine [2 doses]	V505 Formulation 3 Vaccine [2 doses]
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	101	105	101	100
Units: Percentage of participants				
number (not applicable)	8.9	12.4	8.9	7

End point values	qHPV Vaccine [3 doses]			
Subject group type	Subject analysis set			
Number of subjects analysed	99			
Units: Percentage of participants				
number (not applicable)	6.1			

Statistical analyses

Statistical analysis title	Difference in % vs qHPV Vaccine
Statistical analysis description: Difference in % vs qHPV Vaccine	
Comparison groups	V505 Formulation 1 Vaccine [3 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.445
Method	Miettinen & Nurminen method
Parameter estimate	Difference in % vs qHPV Vaccine
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	10.9

Statistical analysis title	Difference in % vs qHPV Vaccine
Statistical analysis description: Difference in % vs qHPV Vaccine	
Comparison groups	V505 Formulation 2 Vaccine [3 doses] v qHPV Vaccine [3

	doses]
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.121
Method	Miettinen & Nurminen method
Parameter estimate	Difference in % vs qHPV Vaccine
Point estimate	6.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	14.8

Statistical analysis title	Difference in % vs qHPV Vaccine
Statistical analysis description: Difference in % vs qHPV Vaccine	
Comparison groups	V505 Formulation 2 Vaccine [2 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.445
Method	Miettinen & Nurminen method
Parameter estimate	Difference in % vs qHPV Vaccine
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	10.9

Statistical analysis title	Difference in % vs qHPV Vaccine
Statistical analysis description: Difference in % vs qHPV Vaccine	
Comparison groups	V505 Formulation 3 Vaccine [2 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.789
Method	Miettinen & Nurminen method
Parameter estimate	Difference in % vs qHPV Vaccine
Point estimate	0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	8.5

Primary: Geometric mean titers (GMTs) to HPV 6 in the vaccines administered in a 3-dose regimen

End point title	Geometric mean titers (GMTs) to HPV 6 in the vaccines administered in a 3-dose regimen

End point description:

GMT (milli Merck Units/mL [mMU/mL]) for all participants who completed a 3-dose vaccination series. The per-protocol immunogenicity population (PPI) included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

End point type	Primary

End point timeframe:

Month 7 (1 month post-dose 3)

End point values	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 Vaccine [3 doses]	qHPV Vaccine [3 doses]	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	68	70	65	
Units: Milli Merck units (mMU)/mL				
geometric mean (confidence interval 95%)	2257 (1814 to 2808)	3567 (2876 to 4423)	856 (685 to 1070)	

Statistical analyses

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines

Statistical analysis description:

Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

Comparison groups	V505 Formulation 1 Vaccine [3 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	2.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.97
upper limit	3.53

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description:	
Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 2 Vaccine [3 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	4.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.09
upper limit	5.63

Primary: GMTs to HPV 11 in the vaccines administered in a 3-dose regimen	
End point title	GMTs to HPV 11 in the vaccines administered in a 3-dose regimen
End point description:	
GMT (mMU/mL) for all participants who completed a 3-dose vaccination series. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.	
End point type	Primary
End point timeframe:	
Month 7 (1 month post-dose 3)	

End point values	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 Vaccine [3 doses]	qHPV Vaccine [3 doses]	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	68	70	65	
Units: mMU/mL				
geometric mean (confidence interval 95%)	1551 (1236 to 1946)	2714 (2170 to 3395)	890 (705 to 1122)	

Statistical analyses

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description:	
Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 1 Vaccine [3 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	2.35

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description:	
Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 2 Vaccine [3 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	3.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.17
upper limit	4.29

Primary: GMTs to HPV 16 in the vaccines administered in a 3-dose regimen

End point title	GMTs to HPV 16 in the vaccines administered in a 3-dose regimen

End point description:

GMT (mMU/mL) for all participants who completed a 3-dose vaccination series. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

End point type	Primary

End point timeframe:

Month 7 (1 month post-dose 3)

End point values	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 Vaccine [3 doses]	qHPV Vaccine [3 doses]	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	67	72	66	
Units: mMU/mL				
geometric mean (confidence interval 95%)	6665 (5607 to 7922)	9911 (8389 to 11709)	3126 (2627 to 3721)	

Statistical analyses

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines

Statistical analysis description:

Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

Comparison groups	V505 Formulation 1 Vaccine [3 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	2.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.73
upper limit	2.62

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines

Statistical analysis description:

Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

Comparison groups	V505 Formulation 2 Vaccine [3 doses] v qHPV Vaccine [3 doses]

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	3.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	4.01

Primary: GMTs to HPV 18 in the vaccines administered in a 3-dose regimen

End point title	GMTs to HPV 18 in the vaccines administered in a 3-dose regimen

End point description:

GMT (mMU/mL) for all participants who completed a 3-dose vaccination series. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

End point type	Primary

End point timeframe:

Month 7 (1 month post-dose 3)

End point values	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 Vaccine [3 doses]	qHPV Vaccine [3 doses]	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	73	74	71	
Units: mMU/mL				
geometric mean (confidence interval 95%)	2112 (1629 to 2737)	3620 (2798 to 4683)	693 (533 to 901)	

Statistical analyses

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines

Statistical analysis description:

Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

Comparison groups	V505 Formulation 1 Vaccine [3 doses] v qHPV Vaccine [3 doses]

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	3.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.15
upper limit	4.32

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description:	
Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 2 Vaccine [3 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	5.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.66
upper limit	7.47

Secondary: GMTs to HPV Types 31, 33, 45, 52, and 58 in the vaccines administered in a 3-dose regimen

End point title	GMTs to HPV Types 31, 33, 45, 52, and 58 in the vaccines administered in a 3-dose regimen
End point description:	
GMT (mMU/mL) for all participants who completed a 3-dose vaccination series. Gardasil does not contain the following HPV types, HPV 31/33/45/52/58. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range. A value of 99999 indicates a GMT that is less than quantifiable.	
End point type	Secondary
End point timeframe:	
Month 7 (1 month post-dose 3)	

End point values	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 Vaccine [3 doses]	qHPV Vaccine [3 doses]	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	101	105	101	
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 31 (n=68, 77, 68)	2265 (1752 to 2929)	2632 (2067 to 3351)	10 (8 to 13)	
Anti-HPV 33 (n=73, 76, 70)	930 (749 to 1155)	1244 (1006 to 1539)	99999 (99999 to 99999)	
Anti-HPV 45 (n=74, 78, 73)	797 (624 to 1019)	1136 (894 to 1443)	99999 (99999 to 99999)	
Anti-HPV 52 (n=74, 74, 71)	1058 (826 to 1356)	1814 (1415 to 2325)	99999 (99999 to 99999)	
Anti-HPV 58 (n=68, 74, 71)	1940 (1460 to 2579)	2642 (2011 to 3471)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs to HPV 6 in the vaccines administered in a 2-dose or 3-dose regimen

End point title	GMTs to HPV 6 in the vaccines administered in a 2-dose or 3-dose regimen

End point description:

GMT (mMU/mL) for all participants who completed a 2-dose or 3-dose vaccination series. Participants who received a 2-dose vaccination regimen received in addition placebo at Month 2. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

End point type	Secondary

End point timeframe:

Month 7 (1 month post-dose 3)

End point values	V505 Formulation 2 Vaccine [2 doses]	V505 Formulation 3 Vaccine [2 doses]	qHPV Vaccine [3 doses]	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	62	65	
Units: mMU/mL				
geometric mean (confidence interval 95%)	3140 (2489 to 3962)	3805 (3027 to 4783)	856 (685 to 1070)	

Statistical analyses

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description: Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 2 Vaccine [2 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	3.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.72
upper limit	4.94

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description: Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 3 Vaccine [2 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	4.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.22
upper limit	6.13

Secondary: GMTs to HPV 11 in the vaccines administered in a 2-dose or 3-dose regimen

End point title	GMTs to HPV 11 in the vaccines administered in a 2-dose or 3-dose regimen

End point description:

GMT (mMU/mL) for all participants who completed a 2-dose or 3-dose vaccination series. Participants who received a 2-dose vaccination regimen received in addition placebo at Month 2. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

End point type	Secondary

End point timeframe:

Month 7 (1 month post-dose 3)

End point values	V505 Formulation 2 Vaccine [2 doses]	V505 Formulation 3 Vaccine [2 doses]	qHPV Vaccine [3 doses]	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	62	65	
Units: mMU/mL				
geometric mean (confidence interval 95%)	2533 (1989 to 3225)	2425 (1912 to 3075)	890 (705 to 1122)	

Statistical analyses

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description:	
Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 2 Vaccine [2 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	2.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.08
upper limit	3.89

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description:	
Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 3 Vaccine [2 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001 [2]
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	2.73

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.94
upper limit	3.82

Notes:

[2] - Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

Secondary: GMTs to HPV 16 in the vaccines administered in a 2-dose or 3-dose regimen

End point title	GMTs to HPV 16 in the vaccines administered in a 2-dose or 3-dose regimen

End point description:

GMT (mMU/mL) for all participants who completed a 2-dose or 3-dose vaccination series. Participants who received a 2-dose vaccination regimen received in addition placebo at Month 2. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.

End point type	Secondary

End point timeframe:

Month 7 (1 month post-dose 3)

End point values	V505 Formulation 2 Vaccine [2 doses]	V505 Formulation 3 Vaccine [2 doses]	qHPV Vaccine [3 doses]	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	61	66	
Units: mMU/mL				
geometric mean (confidence interval 95%)	9717 (8095 to 11664)	10561 (8811 to 12658)	3126 (2627 to 3721)	

Statistical analyses

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines

Statistical analysis description:

Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.

Comparison groups	V505 Formulation 2 Vaccine [2 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	3.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.37
upper limit	4.08

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description:	
Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 3 Vaccine [2 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	127
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	3.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.66
upper limit	4.3

Secondary: GMTs to HPV 18 in the vaccines administered in a 2-dose or 3-dose regimen

End point title	GMTs to HPV 18 in the vaccines administered in a 2-dose or 3-dose regimen
End point description:	
GMT (mMU/mL) for all participants who completed a 2-dose or 3-dose vaccination series. Participants who received a 2-dose vaccination regimen received in addition placebo at Month 2. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range.	
End point type	Secondary
End point timeframe:	
Month 7 (1 month post-dose 3)	

End point values	V505 Formulation 2 Vaccine [2 doses]	V505 Formulation 3 Vaccine [2 doses]	qHPV Vaccine [3 doses]	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	65	69	71	
Units: mMU/mL				
geometric mean (confidence interval 95%)	1948 (1480 to 2564)	3360 (2573 to 4387)	693 (533 to 901)	

Statistical analyses

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description: Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 2 Vaccine [2 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	2.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.01
upper limit	3.93

Statistical analysis title	Estimated Fold Difference Exp./Comparator Vaccines
Statistical analysis description: Non-inferiority for GMTs is defined as statistically less than a 2-fold decrease.	
Comparison groups	V505 Formulation 3 Vaccine [2 doses] v qHPV Vaccine [3 doses]
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Estimated Difference Exp./Comp. Vaccines
Point estimate	4.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.36
upper limit	7

Secondary: GMTs to HPV Types 31, 33, 45, 52, and 58 in the vaccines administered in a 2-dose or 3-dose regimen

End point title	GMTs to HPV Types 31, 33, 45, 52, and 58 in the vaccines

	administered in a 2-dose or 3-dose regimen

End point description:

GMT (mMU/mL) for all participants who completed a 3-dose vaccination series. Participants who received a 2-dose vaccination regimen received in addition placebo at Month 2. The PPI population included all participants who were not general protocol violators, received all vaccinations within acceptable day ranges, were seronegative at Day 1 and PCR-negative Day 1 through Month 7 for the relevant HPV type(s), and had a Month 7 serum sample collected within an acceptable day range. A value of 99999 indicates a GMT that is less than quantifiable.

End point type	Secondary

End point timeframe:

Month 7 (1 month post-dose 3)

End point values	V505 Formulation 2 Vaccine [2 doses]	V505 Formulation 3 Vaccine [2 doses]	qHPV Vaccine [3 doses]	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	103	101	101	
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 31 (n=64, 68, 68)	1938 (1487 to 2526)	2265 (1751 to 2928)	10 (8 to 13)	
Anti-HPV 33 (n=67, 68, 70)	1723 (1374 to 2160)	1692 (1352 to 2118)	99999 (99999 to 99999)	
Anti-HPV 45 (n=67, 70, 73)	520 (402 to 673)	740 (575 to 953)	99999 (99999 to 99999)	
Anti-HPV 52 (n=66, 70, 71)	819 (630 to 1065)	690 (535 to 891)	99999 (99999 to 99999)	
Anti-HPV 58 (n=68, 67, 71)	1840 (1384 to 2445)	2718 (2041 to 3621)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 36 months	
Adverse event reporting additional description:	
For the present vaccine study, the number of participants with follow-up and not the actual count of participants who were randomized and vaccinated are displayed.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	V505 Formulation 1 Vaccine [3 doses]
Reporting group description:	
V505 Formulation 1 vaccine [3 doses] (Day 1, Month 2, Month 6)	
Reporting group title	V505 Formulation 2 [3 doses]
Reporting group description:	
V505 Formulation 2 vaccine [3 doses] (Day 1, Month 2, Month 6)	
Reporting group title	V505 Formulation 2 Vaccine [2 doses]
Reporting group description:	
V505 Formulation 2 vaccine [2 doses] (Day 1 and Month 6)	
Reporting group title	V505 Formulation 3 Vaccine [2 doses]
Reporting group description:	
V505 Formulation 3 vaccine [2 doses] (Day 1 and Month 6)	
Reporting group title	qHPV Vaccine [3 doses]
Reporting group description:	
HPV 6/11/16/18 VLP - 20/40/40/20 mcg (GARDASIL™), 3 doses (Day 1, Month 2, and Month 6)	

Serious adverse events	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 [3 doses]	V505 Formulation 2 Vaccine [2 doses]
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 101 (4.95%)	2 / 105 (1.90%)	3 / 102 (2.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blighted ovum			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 102 (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
Brow presentation			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 102 (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
Foetal distress syndrome			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 102 (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
Pre-eclampsia			
subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	0 / 102 (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
Premature separation of placenta			
subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	0 / 102 (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
Prolonged labour			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	0 / 102 (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
Infections and infestations			
Bartholin's abscess			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			

subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 102 (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	V505 Formulation 3 Vaccine [2 doses]	qHPV Vaccine [3 doses]	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 100 (3.00%)	6 / 99 (6.06%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	2 / 100 (2.00%)	4 / 99 (4.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 100 (1.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blighted ovum			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brow presentation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal distress syndrome			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pre-eclampsia			

subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature separation of placenta			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolonged labour			
subjects affected / exposed	0 / 100 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bartholin's abscess			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	V505 Formulation 1 Vaccine [3 doses]	V505 Formulation 2 [3 doses]	V505 Formulation 2 Vaccine [2 doses]
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 101 (99.01%)	105 / 105 (100.00%)	101 / 102 (99.02%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 101 (4.95%)	13 / 105 (12.38%)	8 / 102 (7.84%)
occurrences (all)	5	17	9
Headache			
subjects affected / exposed	47 / 101 (46.53%)	61 / 105 (58.10%)	48 / 102 (47.06%)
occurrences (all)	84	113	74
Lethargy			

subjects affected / exposed	2 / 101 (1.98%)	6 / 105 (5.71%)	1 / 102 (0.98%)
occurrences (all)	2	8	1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	3 / 101 (2.97%)	5 / 105 (4.76%)	7 / 102 (6.86%)
occurrences (all)	3	6	7
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 101 (9.90%)	13 / 105 (12.38%)	16 / 102 (15.69%)
occurrences (all)	11	14	17
Injection site erythema			
subjects affected / exposed	50 / 101 (49.50%)	51 / 105 (48.57%)	35 / 102 (34.31%)
occurrences (all)	77	75	44
Injection site haematoma			
subjects affected / exposed	6 / 101 (5.94%)	8 / 105 (7.62%)	4 / 102 (3.92%)
occurrences (all)	7	10	4
Injection site mass			
subjects affected / exposed	3 / 101 (2.97%)	6 / 105 (5.71%)	3 / 102 (2.94%)
occurrences (all)	4	7	5
Injection site pain			
subjects affected / exposed	99 / 101 (98.02%)	105 / 105 (100.00%)	100 / 102 (98.04%)
occurrences (all)	267	289	228
Injection site pruritus			
subjects affected / exposed	8 / 101 (7.92%)	11 / 105 (10.48%)	2 / 102 (1.96%)
occurrences (all)	12	14	3
Injection site swelling			
subjects affected / exposed	60 / 101 (59.41%)	68 / 105 (64.76%)	49 / 102 (48.04%)
occurrences (all)	106	124	74
Pain			
subjects affected / exposed	2 / 101 (1.98%)	12 / 105 (11.43%)	5 / 102 (4.90%)
occurrences (all)	4	14	5
Pyrexia			
subjects affected / exposed	9 / 101 (8.91%)	12 / 105 (11.43%)	11 / 102 (10.78%)
occurrences (all)	9	18	13
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	4 / 101 (3.96%)	0 / 105 (0.00%)	3 / 102 (2.94%)
occurrences (all)	4	0	3
Diarrhoea			
subjects affected / exposed	4 / 101 (3.96%)	3 / 105 (2.86%)	3 / 102 (2.94%)
occurrences (all)	4	3	3
Nausea			
subjects affected / exposed	13 / 101 (12.87%)	14 / 105 (13.33%)	19 / 102 (18.63%)
occurrences (all)	14	18	26
Vomiting			
subjects affected / exposed	3 / 101 (2.97%)	6 / 105 (5.71%)	7 / 102 (6.86%)
occurrences (all)	4	6	7
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	8 / 101 (7.92%)	3 / 105 (2.86%)	4 / 102 (3.92%)
occurrences (all)	9	4	4
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	10 / 101 (9.90%)	8 / 105 (7.62%)	7 / 102 (6.86%)
occurrences (all)	11	10	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 101 (0.00%)	4 / 105 (3.81%)	2 / 102 (1.96%)
occurrences (all)	0	5	2
Back pain			
subjects affected / exposed	3 / 101 (2.97%)	8 / 105 (7.62%)	3 / 102 (2.94%)
occurrences (all)	4	10	3
Myalgia			
subjects affected / exposed	4 / 101 (3.96%)	10 / 105 (9.52%)	6 / 102 (5.88%)
occurrences (all)	5	10	8
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	8 / 101 (7.92%)	5 / 105 (4.76%)	10 / 102 (9.80%)
occurrences (all)	8	5	12

Non-serious adverse events	V505 Formulation 3 Vaccine [2 doses]	qHPV Vaccine [3 doses]	

Total subjects affected by non-serious adverse events subjects affected / exposed	100 / 100 (100.00%)	94 / 99 (94.95%)	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	4 / 100 (4.00%) 4	4 / 99 (4.04%) 5	
Headache subjects affected / exposed occurrences (all)	57 / 100 (57.00%) 103	39 / 99 (39.39%) 61	
Lethargy subjects affected / exposed occurrences (all)	5 / 100 (5.00%) 6	3 / 99 (3.03%) 5	
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	2 / 100 (2.00%) 2	2 / 99 (2.02%) 2	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	10 / 100 (10.00%) 11	11 / 99 (11.11%) 14	
Injection site erythema subjects affected / exposed occurrences (all)	46 / 100 (46.00%) 62	24 / 99 (24.24%) 35	
Injection site haematoma subjects affected / exposed occurrences (all)	9 / 100 (9.00%) 11	6 / 99 (6.06%) 7	
Injection site mass subjects affected / exposed occurrences (all)	2 / 100 (2.00%) 2	2 / 99 (2.02%) 2	
Injection site pain subjects affected / exposed occurrences (all)	100 / 100 (100.00%) 231	87 / 99 (87.88%) 181	
Injection site pruritus subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	4 / 99 (4.04%) 4	
Injection site swelling			

subjects affected / exposed	60 / 100 (60.00%)	24 / 99 (24.24%)	
occurrences (all)	88	38	
Pain			
subjects affected / exposed	8 / 100 (8.00%)	3 / 99 (3.03%)	
occurrences (all)	10	4	
Pyrexia			
subjects affected / exposed	11 / 100 (11.00%)	7 / 99 (7.07%)	
occurrences (all)	12	7	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 100 (3.00%)	6 / 99 (6.06%)	
occurrences (all)	3	6	
Diarrhoea			
subjects affected / exposed	5 / 100 (5.00%)	6 / 99 (6.06%)	
occurrences (all)	5	7	
Nausea			
subjects affected / exposed	14 / 100 (14.00%)	12 / 99 (12.12%)	
occurrences (all)	18	13	
Vomiting			
subjects affected / exposed	5 / 100 (5.00%)	4 / 99 (4.04%)	
occurrences (all)	5	4	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 100 (3.00%)	4 / 99 (4.04%)	
occurrences (all)	3	4	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	10 / 100 (10.00%)	7 / 99 (7.07%)	
occurrences (all)	10	7	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 100 (6.00%)	0 / 99 (0.00%)	
occurrences (all)	6	0	
Back pain			

subjects affected / exposed	6 / 100 (6.00%)	5 / 99 (5.05%)	
occurrences (all)	6	5	
Myalgia			
subjects affected / exposed	8 / 100 (8.00%)	4 / 99 (4.04%)	
occurrences (all)	8	4	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 100 (7.00%)	6 / 99 (6.06%)	
occurrences (all)	7	6	

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