Clinical trial results:
A Phase 3, Open-label Clinical Study to Evaluate the Immunogenicity and Safety of 9vHPV Vaccine, in Japanese Boys and Girls, 9 to 15 Years of Age.

Summary

EudraCT number	2020-001170-29
Trial protocol	Outside EU/EEA
Global end of trial date	11 June 2024

Results information

Result version number	v1 (current)
This version publication date	21 December 2024
First version publication date	21 December 2024

Trial information

Trial identification

Sponsor protocol code	V503-066

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04772534
WHO universal trial number (UTN)	-
Other trial identifiers	jRCT: jRCT2031210080

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	06 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 April 2024
Global end of trial reached?	Yes
Global end of trial date	11 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is the estimation of the human papillomavirus (HPV) 6, 11, 16, 18, 31, 33, 45, 52 and 58 seroconversion at 1 month post last dose (Month 7) following 3 doses and 2 doses of the 9vHPV vaccine. No hypothesis will be tested since this study is an estimation-only 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	17 May 2021
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: 314
Worldwide total number of subjects	314
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)	158
Adolescents (12-17 years)	156
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 boys aged 9 to 15 years and healthy girls aged 9 to 14 years who had not yet had coitarche and had not previously received an HPV vaccine were enrolled at study sites in Japan.

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	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys

Arm description:

9 to 15 year old boys received a 3-dose regimen of 9-valent human papillomavirus (9vHPV) vaccine (Day 1, Month 2 and Month 6).

Arm type	Experimental
Investigational medicinal product name	9vHPV Vaccine
Investigational medicinal product code	
Other name	V503 SILGARD®9 GARDASIL™9
Pharmaceutical forms	Solution 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-mL intramuscular injection

Arm title	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys

Arm description:

9 to 14 year old boys received a 2-dose regimen of 9vHPV vaccine (Day 1 and Month 6).

Arm type	Experimental
Investigational medicinal product name	9vHPV Vaccine
Investigational medicinal product code	
Other name	V503 SILGARD®9 GARDASIL™9
Pharmaceutical forms	Solution 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-mL intramuscular injection

Arm title	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls

Arm description:

9 to 14 year old girls received a 2-dose regimen of 9vHPV vaccine (Day 1 and Month 6).

Arm type	Experimental

Investigational medicinal product name	9vHPV Vaccine
Investigational medicinal product code	
Other name	V503 SILGARD®9 GARDASIL™9
Pharmaceutical forms	Solution 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-mL intramuscular injection

Number of subjects in period 1	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls
Started	105	104	105
Completed	101	104	104
Not completed	4	0	1
Physician decision	1	-	-
Consent withdrawn by subject	3	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys
Reporting group description:	
9 to 15 year old boys received a 3-dose regimen of 9-valent human papillomavirus (9vHPV) vaccine (Day 1, Month 2 and Month 6).	
Reporting group title	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys
Reporting group description:	
9 to 14 year old boys received a 2-dose regimen of 9vHPV vaccine (Day 1 and Month 6).	
Reporting group title	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls
Reporting group description:	
9 to 14 year old girls received a 2-dose regimen of 9vHPV vaccine (Day 1 and Month 6).	

Reporting group values	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls
Number of subjects	105	104	105
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)	49	53	56
Adolescents (12-17 years)	56	51	49
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			
median	12.0	11.0	11.0
full range (min-max)	9 to 15	9 to 14	9 to 14
Gender Categorical			
Units: Subjects			
Female	0	0	105
Male	105	104	0
Race			
Units: Subjects			
Japanese	105	104	105

Reporting group values	Total		
Number of subjects	314		
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)	158		
Adolescents (12-17 years)	156		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: years			
median			
full range (min-max)	-		
Gender Categorical			
Units: Subjects			
Female	105		
Male	209		
Race			
Units: Subjects			
Japanese	314		

End points

End points reporting groups

Reporting group title	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys
Reporting group description:	
9 to 15 year old boys received a 3-dose regimen of 9-valent human papillomavirus (9vHPV) vaccine (Day 1, Month 2 and Month 6).	
Reporting group title	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys
Reporting group description:	
9 to 14 year old boys received a 2-dose regimen of 9vHPV vaccine (Day 1 and Month 6).	
Reporting group title	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls
Reporting group description:	
9 to 14 year old girls received a 2-dose regimen of 9vHPV vaccine (Day 1 and Month 6).	

Primary: Seroconversion Percentages for the HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58

End point title	Seroconversion Percentages for the HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58[1]
End point description:	
The percentage of seropositive participants is reported. Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58 were determined using competitive Luminex Immunoassay (cLIA). Seroconversion is defined as changing serostatus from seronegative at Day 1 to seropositive at 4 weeks post last vaccination. Participants who were seronegative on Day 1, received all vaccinations of 9vHPV within the acceptable day ranges, and provided blood samples are included.	
End point type	Primary
End point timeframe:	
4 weeks post last vaccination (Month 7)	

Notes:

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

End point values	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	104	104	
Units: Percentage of participants				
number (confidence interval 95%)				
Anti-HPV 6	100.0 (96.0 to 100.0)	100.0 (96.0 to 100.0)	100.0 (96.1 to 100.0)	
Anti-HPV 11	100.0 (96.0 to 100.0)	100.0 (96.0 to 100.0)	100.0 (96.1 to 100.0)	
Anti-HPV 16	100.0 (96.3 to 100.0)	100.0 (96.3 to 100.0)	100.0 (96.3 to 100.0)	
Anti-HPV 18	100.0 (96.2 to 100.0)	100.0 (96.1 to 100.0)	100.0 (95.7 to 100.0)	
Anti-HPV 31	100.0 (96.0 to 100.0)	100.0 (96.1 to 100.0)	100.0 (96.0 to 100.0)	
Anti-HPV 33	100.0 (95.8 to 100.0)	100.0 (96.0 to 100.0)	100.0 (96.2 to 100.0)	
Anti-HPV 45	100.0 (96.2 to 100.0)	100.0 (96.2 to 100.0)	100.0 (96.3 to 100.0)	

Anti-HPV 52	100.0 (96.3 to 100.0)	100.0 (96.2 to 100.0)	100.0 (96.3 to 100.0)	
Anti-HPV 58	100.0 (96.4 to 100.0)	100.0 (96.4 to 100.0)	100.0 (96.3 to 100.0)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With at Least 1 Serious Adverse Event (SAE)

End point title	Percentage of Participants With at Least 1 Serious Adverse Event (SAE)[2]

End point description:

A serious adverse event (SAE) is defined as one that results in death, is life threatening, or requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly or birth defect, or other important medical event that may require medical intervention. All participants who received ≥1 study vaccination are included.

End point type	Primary

End point timeframe:

Up to ~Month 30

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: Per protocol, only descriptive statistics are presented.

End point values	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	103	104	104	
Units: Percentage of Participants				
number (not applicable)	0.0	1.9	2.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with at Least 1 Injection-site Adverse Event

End point title	Percentage of Participants with at Least 1 Injection-site Adverse Event

End point description:

An adverse event (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. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. All participants who received ≥1 study vaccination are included.

End point type	Secondary

End point timeframe:

Up to 15 days after each vaccination

End point values	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	103	104	104	
Units: Percentage of Participants				
number (not applicable)	84.5	81.7	88.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With at Least 1 Systemic Adverse Even

End point title	Percentage of Participants With at Least 1 Systemic Adverse Even

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. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. All participants who received ≥1 study vaccination are included.

End point type	Secondary

End point timeframe:

Up to 15 days after each vaccination

End point values	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	103	104	104	
Units: Percentage of Participants				
number (not applicable)	53.4	39.4	31.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With at Least 1 Vaccine-related Serious Adverse Event

End point title	Percentage of Participants With at Least 1 Vaccine-related Serious Adverse Event

End point description:

A serious adverse event (SAE) is defined as one that results in death, is life threatening, or requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly or birth defect, or other important medical event that may require medical intervention. An SAE that is judged by the investigator to be related to the study vaccine is defined as a vaccine-related SAE. All participants who received ≥1 study vaccination are included.

End point type	Secondary

End point timeframe:

Up to ~Month 30

End point values	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	103	104	104	
Units: Percentage of Participants				
number (not applicable)	0.0	0.0	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers of Anti-HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58

End point title	Geometric Mean Titers of Anti-HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58

End point description:

Serum antibodies to HPV types 6, 11, 16, 18 31, 33, 45, 52, and 58 will be measured with a cLIA. Titers are reported in milli Merck Units/mL. Participants who were seronegative on Day 1, received all vaccinations of 9vHPV within the acceptable day ranges, and provided blood samples are included.

End point type	Secondary

End point timeframe:

4 weeks post last vaccination (Month 7)

End point values	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	104	105	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-HPV 6	1759.8 (1481.2 to 2090.8)	2417.0 (2057.3 to 2839.6)	2343.2 (2036.1 to 2696.5)	

Anti-HPV 11	1341.8 (1136.1 to 1584.9)	1510.1 (1310.3 to 1740.4)	1508.5 (1340.8 to 1697.0)	
Anti-HPV 16	7020.8 (5955.3 to 8277.1)	9808.5 (8437.7 to 11402.0)	9800.0 (8440.1 to 11379.1)	
Anti-HPV 18	2629.6 (2154.7 to 3209.1)	2464.6 (2095.6 to 2898.5)	2999.8 (2509.3 to 3586.3)	
Anti-HPV 31	2095.0 (1717.2 to 2555.9)	1908.5 (1619.3 to 2249.4)	1838.7 (1571.8 to 2151.0)	
Anti-HPV 33	894.9 (753.1 to 1063.4)	1272.1 (1085.2 to 1491.2)	1283.1 (1132.4 to 1453.8)	
Anti-HPV 45	848.9 (701.1 to 1027.8)	508.4 (431.7 to 598.8)	599.6 (520.6 to 690.4)	
Anti-HPV 52	925.3 (774.9 to 1105.0)	587.4 (503.3 to 685.5)	582.7 (517.3 to 656.4)	
Anti-HPV 58	1401.7 (1177.4 to 1668.8)	1350.6 (1155.1 to 1579.1)	1379.8 (1216.4 to 1565.1)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to ~30 months	
Adverse event reporting additional description:	
All participants who received ≥1 dose of study treatment are included.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups	
Reporting group title	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys
Reporting group description:	
9 to 15 year old boys received a 3-dose regimen of 9-valent human papillomavirus (9vHPV) vaccine (Day 1, Month 2 and Month 6).	
Reporting group title	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls
Reporting group description:	
9 to 14 year old girls received a 2-dose regimen of 9vHPV vaccine (Day 1 and Month 6).	
Reporting group title	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys
Reporting group description:	
9 to 14 year old boys received a 2-dose regimen of 9vHPV vaccine (Day 1 and Month 6).	

Serious adverse events	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 103 (0.00%)	3 / 104 (2.88%)	2 / 104 (1.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 103 (0.00%)	0 / 104 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 103 (0.00%)	1 / 104 (0.96%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Strabismus			

subjects affected / exposed	0 / 103 (0.00%)	1 / 104 (0.96%)	0 / 104 (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
Infections and infestations			
Pyelonephritis acute			
subjects affected / exposed	0 / 103 (0.00%)	1 / 104 (0.96%)	0 / 104 (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

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

Non-serious adverse events	Arm 1: 3-Dose Regimen in 9 to 15 Year Old Boys	Arm 3: 2-Dose Regimen in 9 to 14 Year Old Girls	Arm 2: 2-Dose Regimen in 9 to 14 Year Old Boys
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 103 (33.01%)	18 / 104 (17.31%)	24 / 104 (23.08%)
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 103 (9.71%)	6 / 104 (5.77%)	9 / 104 (8.65%)
occurrences (all)	10	6	9
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	18 / 103 (17.48%)	8 / 104 (7.69%)	12 / 104 (11.54%)
occurrences (all)	18	8	12
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 103 (5.83%)	4 / 104 (3.85%)	3 / 104 (2.88%)
occurrences (all)	6	4	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2021	AM1: The primary purpose of the amendment was to initiate enrollment of girls earlier than boys.
19 September 2022	AM2: The primary purpose of the amendment was to update Sponsor name and address.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported