Clinical trial results:
A Phase 3 Open-Label Clinical Trial to Study the Immunogenicity and Safety of 9-Valent Human Papillomavirus (HPV) L1 Virus-Like Particle (VLP) Vaccine (V503) in Chinese females 9 to 45 Years of Age

Summary

EudraCT number	2024-000582-24
Trial protocol	Outside EU/EEA
Global end of trial date	22 July 2025

Results information

Result version number	v1
This version publication date	01 February 2026
First version publication date	01 February 2026

Trial information

Trial identification

Sponsor protocol code	V503-024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03903562
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.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	22 July 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2025
Global end of trial reached?	Yes
Global end of trial date	22 July 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will investigate the immunogenicity and safety of the 9vHPV vaccine in healthy Chinese females 9 to 45 years of age. The study consists of Stage I (Day 1 to Month 7) and Stage II (post Month 7 to Month 60). Stage II will report the long-term immunogenicity and safety in 9 to 19 years of age group only. Dual-primary hypotheses of Stage I: 9vHPV vaccine induces non-inferior immune responses in females 9 to 19 years of age who are seronegative at Day 1 to the relevant HPV type compared to females 20 to 26 years of age who are seronegative at Day 1 to relevant HPV type, as measured by anti-HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58 geometric mean titers at 1 month post Dose 3; 9vHPV vaccine induces non-inferior immune responses in females 27 to 45 years of age who are seronegative Day 1 to relevant HPV type compared to females 20 to 26 years of age who are seronegative Day 1 to relevant HPV type, measured by seroconversion percentages to each of HPV types at 1 month post Dose 3.

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	27 April 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Regulatory reason, Scientific research
Long term follow-up duration	53 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 1990
Worldwide total number of subjects	1990
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	166
Adolescents (12-17 years)	425
Adults (18-64 years)	1399
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy Chinese females received 9-Valent Human Papillomavirus (HPV) L1 Virus-Like Particle (VLP) Vaccine (V503). The study consists of two stages. Stage I is from Day 1 through 1 month post last dose (Month 7). Participants in the 9 to 19 years of age group who completed 3 doses of V503 were eligible for Stage II and followed up to Month 60.

Pre-assignment

Screening details:

1990 participants were enrolled, and 1988 received at least one dose of study vaccination.

Period 1

Period 1 title	Stage I
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	9 to 19 Years of Age

Arm description:

Chinese females 9 to 19 years of age received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Arm type	Experimental
Investigational medicinal product name	9-valent human papillomavirus (HPV) (types 6, 11, 16, 18, 31, 33, 45, 52, and 58) L1 VLP vaccine
Investigational medicinal product code	
Other name	V503 GARDASIL 9
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Arm title	20 to 26 Years of Age

Arm description:

Chinese females 20 to 26 years of age received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Arm type	Experimental
Investigational medicinal product name	9vHPV (types 6, 11, 16, 18, 31, 33, 45, 52, and 58) L1 VLP vaccine
Investigational medicinal product code	
Other name	V503 GARDASIL 9
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Arm title	27 to 45 Years of Age

Arm description:

Chinese females 27 to 45 years of received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Arm type	Experimental

Investigational medicinal product name	9vHPV (types 6, 11, 16, 18, 31, 33, 45, 52, and 58) L1 VLP vaccine
Investigational medicinal product code	
Other name	V503 GARDASIL 9
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Number of subjects in period 1	9 to 19 Years of Age	20 to 26 Years of Age	27 to 45 Years of Age
Started	690	650	650
Vaccination 1	688	650	650
Vaccination 2	683	647	644
Vaccination 3	682	635	641
Completed	682	635	641
Not completed	8	15	9
Consent withdrawn by subject	5	15	9
withdrawal by parent/guardian	3	-	-

Period 2

Period 2 title	Stage II
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	9 to 19 Years of Age

Arm description:

Participants in the 9 to 19 years of age group who completed 3 doses of V503 were eligible for Stage II and followed up to Month 60.

Arm type	Experimental
Investigational medicinal product name	9vHPV (types 6, 11, 16, 18, 31, 33, 45, 52, and 58) L1 VLP vaccine
Investigational medicinal product code	
Other name	V503 GARDASIL 9
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Number of subjects in period 2[1]	9 to 19 Years of Age
Started	682
Completed	645
Not completed	37
Consent withdrawn by subject	25
Lost to follow-up	12

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: The number that started Stage II is the number that completed 3 vaccinations in Arm 1.

Baseline characteristics

Reporting groups	
Reporting group title	9 to 19 Years of Age
Reporting group description:	
Chinese females 9 to 19 years of age received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.	
Reporting group title	20 to 26 Years of Age
Reporting group description:	
Chinese females 20 to 26 years of age received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.	
Reporting group title	27 to 45 Years of Age
Reporting group description:	
Chinese females 27 to 45 years of received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.	

Reporting group values	9 to 19 Years of Age	20 to 26 Years of Age	27 to 45 Years of Age
Number of subjects	690	650	650
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	166	0	0
Adolescents (12-17 years)	425	0	0
Adults (18-64 years)	99	650	650
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	14.0	23.1	35.5
standard deviation	± 3.0	± 1.7	± 5.1
Gender categorical Units: Subjects			
Female	690	650	650
Male	0	0	0
Race Units: Subjects			
Asian	690	650	650
Ethnicity Units: Subjects			
Not Hispanic or Latino	690	650	650
Age Units: Years			
arithmetic mean	14.0	23.1	35.5
standard deviation	± 3.0	± 1.7	± 5.1

Reporting group values	Total		
Number of subjects	1990		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	166		
Adolescents (12-17 years)	425		
Adults (18-64 years)	1399		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	1990		
Male	0		
Race Units: Subjects			
Asian	1990		
Ethnicity Units: Subjects			
Not Hispanic or Latino	1990		
Age Units: Years			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	9 to 19 Years of Age

Reporting group description:

Chinese females 9 to 19 years of age received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Reporting group title	20 to 26 Years of Age

Reporting group description:

Chinese females 20 to 26 years of age received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Reporting group title	27 to 45 Years of Age

Reporting group description:

Chinese females 27 to 45 years of received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Reporting group title	9 to 19 Years of Age

Reporting group description:

Participants in the 9 to 19 years of age group who completed 3 doses of V503 were eligible for Stage II and followed up to Month 60.

Subject analysis set title	Stage I: 9 to 15 Years of Age
Subject analysis set type	Per protocol

Subject analysis set description:

Chinese females 9 to 15 years of age, a subset of the 9 to 19 years of age group, received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Primary: Stage I: Competitive Luminex Immunoassay (cLIA) Geometric Mean Titers (GMTs) for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 Years of Age and 20 to 26 Years of Age: Month 7

End point title	Stage I: Competitive Luminex Immunoassay (cLIA) Geometric Mean Titers (GMTs) for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 Years of Age and 20 to 26 Years of Age: Month 7[1]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using cLIA. The HPV-9 cLIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as milli Merck units/mL (mMU/mL). Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant’s immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

1 month post vaccination 3 (Month 7)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No statistical analyses were planned for arm 3 (27 to 45 Years of Age) for this endpoint.

End point values	9 to 19 Years of Age	20 to 26 Years of Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	688	650		
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=640, 567)	1129.7 (1069.8 to 1193.0)	861.7 (817.5 to 908.4)		
Anti-HPV 11 (n=640, 567)	926.7 (876.4 to 979.8)	702.6 (662.7 to 744.9)		
Anti-HPV 16 (n=662, 595)	4972.3 (4696.9 to 5263.9)	3723.7 (3513.0 to 3946.9)		
Anti-HPV 18 (n=630, 574)	1438.4 (1349.0 to 1533.6)	1031.6 (964.4 to 1103.6)		
Anti-HPV 31 (n=657, 587)	1161.5 (1093.2 to 1234.2)	821.9 (770.5 to 876.7)		
Anti-HPV 33 (n=642, 589)	664.3 (626.3 to 704.7)	497.5 (468.1 to 528.8)		
Anti-HPV 45 (n=655, 598)	442.9 (415.0 to 472.7)	299.1 (279.8 to 319.9)		
Anti-HPV 52 (n=649, 572)	505.9 (478.4 to 535.0)	397.8 (374.4 to 422.8)		
Anti-HPV 58 (n=645, 580)	725.3 (685.6 to 767.4)	535.9 (503.2 to 570.8)		

Statistical analyses

Statistical analysis title	Anti-HPV 6
Statistical analysis description: GMT Ratio	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.31
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.2
upper limit	1.43

Notes:

[2] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 19 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 11

Statistical analysis description:	
GMT Ratio	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.32
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.2
upper limit	1.45

Notes:

[3] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 19 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 16
Statistical analysis description:	
GMT Ratio	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.34
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.22
upper limit	1.47

Notes:

[4] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 19 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 18
Statistical analysis description:	
GMT Ratio	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.39

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.25
upper limit	1.55

Notes:

[5] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 19 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 31

Statistical analysis description:

GMT Ratio

Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.41
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.28
upper limit	1.56

Notes:

[6] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 19 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 45

Statistical analysis description:

GMT Ratio

Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.48
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.33
upper limit	1.65

Notes:

[7] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 19 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 33
Statistical analysis description:	
GMT Ratio	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.34
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.21
upper limit	1.47

Notes:

[8] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 19 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 52
Statistical analysis description:	
GMT Ratio	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.27
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.16
upper limit	1.4

Notes:

[9] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 19 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 58
Statistical analysis description:	
GMT Ratio	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age

Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.35
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.23
upper limit	1.49

Notes:

[10] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 19 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Primary: Stage I: Percentage of Participants 27 to 45 Years of Age and 20 to 26 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 7

End point title	Stage I: Percentage of Participants 27 to 45 Years of Age and 20 to 26 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 7[11]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using cLIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥50, 29, 41, 59, 29, 22, 15, 20, and 15 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

1 month post vaccination 3 (Month 7)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were performed for arm 1 (9 to 19 Years of Age) for this endpoint.

End point values	20 to 26 Years of Age	27 to 45 Years of Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	650	650		
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥50 mMU/mL (n=567, 517)	100.0 (99.4 to 100.0)	100.0 (99.3 to 100.0)		
Anti-HPV 11 ≥29 mMU/mL (n=567, 517)	100.0 (99.4 to 100.0)	100.0 (99.3 to 100.0)		
Anti-HPV 16 ≥41 mMU/mL (n=595, 575)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 18 ≥59 mMU/mL (n=574, 575)	99.8 (99.0 to 100.0)	100.0 (99.4 to 100.0)		

Anti-HPV 31 ≥29 mMU/mL (n=587, 576)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 33 ≥22 mMU/mL (n=589, 569)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 45 ≥15 mMU/mL (n=598, 598)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 52 ≥20 mMU/mL (n=572, 578)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 58 ≥15 mMU/mL (n=580, 534)	100.0 (99.4 to 100.0)	100.0 (99.3 to 100.0)		

Statistical analyses

Statistical analysis title	Anti-HPV 6 ≥50 mMU/mL
Statistical analysis description:	
Difference of Seroconversion Percentages (27 to 45 years of age) - (20 to 26 years of age)	
Comparison groups	20 to 26 Years of Age v 27 to 45 Years of Age
Number of subjects included in analysis	1300
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1
upper limit	0.9

Notes:

[12] - Criterion for non-inferiority with respect to the difference (females 27 to 45 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 11 ≥29 mMU/mL
Statistical analysis description:	
Difference of Seroconversion Percentages (27 to 45 years of age) - (20 to 26 years of age)	
Comparison groups	20 to 26 Years of Age v 27 to 45 Years of Age
Number of subjects included in analysis	1300
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1
upper limit	0.9

Notes:

[13] - Criterion for non-inferiority with respect to the difference (females 27 to 45 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 16 ≥41 mMU/mL
Statistical analysis description:	
Difference of Seroconversion Percentages (27 to 45 years of age) - (20 to 26 years of age)	
Comparison groups	20 to 26 Years of Age v 27 to 45 Years of Age
Number of subjects included in analysis	1300
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.9
upper limit	0.8

Notes:

[14] - Criterion for non-inferiority with respect to the difference (females 27 to 45 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 18 ≥59 mMU/mL
Statistical analysis description:	
Difference of Seroconversion Percentages (27 to 45 years of age) - (20 to 26 years of age)	
Comparison groups	20 to 26 Years of Age v 27 to 45 Years of Age
Number of subjects included in analysis	1300
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.7
upper limit	1.2

Notes:

[15] - Criterion for non-inferiority with respect to the difference (females 27 to 45 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 31 ≥29 mMU/mL
Statistical analysis description:	
Difference of Seroconversion Percentages (27 to 45 years of age) - (20 to 26 years of age)	
Comparison groups	20 to 26 Years of Age v 27 to 45 Years of Age

Number of subjects included in analysis	1300
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.9
upper limit	0.8

Notes:

[16] - Criterion for non-inferiority with respect to the difference (females 27 to 45 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 45 ≥15 mMU/mL

Statistical analysis description:

Difference of Seroconversion Percentages (27 to 45 years of age) - (20 to 26 years of age)

Comparison groups	20 to 26 Years of Age v 27 to 45 Years of Age
Number of subjects included in analysis	1300
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.8
upper limit	0.8

Notes:

[17] - Criterion for non-inferiority with respect to the difference (females 27 to 45 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 33 ≥22 mMU/mL

Statistical analysis description:

Difference of Seroconversion Percentages (27 to 45 years of age) - (20 to 26 years of age)

Comparison groups	20 to 26 Years of Age v 27 to 45 Years of Age
Number of subjects included in analysis	1300
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.9
upper limit	0.8

Notes:

[18] - Criterion for non-inferiority with respect to the difference (females 27 to 45 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 52 ≥20 mMU/mL

Statistical analysis description:

Difference of Seroconversion Percentages (27 to 45 years of age) - (20 to 26 years of age)

Comparison groups	20 to 26 Years of Age v 27 to 45 Years of Age
Number of subjects included in analysis	1300
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.9
upper limit	0.9

Notes:

[19] - Criterion for non-inferiority with respect to the difference (females 27 to 45 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 58 ≥15 mMU/mL

Statistical analysis description:

Difference of Seroconversion Percentages (27 to 45 years of age) - (20 to 26 years of age)

Comparison groups	20 to 26 Years of Age v 27 to 45 Years of Age
Number of subjects included in analysis	1300
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.9
upper limit	0.9

Notes:

[20] - Criterion for non-inferiority with respect to the difference (females 27 to 45 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Primary: Stage II: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 Years of Age: Month 12

End point title	Stage II: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 Years of Age: Month 12[21]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using cLIA. The HPV-9 cLIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 12

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=638)	420.3 (393.3 to 449.1)			
Anti-HPV 11 (n=638)	341.9 (320.1 to 365.3)			
Anti-HPV 16 (n=660)	1748.7 (1636.7 to 1868.3)			
Anti-HPV 18 (n=628)	472.2 (440.6 to 506.1)			
Anti-HPV 31 (n=655)	403.5 (375.6 to 433.5)			
Anti-HPV 33 (n=640)	237.7 (221.8 to 254.8)			
Anti-HPV 45 (n=653)	144.0 (133.4 to 155.3)			
Anti-HPV 52 (n=647)	187.6 (175.8 to 200.2)			
Anti-HPV 58 (n=643)	272.5 (255.5 to 290.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 24

End point title	Stage II: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 24[22]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using cLIA. The HPV-9 cLIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 24

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=636)	210.2 (196.4 to 225.0)			
Anti-HPV 11 (n=636)	172.2 (160.7 to 184.5)			
Anti-HPV 16 (n=658)	774.8 (717.2 to 837.1)			
Anti-HPV 18 (n=627)	226.9 (211.8 to 243.0)			
Anti-HPV 31 (n=653)	205.3 (190.4 to 221.4)			
Anti-HPV 33 (n=638)	120.4 (112.2 to 129.2)			
Anti-HPV 45 (n=651)	72.1 (66.8 to 77.8)			
Anti-HPV 52 (n=645)	97.5 (91.3 to 104.2)			
Anti-HPV 58 (n=641)	125.8 (117.0 to 135.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 36

End point title	Stage II: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 36[23]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using cLIA. The HPV-9 cLIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Participants who 1) received all vaccinations in the

planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 36

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=616)	172.6 (161.6 to 184.4)			
Anti-HPV 11 (n=616)	136.5 (127.6 to 146.0)			
Anti-HPV 16 (n=637)	600.5 (554.3 to 650.6)			
Anti-HPV 18 (n=609)	178.0 (166.3 to 190.5)			
Anti-HPV 31 (n=633)	166.9 (154.7 to 180.0)			
Anti-HPV 33 (n=618)	95.1 (88.6 to 102.1)			
Anti-HPV 45 (n=631)	56.9 (52.8 to 61.4)			
Anti-HPV 52 (n=626)	78.1 (73.2 to 83.4)			
Anti-HPV 58 (n=620)	100.9 (93.9 to 108.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 48

End point title	Stage II: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 48[24]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using cLIA. The HPV-9 cLIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 48

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=616)	170.3 (158.9 to 182.6)			
Anti-HPV 11 (n=616)	123.4 (115.0 to 132.3)			
Anti-HPV 16 (n=636)	612.6 (568.8 to 659.8)			
Anti-HPV 18 (n=607)	151.9 (140.1 to 164.8)			
Anti-HPV 31 (n=632)	165.6 (153.2 to 178.9)			
Anti-HPV 33 (n=617)	87.9 (81.4 to 94.9)			
Anti-HPV 45 (n=630)	53.5 (49.4 to 57.9)			
Anti-HPV 52 (n=625)	75.3 (70.5 to 80.4)			
Anti-HPV 58 (n=619)	97.1 (90.5 to 104.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 60

End point title	Stage II: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 60[25]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using cLIA. The HPV-9 cLIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant’s immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 60

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=604)	154.2 (143.5 to 165.6)			
Anti-HPV 11 (n=604)	111.3 (103.5 to 119.6)			
Anti-HPV 16 (n=624)	541.7 (502.0 to 584.5)			
Anti-HPV 18 (n=597)	132.9 (122.5 to 144.1)			
Anti-HPV 31 (n=620)	147.1 (135.9 to 159.2)			
Anti-HPV 33 (n=605)	79.0 (73.1 to 85.3)			
Anti-HPV 45 (n=619)	48.3 (44.5 to 52.4)			
Anti-HPV 52 (n=613)	68.6 (64.1 to 73.3)			
Anti-HPV 58 (n=608)	86.8 (80.6 to 93.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 12

End point title	Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 12[26]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using cLIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥50, 29, 41, 59, 29, 22, 15, 20, and 15 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 12

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥50 mMU/mL (n=638)	99.5 (98.6 to 99.9)			
Anti-HPV 11 ≥29 mMU/mL (n=638)	100.0 (99.4 to 100.0)			
Anti-HPV 16 ≥41 mMU/mL (n=660)	100.0 (99.4 to 100.0)			
Anti-HPV 18 ≥59 mMU/mL (n=628)	99.0 (97.9 to 99.6)			
Anti-HPV 31 ≥29 mMU/mL (n=655)	99.4 (98.4 to 99.8)			
Anti-HPV 33 ≥22 mMU/mL (n=640)	99.5 (98.6 to 99.9)			
Anti-HPV 45 ≥15 mMU/mL (n=653)	98.9 (97.8 to 99.6)			
Anti-HPV 52 ≥20 mMU/mL (n=647)	99.7 (98.9 to 100.0)			
Anti-HPV 58 ≥15 mMU/mL (n=643)	100.0 (99.4 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 24

End point title	Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 24[27]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using cLIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥50, 29, 41, 59, 29, 22, 15, 20, and 15 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 24

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥50 mMU/mL (n=636)	96.4 (94.6 to 97.7)			
Anti-HPV 11 ≥29 mMU/mL (n=636)	98.3 (96.9 to 99.1)			
Anti-HPV 16 ≥41 mMU/mL (n=658)	99.1 (98.0 to 99.7)			
Anti-HPV 18 ≥59 mMU/mL (n=627)	95.7 (93.8 to 97.1)			
Anti-HPV 31 ≥29 mMU/mL (n=653)	98.0 (96.6 to 98.9)			
Anti-HPV 33 ≥22 mMU/mL (n=638)	98.0 (96.5 to 98.9)			
Anti-HPV 45 ≥15 mMU/mL (n=651)	96.8 (95.1 to 98.0)			
Anti-HPV 52 ≥20 mMU/mL (n=645)	96.9 (95.3 to 98.1)			
Anti-HPV 58 ≥15 mMU/mL (n=641)	98.0 (96.6 to 98.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 36

End point title	Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 36[28]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using cLIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥65, 37, 79, 85, 46, 26, 21, 30 and 31 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 36

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥65 mMU/mL (n=616)	87.3 (84.5 to 89.9)			
Anti-HPV 11 ≥37 mMU/mL (n=616)	94.5 (92.4 to 96.1)			
Anti-HPV 16 ≥79 mMU/mL (n=637)	97.0 (95.4 to 98.2)			
Anti-HPV 18 ≥85 mMU/mL (n=609)	80.5 (77.1 to 83.5)			
Anti-HPV 31 ≥46 mMU/mL (n=633)	90.5 (88.0 to 92.7)			
Anti-HPV 33 ≥26 mMU/mL (n=618)	94.8 (92.8 to 96.4)			
Anti-HPV 45 ≥21 mMU/mL (n=631)	84.9 (81.9 to 87.6)			
Anti-HPV 52 ≥30 mMU/mL (n=626)	86.9 (84.0 to 89.4)			
Anti-HPV 58 ≥31 mMU/mL (n=620)	90.2 (87.5 to 92.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 48

End point title	Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 48[29]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using cLIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥34, 25, 32, 26, 15, 10, 10, 14 and 10 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 48

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥34 mMU/mL (n=616)	94.2 (92.0 to 95.9)			
Anti-HPV 11 ≥25 mMU/mL (n=616)	95.9 (94.1 to 97.4)			
Anti-HPV 16 ≥32 mMU/mL (n=636)	99.1 (98.0 to 99.7)			
Anti-HPV 18 ≥26 mMU/mL (n=607)	92.3 (89.8 to 94.3)			
Anti-HPV 31 ≥15 mMU/mL (n=632)	98.3 (96.9 to 99.1)			
Anti-HPV 33 ≥10 mMU/mL (n=617)	97.4 (95.8 to 98.5)			
Anti-HPV 45 ≥10 mMU/mL (n=630)	92.7 (90.4 to 94.6)			
Anti-HPV 52 ≥14 mMU/mL (n=625)	96.8 (95.1 to 98.0)			
Anti-HPV 58 ≥10 mMU/mL (n=619)	98.5 (97.3 to 99.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Percentage of Participants 9 to 19 years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 60

End point title	Stage II: Percentage of Participants 9 to 19 years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 60[30]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using cLIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥34, 25, 32, 26, 15, 10, 10, 14 and 10 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 60

Notes:

[30] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥34 mMU/mL (n=604)	92.5 (90.2 to 94.5)			
Anti-HPV 11 ≥25 mMU/mL (n=604)	93.5 (91.3 to 95.4)			
Anti-HPV 16 ≥32 mMU/mL (n=624)	98.9 (97.7 to 99.5)			
Anti-HPV 18 ≥26 mMU/mL (n=597)	90.3 (87.6 to 92.5)			
Anti-HPV 31 ≥15 mMU/mL (n=620)	97.6 (96.0 to 98.6)			
Anti-HPV 33 ≥10 mMU/mL (n=605)	96.2 (94.4 to 97.6)			
Anti-HPV 45 ≥10 mMU/mL (n=619)	89.7 (87.0 to 91.9)			
Anti-HPV 52 ≥14 mMU/mL (n=613)	95.3 (93.3 to 96.8)			
Anti-HPV 58 ≥10 mMU/mL (n=608)	97.9 (96.4 to 98.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Immunoglobulin G Luminex Immunoassay (IgG LIA) GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 12

End point title	Stage II: Immunoglobulin G Luminex Immunoassay (IgG LIA) GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 12[31]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using IgG LIA. The HPV-9 IgG LIA assay was used to quantify the antibodies. This assay evaluated serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Although the same name (mMU/mL) is used for the unit of measurement of cLIA and IgG LIA, the 'cLIA mMU/mL' and the 'IgG LIA mMU/mL' are different units of measurement and cannot be directly compared. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no protocol violations that could interfere with evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 12

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=638)	355.1 (329.4 to 382.7)			
Anti-HPV 11 (n=638)	290.5 (270.1 to 312.4)			
Anti-HPV 16 (n=660)	1505.2 (1405.6 to 1611.9)			
Anti-HPV 18 (n=628)	340.1 (314.5 to 367.8)			
Anti-HPV 31 (n=655)	331.7 (307.2 to 358.2)			
Anti-HPV 33 (n=640)	194.7 (180.6 to 210.0)			
Anti-HPV 45 (n=653)	112.1 (103.3 to 121.7)			
Anti-HPV 52 (n=647)	153.3 (142.7 to 164.8)			
Anti-HPV 58 (n=643)	230.0 (214.6 to 246.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: IgG LIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 24

End point title	Stage II: IgG LIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 24[32]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using IgG LIA. The HPV-9 IgG LIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 24

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=636)	186.3 (172.2 to 201.5)			
Anti-HPV 11 (n=636)	159.0 (147.3 to 171.7)			
Anti-HPV 16 (n=658)	750.8 (695.2 to 810.8)			
Anti-HPV 18 (n=627)	153.6 (140.4 to 168.0)			
Anti-HPV 31 (n=653)	174.8 (161.1 to 189.6)			
Anti-HPV 33 (n=638)	99.1 (91.3 to 107.5)			
Anti-HPV 45 (n=651)	58.4 (53.5 to 63.9)			
Anti-HPV 52 (n=645)	82.6 (76.7 to 89.1)			
Anti-HPV 58 (n=641)	115.2 (106.8 to 124.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: IgG LIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 36

End point title	Stage II: IgG LIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 36[33]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using IgG LIA. The HPV-9 IgG LIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 36

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=616)	143.2 (132.0 to 155.5)			
Anti-HPV 11 (n=616)	121.9 (112.5 to 132.2)			
Anti-HPV 16 (n=637)	566.1 (521.8 to 614.2)			
Anti-HPV 18 (n=609)	112.3 (102.1 to 123.4)			
Anti-HPV 31 (n=633)	137.3 (126.1 to 149.5)			
Anti-HPV 33 (n=618)	75.4 (69.2 to 82.1)			
Anti-HPV 45 (n=631)	44.2 (40.3 to 48.4)			
Anti-HPV 52 (n=626)	65.0 (60.2 to 70.3)			
Anti-HPV 58 (n=620)	90.0 (83.1 to 97.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: IgG LIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 48

End point title	Stage II: IgG LIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 48[34]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using IgG LIA. The HPV-9 IgG LIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 48

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=616)	121.4 (111.9 to 131.8)			
Anti-HPV 11 (n=616)	104.4 (96.3 to 113.2)			
Anti-HPV 16 (n=636)	491.4 (452.7 to 533.4)			
Anti-HPV 18 (n=607)	96.0 (87.2 to 105.7)			
Anti-HPV 31 (n=632)	122.0 (112.0 to 133.0)			
Anti-HPV 33 (n=617)	65.8 (60.4 to 71.8)			
Anti-HPV 45 (n=630)	38.7 (35.4 to 42.4)			
Anti-HPV 52 (n=625)	56.6 (52.3 to 61.3)			
Anti-HPV 58 (n=619)	79.7 (73.5 to 86.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: IgG LIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 60

End point title	Stage II: IgG LIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 years of Age: Month 60[35]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using IgG LIA. The HPV-9 IgG LIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 60

Notes:

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=604)	106.8 (98.1 to 116.3)			
Anti-HPV 11 (n=604)	91.3 (83.9 to 99.2)			
Anti-HPV 16 (n=624)	433.6 (398.2 to 472.2)			
Anti-HPV 18 (n=597)	81.9 (74.2 to 90.3)			
Anti-HPV 31 (n=620)	106.1 (97.1 to 115.9)			
Anti-HPV 33 (n=605)	58.3 (53.4 to 63.6)			
Anti-HPV 45 (n=619)	33.6 (30.6 to 36.9)			
Anti-HPV 52 (n=613)	49.6 (45.7 to 54.0)			
Anti-HPV 58 (n=608)	70.8 (65.0 to 77.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 12

End point title	Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 12[36]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using IgG LIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥9, 6, 5, 5, 3, 4, 3, 5 and 5 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 12

Notes:

[36] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥9 mMU/mL (n=638)	100.0 (99.4 to 100.0)			
Anti-HPV 11 ≥6 mMU/mL (n=638)	100.0 (99.4 to 100.0)			
Anti-HPV 16 ≥5 mMU/mL (n=660)	100.0 (99.4 to 100.0)			
Anti-HPV 18 ≥5 mMU/mL (n=628)	100.0 (99.4 to 100.0)			
Anti-HPV 31 ≥3 mMU/mL (n=655)	100.0 (99.4 to 100.0)			
Anti-HPV 33 ≥4 mMU/mL (n=640)	100.0 (99.4 to 100.0)			
Anti-HPV 45 ≥3 mMU/mL (n=653)	99.8 (99.1 to 100.0)			
Anti-HPV 52 ≥5 mMU/mL (n=647)	99.8 (99.1 to 100.0)			
Anti-HPV 58 ≥5 mMU/mL (n=643)	99.8 (99.1 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 24

End point title	Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 24[37]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using IgG LIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥9, 6, 5, 5, 3, 4, 3, 5 and 5 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 24

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥9 mMU/mL (n=636)	99.8 (99.1 to 100.0)			
Anti-HPV 11 ≥6 mMU/mL (n=636)	100.0 (99.4 to 100.0)			
Anti-HPV 16 ≥5 mMU/mL (n=658)	100.0 (99.4 to 100.0)			
Anti-HPV 18 ≥5 mMU/mL (n=627)	99.4 (98.4 to 99.8)			
Anti-HPV 31 ≥3 mMU/mL (n=653)	99.8 (99.1 to 100.0)			
Anti-HPV 33 ≥4 mMU/mL (n=638)	99.8 (99.1 to 100.0)			
Anti-HPV 45 ≥3 mMU/mL (n=651)	99.1 (98.0 to 99.7)			
Anti-HPV 52 ≥5 mMU/mL (n=645)	99.8 (99.1 to 100.0)			
Anti-HPV 58 ≥5 mMU/mL (n=641)	99.5 (98.6 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 36

End point title	Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 36[38]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using IgG LIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥9, 6, 5, 5, 3, 4, 3, 5 and 5 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 36

Notes:

[38] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥9 mMU/mL (n=616)	99.7 (98.8 to 100.0)			
Anti-HPV 11 ≥6 mMU/mL (n=616)	99.7 (98.8 to 100.0)			
Anti-HPV 16 ≥5 mMU/mL (n=637)	100.0 (99.4 to 100.0)			
Anti-HPV 18 ≥5 mMU/mL (n=609)	98.7 (97.4 to 99.4)			
Anti-HPV 31 ≥3 mMU/mL (n=633)	99.8 (99.1 to 100.0)			
Anti-HPV 33 ≥4 mMU/mL (n=618)	99.4 (98.4 to 99.8)			
Anti-HPV 45 ≥3 mMU/mL (n=631)	98.4 (97.1 to 99.2)			
Anti-HPV 52 ≥5 mMU/mL (n=626)	99.2 (98.1 to 99.7)			
Anti-HPV 58 ≥5 mMU/mL (n=620)	99.0 (97.9 to 99.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 48

End point title	Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 48[39]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using IgG LIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥9, 6, 5, 5, 3, 4, 3, 5 and 5 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 48

Notes:

[39] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥9 mMU/mL (n=616)	99.2 (98.1 to 99.7)			
Anti-HPV 11 ≥6 mMU/mL (n=616)	99.2 (98.1 to 99.7)			
Anti-HPV 16 ≥5 mMU/mL (n=636)	100.0 (99.4 to 100.0)			
Anti-HPV 18 ≥5 mMU/mL (n=607)	98.5 (97.2 to 99.3)			
Anti-HPV 31 ≥3 mMU/mL (n=632)	99.5 (98.6 to 99.9)			
Anti-HPV 33 ≥4 mMU/mL (n=617)	98.5 (97.2 to 99.3)			
Anti-HPV 45 ≥3 mMU/mL (n=630)	98.6 (97.3 to 99.3)			
Anti-HPV 52 ≥5 mMU/mL (n=625)	98.7 (97.5 to 99.4)			
Anti-HPV 58 ≥5 mMU/mL (n=619)	99.0 (97.9 to 99.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 60

End point title	Stage II: Percentage of Participants 9 to 19 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 60[40]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using IgG LIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥9, 6, 5, 5, 3, 4, 3, 5 and 5 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Primary

End point timeframe:

Month 60

Notes:

[40] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No between-group statistical analyses were performed for this endpoint.

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥9 mMU/mL (n=604)	99.0 (97.9 to 99.6)			
Anti-HPV 11 ≥6 mMU/mL (n=604)	99.0 (97.9 to 99.6)			
Anti-HPV 16 ≥5 mMU/mL (n=624)	100.0 (99.4 to 100.0)			
Anti-HPV 18 ≥5 mMU/mL (n=597)	97.5 (95.9 to 98.6)			
Anti-HPV 31 ≥3 mMU/mL (n=620)	99.7 (98.8 to 100.0)			
Anti-HPV 33 ≥4 mMU/mL (n=605)	98.2 (96.8 to 99.1)			
Anti-HPV 45 ≥3 mMU/mL (n=619)	97.9 (96.4 to 98.9)			
Anti-HPV 52 ≥5 mMU/mL (n=613)	98.2 (96.8 to 99.1)			
Anti-HPV 58 ≥5 mMU/mL (n=608)	98.7 (97.4 to 99.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Stage I: Percentage of Participants 9 to 19 Years of Age and 20 to 26 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 7

End point title	Stage I: Percentage of Participants 9 to 19 Years of Age and 20 to 26 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 7[41]

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using cLIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥50, 29, 41, 59, 29, 22, 15, 20, and 15 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant’s immune response to the study vaccine were analyzed.

End point type	Secondary

End point timeframe:

1 month post vaccination 3 (Month 7)

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were planned for arm 3 (27 to 45 Years of Age) for this endpoint.

End point values	9 to 19 Years of Age	20 to 26 Years of Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	688	650		
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥50 mMU/mL (n=640, 567)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 11 ≥29 mMU/mL (n=640, 567))	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 16 ≥41 mMU/mL (n=662, 595)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 18 ≥59 mMU/mL (n=630, 574)	100.0 (99.4 to 100.0)	99.8 (99.0 to 100.0)		
Anti-HPV 31 ≥29 mMU/mL (n=657, 587)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 33 ≥22 mMU/mL (n=642, 589)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 45 ≥15 mMU/mL (n=655, 598)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 52 ≥20 mMU/mL (n=649. 572)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		
Anti-HPV 58 ≥15 mMU/mL (n=645, 580)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)		

Statistical analyses

Statistical analysis title	Anti-HPV 18 ≥59 mMU/mL
Statistical analysis description:	
Difference of Seroconversion Percentages (9 to 19 years of age) - (20 to 26 years of age)	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[42]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.6
upper limit	1.2

Notes:

[42] - Criterion for non-inferiority with respect to the difference (females 9 to 19 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 16 ≥41 mMU/mL
Statistical analysis description:	
Difference of Seroconversion Percentages (9 to 19 years of age) - (20 to 26 years of age)	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age

Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[43]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.8
upper limit	0.8

Notes:

[43] - Criterion for non-inferiority with respect to the difference (females 9 to 19 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 11 ≥29 mMU/mL

Statistical analysis description:

Difference of Seroconversion Percentages (9 to 19 years of age) - (20 to 26 years of age)

Comparison groups	20 to 26 Years of Age v 9 to 19 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[44]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.8
upper limit	0.9

Notes:

[44] - Criterion for non-inferiority with respect to the difference (females 9 to 19 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 6 ≥50 mMU/mL

Statistical analysis description:

Difference of Seroconversion Percentages (9 to 19 years of age) - (20 to 26 years of age)

Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[45]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.8
upper limit	0.9

Notes:

[45] - Criterion for non-inferiority with respect to the difference (females 9 to 19 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 52 ≥20 mMU/mL

Statistical analysis description:

Difference of Seroconversion Percentages (9 to 19 years of age) - (20 to 26 years of age)

Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[46]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.8
upper limit	0.9

Notes:

[46] - Criterion for non-inferiority with respect to the difference (females 9 to 19 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 45 ≥15 mMU/mL

Statistical analysis description:

Difference of Seroconversion Percentages (9 to 19 years of age) - (20 to 26 years of age)

Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[47]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.8
upper limit	0.8

Notes:

[47] - Criterion for non-inferiority with respect to the difference (females 9 to 19 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 33 ≥22 mMU/mL

Statistical analysis description:	
Difference of Seroconversion Percentages (9 to 19 years of age) - (20 to 26 years of age)	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[48]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.8
upper limit	0.8

Notes:

[48] - Criterion for non-inferiority with respect to the difference (females 9 to 19 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 58 ≥15 mMU/mL
Statistical analysis description:	
Difference of Seroconversion Percentages (9 to 19 years of age) - (20 to 26 years of age)	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[49]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.8
upper limit	0.9

Notes:

[49] - Criterion for non-inferiority with respect to the difference (females 9 to 19 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Statistical analysis title	Anti-HPV 31 ≥29 mMU/mL
Statistical analysis description:	
Difference of Seroconversion Percentages (9 to 19 years of age) - (20 to 26 years of age)	
Comparison groups	9 to 19 Years of Age v 20 to 26 Years of Age
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[50]
P-value	< 0.0001
Method	Miettinen & Nurminen method
Parameter estimate	Difference of Seroconversion Percentages
Point estimate	0

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.8
upper limit	0.8

Notes:

[50] - Criterion for non-inferiority with respect to the difference (females 9 to 19 years of age - females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than -5% for each HPV type.

Secondary: Stage I: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 15 Years of Age and 20 to 26 Years of Age: Month 7

End point title	Stage I: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 15 Years of Age and 20 to 26 Years of Age: Month 7[51]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using cLIA. The HPV-9 cLIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type were expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Secondary

End point timeframe:

1 month post vaccination 3 (Month 7)

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were planned for arms 1 and 3 for this endpoint.

End point values	20 to 26 Years of Age	Stage I: 9 to 15 Years of Age		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	650	458		
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=567, 426)	861.7 (817.5 to 908.4)	1201.1 (1123.6 to 1284.0)		
Anti-HPV 11 (n=567, 426)	702.6 (662.7 to 744.9)	981.6 (917.5 to 1050.2)		
Anti-HPV 16 (n=595, 441)	3723.7 (3513.0 to 3946.9)	5279.6 (4943.8 to 5638.3)		
Anti-HPV 18 (n=574, 422)	1031.6 (964.4 to 1103.6)	1582.4 (1469.4 to 1704.1)		
Anti-HPV 31 (n=587, 436)	821.9 (770.5 to 876.7)	1253.1 (1167.7 to 1344.9)		
Anti-HPV 33 (n=589, 432)	497.5 (468.1 to 528.8)	699.6 (653.5 to 748.9)		
Anti-HPV 45 (n=598, 437)	299.1 (279.8 to 319.9)	490.5 (454.3 to 529.6)		

Anti-HPV 52 (n=572, 430)	397.8 (374.4 to 422.8)	535.1 (501.4 to 571.1)		
Anti-HPV 58 (n=580, 429)	535.9 (503.2 to 570.8)	771.5 (721.8 to 824.6)		

Statistical analyses

Statistical analysis title	Anti-HPV 6
Statistical analysis description: GMT Ratio	
Comparison groups	20 to 26 Years of Age v Stage I: 9 to 15 Years of Age
Number of subjects included in analysis	1108
Analysis specification	Pre-specified
Analysis type	non-inferiority[52]
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.39
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.27
upper limit	1.53

Notes:

[52] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 15 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 11
Statistical analysis description: GMT Ratio	
Comparison groups	20 to 26 Years of Age v Stage I: 9 to 15 Years of Age
Number of subjects included in analysis	1108
Analysis specification	Pre-specified
Analysis type	non-inferiority[53]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.26
upper limit	1.55

Notes:

[53] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 15 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 16

Statistical analysis description:	
GMT Ratio	
Comparison groups	20 to 26 Years of Age v Stage I: 9 to 15 Years of Age
Number of subjects included in analysis	1108
Analysis specification	Pre-specified
Analysis type	non-inferiority[54]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.42
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.28
upper limit	1.57

Notes:

[54] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 15 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 18
Statistical analysis description:	
GMT Ratio	
Comparison groups	20 to 26 Years of Age v Stage I: 9 to 15 Years of Age
Number of subjects included in analysis	1108
Analysis specification	Pre-specified
Analysis type	non-inferiority[55]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.53
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.37
upper limit	1.72

Notes:

[55] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 15 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 31
Statistical analysis description:	
GMT Ratio	
Comparison groups	20 to 26 Years of Age v Stage I: 9 to 15 Years of Age
Number of subjects included in analysis	1108
Analysis specification	Pre-specified
Analysis type	non-inferiority[56]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.52

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.37
upper limit	1.7

Notes:

[56] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 15 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 33

Statistical analysis description:

GMT Ratio

Comparison groups	20 to 26 Years of Age v Stage I: 9 to 15 Years of Age
Number of subjects included in analysis	1108
Analysis specification	Pre-specified
Analysis type	non-inferiority[57]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.41
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.27
upper limit	1.56

Notes:

[57] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 15 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 45

Statistical analysis description:

GMT Ratio

Comparison groups	20 to 26 Years of Age v Stage I: 9 to 15 Years of Age
Number of subjects included in analysis	1108
Analysis specification	Pre-specified
Analysis type	non-inferiority[58]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.64
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.46
upper limit	1.84

Notes:

[58] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 15 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 52
Statistical analysis description:	
GMT Ratio	
Comparison groups	20 to 26 Years of Age v Stage I: 9 to 15 Years of Age
Number of subjects included in analysis	1108
Analysis specification	Pre-specified
Analysis type	non-inferiority[59]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.35
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.21
upper limit	1.49

Notes:

[59] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 15 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Statistical analysis title	Anti-HPV 58
Statistical analysis description:	
GMT Ratio	
Comparison groups	20 to 26 Years of Age v Stage I: 9 to 15 Years of Age
Number of subjects included in analysis	1108
Analysis specification	Pre-specified
Analysis type	non-inferiority[60]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.44
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.29
upper limit	1.6

Notes:

[60] - Criterion for non-inferiority with respect to GMT ratio (females 9 to 15 years of age / females 20 to 26 years of age) required that the lower bound of 97.5% confidence be greater than 0.67 for each HPV type. An analysis of variance model with a response of log individual titers and fixed effect for group was used.

Secondary: Stage I: Percentage of Participants 9 to 15 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 7

End point title	Stage I: Percentage of Participants 9 to 15 Years of Age Who Are Seropositive by cLIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 7

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using cLIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥50, 29, 41, 59, 29, 22, 15, 20, and 15 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type, 3) had a serum sample collected 1 month after last dose within an

acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Secondary

End point timeframe:

1 month post vaccination 3 (Month 7)

End point values	Stage I: 9 to 15 Years of Age			
Subject group type	Subject analysis set			
Number of subjects analysed	458			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥50 mMU/mL (n=426)	100.0 (99.1 to 100.0)			
Anti-HPV 11 ≥29 mMU/mL (n=426)	100.0 (99.1 to 100.0)			
Anti-HPV 16 ≥41 mMU/mL (n=441)	100.0 (99.2 to 100.0)			
Anti-HPV 18 ≥59 mMU/mL (n=422)	100.0 (99.1 to 100.0)			
Anti-HPV 31 ≥29 mMU/mL (n=436)	100.0 (99.2 to 100.0)			
Anti-HPV 33 ≥22 mMU/mL (n=432)	100.0 (99.1 to 100.0)			
Anti-HPV 45 ≥15 mMU/mL (n=437)	100.0 (99.2 to 100.0)			
Anti-HPV 52 ≥20 mMU/mL (n=430)	100.0 (99.1 to 100.0)			
Anti-HPV 58 ≥15 mMU/mL (n=429)	100.0 (99.1 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Stage I: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 27 to 45 Years of Age: Month 7

End point title	Stage I: cLIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 27 to 45 Years of Age: Month 7[61]

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using cLIA. The HPV-9 cLIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type were expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Secondary

End point timeframe:

1 month post vaccination 3 (Month 7)

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses were planned for arms 1 and 2 for this endpoint.

End point values	27 to 45 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	650			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=517)	784.1 (738.9 to 832.1)			
Anti-HPV 11 (n=517)	634.7 (596.1 to 675.8)			
Anti-HPV 16 (n=575)	3175.0 (2983.0 to 3379.5)			
Anti-HPV 18 (n=575)	838.9 (783.8 to 897.8)			
Anti-HPV 31 (n=576)	699.9 (658.3 to 744.1)			
Anti-HPV 33 (n=569)	422.7 (396.9 to 450.1)			
Anti-HPV 45 (n=598)	245.1 (229.8 to 261.5)			
Anti-HPV 52 (n=578)	342.1 (322.2 to 363.2)			
Anti-HPV 58 (n=534)	435.2 (408.1 to 464.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Stage I: IgG LIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 Years of Age, 20 to 26 Years of Age, and 27 to 45 Years of Age: Month 7

End point title	Stage I: IgG LIA GMTs for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in Participants 9 to 19 Years of Age, 20 to 26 Years of Age, and 27 to 45 Years of Age: Month 7

End point description:

Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using IgG LIA. The HPV-9 IgG LIA assay was used to quantify the antibodies. This assay evaluated the serological response before and after 9vHPV vaccination and measured HPV infection-induced antibodies. The GMT for each HPV type was expressed as mMU/mL. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type and in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant’s immune response to the study vaccine were analyzed.

End point type	Secondary

End point timeframe:

1 month post vaccination 3 (Month 7)

End point values	9 to 19 Years of Age	20 to 26 Years of Age	27 to 45 Years of Age	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	688	650	650	
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=640, 567, 517)	1177.1 (1105.1 to 1253.7)	835.9 (785.7 to 889.3)	717.2 (668.3 to 769.8)	
Anti-HPV 11 (n=640, 567, 517)	939.9 (884.2 to 999.1)	670.6 (628.8 to 715.2)	566.1 (526.0 to 609.1)	
Anti-HPV 16 (n=662, 595, 575)	4746.8 (4473.9 to 5036.4)	3435.0 (3232.2 to 3650.5)	2867.6 (2685.8 to 3061.7)	
Anti-HPV 18 (n=630, 574, 575)	1303.8 (1219.5 to 1393.8)	910.3 (848.6 to 976.5)	741.7 (690.6 to 796.5)	
Anti-HPV 31 (n=657, 587, 576)	1082.5 (1016.4 to 1152.9)	744.2 (695.5 to 796.2)	630.2 (589.5 to 673.6)	
Anti-HPV 33 (n=642, 589, 569)	647.1 (607.3 to 689.5)	461.7 (433.0 to 492.4)	384.5 (359.0 to 411.9)	
Anti-HPV 45 (n=655, 598, 598)	397.9 (371.7 to 425.9)	260.7 (243.0 to 279.6)	213.7 (199.6 to 228.8)	
Anti-HPV 52 (n=649, 572, 578)	478.8 (450.7 to 508.8)	354.7 (332.0 to 379.0)	278.3 (259.2 to 298.8)	
Anti-HPV 58 (n=645, 580, 534)	698.8 (659.0 to 741.1)	501.0 (469.4 to 534.8)	399.3 (373.2 to 427.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage I: Percentage of Participants 9 to 19 Years of Age, 20 to 26 Years of Age, and 27 to 45 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 7

End point title	Stage I: Percentage of Participants 9 to 19 Years of Age, 20 to 26 Years of Age, and 27 to 45 Years of Age Who Are Seropositive by IgG LIA to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58: Month 7

End point description:

The percentage of participants who are seropositive for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 was determined using IgG LIA. Seroconversion was defined as changing serostatus from seronegative at baseline (Day 1) to seropositive at 1 month after last dose. Cutoff values for HPV seropositivity are ≥9, 6, 5, 5, 3, 4, 3, 5 and 5 mMU/mL for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively. Participants who 1) received all vaccinations in the planned regimen, 2) were seronegative at Day 1 for the relevant HPV type in the analysis of HPV types 6 and 11, the participant must be seronegative to both HPV 6 and 11, 3) had a serum sample collected 1 month after last dose within an acceptable day range, and 4) had no other protocol violations that could interfere with the evaluation of participant's immune response to the study vaccine were analyzed.

End point type	Secondary

End point timeframe:

1 month post vaccination 3 (Month 7)

End point values	9 to 19 Years of Age	20 to 26 Years of Age	27 to 45 Years of Age	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	688	650	650	
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 ≥9 mMU/mL (n=640, 567, 517)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	100.0 (99.3 to 100.0)	
Anti-HPV 11 ≥6 mMU/mL (n=640, 567, 517)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	100.0 (99.3 to 100.0)	
Anti-HPV 16 ≥5 mMU/mL (n=662, 595, 575)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	
Anti-HPV 18 ≥5 mMU/mL (n=630, 574, 575)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	
Anti-HPV 31 ≥3 mMU/mL (n=657, 587, 576)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	
Anti-HPV 33 ≥4 mMU/mL (n=642, 589, 569)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	
Anti-HPV 45 ≥3 mMU/mL (n=655, 598, 598)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	
Anti-HPV 52 ≥5 mMU/mL (n=649, 572, 578)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	
Anti-HPV 58 ≥5 mMU/mL (n=645, 580, 534)	100.0 (99.4 to 100.0)	100.0 (99.4 to 100.0)	100.0 (99.3 to 100.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage I: Percentage of Participants Who Experience at Least 1 Solicited Injection-site Adverse Event (AE)

End point title	Stage I: Percentage of Participants Who Experience at Least 1 Solicited Injection-site Adverse Event (AE)

End point description:

An AE is defined as any untoward medical occurrence in a participant which does not necessarily have a causal relationship with study vaccine. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study vaccine or a protocol-specified procedure, whether or not considered related to the study vaccine or protocol-specified procedure. Any worsening of a preexisting condition that is temporally associated with the study vaccine or protocol-specified procedure is also an AE. The participant or the parent/guardian of the participant were to record the presence of any vaccination report card (VRC)-prompted injection-site AEs that occurred in the 8 days after any vaccination. The percentage of participants with an injection-site AE prompted on the VRC (erythema, pain, swelling and induration) is reported. The analysis population consisted of all participants who received at least 1 dose of study vaccination.

End point type	Secondary

End point timeframe:

Up to 8 days post any vaccination (Up to ~Day 192)

End point values	9 to 19 Years of Age	20 to 26 Years of Age	27 to 45 Years of Age	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	688	650	650	
Units: Percentage of Participants				
number (confidence interval 95%)				
Injection site pain	39.1 (35.4 to 42.9)	44.5 (40.6 to 48.4)	39.1 (35.3 to 42.9)	
Injection site erythema	9.3 (7.2 to 11.7)	11.1 (8.8 to 13.7)	7.4 (5.5 to 9.7)	
Injection site swelling	8.1 (6.2 to 10.4)	8.9 (6.8 to 11.4)	5.4 (3.8 to 7.4)	
Injection site induration	6.3 (4.6 to 8.3)	8.0 (6.0 to 10.4)	6.0 (4.3 to 8.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage I: Percentage of Participants Who Experience at Least 1 Systemic AE

End point title	Stage I: Percentage of Participants Who Experience at Least 1 Systemic AE

End point description:

An AE is defined as any untoward medical occurrence in a participant which does not necessarily have a causal relationship with study vaccine. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study vaccine or a protocol-specified procedure, whether or not considered related to the study vaccine or protocol-specified procedure. Any worsening of a preexisting condition that is temporally associated with the study vaccine or protocol-specified procedure is also an AE. The percentage of participants with a systemic AE is reported. The analysis population consisted of all participants who received at least 1 dose of study vaccination.

End point type	Secondary

End point timeframe:

Up to 31 days post any vaccination (Up to ~Month 7)

End point values	9 to 19 Years of Age	20 to 26 Years of Age	27 to 45 Years of Age	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	688	650	650	
Units: Percentage of Participants				
number (confidence interval 95%)	50.9 (47.1 to 54.7)	57.1 (53.2 to 60.9)	43.4 (39.5 to 47.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage I: Percentage of Participants Who Experience at Least 1 Serious Adverse Event (SAE)

End point title	Stage I: Percentage of Participants Who Experience at Least 1 Serious Adverse Event (SAE)

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the study vaccine. An SAE is an AE that results in death, is life threatening, results in a persistent or significant disability or incapacity, results in or prolongs an existing hospitalization, is a congenital anomaly or birth defect, or is another important medical event. The percentage of participants that experienced 1 or more SAEs is reported. The analysis population consisted of all participants who received at least 1 dose of study vaccination.

End point type	Secondary

End point timeframe:

Day 1 to Month 7

End point values	9 to 19 Years of Age	20 to 26 Years of Age	27 to 45 Years of Age	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	688	650	650	
Units: Percentage of Participants				
number (confidence interval 95%)	1.0 (0.4 to 2.1)	2.6 (1.5 to 4.2)	2.6 (1.5 to 4.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage I: Percentage of Participants with Elevated Axillary Temperature (≥37.1 C)

End point title	Stage I: Percentage of Participants with Elevated Axillary Temperature (≥37.1 C)

End point description:

Participant or participant’s legally acceptable representative will be asked to record axillary temperature in the evening after each study vaccination and daily, at the same time of day whenever possible, for 8 days after each study vaccination in the VRC. The percentage of participant’s who had an axillary temperature ≥37.1°C is reported. The analysis population consisted of all participants who received at least 1 dose of study vaccination.

End point type	Secondary

End point timeframe:

Up to 8 days post any vaccination (Up to ~Day 192)

End point values	9 to 19 Years of Age	20 to 26 Years of Age	27 to 45 Years of Age	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	688	650	650	
Units: Percentage of Participants				
number (confidence interval 95%)				
≥37.1°C (98.8°F) and <37.6°C (99.7°F)	20.8 (17.8 to 24.0)	23.8 (20.6 to 27.3)	11.7 (9.3 to 14.4)	
≥37.6°C (99.7°F) and <39.1°C (102.4°F)	2.2 (1.2 to 3.6)	2.0 (1.1 to 3.4)	0.5 (0.1 to 1.3)	
≥39.1°C (102.4°F)	0.3 (0.0 to 1.0)	0.2 (0.0 to 0.9)	0.0 (0.0 to 0.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Stage II: Percentage of Participants 9 to 19 years of Age Who Experience at Least 1 Serious Adverse Event (SAE): Month 7 to Month 60

End point title	Stage II: Percentage of Participants 9 to 19 years of Age Who Experience at Least 1 Serious Adverse Event (SAE): Month 7 to Month 60

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the study vaccine. An SAE is an AE that results in death, is life threatening, results in a persistent or significant disability or incapacity, results in or prolongs an existing hospitalization, is a congenital anomaly or birth defect, or is another important medical event. The percentage of participants that experienced 1 or more SAEs is reported. The analysis population consisted of all participants who received at least 1 dose of study vaccination.

End point type	Secondary

End point timeframe:

Month 7 to Month 60

End point values	9 to 19 Years of Age			
Subject group type	Reporting group			
Number of subjects analysed	682			
Units: Percentage of Participants				
number (not applicable)	1.5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Stage I: Day 1 to Month 7; Stage II: Post Month 7 to Month 60

Adverse event reporting additional description:

The analysis population for deaths (all-causes) included all enrolled participants (N=690, N=650, N=650, N=682). The analysis population for AEs included all enrolled participants who received at least 1 dose of study vaccination.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28.0

Reporting groups

Reporting group title	9 to 19 Years of Age Stage I

Reporting group description:

Chinese females 9 to 19 years of age received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Reporting group title	20 to 26 Years of Age Stage I

Reporting group description:

Chinese females 20 to 26 years of age received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Reporting group title	27 to 45 Years of Age Stage I

Reporting group description:

Chinese females 27 to 45 years of age received a 0.5 mL per dose was administered as an intramuscular injection at Day 1, Month 2, and Month 6.

Reporting group title	9 to 19 Years of Age Stage II

Reporting group description:

Participants in the 9 to 19 years of age group who completed 3 doses of V503 were eligible for Stage II and followed up to Month 60.

Serious adverse events	9 to 19 Years of Age Stage I	20 to 26 Years of Age Stage I	27 to 45 Years of Age Stage I
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 688 (1.31%)	17 / 650 (2.62%)	17 / 650 (2.62%)
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)			
Uterine leiomyoma			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nipple neoplasm			

subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipoma			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	0 / 650 (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
Fibroadenoma of breast			
subjects affected / exposed	1 / 688 (0.15%)	3 / 650 (0.46%)	0 / 650 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Biochemical pregnancy			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Abortion spontaneous			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Abortion missed			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	2 / 650 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ectopic pregnancy			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Cervical dysplasia			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	2 / 650 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abnormal uterine bleeding			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	0 / 650 (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
Ovarian cyst ruptured			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Uterine adhesions			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine diverticulum			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	2 / 650 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Nasal polyps			
subjects affected / exposed	1 / 688 (0.15%)	0 / 650 (0.00%)	0 / 650 (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
Dyspnoea			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Injury, poisoning and procedural complications			
Closed globe injury			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Craniofacial fracture			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Blood and lymphatic system disorders			
Immune thrombocytopenia			

subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	0 / 650 (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
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Embedded tooth			
subjects affected / exposed	1 / 688 (0.15%)	0 / 650 (0.00%)	0 / 650 (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
Enteritis			
subjects affected / exposed	1 / 688 (0.15%)	0 / 650 (0.00%)	0 / 650 (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
Gastritis			
subjects affected / exposed	1 / 688 (0.15%)	0 / 650 (0.00%)	0 / 650 (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
Haemoperitoneum			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammatory bowel disease			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	0 / 650 (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
Tooth impacted			

subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 688 (0.15%)	0 / 650 (0.00%)	0 / 650 (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
Hepatic function abnormal			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	0 / 650 (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
Cholecystitis chronic			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Skin and subcutaneous tissue disorders			
Bromhidrosis			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	0 / 650 (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
Musculoskeletal and connective tissue disorders			
Jaw cyst			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chondropathy			
subjects affected / exposed	1 / 688 (0.15%)	0 / 650 (0.00%)	0 / 650 (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
Infections and infestations			
Appendicitis perforated			

subjects affected / exposed	1 / 688 (0.15%)	0 / 650 (0.00%)	0 / 650 (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
Anal abscess			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Diarrhoea infectious			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Lymphadenitis bacterial			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	0 / 650 (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
Tonsillitis bacterial			
subjects affected / exposed	0 / 688 (0.00%)	0 / 650 (0.00%)	0 / 650 (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 mycoplasmal			
subjects affected / exposed	1 / 688 (0.15%)	0 / 650 (0.00%)	0 / 650 (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
Pneumonia			
subjects affected / exposed	0 / 688 (0.00%)	1 / 650 (0.15%)	1 / 650 (0.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	9 to 19 Years of Age Stage II		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 682 (1.47%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nipple neoplasm			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lipoma			
subjects affected / exposed	1 / 682 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fibroadenoma of breast			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Biochemical pregnancy			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abortion spontaneous			

subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abortion missed				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ectopic pregnancy				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Ovarian cyst				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervical dysplasia				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abnormal uterine bleeding				
subjects affected / exposed	1 / 682 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ovarian cyst ruptured				
subjects affected / exposed	1 / 682 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine adhesions				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine polyp				

subjects affected / exposed	1 / 682 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine diverticulum				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Nasal polyps				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Schizophrenia				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Closed globe injury				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Craniofacial fracture				
subjects affected / exposed	0 / 682 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thoracic vertebral fracture				

subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 682 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Immune thrombocytopenia			
subjects affected / exposed	1 / 682 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Embedded tooth			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemoperitoneum			

subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inflammatory bowel disease			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 682 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tooth impacted			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic function abnormal			
subjects affected / exposed	1 / 682 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis chronic			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Bromhidrosis			
subjects affected / exposed	1 / 682 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue			

disorders			
Jaw cyst			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chondropathy			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis perforated			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea infectious			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphadenitis bacterial			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsillitis bacterial			
subjects affected / exposed	1 / 682 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pneumonia			
subjects affected / exposed	1 / 682 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	9 to 19 Years of Age Stage I	20 to 26 Years of Age Stage I	27 to 45 Years of Age Stage I
Total subjects affected by non-serious adverse events			
subjects affected / exposed	411 / 688 (59.74%)	424 / 650 (65.23%)	346 / 650 (53.23%)
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	64 / 688 (9.30%)	73 / 650 (11.23%)	48 / 650 (7.38%)
occurrences (all)	76	93	61
Injection site induration			
subjects affected / exposed	46 / 688 (6.69%)	58 / 650 (8.92%)	45 / 650 (6.92%)
occurrences (all)	52	68	51
Injection site pain			
subjects affected / exposed	270 / 688 (39.24%)	294 / 650 (45.23%)	259 / 650 (39.85%)
occurrences (all)	411	492	407
Injection site swelling			
subjects affected / exposed	60 / 688 (8.72%)	63 / 650 (9.69%)	38 / 650 (5.85%)
occurrences (all)	69	72	48
Pyrexia			
subjects affected / exposed	172 / 688 (25.00%)	175 / 650 (26.92%)	85 / 650 (13.08%)
occurrences (all)	256	261	117
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	51 / 688 (7.41%)	35 / 650 (5.38%)	27 / 650 (4.15%)
occurrences (all)	57	36	29
Oropharyngeal pain			
subjects affected / exposed	45 / 688 (6.54%)	44 / 650 (6.77%)	22 / 650 (3.38%)
occurrences (all)	53	45	24
Rhinorrhoea			

subjects affected / exposed	42 / 688 (6.10%)	40 / 650 (6.15%)	19 / 650 (2.92%)
occurrences (all)	46	44	19

Non-serious adverse events	9 to 19 Years of Age Stage II		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 682 (0.00%)		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences (all)	0		
Injection site induration			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences (all)	0		
Injection site swelling			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 682 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 May 2020	Amendment 01: Primary reason for amendment was to extend the visit window of Dose 3 vaccination.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported