Clinical trial results:
A Phase III Clinical Trial to Study the Tolerability and Immunogenicity of a 2-dose regimen of V503, a Multivalent Human Papillomavirus (HPV) L1 Virus-Like Particle (VLP) Vaccine, administered in Preadolescents and Adolescents (9 to 14 year olds) with a Comparison to Young Women (16 to 26 year olds)

Summary

EudraCT number	2013-001314-15
Trial protocol	CZ NO DK ES Outside EU/EEA
Global end of trial date	15 September 2017

Results information

Result version number	v1
This version publication date	09 February 2018
First version publication date	09 February 2018

Trial information

Trial identification

Sponsor protocol code	V503-010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01984697
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	15 September 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was a 37-month safety and immunogenicity study conducted in boys and girls 9 to 14 years of age and in young women 16 to 26 years of age. From this study, the goal was to establish that the investigational 2-dose regimens (0, 6 months and 0, 12 months) studied in boys and girls 9 to 14 years of age are generally safe and immunogenic, with an antibody response that is not inferior to that observed in young women 16 to 26 years of age who received the standard 3-dose regimen of V503 (i.e., the population and dose regimen used to establish V503 efficacy).

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	12 December 2013
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: 116
Country: Number of subjects enrolled	Chile: 95
Country: Number of subjects enrolled	Colombia: 151
Country: Number of subjects enrolled	Czech Republic: 116
Country: Number of subjects enrolled	Denmark: 132
Country: Number of subjects enrolled	Israel: 62
Country: Number of subjects enrolled	Korea, Republic of: 46
Country: Number of subjects enrolled	Malaysia: 72
Country: Number of subjects enrolled	Norway: 106
Country: Number of subjects enrolled	South Africa: 107
Country: Number of subjects enrolled	Spain: 116
Country: Number of subjects enrolled	Taiwan: 42
Country: Number of subjects enrolled	Thailand: 76
Country: Number of subjects enrolled	Turkey: 22
Country: Number of subjects enrolled	United States: 259
Worldwide total number of subjects	1518
EEA total number of subjects	470

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)	606
Adolescents (12-17 years)	633
Adults (18-64 years)	279
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1536 participants were screened and 1518 were randomized into the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Girls 9 to 14 Years V503 at Months 0 and 6

Arm description:

Girls aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL intramuscular (IM) injection at Months 0 and 6.

Arm type	Experimental
Investigational medicinal product name	V503
Investigational medicinal product code	
Other name	9-valent (Types 6, 11, 16, 18, 31, 33, 45, 52, 58) Human Papillomavirus [HPV] L1 Virus-Like Particle [VLP] vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL IM injection at Months 0 and 6 (initial 2-dose regimen)

Arm title	Boys 9 to 14 Years V503 at Months 0 and 6

Arm description:

Boys aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL IM injection at Months 0 and 6.

Arm type	Experimental
Investigational medicinal product name	V503
Investigational medicinal product code	
Other name	9-valent (Types 6, 11, 16, 18, 31, 33, 45, 52, 58) Human Papillomavirus [HPV] L1 Virus-Like Particle [VLP] vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL IM injection at Months 0 and 6 (initial 2-dose regimen)

Arm title	Girls and Boys 9 to 14 Years V503 at Months 0 and 12

Arm description:

Girls and boys aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL IM injection at Months 0 and 12.

Arm type	Experimental
Investigational medicinal product name	V503
Investigational medicinal product code	
Other name	9-valent (Types 6, 11, 16, 18, 31, 33, 45, 52, 58) Human Papillomavirus [HPV] L1 Virus-Like Particle [VLP] vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL IM injection at Months 0 and 12 (initial 2-dose regimen)

Arm title	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Arm description:	
Girls aged 9 to 14 years received a 3-dose regimen of V503 0.5 mL IM injection at Months 0, 2, and 6.	
Arm type	Experimental
Investigational medicinal product name	V503
Investigational medicinal product code	
Other name	9-valent (Types 6, 11, 16, 18, 31, 33, 45, 52, 58) Human Papillomavirus [HPV] L1 Virus-Like Particle [VLP] vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL IM injection at Months 0, 2, and 6 (initial 3-dose regimen)	
Arm title	Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Arm description:	
Young Women aged 16 to 26 years received a 3-dose regimen of V503 0.5 mL IM injection at Months 0, 2, and 6.	
Arm type	Active comparator
Investigational medicinal product name	V503
Investigational medicinal product code	
Other name	9-valent (Types 6, 11, 16, 18, 31, 33, 45, 52, 58) Human Papillomavirus [HPV] L1 Virus-Like Particle [VLP] vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL IM injection at Months 0, 2, and 6 (initial 3-dose regimen)	

Number of subjects in period 1	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12
Started	301	301	301
Vaccination 1	301	301	300
Vaccination 2	293	296	291
Vaccination 3	0 [1]	0 [2]	0 [3]
Month 36 Vaccination	270	281	280
Completed	258	270	272
Not completed	43	31	29
Consent withdrawn by subject	15	21	13
Physician decision	3	-	-
Adverse event, non-fatal	-	-	2
Death	-	-	-
Pregnancy	2	-	1

Missed last follow-up visit	1	-	-
Lost to follow-up	14	5	10
Protocol deviation	8	5	3

Number of subjects in period 1	Girls 9 to 14 Years V503 at Months 0, 2, and 6	Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Started	301	314
Vaccination 1	300	314
Vaccination 2	298	313
Vaccination 3	293	311
Month 36 Vaccination	9 [4]	31 [5]
Completed	280	279
Not completed	21	35
Consent withdrawn by subject	11	13
Physician decision	1	-
Adverse event, non-fatal	-	-
Death	1	-
Pregnancy	-	1
Missed last follow-up visit	-	-
Lost to follow-up	6	21
Protocol deviation	2	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants in this group did not received Vaccination 3 per protocol

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants in this group did not received Vaccination 3 per protocol

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants in this group did not received Vaccination 3 per protocol

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A total of 9 participants in this group received the Month 36 vaccination

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A total of 31 participants in this group received the Month 36 vaccination

Baseline characteristics

Reporting groups	
Reporting group title	Girls 9 to 14 Years V503 at Months 0 and 6
Reporting group description:	
Girls aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL intramuscular (IM) injection at Months 0 and 6.	
Reporting group title	Boys 9 to 14 Years V503 at Months 0 and 6
Reporting group description:	
Boys aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL IM injection at Months 0 and 6.	
Reporting group title	Girls and Boys 9 to 14 Years V503 at Months 0 and 12
Reporting group description:	
Girls and boys aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL IM injection at Months 0 and 12.	
Reporting group title	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Reporting group description:	
Girls aged 9 to 14 years received a 3-dose regimen of V503 0.5 mL IM injection at Months 0, 2, and 6.	
Reporting group title	Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Reporting group description:	
Young Women aged 16 to 26 years received a 3-dose regimen of V503 0.5 mL IM injection at Months 0, 2, and 6.	

Reporting group values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12
Number of subjects	301	301	301
Age, Customized Units: Subjects			
Between 9 and 10 years	100	98	100
Between 11 and 12 years	102	102	106
Between 13 and 14 years	99	101	95
Between 16 and 26 years	0	0	0
Age Continuous Units: Years			
arithmetic mean	11.4	11.5	11.4
standard deviation	± 1.7	± 1.7	± 1.6
Gender, Male/Female Units: Subjects			
Female	301	0	151
Male	0	301	150

Reporting group values	Girls 9 to 14 Years V503 at Months 0, 2, and 6	Young Women 16 to 26 Years V503 at Months 0, 2, and 6	Total
Number of subjects	301	314	1518
Age, Customized Units: Subjects			
Between 9 and 10 years	101	0	399
Between 11 and 12 years	100	0	410
Between 13 and 14 years	100	0	395
Between 16 and 26 years	0	314	314

Age Continuous Units: Years			
arithmetic mean	11.4	21.0	
standard deviation	± 1.7	± 2.7	-
Gender, Male/Female Units: Subjects			
Female	301	314	1067
Male	0	0	451

End points

End points reporting groups

Reporting group title	Girls 9 to 14 Years V503 at Months 0 and 6
Reporting group description:	
Girls aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL intramuscular (IM) injection at Months 0 and 6.	
Reporting group title	Boys 9 to 14 Years V503 at Months 0 and 6
Reporting group description:	
Boys aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL IM injection at Months 0 and 6.	
Reporting group title	Girls and Boys 9 to 14 Years V503 at Months 0 and 12
Reporting group description:	
Girls and boys aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL IM injection at Months 0 and 12.	
Reporting group title	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Reporting group description:	
Girls aged 9 to 14 years received a 3-dose regimen of V503 0.5 mL IM injection at Months 0, 2, and 6.	
Reporting group title	Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Reporting group description:	
Young Women aged 16 to 26 years received a 3-dose regimen of V503 0.5 mL IM injection at Months 0, 2, and 6.	

Primary: Geometric Mean Titers to HPV Type 6 at Four Weeks After the Last Dose of V503

End point title	Geometric Mean Titers to HPV Type 6 at Four Weeks After the Last Dose of V503
End point description:	
Antibodies to HPV virus-like particles (VLP) type 6 were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.	
End point type	Primary
End point timeframe:	
4 weeks after the last dose of V503 (Month 7 or Month 13)	

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	263	257	254
Units: mMU/mL				
geometric mean (confidence interval 95%)	1657.9 (1479.6 to 1857.6)	1557.4 (1391.5 to 1743.1)	2678.8 (2390.2 to 3002.1)	1496.1 (1334.1 to 1677.8)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	238			
Units: mMU/mL				
geometric mean (confidence interval 95%)	770.9 (684.8 to 867.9)			

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	2.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.83
upper limit	2.53

Notes:

[1] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the Geometric Mean Titer (GMT) ratio for Girls 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	2.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.73
upper limit	2.36

Notes:

[2] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	3.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.93
upper limit	4.11

Notes:

[3] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls and Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Primary: Geometric Mean Titers to HPV Type 11 at Four Weeks After the Last Dose of V503

End point title	Geometric Mean Titers to HPV Type 11 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 11 were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Primary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	264	257	254
Units: mMU/mL				
geometric mean (confidence interval 95%)	1388.9 (1240.4 to 1555.3)	1423.9 (1273.2 to 1592.3)	2941.8 (2626.6 to 3294.9)	1306.3 (1165.5 to 1464.0)

End point values	Young Women			

	16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	238			
Units: mMU/mL				
geometric mean (confidence interval 95%)	580.5 (516.0 to 653.0)			

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	2.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.03
upper limit	2.82

Notes:

[4] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	502
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	2.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.09
upper limit	2.88

Notes:

[5] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young

	Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	5.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.32
upper limit	5.94

Notes:

[6] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls and Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Primary: Geometric Mean Titers to HPV Type 16 at Four Weeks After the Last Dose of V503

End point title	Geometric Mean Titers to HPV Type 16 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 16 were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Primary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	272	273	264	269
Units: mMU/mL				
geometric mean (confidence interval 95%)	8004.9 (7160.5 to 8948.8)	8474.8 (7582.4 to 9472.3)	14329.3 (12796.4 to 16045.9)	6996.0 (6254.1 to 7825.8)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	249			

Units: mMU/mL				
geometric mean (confidence interval 95%)	3154.0 (2807.1 to 3543.7)			

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	2.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.14
upper limit	3

Notes:

[7] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.29
upper limit	3.15

Notes:

[8] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	4.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.84
upper limit	5.37

Notes:

[9] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls and Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Primary: Geometric Mean Titers to HPV Type 18 at Four Weeks After the Last Dose of V503

End point title	Geometric Mean Titers to HPV Type 18 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 18 were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Primary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	272	272	266	270
Units: mMU/mL				
geometric mean (confidence interval 95%)	1872.8 (1651.6 to 2123.6)	1860.9 (1641.1 to 2110.2)	2810.4 (2474.9 to 3191.3)	2049.3 (1806.4 to 2324.8)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	267			
Units: mMU/mL				

geometric mean (confidence interval 95%)	761.5 (670.8 to 864.5)			

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	539
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	2.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.05
upper limit	2.96

Notes:

[10] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	539
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	2.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.04
upper limit	2.92

Notes:

[11] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	533
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	3.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.06
upper limit	4.45

Notes:

[12] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls and Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Primary: Geometric Mean Titers to HPV Type 31 at Four Weeks After the Last Dose of V503

End point title	Geometric Mean Titers to HPV Type 31 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 31 were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Primary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	272	271	268	271
Units: mMU/mL				
geometric mean (confidence interval 95%)	1436.3 (1272.1 to 1621.8)	1498.2 (1326.5 to 1692.0)	2117.5 (1873.7 to 2393.1)	1748.3 (1548.1 to 1974.5)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	264			
Units: mMU/mL				

geometric mean (confidence interval 95%)	572.1 (505.8 to 647.2)			

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	536
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	2.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.1
upper limit	3

Notes:

[13] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	535
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	2.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	3.12

Notes:

[14] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	532
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.08
upper limit	4.45

Notes:

[15] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls and Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Primary: Geometric Mean Titers to HPV Type 33 at Four Weeks After the Last Dose of V503

End point title	Geometric Mean Titers to HPV Type 33 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 33 were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Primary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	273	271	269	275
Units: mMU/mL				
geometric mean (confidence interval 95%)	1030.0 (920.4 to 1152.7)	1040.0 (928.9 to 1164.3)	2197.5 (1961.9 to 2461.3)	796.4 (712.0 to 890.9)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	279			
Units: mMU/mL				

geometric mean (confidence interval 95%)	348.1 (311.5 to 389.1)			

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	552
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	2.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	3.5

Notes:

[16] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	550
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	2.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.55
upper limit	3.5

Notes:

[17] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	548
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	6.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.36
upper limit	7.43

Notes:

[18] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls and Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Primary: Geometric Mean Titers to HPV Type 45 at Four Weeks After the Last Dose of V503

End point title	Geometric Mean Titers to HPV Type 45 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 45 were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Primary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	274	273	268	275
Units: mMU/mL				
geometric mean (confidence interval 95%)	357.6 (313.7 to 407.6)	352.3 (309.0 to 401.7)	417.7 (365.9 to 476.9)	661.7 (580.6 to 754.1)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	280			
Units: mMU/mL				
geometric mean (confidence interval	213.6 (187.7			

95%)	to 243.2)

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	2.03

Notes:

[19] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	553
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.37
upper limit	1.99

Notes:

[20] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	548
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.61
upper limit	2.37

Notes:

[21] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls and Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Primary: Geometric Mean Titers to HPV Type 52 at Four Weeks After the Last Dose of V503

End point title	Geometric Mean Titers to HPV Type 52 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 52 were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Primary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	272	273	268	275
Units: mMU/mL				
geometric mean (confidence interval 95%)	581.1 (521.9 to 647.1)	640.4 (575.2 to 713.0)	1123.4 (1008.1 to 1251.9)	909.9 (817.6 to 1012.5)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	271			
Units: mMU/mL				

geometric mean (confidence interval 95%)	364.2 (327.0 to 405.6)			

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.36
upper limit	1.87

Notes:

[22] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.51
upper limit	2.05

Notes:

[23] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	539
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	3.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.64
upper limit	3.61

Notes:

[24] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls and Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Primary: Geometric Mean Titers to HPV Type 58 at Four Weeks After the Last Dose of V503

End point title	Geometric Mean Titers to HPV Type 58 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 58 were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Primary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	265	273
Units: mMU/mL				
geometric mean (confidence interval 95%)	1251.2 (1119.6 to 1398.4)	1325.7 (1186.2 to 1481.6)	2444.6 (2185.2 to 2734.9)	1229.3 (1100.7 to 1373.0)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	261			
Units: mMU/mL				

geometric mean (confidence interval 95%)	491.1 (438.6 to 549.8)			

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	531
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	2.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.15
upper limit	3.01

Notes:

[25] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	531
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	3.16

Notes:

[26] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	non-inferiority[27]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	4.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.23
upper limit	5.86

Notes:

[27] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the GMT ratio for Girls and Boys 9 to 14 Years / Young Women 16 to 26 years is >0.67.

Secondary: Percentage of Participants with Seroconversion to HPV Type 6 at Four Weeks After the Last Dose of V503

End point title	Percentage of Participants with Seroconversion to HPV Type 6 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 6 were measured using a competitive Luminex immunoassay. Seroconversion to HPV type 6 was defined as a titer >=30 mMU/mL. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Secondary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	263	257	254
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (97.9 to 100)	100 (98.6 to 100)	100 (98.6 to 100)	99.2 (97.2 to 99.9)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	238			
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (97.7 to			

100)

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	non-inferiority[28]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	2

Notes:

[28] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	non-inferiority[29]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.3

Notes:

[29] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	non-inferiority[30]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.3

Notes:

[30] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls and Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Secondary: Percentage of Participants with Seroconversion to HPV Type 11 at Four Weeks After the Last Dose of V503

End point title	Percentage of Participants with Seroconversion to HPV Type 11 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 11 were measured using a competitive Luminex immunoassay. Seroconversion to HPV type 11 was defined as a titer >=16 mMU/mL. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Secondary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	258	264	257	254
Units: Percentage of participants				
number (confidence interval 95%)	100 (98.6 to 100)	100 (98.6 to 100)	100 (98.6 to 100)	99.6 (97.8 to 100)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	238			
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (97.7 to			

100)

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	non-inferiority[31]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.3

Notes:

[31] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	502
Analysis specification	Pre-specified
Analysis type	non-inferiority[32]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.3

Notes:

[32] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	non-inferiority[33]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.3

Notes:

[33] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls and Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Secondary: Percentage of Participants with Seroconversion to HPV Type 16 at Four Weeks After the Last Dose of V503

End point title	Percentage of Participants with Seroconversion to HPV Type 16 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 16 were measured using a competitive Luminex immunoassay. Seroconversion to HPV type 16 was defined as a titer >=20 mMU/mL. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Secondary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	272	273	264	269
Units: Percentage of participants				
number (confidence interval 95%)	100 (98.7 to 100)	100 (98.7 to 100)	100 (98.6 to 100)	100 (98.6 to 100)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	249			
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (97.8 to			

100)

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	non-inferiority[34]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.2

Notes:

[34] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	non-inferiority[35]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.2

Notes:

[35] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	513
Analysis specification	Pre-specified
Analysis type	non-inferiority[36]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.2

Notes:

[36] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls and Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Secondary: Percentage of Participants with Seroconversion to HPV Type 18 at Four Weeks After the Last Dose of V503

End point title	Percentage of Participants with Seroconversion to HPV Type 18 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 18 were measured using a competitive Luminex immunoassay. Seroconversion to HPV type 18 was defined as a titer >=24 mMU/mL. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Secondary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	272	272	266	270
Units: Percentage of participants				
number (confidence interval 95%)	100 (98.7 to 100)	100 (98.7 to 100)	100 (98.6 to 100)	99.6 (98.0 to 100)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	267			
Units: Percentage of participants				
number (confidence interval 95%)	98.5 (96.2 to			

99.6)

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	539
Analysis specification	Pre-specified
Analysis type	non-inferiority[37]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	3.8

Notes:

[37] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	539
Analysis specification	Pre-specified
Analysis type	non-inferiority[38]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	3.8

Notes:

[38] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	533
Analysis specification	Pre-specified
Analysis type	non-inferiority[39]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	3.8

Notes:

[39] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls and Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Secondary: Percentage of Participants with Seroconversion to HPV Type 31 at Four Weeks After the Last Dose of V503

End point title	Percentage of Participants with Seroconversion to HPV Type 31 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 31 were measured using a competitive Luminex immunoassay. Seroconversion to HPV type 31 was defined as a titer >=10 mMU/mL. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Secondary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	272	271	268	271
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (98.0 to 100)	100 (98.6 to 100)	100 (98.6 to 100)	100 (98.6 to 100)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	264			
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (97.9 to			

100)

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	536
Analysis specification	Pre-specified
Analysis type	non-inferiority[40]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.8

Notes:

[40] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	535
Analysis specification	Pre-specified
Analysis type	non-inferiority[41]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.1

Notes:

[41] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	532
Analysis specification	Pre-specified
Analysis type	non-inferiority[42]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.1

Notes:

[42] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls and Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Secondary: Percentage of Participants with Seroconversion to HPV Type 33 at Four Weeks After the Last Dose of V503

End point title	Percentage of Participants with Seroconversion to HPV Type 33 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 33 were measured using a competitive Luminex immunoassay. Seroconversion to HPV type 33 was defined as a titer >=8 mMU/mL. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Secondary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	273	271	269	275
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (98.0 to 100)	100 (98.6 to 100)	100 (98.6 to 100)	100 (98.7 to 100)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	279			
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (98.0 to			

100)

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	552
Analysis specification	Pre-specified
Analysis type	non-inferiority[43]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.7

Notes:

[43] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	550
Analysis specification	Pre-specified
Analysis type	non-inferiority[44]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2

Notes:

[44] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	548
Analysis specification	Pre-specified
Analysis type	non-inferiority[45]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2

Notes:

[45] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls and Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Secondary: Percentage of Participants with Seroconversion to HPV Type 45 at Four Weeks After the Last Dose of V503

End point title	Percentage of Participants with Seroconversion to HPV Type 45 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 45 were measured using a competitive Luminex immunoassay. Seroconversion to HPV type 45 was defined as a titer >=8 mMU/mL. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Secondary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	274	273	268	275
Units: Percentage of participants				
number (confidence interval 95%)	99.3 (97.4 to 99.9)	99.3 (97.4 to 99.9)	100 (98.6 to 100)	99.3 (97.4 to 99.9)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	280			
Units: Percentage of participants				
number (confidence interval 95%)	97.9 (95.4 to			

99.2)

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	non-inferiority[46]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	4

Notes:

[46] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	553
Analysis specification	Pre-specified
Analysis type	non-inferiority[47]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	4

Notes:

[47] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	548
Analysis specification	Pre-specified
Analysis type	non-inferiority[48]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	4.6

Notes:

[48] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls and Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Secondary: Percentage of Participants with Seroconversion to HPV Type 52 at Four Weeks After the Last Dose of V503

End point title	Percentage of Participants with Seroconversion to HPV Type 52 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 52 were measured using a competitive Luminex immunoassay. Seroconversion to HPV type 52 was defined as a titer >=8 mMU/mL. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Secondary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	272	273	268	275
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (98.0 to 100)	100 (98.7 to 100)	100 (98.6 to 100)	99.6 (98.0 to 100)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	271			
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (98.0 to			

100)

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	543
Analysis specification	Pre-specified
Analysis type	non-inferiority[49]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.7

Notes:

[49] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	non-inferiority[50]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.1

Notes:

[50] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	539
Analysis specification	Pre-specified
Analysis type	non-inferiority[51]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.1

Notes:

[51] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls and Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Secondary: Percentage of Participants with Seroconversion to HPV Type 58 at Four Weeks After the Last Dose of V503

End point title	Percentage of Participants with Seroconversion to HPV Type 58 at Four Weeks After the Last Dose of V503

End point description:

Antibodies to HPV VLP type 58 were measured using a competitive Luminex immunoassay. Seroconversion to HPV type 58 was defined as a titer >=8 mMU/mL. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Secondary

End point timeframe:

4 weeks after the last dose of V503 (Month 7 or Month 13)

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	270	265	273
Units: Percentage of participants				
number (confidence interval 95%)	100 (98.6 to 100)	100 (98.6 to 100)	100 (98.6 to 100)	99.6 (98.0 to 100)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	261			
Units: Percentage of participants				
number (confidence interval 95%)	99.6 (97.9 to			

100)

Statistical analyses

Statistical analysis title	Non-inferiority
Comparison groups	Girls 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	531
Analysis specification	Pre-specified
Analysis type	non-inferiority[52]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.1

Notes:

[52] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Boys 9 to 14 Years V503 at Months 0 and 6 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6
Number of subjects included in analysis	531
Analysis specification	Pre-specified
Analysis type	non-inferiority[53]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2.1

Notes:

[53] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Statistical analysis title	Non-inferiority
Comparison groups	Girls and Boys 9 to 14 Years V503 at Months 0 and 12 v Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Number of subjects included in analysis	526
Analysis specification	Pre-specified
Analysis type	non-inferiority[54]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Seroconversion percentage difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.1

Notes:

[54] - Non-inferiority is demonstrated if the lower limit of the 95% confidence interval of the seroconversion percentage difference for Girls and Boys 9 to 14 Years - Young Women 16 to 26 years is > -5.

Other pre-specified: Antibody Persistence: Geometric Mean Titers to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 24

End point title	Antibody Persistence: Geometric Mean Titers to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 24

End point description:

Antibodies to HPV VLP types were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Other pre-specified

End point timeframe:

Month 24

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	301	301	300	300
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=253, 259, 252, 249, 232)	260.7 (231.5 to 293.6)	209.1 (185.9 to 235.1)	574.0 (509.6 to 646.5)	300.7 (266.8 to 339.0)
Anti-HPV Type 11 (n=253, 260, 252, 249, 232)	169.8 (150.5 to 191.7)	150.6 (133.6 to 169.7)	443.7 (392.9 to 501.0)	201.9 (178.7 to 228.1)
Anti-HPV Type 16 (n=266, 269, 259, 264, 241)	900.5 (788.0 to 1028.9)	801.0 (701.5 to 914.6)	2316.2 (2023.5 to 2651.4)	1041.3 (910.8 to 1190.4)
Anti-HPV Type 18 (n=266, 268, 261, 265, 259)	196.8 (174.9 to 221.6)	169.6 (150.7 to 190.8)	380.8 (337.9 to 429.1)	255.8 (227.2 to 288.0)
Anti-HPV Type 31 (n=266, 267, 263, 266, 258)	160.6 (140.8 to 183.3)	139.1 (122.0 to 158.7)	312.8 (273.9 to 357.1)	260.6 (228.4 to 297.3)
Anti-HPV Type 33 (n=267, 267, 264, 270, 269)	131.2 (116.9 to 147.2)	121.5 (108.3 to 136.4)	341.7 (304.3 to 383.6)	120.8 (107.7 to 135.4)

Anti-HPV Type 45 (n=268, 269, 263, 270, 271)	37.8 (33.2 to 43.0)	31.9 (28.0 to 36.3)	62.3 (54.7 to 71.1)	86.9 (76.4 to 98.9)
Anti-HPV Type 52 (n=266, 269, 263, 270, 261)	85.1 (76.4 to 94.7)	80.9 (72.7 to 90.0)	199.4 (179.0 to 222.2)	150.4 (135.2 to 167.4)
Anti-HPV Type 58 (n=264, 266, 260, 268, 253)	155.4 (138.0 to 175.1)	149.8 (133.1 to 168.6)	380.2 (337.3 to 428.6)	183.7 (163.3 to 206.7)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	314			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=253, 259, 252, 249, 232)	153.2 (135.4 to 173.5)			
Anti-HPV Type 11 (n=253, 260, 252, 249, 232)	98.3 (86.6 to 111.6)			
Anti-HPV Type 16 (n=266, 269, 259, 264, 241)	461.6 (401.2 to 531.0)			
Anti-HPV Type 18 (n=266, 268, 261, 265, 259)	122.2 (108.4 to 137.7)			
Anti-HPV Type 31 (n=266, 267, 263, 266, 258)	89.6 (78.4 to 102.5)			
Anti-HPV Type 33 (n=267, 267, 264, 270, 269)	61.3 (54.6 to 68.7)			
Anti-HPV Type 45 (n=268, 269, 263, 270, 271)	30.7 (27.0 to 34.9)			
Anti-HPV Type 52 (n=266, 269, 263, 270, 261)	73.7 (66.1 to 82.1)			
Anti-HPV Type 58 (n=264, 266, 260, 268, 253)	76.8 (68.0 to 86.7)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Antibody Persistence: Percentage of Participants with Seroconversion to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 24

End point title	Antibody Persistence: Percentage of Participants with Seroconversion to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 24

End point description:

Antibodies to HPV VLP types were measured using a competitive Luminex immunoassay. Seroconversion to HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 were defined as a titer >=41, 24, 34, 38, 24, 18, 12, 16, and 12 mMU/mL, respectively. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Other pre-specified

End point timeframe:
Month 24

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	301	301	300	300
Units: Percentage of participants				
number (confidence interval 95%)				
Anti-HPV Type 6 (n=253, 259, 252, 249, 232)	98.4 (96.0 to 99.6)	96.9 (94.0 to 98.7)	99.2 (97.2 to 99.9)	99.6 (97.8 to 100)
Anti-HPV Type 11 (n=253, 260, 252, 249, 232)	98.0 (95.4 to 99.4)	95.8 (92.6 to 97.9)	99.6 (97.8 to 100)	98.8 (96.5 to 99.8)
Anti-HPV Type 16 (n=266, 269, 259, 264, 241)	98.9 (96.7 to 99.8)	99.6 (97.9 to 100)	100 (98.6 to 100)	99.6 (97.9 to 100)
Anti-HPV Type 18 (n=266, 268, 261, 265, 259)	98.5 (96.2 to 99.6)	95.9 (92.8 to 97.9)	98.9 (96.7 to 99.8)	99.2 (97.3 to 99.9)
Anti-HPV Type 31 (n=266, 267, 263, 266, 258)	97.0 (94.2 to 98.7)	94.8 (91.4 to 97.1)	98.5 (96.2 to 99.6)	97.7 (95.2 to 99.2)
Anti-HPV Type 33 (n=267, 267, 264, 270, 269)	97.8 (95.2 to 99.2)	96.6 (93.7 to 98.4)	99.2 (97.3 to 99.9)	98.9 (96.8 to 99.8)
Anti-HPV Type 45 (n=268, 269, 263, 270, 271)	88.4 (84.0 to 92.0)	85.9 (81.1 to 89.8)	93.9 (90.3 to 96.5)	96.7 (93.8 to 98.5)
Anti-HPV Type 52 (n=266, 269, 263, 270, 261)	96.6 (93.7 to 98.4)	95.2 (91.9 to 97.4)	99.2 (97.3 to 99.9)	99.3 (97.3 to 99.9)
Anti-HPV Type 58 (n=264, 266, 260, 268, 253)	98.9 (96.7 to 99.8)	99.6 (97.9 to 100)	100 (98.6 to 100)	100 (98.6 to 100)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	314			
Units: Percentage of participants				
number (confidence interval 95%)				
Anti-HPV Type 6 (n=253, 259, 252, 249, 232)	94.0 (90.1 to 96.7)			
Anti-HPV Type 11 (n=253, 260, 252, 249, 232)	94.8 (91.1 to 97.3)			
Anti-HPV Type 16 (n=266, 269, 259, 264, 241)	99.6 (97.7 to 100)			
Anti-HPV Type 18 (n=266, 268, 261, 265, 259)	95.0 (91.6 to 97.3)			
Anti-HPV Type 31 (n=266, 267, 263, 266, 258)	91.5 (87.4 to 94.6)			
Anti-HPV Type 33 (n=267, 267, 264, 270, 269)	94.8 (91.4 to 97.1)			
Anti-HPV Type 45 (n=268, 269, 263, 270, 271)	82.7 (77.6 to 87.0)			

Anti-HPV Type 52 (n=266, 269, 263, 270, 261)	97.3 (94.6 to 98.9)			
Anti-HPV Type 58 (n=264, 266, 260, 268, 253)	96.0 (92.9 to 98.1)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Antibody Persistence: Geometric Mean Titers to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 36

End point title	Antibody Persistence: Geometric Mean Titers to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 36

End point description:

Antibodies to HPV VLP types were measured using a competitive Luminex immunoassay. Antibody titers were expressed as milli Merck units/mL (mMU/mL). The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Other pre-specified

End point timeframe:

Month 36

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	301	301	300	300
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=236, 254, 246, 240, 214)	209.6 (184.9 to 237.6)	160.1 (141.9 to 180.7)	401.2 (354.8 to 453.7)	232.2 (205.1 to 263.0)
Anti-HPV Type 11 (n=236, 255, 246, 240, 214)	133.7 (117.6 to 152.1)	115.2 (101.8 to 130.3)	308.2 (271.8 to 349.6)	159.1 (140.0 to 180.7)
Anti-HPV Type 16 (n=248, 263, 253, 255, 222)	673.8 (582.8 to 779.1)	592.6 (514.7 to 682.4)	1534.3 (1328.8 to 1771.5)	792.4 (686.7 to 914.4)
Anti-HPV Type 18 (n=248, 262, 255, 256, 239)	158.9 (140.8 to 179.4)	141.7 (125.9 to 159.4)	276.4 (245.3 to 311.6)	206.5 (183.3 to 232.7)
Anti-HPV Type 31 (n=248, 261, 257, 258, 235)	127.8 (111.4 to 146.5)	106.9 (93.5 to 122.1)	218.0 (190.6 to 249.4)	205.9 (180.0 to 235.5)
Anti-HPV Type 33 (n=249, 261, 258, 261, 246)	106.0 (94.1 to 119.5)	95.7 (85.1 to 107.5)	240.4 (213.8 to 270.3)	95.5 (85.0 to 107.3)
Anti-HPV Type 45 (n=250, 263, 257, 261, 248)	30.6 (26.9 to 35.0)	26.8 (23.6 to 30.4)	43.6 (38.3 to 49.7)	66.1 (58.1 to 75.2)
Anti-HPV Type 52 (n=248, 263, 257, 261, 239)	66.2 (59.1 to 74.0)	63.4 (56.8 to 70.7)	143.2 (128.3 to 159.9)	115.9 (103.9 to 129.3)
Anti-HPV Type 58 (n=246, 261, 255, 259, 231)	125.8 (111.1 to 142.5)	119.2 (105.6 to 134.5)	265.3 (234.8 to 299.8)	143.0 (126.7 to 161.5)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	314			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=236, 254, 246, 240, 214)	133.8 (117.3 to 152.7)			
Anti-HPV Type 11 (n=236, 255, 246, 240, 214)	82.9 (72.4 to 94.9)			
Anti-HPV Type 16 (n=248, 263, 253, 255, 222)	368.9 (316.4 to 430.0)			
Anti-HPV Type 18 (n=248, 262, 255, 256, 239)	104.1 (92.0 to 117.8)			
Anti-HPV Type 31 (n=248, 261, 257, 258, 235)	74.6 (64.8 to 85.9)			
Anti-HPV Type 33 (n=249, 261, 258, 261, 246)	52.2 (46.3 to 58.9)			
Anti-HPV Type 45 (n=250, 263, 257, 261, 248)	27.3 (23.9 to 31.1)			
Anti-HPV Type 52 (n=248, 263, 257, 261, 239)	61.5 (54.8 to 68.9)			
Anti-HPV Type 58 (n=246, 261, 255, 259, 231)	64.7 (56.9 to 73.6)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Antibody Persistence: Percentage of Participants with Seroconversion to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 36

End point title	Antibody Persistence: Percentage of Participants with Seroconversion to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 36

End point description:

Antibodies to HPV VLP types were measured using a competitive Luminex immunoassay. Seroconversion to HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 were defined as a titer >=41, 24, 34, 38, 24, 18, 12, 16, and 12 mMU/mL, respectively. The per-protocol population included all participants who 1) received all vaccinations in the planned regimen, 2) had a serum sample collected 4 weeks after the last vaccination in the planned regimen, 3) were seronegative at Day 1 for the relevant HPV type, and 4) had no protocol violations that would interfere with evaluation of the immune response.

End point type	Other pre-specified

End point timeframe:

Month 36

End point values	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12	Girls 9 to 14 Years V503 at Months 0, 2, and 6
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	301	301	300	300
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=236, 254, 246, 240, 214)	95.3 (91.8 to 97.7)	91.3 (87.2 to 94.5)	99.2 (97.1 to 99.9)	97.9 (95.2 to 99.3)
Anti-HPV Type 11 (n=236, 255, 246, 240, 214)	94.1 (90.2 to 96.7)	92.9 (89.1 to 95.8)	99.2 (97.1 to 99.9)	98.8 (96.4 to 99.7)
Anti-HPV Type 16 (n=248, 263, 253, 255, 222)	97.2 (94.3 to 98.9)	98.5 (96.2 to 99.6)	100 (98.6 to 100)	99.2 (97.2 to 99.9)
Anti-HPV Type 18 (n=248, 262, 255, 256, 239)	95.6 (92.2 to 97.8)	94.3 (90.7 to 96.8)	97.6 (94.9 to 99.1)	97.3 (94.4 to 98.9)
Anti-HPV Type 31 (n=248, 261, 257, 258, 235)	94.0 (90.2 to 96.6)	91.2 (87.1 to 94.3)	96.5 (93.5 to 98.4)	97.7 (95.0 to 99.1)
Anti-HPV Type 33 (n=249, 261, 258, 261, 246)	94.0 (90.3 to 96.6)	96.9 (94.1 to 98.7)	99.2 (97.2 to 99.9)	98.1 (95.6 to 99.4)
Anti-HPV Type 45 (n=250, 263, 257, 261, 248)	83.6 (78.4 to 88.0)	81.4 (76.1 to 85.9)	87.9 (83.3 to 91.7)	91.2 (87.1 to 94.3)
Anti-HPV Type 52 (n=248, 263, 257, 261, 239)	93.5 (89.7 to 96.3)	93.9 (90.3 to 96.5)	98.8 (96.6 to 99.8)	97.7 (95.1 to 99.2)
Anti-HPV Type 58 (n=246, 261, 255, 259, 231)	98.0 (95.3 to 99.3)	99.2 (97.3 to 99.9)	100 (98.6 to 100)	98.8 (96.7 to 99.8)

End point values	Young Women 16 to 26 Years V503 at Months 0, 2, and 6			
Subject group type	Reporting group			
Number of subjects analysed	314			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=236, 254, 246, 240, 214)	92.1 (87.6 to 95.3)			
Anti-HPV Type 11 (n=236, 255, 246, 240, 214)	92.1 (87.6 to 95.3)			
Anti-HPV Type 16 (n=248, 263, 253, 255, 222)	98.2 (95.5 to 99.5)			
Anti-HPV Type 18 (n=248, 262, 255, 256, 239)	90.8 (86.4 to 94.1)			
Anti-HPV Type 31 (n=248, 261, 257, 258, 235)	86.0 (80.8 to 90.1)			
Anti-HPV Type 33 (n=249, 261, 258, 261, 246)	91.9 (87.7 to 95.0)			
Anti-HPV Type 45 (n=250, 263, 257, 261, 248)	77.8 (72.1 to 82.8)			
Anti-HPV Type 52 (n=248, 263, 257, 261, 239)	95.0 (91.4 to 97.4)			
Anti-HPV Type 58 (n=246, 261, 255, 259, 231)	94.8 (91.1 to 97.3)			

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 37; Non-injection site adverse events: up to Day 15 following any vaccination; Injection site adverse events: up to Day 5 following any vaccination

Adverse event reporting additional description:

Participants at risk for adverse events includes those who were vaccinated and had safety follow-up data

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Girls 9 to 14 Years V503 at Months 0 and 6

Reporting group description:

Girls aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL intramuscular (IM) injection at Months 0 and 6. A challenge dose of V503 0.5 mL IM injection was administered at Month 36.

Reporting group title	Boys 9 to 14 Years V503 at Months 0 and 6

Reporting group description:

Boys aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL IM injection at Months 0 and 6. A challenge dose of V503 0.5 mL IM injection was administered at Month 36.

Reporting group title	Girls and Boys 9 to 14 Years V503 at Months 0 and 12

Reporting group description:

Girls and boys aged 9 to 14 years received a 2-dose regimen of V503 0.5 mL IM injection at Months 0 and 12. A challenge dose of V503 0.5 mL IM injection was administered at Month 36.

Reporting group title	Girls 9 to 14 Years V503 at Months 0, 2, and 6

Reporting group description:

Girls aged 9 to 14 years received a 3-dose regimen of V503 0.5 mL IM injection at Months 0, 2, and 6. A challenge dose of V503 0.5 mL IM injection was administered at Month 36 for a subset of participants.

Reporting group title	Young Women 16 to 26 Years V503 at Months 0, 2, and 6

Reporting group description:

Young Women aged 16 to 26 years received a 3-dose regimen of V503 0.5 mL IM injection at Months 0, 2, and 6. A challenge dose of V503 0.5 mL IM injection was administered at Month 36 for a subset of participants.

Serious adverse events	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 294 (2.04%)	9 / 296 (3.04%)	6 / 293 (2.05%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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

Vascular disorders			
Venous thrombosis limb			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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
Pregnancy, puerperium and perinatal conditions			
Premature delivery			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 294 (0.34%)	0 / 296 (0.00%)	0 / 293 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 294 (0.00%)	1 / 296 (0.34%)	0 / 293 (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
Concussion			
subjects affected / exposed	0 / 294 (0.00%)	1 / 296 (0.34%)	0 / 293 (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

Forearm fracture			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			
subjects affected / exposed	1 / 294 (0.34%)	0 / 296 (0.00%)	0 / 293 (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
Spinal fracture			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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
Wolff-Parkinson-White syndrome			
subjects affected / exposed	0 / 294 (0.00%)	1 / 296 (0.34%)	0 / 293 (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
Nervous system disorders			
Encephalitis autoimmune			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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
Epilepsy			
subjects affected / exposed	0 / 294 (0.00%)	1 / 296 (0.34%)	0 / 293 (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
Radiculopathy			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Status epilepticus			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 294 (0.68%)	0 / 296 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 294 (0.00%)	1 / 296 (0.34%)	0 / 293 (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
Gastritis			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 294 (0.34%)	1 / 296 (0.34%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chikungunya virus infection			

subjects affected / exposed	0 / 294 (0.00%)	1 / 296 (0.34%)	0 / 293 (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
Dengue fever			
subjects affected / exposed	1 / 294 (0.34%)	0 / 296 (0.00%)	0 / 293 (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
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 294 (0.00%)	1 / 296 (0.34%)	0 / 293 (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
Meningitis bacterial			
subjects affected / exposed	0 / 294 (0.00%)	1 / 296 (0.34%)	0 / 293 (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
Oral herpes			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	1 / 294 (0.34%)	0 / 296 (0.00%)	0 / 293 (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
Pharyngotonsillitis			
subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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
Pneumonia			
subjects affected / exposed	0 / 294 (0.00%)	1 / 296 (0.34%)	0 / 293 (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
Subcutaneous abscess			

subjects affected / exposed	0 / 294 (0.00%)	0 / 296 (0.00%)	0 / 293 (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

Serious adverse events	Girls 9 to 14 Years V503 at Months 0, 2, and 6	Young Women 16 to 26 Years V503 at Months 0, 2, and 6	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 300 (2.00%)	11 / 313 (3.51%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	1 / 300 (0.33%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Venous thrombosis limb			
subjects affected / exposed	0 / 300 (0.00%)	1 / 313 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 300 (0.00%)	4 / 313 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Premature delivery			
subjects affected / exposed	0 / 300 (0.00%)	1 / 313 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 300 (0.33%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 300 (0.33%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 300 (0.00%)	1 / 313 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 300 (0.33%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Wolff-Parkinson-White syndrome			

subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Encephalitis autoimmune			
subjects affected / exposed	1 / 300 (0.33%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	1 / 300 (0.33%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 300 (0.00%)	1 / 313 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 300 (0.00%)	1 / 313 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	0 / 300 (0.00%)	1 / 313 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chikungunya virus infection			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pharyngitis			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 313 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 300 (0.00%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 300 (0.33%)	0 / 313 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Girls 9 to 14 Years V503 at Months 0 and 6	Boys 9 to 14 Years V503 at Months 0 and 6	Girls and Boys 9 to 14 Years V503 at Months 0 and 12
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 294 (18.03%)	32 / 296 (10.81%)	46 / 293 (15.70%)
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 294 (2.72%)	9 / 296 (3.04%)	7 / 293 (2.39%)
occurrences (all)	9	9	8
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	49 / 294 (16.67%)	28 / 296 (9.46%)	41 / 293 (13.99%)
occurrences (all)	65	31	52

Non-serious adverse events	Girls 9 to 14 Years V503 at Months 0, 2, and 6	Young Women 16 to 26 Years V503 at Months 0, 2, and 6	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 300 (18.33%)	90 / 313 (28.75%)	

Nervous system disorders Headache subjects affected / exposed occurrences (all)	 7 / 300 (2.33%) 8	 16 / 313 (5.11%) 19	
General disorders and administration site conditions Injection site pain subjects affected / exposed occurrences (all)	 53 / 300 (17.67%) 81	 80 / 313 (25.56%) 148	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 February 2015	Amendment 1: Added peripheral blood mononuclear cell (PBMC) collection and testing at Month 24; added U.S. sites and IND number; added participants for PBMC testing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported