Clinical trial results:
A Phase 3, Multicenter, Open-Label Study to Evaluate the Safety and Immunogenicity of 2-dose Regimens of 9vHPV and mRNA-1273 SARS-CoV-2 Vaccines Where the First Dose of Each Vaccine Are Given Concomitantly in Boys and Girls 9 to 11 Years of Age

Summary

EudraCT number	2021-003591-13
Trial protocol	Outside EU/EEA
Global end of trial date	25 February 2025

Results information

Result version number	v1 (current)
This version publication date	17 July 2025
First version publication date	17 July 2025

Trial information

Trial identification

Sponsor protocol code	V503-076

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05119855
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	12 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 December 2023
Global end of trial reached?	Yes
Global end of trial date	25 February 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study to evaluate the safety and immunogenicity of a 2-dose regimen of 9-valent Human Papillomavirus (9vHPV) vaccine, where the first dose is administered concomitantly with a first dose of a 2-dose regimen of messenger ribonucleic acid (mRNA)-1273 Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (COVID-19) Vaccine (mRNA-1273) vaccine versus non-concomitant administration of 9vHPV and mRNA-1273 vaccines in boys and girls 9 to 11 years of age.

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	28 March 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 165
Worldwide total number of subjects	165
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)	165
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Healthy children 9 to 11 years of age were enrolled in this study; 165 participants were randomly assigned in a 1:1 ratio to the Concomitant Group and the Non-concomitant Group.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Concomitant Group

Arm description:

Participants received Dose 1 of 9-valent human papillomavirus [Types 6, 11, 16, 18, 31, 33, 45, 52, 58] (9vHPV) vaccine administered into the left arm as an intramuscular (IM) injection, AND Dose 1 of the messenger ribonucleic acid (mRNA)-1273 vaccine administered into the right arm as an IM injection on Day 1; participants then received Dose 2 of the mRNA-1273 vaccine administered into the right arm as an IM injection at Month 1 and Dose 2 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 6.

Arm type	Experimental
Investigational medicinal product name	9vHPV Vaccine
Investigational medicinal product code	
Other name	V503 GARDASIL®9 SILGARD®9
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

9-valent human papillomavirus (Types 6, 11,16, 18, 31, 33, 45, 52, 58) administered as a 0.5-mLintramuscular (IM) injection

Investigational medicinal product name	mRNA-1273 Vaccine
Investigational medicinal product code	
Other name	SARS-CoV-2 Vaccine Moderna COVID-19Vaccine
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

mRNA-1273 50 mcg dose administered as a 0.25-mLIM injection

Arm title	Non-concomitant Group

Arm description:

Participants received Dose 1 of the mRNA-1273 vaccine administered into the right arm as an IM injection on Day 1 and Dose 2 of the mRNA-1273 vaccine administered into the right arm as an IM injection at Month 1. Participants then received Dose 1 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 2 and Dose 2 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 8.

Arm type	Experimental

Investigational medicinal product name	mRNA-1273 Vaccine
Investigational medicinal product code	
Other name	SARS-CoV-2 Vaccine Moderna COVID-19Vaccine
Pharmaceutical forms	Dispersion for injection
Routes of administration	Intramuscular use

Dosage and administration details:

mRNA-1273 50 mcg dose administered as a 0.25-mLIM injection

Investigational medicinal product name	9vHPV Vaccine
Investigational medicinal product code	
Other name	V503 GARDASIL®9 SILGARD®9
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

9-valent human papillomavirus (Types 6, 11,16, 18, 31, 33, 45, 52, 58) administered as a 0.5-mLintramuscular (IM) injection

Number of subjects in period 1	Concomitant Group	Non-concomitant Group
Started	82	83
Vaccinated: mRNA-1273 Dose 1	81	81
Vaccinated: 9vHPV Dose 1	81	72
Vaccinated: mRNA-1273 Dose 2	78	78
Vaccinated: 9vHPV Dose 2	67	66
Concomitant Dose 1 Day 1 9vHPV	81	0 [1]
Concomitant Dose 1 Day 1 mRNA-1273	81	0 [2]
Concomitant Dose 2 Month 1 mRNA-1273	78	0 [3]
Concomitant Dose 2 Month 6 9vHPV	67	0 [4]
Non-concomitant Dose 1 Day 1 mRNA-1273	0 [5]	81
Non-concomitant Dose 2 Month 1 mRNA-1273	0 [6]	78
Non-concomitant Dose 1 Month 2 9vHPV	0 [7]	72
Non-concomitant Dose 2 Month 8 9vHPV	0 [8]	66
Completed	66	64
Not completed	16	19
Withdrawal By Parent/Guardian	10	10
Lost to follow-up	6	8
Randomized by Mistake Without Study Treatment	-	1

Notes:

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

Justification: Per protocol, Non-Concomitant Dose 2 Month 1 mRNA-1273 is not applicable to Concomitant Arm.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Per protocol, Non-Concomitant Dose 1 Month 2 9vHPV is not applicable to Concomitant Arm.
[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Per protocol, Non-Concomitant Dose 2 Month 8 9vHPV is not applicable to Concomitant Arm.
[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Per protocol, Non-Concomitant Dose 1 Day 1 mRNA-1273 is not applicable to Concomitant Arm.
[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Per protocol, Concomitant Dose 1 Day 1 9vHPV is not applicable to Non-Concomitant Arm.
[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Per protocol, Concomitant Dose 1 Day 1 mRNA-1273 is not applicable to Non-Concomitant Arm.
[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Per protocol, Concomitant Dose 2 Month 1 mRNA-1273 is not applicable to Non-Concomitant Arm.
[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Per protocol, Concomitant Dose 2 Month 6 9vHPV is not applicable to Non-Concomitant Arm.

Baseline characteristics

Reporting groups	
Reporting group title	Concomitant Group
Reporting group description:	
Participants received Dose 1 of 9-valent human papillomavirus [Types 6, 11, 16, 18, 31, 33, 45, 52, 58] (9vHPV) vaccine administered into the left arm as an intramuscular (IM) injection, AND Dose 1 of the messenger ribonucleic acid (mRNA)-1273 vaccine administered into the right arm as an IM injection on Day 1; participants then received Dose 2 of the mRNA-1273 vaccine administered into the right arm as an IM injection at Month 1 and Dose 2 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 6.	
Reporting group title	Non-concomitant Group
Reporting group description:	
Participants received Dose 1 of the mRNA-1273 vaccine administered into the right arm as an IM injection on Day 1 and Dose 2 of the mRNA-1273 vaccine administered into the right arm as an IM injection at Month 1. Participants then received Dose 1 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 2 and Dose 2 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 8.	

Reporting group values	Concomitant Group	Non-concomitant Group	Total
Number of subjects	82	83	165
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)	82	83	165
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	9.9	9.9	
standard deviation	± 0.9	± 0.8	-
Sex: Female, Male Units: Participants			
Female	43	45	88
Male	39	38	77
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	28	31	59
White	53	48	101
More than one race	0	2	2
Unknown or Not Reported	0	2	2

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	50	46	96
Not Hispanic or Latino	32	37	69
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Concomitant Group
Reporting group description:	
Participants received Dose 1 of 9-valent human papillomavirus [Types 6, 11, 16, 18, 31, 33, 45, 52, 58] (9vHPV) vaccine administered into the left arm as an intramuscular (IM) injection, AND Dose 1 of the messenger ribonucleic acid (mRNA)-1273 vaccine administered into the right arm as an IM injection on Day 1; participants then received Dose 2 of the mRNA-1273 vaccine administered into the right arm as an IM injection at Month 1 and Dose 2 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 6.	
Reporting group title	Non-concomitant Group
Reporting group description:	
Participants received Dose 1 of the mRNA-1273 vaccine administered into the right arm as an IM injection on Day 1 and Dose 2 of the mRNA-1273 vaccine administered into the right arm as an IM injection at Month 1. Participants then received Dose 1 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 2 and Dose 2 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 8.	

Primary: Geometric Mean Titers of Anti-Human Papillomavirus Vaccine Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 (9vHPV)

End point title	Geometric Mean Titers of Anti-Human Papillomavirus Vaccine Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 (9vHPV)
End point description:	
Antibodies to HPV types 6/11/16/18/31/33/45/52/58 were measured using a competitive Luminex immunoassay (cLIA). Per protocol, antibody titers were expressed as milli Merck units/milliliter (mMU/mL). Geometric Mean Titers (GMTs) are reported for both arms for all randomized participants included in the per-protocol immunogenicity (PPI) population. The PPI population is HPV-type specific. HPV-type specific PPI population included all randomized participants who; were seronegative pre 9vHPV vaccination to the relevant HPV type(s); had all protocol planned 9vHPV vaccinations; had evaluable serology results post 9vHPV Dose 2 vaccination; no protocol deviations that may affect evaluation of participant's immune response to 9vHPV vaccination. The number of subjects analyzed is the total number of participants for inclusion in any HPV type specific PPI.	
End point type	Primary
End point timeframe:	
Up to approximately 4 weeks post vaccination with 9vHPV Dose 2	

End point values	Concomitant Group	Non-concomitant Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51[1]	49[2]		
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=47, 46)	2198.5 (1806.9 to 2674.8)	1806.8 (1481.8 to 2202.9)		
Anti-HPV 11 (n=46, 49)	1517.6 (1247.5 to 1846.2)	1138.2 (941.4 to 1376.2)		

Anti-HPV 16 (n=47, 46)	9595.8 (7822.5 to 11771.0)	7042.3 (5728.2 to 8657.7)		
Anti-HPV 18 (n=48, 46)	2139.2 (1721.3 to 2658.6)	1713.2 (1372.1 to 2139.1)		
Anti-HPV 31 (n=46, 47)	1695.6 (1383.9 to 2077.3)	1404.7 (1149.0 to 1717.2)		
Anti-HPV 33 (n=48, 47)	1172.3 (950.8 to 1445.5)	889.9 (720.2 to 1099.6)		
Anti-HPV 45 (n=50, 47)	518.0 (413.0 to 649.6)	370.8 (293.6 to 468.4)		
Anti-HPV 52 (n=49, 48)	733.6 (614.4 to 875.9)	504.7 (421.9 to 603.7)		
Anti-HPV 58 (n= 48, 48)	1095.2 (900.5 to 1332.1)	912.6 (750.3 to 1110.0)		

Notes:

[1] - Number of subjects analyzed is number of participants included in any HPV type specific PPI.

[2] - Number of subjects analyzed is number of participants included in any HPV type specific PPI.

Statistical analyses

Statistical analysis title	GMT Ratio for Anti-HPV 11

Statistical analysis description:

Geometric Mean Titer (GMT) Ratio with corresponding 2-sided 95% confidence interval (CI) was calculated using an analysis of variance model (ANOVA) with a response of log individual anti-HPV titers and a fixed effect for the vaccination groups, Concomitant versus Non-Concomitant. Number of subjects analyzed is type-specific PPI; HPV type n-value denotes PPI population with GMT data available: Anti-HPV 11 Concomitant Group n=46; Anti-HPV 11 Non-concomitant Group n=49.

Comparison groups	Concomitant Group v Non-concomitant Group
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Titer (GMT) Ratio
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.75

Statistical analysis title	GMT Ratio for Anti-HPV 6

Statistical analysis description:

Geometric Mean Titer (GMT) Ratio with corresponding 2-sided 95% confidence interval (CI) was calculated using an analysis of variance model (ANOVA) with a response of log individual anti-HPV titers and a fixed effect for the vaccination groups, Concomitant versus Non-Concomitant. Number of subjects analyzed is type-specific PPI; HPV type n-value denotes PPI population with GMT data available: Anti-HPV 6 Concomitant Group n=47; Anti-HPV 6 Non-concomitant Group n=46.

Comparison groups	Concomitant Group v Non-concomitant Group

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Titer (GMT) Ratio
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.61

Statistical analysis title	GMT Ratio for Anti-HPV 58

Statistical analysis description:

Geometric Mean Titer (GMT) Ratio with corresponding 2-sided 95% confidence interval (CI) was calculated using an analysis of variance model (ANOVA) with a response of log individual anti-HPV titers and a fixed effect for the vaccination groups, Concomitant versus Non-Concomitant. Number of subjects analyzed is type-specific PPI; HPV type n-value denotes PPI population with GMT data available: Anti-HPV 58 Concomitant Group n=48; Anti-HPV 58 Non-concomitant Group n=48.

Comparison groups	Concomitant Group v Non-concomitant Group
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Titer (GMT) Ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.58

Statistical analysis title	GMT Ratio for Anti-HPV 33

Statistical analysis description:

Geometric Mean Titer (GMT) Ratio with corresponding 2-sided 95% confidence interval (CI) was calculated using an analysis of variance model (ANOVA) with a response of log individual anti-HPV titers and a fixed effect for the vaccination groups, Concomitant versus Non-Concomitant. Number of subjects analyzed is type-specific PPI; HPV type n-value denotes PPI population with GMT data available: Anti-HPV 33 Concomitant Group n=48; Anti-HPV 33 Non-concomitant Group n=47.

Comparison groups	Concomitant Group v Non-concomitant Group
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Titer (GMT) Ratio
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.77

Statistical analysis title	GMT Ratio Anti-HPV 45

Statistical analysis description:

Geometric Mean Titer (GMT) Ratio with corresponding 2-sided 95% confidence interval (CI) was calculated using an analysis of variance model (ANOVA) with a response of log individual anti-HPV titers and a fixed effect for the vaccination groups, Concomitant versus Non-Concomitant. Number of subjects analyzed is type-specific PPI; HPV type n-value denotes PPI population with GMT data available: Anti-HPV 45 Concomitant Group n=50; Anti-HPV 45 Non-concomitant Group n=47.

Comparison groups	Concomitant Group v Non-concomitant Group
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Titer (GMT) Ratio
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.93

Statistical analysis title	GMT Ratio for Anti-HPV 52

Statistical analysis description:

Geometric Mean Titer (GMT) Ratio with corresponding 2-sided 95% confidence interval (CI) was calculated using an analysis of variance model (ANOVA) with a response of log individual anti-HPV titers and a fixed effect for the vaccination groups, Concomitant versus Non-Concomitant. Number of subjects analyzed is type-specific PPI; HPV type n-value denotes PPI population with GMT data available: Anti-HPV 52 Concomitant Group n=49; Anti-HPV 52 Non-concomitant Group n=48.

Comparison groups	Concomitant Group v Non-concomitant Group
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Titer (GMT) Ratio
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	1.87

Statistical analysis title	GMT Ratio for Anti-HPV 18

Statistical analysis description:

Geometric Mean Titer (GMT) Ratio with corresponding 2-sided 95% confidence interval (CI) was calculated using an analysis of variance model (ANOVA) with a response of log individual anti-HPV titers and a fixed effect for the vaccination groups, Concomitant versus Non-Concomitant. Number of subjects analyzed is type-specific PPI; HPV type n-value denotes PPI population with data available: Anti-HPV 18 Concomitant Group n=48; Anti-HPV 18 Non-concomitant Group n=46.

Comparison groups	Concomitant Group v Non-concomitant Group

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Titer (GMT) Ratio
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.7

Statistical analysis title	GMT Ratio for Anti-HPV 16

Statistical analysis description:

Geometric Mean Titer (GMT) Ratio with corresponding 2-sided 95% confidence interval (CI) was calculated using an analysis of variance model (ANOVA) with a response of log individual anti-HPV titers and a fixed effect for the vaccination groups, Concomitant versus Non-Concomitant. Number of subjects analyzed is type-specific PPI; HPV type n-value denotes PPI population with GMT data available: Anti-HPV 16 Concomitant Group n=47; Anti-HPV 16 Non-concomitant Group n=46.

Comparison groups	Concomitant Group v Non-concomitant Group
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Titer (GMT) Ratio
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.82

Statistical analysis title	GMT Ratio for Ant-HPV 31

Statistical analysis description:

Geometric Mean Titer (GMT) Ratio with corresponding 2-sided 95% confidence interval (CI) was calculated using an analysis of variance model (ANOVA) with a response of log individual anti-HPV titers and a fixed effect for the vaccination groups, Concomitant versus Non-Concomitant. Number of subjects analyzed is type-specific PPI; HPV type n-value denotes PPI population with GMT data available: Anti-HPV 31 Concomitant Group n=46; Anti-HPV 31 Non-concomitant Group n=47.

Comparison groups	Concomitant Group v Non-concomitant Group
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Titer (GMT) Ratio
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.61

Primary: Percentage of Participants with ≥1 Solicited Injection-site Adverse Event (AE)

End point title	Percentage of Participants with ≥1 Solicited Injection-site Adverse Event (AE)[3]

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to study intervention. Solicited AEs are predefined AEs at injection site. Participants used vaccination report card (VRC) to note injection site AEs based on questions asked. Per protocol, percentage of participants with ≥1 solicited injection site AE is reported by injection site for participants in Concomitant (Day 1 mRNA-1273 [right arm] Dose 1; Day 1 9vHPV [left arm] Dose 1; Month 1 mRNA-1273 Dose 2; Month 6 9vHPV Dose 2) and Non-Concomitant (Day 1 mRNA-1273 Dose 1; Month 1 mRNA-1273 Dose 2; Month 2 9vHPV Dose 1; Month 8 9vHPV Dose 2). Per protocol, reporting by injection site for Concomitant Day 1 Dose 1 is specific to this safety endpoint. Per protocol, safety analyses population included all randomized participants who had ≥1 dose of any study vaccine and included by study vaccine given. 9999 indicates data not available.

End point type	Primary

End point timeframe:

Up to approximately Day 7 post vaccination with any study vaccine

Notes:

[3] - 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: Per protocol, only descriptive statistics were planned and are presented for this endpoint.

End point values	Concomitant Group	Non-concomitant Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81[4]	81[5]		
Units: Percentage of Participants				
number (not applicable)				
Concomitant Day 1 mRNA-1273 Dose 1 (n=81,0)	49.4	9999		
Concomitant Day 1 9vHPV Dose 1 (n=81,0)	39.5	9999		
Concomitant Month 1 mRNA-1273 Dose 2 (n=78,0)	35.9	9999		
Concomitant Month 6 9vHPV Dose 2 (n=67,0)	26.9	9999		
Non-concomitant Day 1 mRNA-1273 Dose 1 (n=0,81)	9999	55.6		
Non-concomitant Month 1 mRNA-1273 Dose 2 (n=0,78)	9999	44.9		
Non-Concomitant Month 2 9vHPV Dose 1 (n=0,72)	9999	29.2		
Non-concomitant Month 8 9vHPV Dose 2 (n=0,66)	9999	43.9		

Notes:

[4] - Number of subjects analyzed is safety analyses population.

[5] - Number of subjects analyzed is safety analyses population.

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations of SARS-CoV-2 Spike Protein-Specific

Binding Antibodies

End point title	Geometric Mean Concentrations of SARS-CoV-2 Spike Protein-Specific Binding Antibodies

End point description:

The geometric mean concentration (GMC) of serum-derived antibodies to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spike protein was determined using an electrochemiluminescence (ECL) assay. GMCs are reported for both arms for all randomized participants included in the mRNA-1273 per-protocol (mRNA-1273-PP) population. The analysis mRNA-1273-PP population included all randomized participants who; had all protocol planned mRNA-1273 vaccinations; had evaluable serology results post mRNA-1273 Dose 2 vaccination; no protocol deviations that may affect evaluation of participant's immune response to mRNA-1273 vaccination.

End point type	Primary

End point timeframe:

Up to approximately 4 weeks post vaccination with mRNA-1273 Dose 2

End point values	Concomitant Group	Non-concomitant Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56[6]	60[7]		
Units: µg/mL				
geometric mean (confidence interval 95%)	763084.3 (673224.4 to 864938.4)	650527.9 (576365.9 to 734232.5)		

Notes:

[6] - Number of subjects analyzed is mRNA-1273-PP population.

[7] - Number of subjects analyzed is mRNA-1273-PP population.

Statistical analyses

Statistical analysis title	GMC Ratio of SARS-CoV-2 Spike Protein

Statistical analysis description:

Geometric Mean Concentration (GMC) Ratio with corresponding 2-sided 95% confidence interval (CI) was calculated using an analysis of variance model (ANOVA) with a response of log individual anti-SARS-CoV-2 concentrations and a fixed effect for the vaccination groups, Concomitant versus Non-Concomitant.

Comparison groups	Concomitant Group v Non-concomitant Group
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Concentration (GMC) Ratio
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.4

Primary: Percentage of Participants with ≥1 Solicited Systemic AE

End point title	Percentage of Participants with ≥1 Solicited Systemic AE[8]

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to study intervention. Solicited AEs are predefined systemic events. Participants used VRC to note solicited AEs based on questions asked. Per protocol the percentage of participants who experienced ≥1 solicited systemic AE are reported for participants in Concomitant (Day 1 mRNA-1273 [right arm] Dose 1; Day 1 9vHPV [left arm] Dose 1; Month 1 mRNA-1273 Dose 2; Month 6 9vHPV Dose 2) and Non-Concomitant (Day 1 mRNA-1273 Dose 1; Month 1 mRNA-1273 Dose 2; Month 2 9vHPV Dose 1; Month 8 9vHPV Dose 2) Groups. Per protocol, reporting based on injection time; 9vHPV and mRNA-1273 Dose 1 were both given on Day 1 of the Concomitant Group and are combined below. Per protocol, safety analyses population included all randomized participants who had ≥1 dose of any study vaccine and included by study vaccine given. 9999 indicates data not available.

End point type	Primary

End point timeframe:

Up to approximately Day 7 post vaccination with any study vaccine

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics were planned and are presented for this endpoint.

End point values	Concomitant Group	Non-concomitant Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81[9]	81[10]		
Units: Percentage of Participants				
number (not applicable)				
Concomitant Day 1 mRNA-1273+9vHPV Dose 1 (n=81,0)	33.3	9999		
Concomitant Month 1 mRNA-1273 Dose 2 (n=78,0)	33.3	9999		
Concomitant Month 6 9vHPV Dose 2 (n=67,0)	17.9	9999		
Non-concomitant Day 1 mRNA-1273 Dose 1 (n=0,81)	9999	55.6		
Non-concomitant Month 1 mRNA-1273 Dose 2 (n=0,78)	9999	44.9		
Non-Concomitant Month 2 9vHPV Dose 1 (n=0,72)	9999	29.2		
Non-concomitant Month 8 9vHPV Dose 2 (n=0,66)	9999	43.9		

Notes:

[9] - Number of subjects analyzed is safety analyses population.

[10] - Number of subjects analyzed is safety analyses population.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with ≥1 Serious Adverse Event (SAE)

End point title	Percentage of Participants with ≥1 Serious Adverse Event (SAE)[11]

End point description:

A SAE was defined as; one that results in death, is life threatening, requires hospitalization/prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or other important medical event that may require medical intervention. Per protocol the percentage of participants who experienced ≥1 SAE are reported here for participants in Concomitant (Day 1 mRNA-1273 [right arm] Dose 1; Day 1 9vHPV [left arm] Dose 1; Month 1 mRNA-1273 Dose 2; Month 6 9vHPV Dose 2) and Non-Concomitant (Day 1 mRNA-1273 Dose 1; Month 1 mRNA-1273 Dose 2; Month 2 9vHPV Dose 1; Month 8 9vHPV Dose 2) Groups. Per protocol, reporting is

based on injection time; 9vHPV and mRNA-1273 Dose 1 were given on Day 1 of the Concomitant Group and are combined below. Per protocol, safety analyses population included all randomized participants who had ≥1 dose of any study vaccine and included by study vaccine given. 9999 indicates data not available.

End point type	Primary

End point timeframe:

Up to approximately Day 28 post vaccination with any study vaccine

Notes:

[11] - 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: Per protocol, only descriptive statistics were planned and are presented for this endpoint.

End point values	Concomitant Group	Non-concomitant Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81[12]	81[13]		
Units: Percentage of Participants				
number (not applicable)				
Concomitant Day 1 mRNA-1273+9vHPV Dose 1 (n=81,0)	0.0	9999		
Concomitant Month 1 mRNA-1273 Dose 2 (n=78,0)	0.0	9999		
Concomitant Month 6 9vHPV Dose 2 (n=67,0)	0.0	9999		
Non-concomitant Day 1 mRNA-1273 Dose 1 (n=0,81)	9999	0.0		
Non-concomitant Month 1 mRNA-1273 Dose 2 (n=0,78)	9999	0.0		
Non-Concomitant Month 2 9vHPV Dose 1 (n=0,72)	9999	0.0		
Non-concomitant Month 8 9vHPV Dose 2 (n=0,66)	9999	0.0		

Notes:

[12] - Number of subjects analyzed is safety analyses population.

[13] - Number of subjects analyzed is safety analyses population.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with ≥1 Vaccine-Related SAE

End point title	Percentage of Participants with ≥1 Vaccine-Related SAE[14]

End point description:

A vaccine related SAE defined as; results in death, is life threatening, requires hospitalization/prolongation of existing hospitalization, results in persistent/significant disability/incapacity, congenital anomaly/birth defect, or event that may require medical intervention; AND related to study vaccine as judged by investigator. Percentage of participants with ≥1 vaccine related SAE are reported here for participants in Concomitant (Day 1 mRNA-1273 [right arm] Dose 1; Day 1 9vHPV [left arm] Dose 1; Month 1 mRNA-1273 Dose 2; Month 6 9vHPV Dose 2) and Non-Concomitant (Day 1 mRNA-1273 Dose 1; Month 1 mRNA-1273 Dose 2; Month 2 9vHPV Dose 1; Month 8 9vHPV Dose 2) Group. Per protocol, reporting is based on injection time; 9vHPV and mRNA-1273 Dose 1 given on Day 1 of Concomitant Group are combined below. Per protocol, safety analyses population included all randomized participants who had ≥1 dose of any study vaccine and included by study vaccine given. 9999 indicates data not available.

End point type	Primary

End point timeframe:

Up to approximately 9 Months

Notes:

[14] - 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: Per protocol, only descriptive statistics were planned and are presented for this endpoint.

End point values	Concomitant Group	Non-concomitant Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81[15]	81[16]		
Units: Percentage of Participants				
number (not applicable)				
Concomitant Day 1 mRNA-1273+9vHPV Dose 1 (n=81,0)	0.0	9999		
Concomitant Month 1 mRNA-1273 Dose 2 (n=78,0)	0.0	9999		
Concomitant Month 6 9vHPV Dose 2 (n=67,0)	0.0	9999		
Non-concomitant Day 1 mRNA-1273 Dose 1 (n=0,81)	9999	0.0		
Non-concomitant Month 1 mRNA-1273 Dose 2 (n=0,78)	9999	0.0		
Non-Concomitant Month 2 9vHPV Dose 1 (n=0,72)	9999	0.0		
Non-concomitant Month 8 9vHPV Dose 2 (n=0,66)	9999	0.0		

Notes:

[15] - Number of subjects analyzed is safety analyses population.

[16] - Number of subjects analyzed is safety analyses population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Seroconvert to Each of the 9vHPV Vaccine Types 6, 11, 16, 18, 31, 33, 45, 52 and 58 Following Administration of a 2-Dose Regimen of 9vHPV Vaccine

End point title	Percentage of Participants Who Seroconvert to Each of the 9vHPV Vaccine Types 6, 11, 16, 18, 31, 33, 45, 52 and 58 Following Administration of a 2-Dose Regimen of 9vHPV Vaccine

End point description:

Serum derived antibodies to HPV types 6, 11, 16, 18, 31, 33, 45, 52, 58 measured with cLIA. Seroconversion defined as shift from anti HPV seronegative at pre vaccination to seropositive 4 weeks post 9vHPV Dose 2. Anti HPV titers ≥serostatus cutoffs were seropositive per HPV type. Serostatus cutoffs milli Merck units/milliliter (mMU/mL) per HPV Type: Type 6: ≥34, Type 11: ≥25, Type 16: ≥32, Type 18: ≥26, Type 31: ≥15, Type 33: ≥10, Type 45: ≥10, Type 52: ≥14, Type 58: ≥10. Percentage of participants who seroconverted are reported for both arms included in the PPI population. PPI is HPV-specific and included all randomized participants who; seronegative by HPV-9 cLIA to HPV type pre 9vHPV vaccination; had all protocol planned 9vHPV vaccines; evaluable serology results collected post 9vHPV Dose 2; no protocol deviations may alter evaluation of participant's immune response to 9vHPV. Number of subjects analyzed is total number of participants included in any HPV type specific PPI.

End point type	Secondary

End point timeframe:

Up to approximately 4 weeks post vaccination with 9vHPV Dose 2

End point values	Concomitant Group	Non-concomitant Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51[17]	49[18]		
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 cLIA ≥34 mMU/mL (n=47, 46)	100.0 (92.5 to 100.0)	100.0 (92.3 to 100)		
Anti-HPV 11 cLIA ≥25 mMU/mL (n=46, 49)	100.0 (92.3 to 100.0)	100.0 (92.7 to 100.0)		
Anti-HPV 16 cLIA ≥32 mMU/mL (n=47, 46)	100.0 (92.5 to 100.0)	100.0 (92.3 to 100.0)		
Anti-HPV 18 cLIA ≥26 mMU/mL (n=48, 46)	100.0 (92.6 to 100.0)	100.0 (92.3 to 100.0)		
Anti-HPV 31 cLIA ≥15 mMU/mL (n=46, 47)	100.0 (92.3 to 100.0)	100.0 (92.5 to 100.0)		
Anti-HPV 33 cLIA ≥10 mMU/mL (n=48, 47)	100.0 (92.6 to 100.0)	100.0 (92.5 to 100.0)		
Anti-HPV 45 cLIA ≥10 mMU/mL (n=50, 47)	100.0 (92.9 to 100.0)	100.0 (92.5 to 100.0)		
Anti-HPV 52 cLIA ≥14 mMU/mL (n=49, 48)	100.0 (92.7 to 100.0)	100.0 (92.6 to 100.0)		
Anti-HPV 58 cLIA ≥10 mMU/mL (n=48, 48)	100.0 (92.6 to 100.0)	100.0 (92.6 to 100.0)		

Notes:

[17] - Number of subjects analyzed is number of participants included in any HPV type specific PPI.

[18] - Number of subjects analyzed is number of participants included in any HPV type specific PPI.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experience Seroresponse Following Administration of a 2-Dose Regimen of mRNA-1273 Vaccine

End point title	Percentage of Participants Who Experience Seroresponse Following Administration of a 2-Dose Regimen of mRNA-1273 Vaccine

End point description:

Serum derived antibodies to SARS-CoV-2 spike protein measured with ECL. Seroresponse is defined as a ≥4-fold rise in SARS-CoV-2 spike protein-specific binding antibody concentration from baseline to 4 weeks post vaccination with mRNA-1273 Dose 2. Percentage of participants who experience seroresponse is reported for both Concomitant Group and Non-concomitant Groups for all randomized participants included in the mRNA-1273 mRNA-1273-PP. The mRNA-1273-PP population included all randomized participants who; had all protocol planned mRNA-1273 vaccinations; had evaluable serology results from samples collected post mRNA-1273 Dose 2 vaccination; no protocol deviations that may affect evaluation of participant's immune response to mRNA-1273 vaccination.

End point type	Secondary

End point timeframe:

Up to approximately 4 weeks post vaccination with mRNA-1273 Dose 2

End point values	Concomitant Group	Non-concomitant Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56[19]	60[20]		
Units: Percentage of Participants				
number (confidence interval 95%)	96.4 (87.7 to 99.6)	95.0 (86.1 to 99.0)		

Notes:

[19] - Number of subjects analyzed is mRNA-1273-PP population.

[20] - Number of subjects analyzed is mRNA-1273-PP population.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 9 Months

Adverse event reporting additional description:

All-Cause Mortality included all randomized participants. The safety analysis population (total subjects exposed) included all randomized participants who were vaccinated with at least 1 dose of any study vaccine; participants were included to the treatment group according to the vaccination they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Non-concomitant Group

Reporting group description:

Participants received Dose 1 of the mRNA-1273 vaccine administered into the right arm as an IM injection on Day 1 and Dose 2 of the mRNA-1273 vaccine administered into the right arm as an IM injection at Month 1. Participants then received Dose 1 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 2 and Dose 2 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 8.

Reporting group title	Concomitant Group

Reporting group description:

Participants received Dose 1 of 9-valent human papillomavirus [Types 6, 11, 16, 18, 31, 33, 45, 52, 58] (9vHPV) vaccine administered into the left arm as an intramuscular (IM) injection, AND Dose 1 of the messenger ribonucleic acid (mRNA)-1273 vaccine administered into the right arm as an IM injection on Day 1; participants then received Dose 2 of the mRNA-1273 vaccine administered into the right arm as an IM injection at Month 1 and Dose 2 of the 9vHPV vaccine administered into the left arm as an IM injection at Month 6.

Serious adverse events	Non-concomitant Group	Concomitant Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 81 (0.00%)	0 / 81 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Non-concomitant Group	Concomitant Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	59 / 81 (72.84%)	55 / 81 (67.90%)	
Nervous system disorders			

Headache			
subjects affected / exposed	30 / 81 (37.04%)	26 / 81 (32.10%)	
occurrences (all)	46	33	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	20 / 81 (24.69%)	6 / 81 (7.41%)	
occurrences (all)	25	6	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	11 / 81 (13.58%)	13 / 81 (16.05%)	
occurrences (all)	11	16	
Fatigue			
subjects affected / exposed	23 / 81 (28.40%)	23 / 81 (28.40%)	
occurrences (all)	38	32	
Injection site erythema			
subjects affected / exposed	12 / 81 (14.81%)	6 / 81 (7.41%)	
occurrences (all)	18	7	
Injection site pain			
subjects affected / exposed	52 / 81 (64.20%)	46 / 81 (56.79%)	
occurrences (all)	122	113	
Pyrexia			
subjects affected / exposed	10 / 81 (12.35%)	11 / 81 (13.58%)	
occurrences (all)	14	15	
Injection site swelling			
subjects affected / exposed	18 / 81 (22.22%)	14 / 81 (17.28%)	
occurrences (all)	27	22	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 81 (6.17%)	9 / 81 (11.11%)	
occurrences (all)	7	10	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	16 / 81 (19.75%)	9 / 81 (11.11%)	
occurrences (all)	19	12	
Arthralgia			

subjects affected / exposed occurrences (all)	10 / 81 (12.35%) 11	7 / 81 (8.64%) 7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 January 2022	Amendment 01: The primary reasons for this amendment are to change the age range for study participants to 9 to 11 years of age and to change the dose (volume) of the mRNA-1273 vaccine to 50 µg (0.25 mL) to reflect emerging clinical data for the mRNA-1273 vaccine.
28 July 2022	Amendment 02: The primary reason for this amendment is to allow enrollment of participants with SARS-CoV-2 infection >90 days prior to enrollment.
24 February 2023	Amendment 03: The primary purpose of this amendment is to change from a hypothesis testing study to an estimation study design due to early closure of enrollment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported