Clinical trial results:
A Phase 3, randomized, placebo-controlled clinical study to evaluate the efficacy, immunogenicity and safety of the 9vHPV vaccine in Japanese males, 16 to 26 years of age.

Summary

EudraCT number	2020-001047-67
Trial protocol	Outside EU/EEA
Global end of trial date	23 July 2025

Results information

Result version number	v1 (current)
This version publication date	22 January 2026
First version publication date	22 January 2026

Trial information

Trial identification

Sponsor protocol code	V503-064

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04635423
WHO universal trial number (UTN)	-
Other trial identifiers	jRCT: jRCT2031200217

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	23 July 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2023
Global end of trial reached?	Yes
Global end of trial date	23 July 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purposes of this study are to evaluate the efficacy of V503 (9-valent human papillomavirus [9vHPV] vaccine) in preventing human papillomavirus (HPV)-related anogenital persistent infection, and to evaluate the safety/tolerability of V503, in Japanese males who are 16 to 26 years of age. It is hypothesized that administration of a 3-dose regimen of V503 reduces the combined incidence of HPV 6/11/16/18-related anogenital persistent infection, as well as the combined incidence of HPV31/33/45/52/58-related anogenital persistent infection, compared with placebo. The study includes a Base Study to assess efficacy and safety of V503, and an Extension Study.

Participants in the placebo arm of the Base Study will be eligible to receive V503 on Day 1, Month 2, and Month 6 of the Extension Study. Participants in the V503 arm of the Base Study who received less than 3 doses of V503 in the Base Study will be offered the opportunity to complete the 3-dose regimen in the Extension Study.

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	30 November 2020
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	Japan: 1059
Worldwide total number of subjects	1059
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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	7
Adults (18-64 years)	1052
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were equally randomized to V503 and placebo in the base study to evaluate efficacy, immunogenicity, and safety outcome measures. After the end of the base study, eligible participants could be enrolled in the optional open label study extension.

Pre-assignment

Screening details:

A total of 1059 participants who met the eligibility criteria were randomized in the base study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	V503

Arm description:

In the base study, participants received an intramuscular (IM) injection of V503 at Day 1, Month 2, and Month 6.

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

Dosage and administration details:

9-valent vaccine, HPV6/11/16/18/31/33/45/52/58, L1 virus-like particle (VLP) 30/40/60/40/20/20/20/20/20mcg per dose.

Arm title	Placebo

Arm description:

In the base study, participants received an IM injection of placebo at Day 1, Month 2, and Month 6.

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

Dosage and administration details:

0.9% sodium chloride (NaCL)

Number of subjects in period 1	V503	Placebo
Started	529	530
Vaccination 1: Day 1	529	530
Vaccination 2: Month 2	523	518
Vaccination 3: Month 6	514	508
Completed	464	472
Not completed	65	58
Consent withdrawn by subject	57	42
Lost to follow-up	8	16

Period 2

Period 2 title	Extension Study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	V503 Open Label V503 Extension Study

Arm description:

Participants from the V503 arm of the base study who did not complete the 3-dose series received 1 or 2 doses of V503, on Day 1, or Day 1 and Month 4 of the open label extension study.

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

Dosage and administration details:

9-valent vaccine, HPV6/11/16/18/31/33/45/52/58, L1 virus-like particle (VLP) 30/40/60/40/20/20/20/20/20mcg per dose.

Arm title	Placebo Open Label V503 Extension Study

Arm description:

Participants from the placebo arm of the base study who did not complete the 3-dose series received 3 doses of V503 on Day 1, Month 2 and Month 6 of the open label extension study.

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

Dosage and administration details:

9-valent vaccine, HPV6/11/16/18/31/33/45/52/58, L1 virus-like particle (VLP) 30/40/60/40/20/20/20/20/20mcg per dose.

Number of subjects in period 2[1]	V503 Open Label V503 Extension Study	Placebo Open Label V503 Extension Study
Started	2	381
Completed	2	367
Not completed	0	14
Physician decision	-	1
Consent withdrawn by subject	-	10
Lost to follow-up	-	3

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: Not all base study participants were enrolled in the extension study because participation in the extension study was optional and participants had to meet certain eligibility criteria.

Baseline characteristics

Reporting groups	
Reporting group title	V503
Reporting group description:	
In the base study, participants received an intramuscular (IM) injection of V503 at Day 1, Month 2, and Month 6.	
Reporting group title	Placebo
Reporting group description:	
In the base study, participants received an IM injection of placebo at Day 1, Month 2, and Month 6.	

Reporting group values	V503	Placebo	Total
Number of subjects	529	530	1059
Age categorical			
Units: Subjects			
Age Continuous			
Units: Years			
arithmetic mean	22.9	22.8	
standard deviation	± 2.1	± 2.1	-
Sex: Female, Male			
Units: Participants			
Female	0	0	0
Male	529	530	1059
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	529	530	1059
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	529	530	1059
Unknown or Not Reported	0	0	0
Sexual Orientation Participant Subgroups			
Participant randomization was stratified by sexual orientation heterosexual males (HM) or males who have sex with males (MSM). For HM, participants must be a heterosexual male, who has had exclusively female sexual partners, and has 1 to 5 lifetime female sexual partners at the time of enrollment. For MSM, participants must identify themselves as a male who has sex with males, must have engaged in either anal intercourse or oral sex with another male sexual partner within the last year, and have 0 to 5 lifetime male and/or female sexual partners at the time of enrollment.			
Units: Subjects			
Heterosexual Males (HM)	473	474	947
Males Who Have Sex With Males (MSM)	56	56	112

End points

End points reporting groups

Reporting group title	V503
Reporting group description:	
In the base study, participants received an intramuscular (IM) injection of V503 at Day 1, Month 2, and Month 6.	
Reporting group title	Placebo
Reporting group description:	
In the base study, participants received an IM injection of placebo at Day 1, Month 2, and Month 6.	
Reporting group title	V503 Open Label V503 Extension Study
Reporting group description:	
Participants from the V503 arm of the base study who did not complete the 3-dose series received 1 or 2 doses of V503, on Day 1, or Day 1 and Month 4 of the open label extension study.	
Reporting group title	Placebo Open Label V503 Extension Study
Reporting group description:	
Participants from the placebo arm of the base study who did not complete the 3-dose series received 3 doses of V503 on Day 1, Month 2 and Month 6 of the open label extension study.	

Primary: Combined incidence of HPV 6/11/16/18-related anogenital persistent infection

End point title	Combined incidence of HPV 6/11/16/18-related anogenital persistent infection
End point description:	
HPV6/11/16/18-related anogenital persistent infection was defined as polymerase chain reaction (PCR) positivity to at least 1 relevant HPV type in anogenital or biopsy samples from at least 2 consecutive visits 6 months (±1 month visit) or longer apart, or pathology diagnosis of condyloma or penile/perineal/perianal lesions together with PCR detection of at least 1 HPV type in an adjacent section and PCR detection for same HPV type in anogenital sample or biopsy at a separate adjacent visit. Incidence was measured as number of cases/100 person-years. Primary analysis was conducted in the per protocol efficacy (PPE) population including participants who received 3 doses of V503 or placebo in 1 year, had Month 7 swab samples collected postdose 3 with PCR result, were seronegative to relevant HPV type(s) at Day 1 and PCR-negative to relevant HPV type(s) on all samples collected from Day 1 to Month 7, and had no protocol deviations that could interfere with evaluation of vaccine efficacy.	
End point type	Primary
End point timeframe:	
Up to approximately 36 Months	

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	496	483		
Units: Cases per 100 Person-years				
number (not applicable)	0.2	2.2		

Statistical analyses

Statistical analysis title	Observed Efficacy
Comparison groups	V503 v Placebo
Number of subjects included in analysis	979
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001 [1]
Method	Exact Binomial Method Chan and Bohidar
Parameter estimate	Observed Efficacy (%)
Point estimate	89.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	55.4
upper limit	98.2

Notes:

[1] - one-sided p-value based on exact binomial method proposed by Chan and Bohidar

Primary: Percentage of participants with solicited injection-site adverse events (AEs)

End point title	Percentage of participants with solicited injection-site adverse events (AEs)

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The participant recorded the presence of any vaccination report card (VRC)-prompted injection-site AEs that occurred in the 5 days after any vaccination. The percentage of participants with an injection-site AE prompted on the VRC (redness/erythema, tenderness/pain, and swelling) is reported here for all randomized participants in the All Participants as Treated (APaT) population. Analysis population included all randomized participants in base study who received at least 1 dose of the V503 vaccine or placebo and have provided safety data at any time during the study.

End point type	Primary

End point timeframe:

Up to 5 days after any vaccination

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	530		
Units: Percentage of Participants				
number (not applicable)	69.8	29.6		

Statistical analyses

Statistical analysis title	Difference in Percentages
Comparison groups	V503 v Placebo

Number of subjects included in analysis	1059
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen & Nurminen method
Parameter estimate	Difference in Percentages
Point estimate	40.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	34.5
upper limit	45.5

Primary: Percentage of participants with ≥1 systemic AE

End point title	Percentage of participants with ≥1 systemic AE

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The percentage of participants who experienced at least 1 systemic AE is reported here for all randomized participants in the All Participants as Treated (APaT) population. Analysis population included all randomized participants in base study who received at least 1 dose of the V503 vaccine or placebo and have provided safety data at any time during the study.

End point type	Primary

End point timeframe:

Up to 15 days after any vaccination

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	530		
Units: Percentage of Participants				
number (not applicable)	20.2	19.8		

Statistical analyses

Statistical analysis title	Difference in Percentage
Comparison groups	V503 v Placebo
Number of subjects included in analysis	1059
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen & Nurminen method
Parameter estimate	Difference in Percentage
Point estimate	0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	5.2

Primary: Percentage of participants with ≥1 SAEs

End point title	Percentage of participants with ≥1 SAEs[2]

End point description:

An SAE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention, that results in death, is life-threatening, requires hospitalization or prolongs existing hospitalization, results in persistent/significant disability/incapacity, is a congenital birth defect, or is another important medical event. The percentage of participants who experienced at least 1 SAE is reported here for all randomized participants in the All Participants as Treated (APaT) population. Analysis population included all randomized participants in the base study who received at least 1 dose of the V503 vaccine or placebo and have provided safety data at any time during the study.

End point type	Primary

End point timeframe:

Up to approximately 37 months

Notes:

[2] - 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 arm comparison were planned for the study.

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	530		
Units: Percentage of Participants				
number (not applicable)	1.3	0.9		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Elevated Oral Body Temperature

End point title	Number of Participants with Elevated Oral Body Temperature[3]

End point description:

Participants collected their oral body temperature in the evening of their vaccination day and at the same time each day thereafter for 4 days. The maximum body temperature obtained within 5 days of any of the 3 vaccinations was recorded using the VRC. Per protocol, fever was defined as an oral temperature of ≥99.5°F(37.5°C). The number of participants who had at least 1 oral body temperature reading that was, <99.5°F (<37.5ºC), ≥99.5°F (≥37.5ºC) and <100.4°F (38.0°C), or ≥100.4°F (38.0°C) and <101.3°F(38.5°C), or ≥101.3°F(38.5°C) is reported here for all randomized participants in the APaT population with temperature data available. Analysis population included all randomized participants in base study who received at least 1 dose of the V503 vaccine or placebo and have provided safety data at any time during the study.

End point type	Primary

End point timeframe:

Up to 5 days after any vaccination

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: No between arm comparison were planned for the study.

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	527	526		
Units: Participants				
<99.5°F (37.5°C)	502	496		
≥99.5°F (≥37.5ºC) and <100.4°F (38.0°C)	19	22		
≥100.4°F (38.0°C) and <101.3°F(38.5°C)	1	1		
≥101.3°F(38.5°C)	5	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean titers (GMTs) to HPV 6/11/16/18/31/33/45/52/58

End point title	Geometric mean titers (GMTs) to HPV 6/11/16/18/31/33/45/52/58

End point description:

Antibodies to the HPV types 6/11/16/18/31/33/45/52/58 contained in V503 were measured using a competitive Luminex immunoassay (cLIA). Per protocol, antibody titers were expressed as milli Merck units/milliliter (mMU/mL). GMTs are reported for all participants of the per-protocol immunogenicity population (PPI) which included participants who satisfied all the criteria for the PPE population, and additionally all vaccinations within acceptable day ranges and provided blood samples for serology testing within the acceptable day range. A value of 8888/9999 indicates results were lower than the lower limit of quantitation of the assay.

End point type	Secondary

End point timeframe:

Month 7

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	456	458		
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6	927.3 (850.2 to 1011.3)	21.1 (-9999 to 22.5)		
Anti-HPV 11	716.5 (654.4 to 784.5)	8888 (-9999 to 9999)		
Anti-HPV 16	3491.6 (3196.5 to 3814.0)	8888 (-9999 to 9999)		
Anti-HPV 18	998.0 (904.3 to 1101.4)	45.5 (43.4 to 47.7)		

HPV-31	832.1 (753.3 to 919.2)	15.4 (14.3 to 16.5)		
HPV-33	489.8 (448.6 to 534.7)	12.7 (11.9 to 13.4)		
Anti-HPV 45	326.6 (293.7 to 363.2)	8.5 (-9999 to 9.0)		
Anti-HPV 52	390.5 (356.3 to 428.0)	10.1 (9.5 to 10.8)		
Anti-HPV 58	588.3 (537.7 to 643.6)	8888 (-9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Combined incidence of HPV 31/33/45/52/58-related anogenital persistent infection

End point title	Combined incidence of HPV 31/33/45/52/58-related anogenital persistent infection

End point description:

HPV31/33/45/52/58-related anogenital persistent infection was defined as polymerase chain reaction (PCR) positivity to at least 1 relevant HPV type in anogenital or biopsy samples from at least 2 consecutive visits 6 months (±1 month visit) or longer apart, or pathology diagnosis of condyloma or penile/perineal/perianal lesions together with PCR detection of at least 1 HPV type in an adjacent section and PCR detection for same HPV type in anogenital sample or biopsy at a separate adjacent visit. Incidence was measured as number of cases/100 person-years. Primary analysis was conducted in the PPE population.

End point type	Secondary

End point timeframe:

Up to approximately 36 Months

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	505	493		
Units: cases per 100 Person-years				
number (not applicable)	0.7	1.9		

Statistical analyses

Statistical analysis title	Observed Efficacy
Comparison groups	V503 v Placebo

Number of subjects included in analysis	998
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.023 [4]
Method	Exact Binomial Method Chan and Bohidar
Parameter estimate	Observed Efficacy (%)
Point estimate	63.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.7
upper limit	86

Notes:

[4] - one-sided p-value based on exact binomial method proposed by Chan and Bohidar

Secondary: GMTs to HPV 6/11/16/18/31/33/45/52/58 - Heterosexual Males (HM) Participant Subgroup

End point title	GMTs to HPV 6/11/16/18/31/33/45/52/58 - Heterosexual Males (HM) Participant Subgroup

End point description:

Antibodies to the HPV types 6/11/16/18/31/33/45/52/58 contained in V503 were measured using a cLIA. Per protocol, antibody titers were expressed as mMU/mL. GMTs are reported for the HM subgroup of the PPI population. A value of 8888/9999 indicates that results were lower than the lower limit of quantitation of the assay.

End point type	Secondary

End point timeframe:

Month 7

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	415		
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6	950.2 (866.8 to 1041.6)	21.0 (-9999 to 22.6)		
Anti-HPV 11	730.6 (664.4 to 803.4)	8888 (-9999 to 9999)		
Anti-HPV 16	3608.3 (3288.6 to 3959.0)	8888 (-9999 to 9999)		
Anti-HPV 18	1044.7 (942.7 to 1157.7)	45.1 (42.9 to 47.3)		
Anti-HPV 31	867.8 (780.7 to 964.7)	15.1 (14.0 to 16.3)		
Anti-HPV 33	495.4 (451.9 to 543.1)	12.6 (11.8 to 13.4)		
Anti-HPV 45	333.8 (298.4 to 373.5)	8.4 (-9999 to 9.0)		
Ant-HPV 52	408.7 (372.1 to 448.9)	10.0 (9.3 to 10.7)		
Anti-HPV 58	609.1 (554.2 to 669.4)	8888 (-9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs to HPV 6/11/16/18/31/33/45/52/58 - Males Who Have Sex with Males (MSM) Participant Subgroup

End point title	GMTs to HPV 6/11/16/18/31/33/45/52/58 - Males Who Have Sex with Males (MSM) Participant Subgroup

End point description:

Antibodies to the HPV types 6/11/16/18/31/33/45/52/58 contained in V503 were measured using a cLIA. Per protocol, antibody titers were expressed as mMU/mL. GMTs are reported for the MSM subgroup of the PPI population. A value of 8888/9999 indicates that results were lower than the lower limit of quantitation of the assay.

End point type	Secondary

End point timeframe:

Month 7

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	46		
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6	740.2 (569.2 to 962.6)	21.5 (-9999 to 27.5)		
Anti-HPV 11	598.8 (438.7 to 817.3)	8888 (-9999 to 9999)		
Anti-HPV 16	2599.5 (1957.4 to 3452.4)	8888 (-9999 to 9999)		
Anti-HPV 18	677.4 (487.6 to 941.0)	49.7 (42.1 to 58.6)		
Anti-HPV 31	593.2 (446.0 to 789.0)	17.7 (14.1 to 22.2)		
Anti-HPV 33	443.6 (327.9 to 600.1)	13.5 (11.5 to 16.0)		
Anti-HPV 45	266.6 (190.1 to 373.8)	9.1 (-9999 to 11.1)		
Anti-HPV 52	262.9 (186.7 to 370.2)	11.3 (9.0 to 14.2)		
Anti-HPV 58	437.7 (327.8 to 584.5)	-9999 (-9999 to 8.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Seroconversion to HPV 6/11/16/18/31/33/45/52/58

End point title	Percentage of Participants with Seroconversion to HPV 6/11/16/18/31/33/45/52/58

End point description:

Percentage of seroconversion to each of HPV 6/11/16/18/31/33/45/52/58 at Month 7 per cLIA from participant serum samples. Seroconversion is defined as a change in participant's serostatus from seronegative at Day 1 to seropositive at 1 month post last dose Month 7. Participant with anti-HPV cLIA titer at/above serostatus cutoff cLIA values for a given HPV type is seropositive for that type. HPV serostatus cutoffs were Type6: ≥65, Type11: ≥37; Type16: ≥79, Type18: ≥85, Type31: ≥46, Type33: ≥26, Type45: ≥21, Type 52: ≥30, & Type58: ≥31. Percentage of participants with seroconversion is reported in all participants in the PPI population.

End point type	Secondary

End point timeframe:

Month 7

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	456	458		
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 cLIA ≥65 mMU/mL	99.7 (98.6 to 100.0)	3.5 (1.9 to 6.0)		
Anti-HPV 11 cLIA ≥37 mMU/mL	99.7 (98.6 to 100.0)	4.1 (2.3 to 6.7)		
Anti-HPV 16 cLIA ≥79 mMU/mL	99.6 (98.4 to 99.9)	4.3 (2.6 to 6.6)		
Anti-HPV 18 cLIA ≥85 mMU/mL	99.3 (97.9 to 99.9)	8.3 (5.8 to 11.4)		
Anti-HPV 31 cLIA ≥46 mMU/mL	98.9 (97.3 to 99.6)	5.6 (3.6 to 8.2)		
Anti-HPV 33 cLIA ≥26 mMU/mL	99.8 (98.8 to 100.0)	11.1 (8.3 to 14.4)		
Anti-HPV 45 cLIA ≥21 mMU/mL	98.9 (97.4 to 99.6)	9.0 (6.5 to 12.1)		
Anti-HPV 52 cLIA ≥30 mMU/mL	98.9 (97.4 to 99.6)	4.2 (2.5 to 6.5)		
Anti-HPV 58 cLIA ≥31 mMU/mL	99.3 (98.1 to 99.9)	1.5 (0.6 to 3.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Seroconversion to HPV 6/11/16/18/31/33/45/52/58 - HM Participant Subgroup

End point title	Percentage of Participants with Seroconversion to HPV 6/11/16/18/31/33/45/52/58 - HM Participant Subgroup

End point description:

Percentage of seroconversion to each of HPV 6/11/16/18/31/33/45/52/58 at Month 7 per cLIA from participant serum samples. Seroconversion is defined as a change in participant's serostatus from seronegative at Day 1 to seropositive at 1 month post last dose Month 7. Participant with anti-HPV cLIA titer at/above serostatus cutoff cLIA values for a given HPV type is seropositive for that HPV type. The HPV serostatus cutoffs were Type 6: ≥65, Type 11: ≥37; Type 16: ≥79, Type 18: ≥85, Type 31: ≥46, Type 33: ≥26, Type 45: ≥21, Type 52: ≥30, and Type 58: ≥31. Percentage of participants with seroconversion is reported in the HM subgroup of the PPI population.

End point type	Secondary

End point timeframe:

Month 7

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	415		
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 cLIA ≥65 mMU/mL	99.7 (98.5 to 100.0)	3.5 (1.8 to 6.1)		
Anti-HPV 11 cLIA ≥37 mMU/mL	99.7 (98.5 to 100.0)	4.4 (2.5 to 7.2)		
Anti-HPV 16 cLIA ≥79 mMU/mL	99.5 (98.2 to 99.9)	3.7 (2.1 to 6.0)		
Anti-HPV 18 cLIA ≥85 mMU/mL	99.5 (98.1 to 99.9)	7.6 (5.1 to 10.8)		
Anti-HPV 31 cLIA ≥46 mMU/mL	99.0 (97.4 to 99.7)	5.2 (3.2 to 7.9)		
Anti-HPV 33 cLIA ≥26 mMU/mL	99.8 (98.6 to 100.0)	11.4 (8.4 to 14.9)		
Anti-HPV 45 cLIA ≥21 mMU/mL	98.7 (97.1 to 99.6)	8.5 (5.9 to 11.7)		
Anti-HPV 52 cLIA ≥30 mMU/mL	99.2 (97.8 to 99.8)	3.8 (2.2 to 6.3)		
Anti-HPV 58 cLIA ≥31 mMU/mL	99.3 (97.9 to 99.8)	1.7 (0.7 to 3.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Seroconversion to HPV 6/11/16/18/31/33/45/52/58 - MSM Participant Subgroup

End point title	Percentage of Participants with Seroconversion to HPV 6/11/16/18/31/33/45/52/58 - MSM Participant Subgroup

End point description:

Percentage of seroconversion to each of HPV 6/11/16/18/31/33/45/52/58 at Month 7 per cLIA from participant serum samples. Seroconversion is defined as a change in a participant's serostatus from seronegative at Day 1 to seropositive at 1 month post last dose Month 7. Participant with anti-HPV cLIA titer at/above the serostatus cutoff cLIA values for a given HPV type is seropositive for that HPV type. The HPV serostatus cutoffs were Type 6: ≥65, Type 11: ≥37; Type 16: ≥79, Type 18: ≥85, Type 31: ≥46, Type 33: ≥26, Type 45: ≥21, Type 52: ≥30, and Type 58: ≥31. Percentage of participants with seroconversion is reported in the MSM subgroup of the PPI population.

End point type	Secondary

End point timeframe:
Month 7

End point values	V503	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	46		
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 cLIA ≥65 mMU/mL	100.0 (91.0 to 100.0)	3.6 (0.1 to 18.3)		
Anti-HPV 11 cLIA ≥37 mMU/mL	100.0 (91.0 to 100.0)	0.0 (0.0 to 12.3)		
Anti-HPV 16 cLIA ≥79 mMU/mL	100.0 (92.1 to 100.0)	9.5 (2.7 to 22.6)		
Anti-HPV 18 cLIA ≥85 mMU/mL	97.7 (88.0 to 99.9)	14.3 (5.4 to 28.5)		
Anti-HPV 31 cLIA ≥46 mMU/mL	97.9 (88.9 to 99.9)	8.9 (2.5 to 21.2)		
Anti-HPV 33 cLIA ≥26 mMU/mL	100.0 (92.5 to 100.0)	8.7 (2.4 to 20.8)		
Anti-HPV 45 cLIA ≥21 mMU/mL	100.0 (91.8 to 100.0)	13.3 (5.1 to 26.8)		
Anti-HPV 52 cLIA ≥30 mMU/mL	95.6 (84.9 to 99.5)	7.0 (1.5 to 19.1)		
Anti-HPV 58 cLIA ≥31 mMU/mL	100.0 (92.6 to 100.0)	0.0 (0.0 to 8.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to approximately 55 months	
Adverse event reporting additional description:	
All-cause mortality included all the randomized participants. Non-serious and serious adverse events were reported on all Participants as Treated (APaT). The APaT population consists of all randomized participants who received at least 1 dose of the V503 or placebo and have provided safety data at any time during the study.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	28.0

Reporting groups	
Reporting group title	Base Study: V503
Reporting group description:	
Participants received an IM injection of V503 at Day 1, Month 2, and Month 6.	
Reporting group title	Base Study: Placebo Open Label V503 Extension Study
Reporting group description:	
Participants from the placebo arm of the base study who did not complete the 3-dose series received 3 doses of V503 on Day 1, Month 2 and Month 6 of the open label extension study.	
Reporting group title	Base Study: V503 Open Label V503 Extension Study
Reporting group description:	
Participants from the V503 arm of the base study who did not complete the 3-dose series received 1 or 2 doses of V503, on Day 1, or Day 1 and Month 4 of the open label extension study.	
Reporting group title	Base Study: Placebo
Reporting group description:	
Participants received an IM injection of placebo at Day 1, Month 2, and Month 6.	

Serious adverse events	Base Study: V503	Base Study: Placebo Open Label V503 Extension Study	Base Study: V503 Open Label V503 Extension Study
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 529 (1.32%)	2 / 381 (0.52%)	0 / 2 (0.00%)
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)			
Anogenital warts			
subjects affected / exposed	0 / 529 (0.00%)	0 / 381 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Tendon rupture			

subjects affected / exposed	0 / 529 (0.00%)	0 / 381 (0.00%)	0 / 2 (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
Radius fracture			
subjects affected / exposed	0 / 529 (0.00%)	0 / 381 (0.00%)	0 / 2 (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
Brain contusion			
subjects affected / exposed	1 / 529 (0.19%)	0 / 381 (0.00%)	0 / 2 (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
Ankle fracture			
subjects affected / exposed	0 / 529 (0.00%)	1 / 381 (0.26%)	0 / 2 (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
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 529 (0.19%)	0 / 381 (0.00%)	0 / 2 (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
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 529 (0.19%)	0 / 381 (0.00%)	0 / 2 (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			
subjects affected / exposed	1 / 529 (0.19%)	0 / 381 (0.00%)	0 / 2 (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
COVID-19			
subjects affected / exposed	1 / 529 (0.19%)	0 / 381 (0.00%)	0 / 2 (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

Campylobacter gastroenteritis			
subjects affected / exposed	1 / 529 (0.19%)	0 / 381 (0.00%)	0 / 2 (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
Peritonitis			
subjects affected / exposed	0 / 529 (0.00%)	0 / 381 (0.00%)	0 / 2 (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
Chronic tonsillitis			
subjects affected / exposed	1 / 529 (0.19%)	0 / 381 (0.00%)	0 / 2 (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
Post procedural infection			
subjects affected / exposed	0 / 529 (0.00%)	0 / 381 (0.00%)	0 / 2 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 529 (0.00%)	1 / 381 (0.26%)	0 / 2 (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

Serious adverse events	Base Study: Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 530 (0.94%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	1 / 530 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Tendon rupture			

subjects affected / exposed	1 / 530 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
subjects affected / exposed	1 / 530 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain contusion			
subjects affected / exposed	0 / 530 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	0 / 530 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 530 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 530 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 530 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	1 / 530 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Campylobacter gastroenteritis			
subjects affected / exposed	0 / 530 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	1 / 530 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic tonsillitis			
subjects affected / exposed	0 / 530 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural infection			
subjects affected / exposed	1 / 530 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	0 / 530 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Base Study: V503	Base Study: Placebo Open Label V503 Extension Study	Base Study: V503 Open Label V503 Extension Study
Total subjects affected by non-serious adverse events			
subjects affected / exposed	374 / 529 (70.70%)	0 / 381 (0.00%)	0 / 2 (0.00%)
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	104 / 529 (19.66%)	0 / 381 (0.00%)	0 / 2 (0.00%)
occurrences (all)	149	0	0
Pyrexia			
subjects affected / exposed	29 / 529 (5.48%)	0 / 381 (0.00%)	0 / 2 (0.00%)
occurrences (all)	35	0	0
Injection site swelling			

subjects affected / exposed	118 / 529 (22.31%)	0 / 381 (0.00%)	0 / 2 (0.00%)
occurrences (all)	164	0	0
Injection site pain			
subjects affected / exposed	360 / 529 (68.05%)	0 / 381 (0.00%)	0 / 2 (0.00%)
occurrences (all)	739	0	0

Non-serious adverse events	Base Study: Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	183 / 530 (34.53%)		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	70 / 530 (13.21%)		
occurrences (all)	101		
Pyrexia			
subjects affected / exposed	33 / 530 (6.23%)		
occurrences (all)	36		
Injection site swelling			
subjects affected / exposed	40 / 530 (7.55%)		
occurrences (all)	50		
Injection site pain			
subjects affected / exposed	122 / 530 (23.02%)		
occurrences (all)	166		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 September 2022	The major change of Amendment 1 (AM1) was to change the Sponsor entity name and address change and to add the capability to enroll underrepresented groups.
05 December 2023	The major change of AM2 was to add the extension study.
24 September 2024	The major change of AM3 was to conduct final efficacy analysis before end of study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported