Clinical trial results:
A Phase III Open-label Safety and Immunogenicity Study of GARDASIL™9 Administered to 9- to 26 Year-Old Females and Males in Vietnam

Summary

EudraCT number	2017-001205-33
Trial protocol	Outside EU/EEA
Global end of trial date	29 January 2019

Results information

Result version number	v1 (current)
This version publication date	22 September 2019
First version publication date	22 September 2019

Trial information

Trial identification

Sponsor protocol code	V503-017

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03546842
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The trial was conducted to assess immunogenicity and safety of the 9-valent human papillomavirus (9vHPV) vaccine in participants from Vietnam.

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	29 June 2018
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	Vietnam: 201
Worldwide total number of subjects	201
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)	41
Adolescents (12-17 years)	99
Adults (18-64 years)	61
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Healthy females or males between the ages of 9 years and 26 years were enrolled in the study. Other inclusion and exclusion criteria applied.

Period 1

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

Arms

Arm title	9vHPV Vaccine

Arm description:

Participants received a single 0.5-mL intramuscular injection at Day 1, Month 2, and Month 6

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

Dosage and administration details:

0.5 mL intramuscualr injection at Day 1, Month 2 and Month 6

Number of subjects in period 1	9vHPV Vaccine
Started	201
Vaccination 1	200
Vaccination 2	200
Vaccination 3	198
Completed	198
Not completed	3
Consent withdrawn by subject	2
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	9vHPV Vaccine
Reporting group description:	
Participants received a single 0.5-mL intramuscular injection at Day 1, Month 2, and Month 6	

Reporting group values	9vHPV Vaccine	Total	
Number of subjects	201	201	
Age Categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	 15.8 ± 4.4	 -	
Gender Categorical Units: Subjects			
Female	135	135	
Male	66	66	
Ethnicity Units: Subjects			
Not Hispanic Or Latino	201	201	
Race Units: Subjects			
Asian	201	201	

End points

End points reporting groups

Reporting group title	9vHPV Vaccine
Reporting group description:	
Participants received a single 0.5-mL intramuscular injection at Day 1, Month 2, and Month 6	
Subject analysis set title	9vHPV Vaccine-Immunogenicity
Subject analysis set type	Per protocol
Subject analysis set description:	
The per-protocol immunogenicity (PPI) population was HPV type-specific and consisted of all allocated participants who were seronegative to the appropriate HPV type at Day 1, received all 3 vaccinations with the correct dose of 9vHPV vaccine within acceptable day ranges, provided a serum sample within 21 to 49 days post-dose 3, and had no protocol deviations that could interfere with the evaluation of participant's immune response to 9vHPV vaccination.	
Subject analysis set title	9vHPV Vaccine-Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
All participants that received at least 1 vaccination with V503 and provided safety data at any time during the study.	

Primary: Seroconversion Percentages to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 7

End point title	Seroconversion Percentages to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 7[1]
End point description:	
Seroconversion is defined as a participant who was anti-HPV seronegative at Day 1 and became seropositive at 4 weeks postdose 3 (Month 7). Anti-HPV antibodies are measured using a Competitive Luminex Immunoassay.	
End point type	Primary
End point timeframe:	
4 weeks postdose 3 (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: System does not allow the posting of the analysis of a single arm study.

End point values	9vHPV Vaccine-Immunogenicity			
Subject group type	Subject analysis set			
Number of subjects analysed	200			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-HPV 6 (n=190)	100.0 (98.1 to 100.0)			
Anti-HPV 11 (n=190)	100.0 (98.1 to 100.0)			
Anti-HPV 16 (n=187)	100.0 (98.0 to 100.0)			
Anti-HPV 18 (n=190)	100.0 (98.1 to 100.0)			
Anti-HPV 31 (n=188)	100.0 (98.1 to 100.0)			
Anti-HPV 33 (n=194)	100.0 (98.1 to 100.0)			

Anti-HPV 45 (n=193)	100.0 (98.1 to 100.0)			
Anti-HPV 52 (n=192)	100.0 (98.1 to 100.0)			
Anti-HPV 58 (n=190)	100.0 (98.1 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Solicited Injection-site Adverse Event

End point title	Percentage of Participants with a Solicited Injection-site Adverse Event

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant which did not necessarily have a causal relationship with study vaccine. An AE could therefore be any unfavourable and unintended sign, symptom, or disease temporally associated with the use of study vaccine or a protocol-specified procedure, whether or not considered related to the study vaccine or protocol-specified procedure. Any worsening of a preexisting condition that was temporally associated with the study vaccine or protocol-specified procedure was also an AE. The participant or the parent/guardian of the participant were to record the presence of any vaccination report card (VRC)-prompted injection-site AEs that occurred in the 5 days after any vaccination. The percentage of participants with an injection-site AE prompted on the VRC (erythema, pain, and swelling) was summarized.

End point type	Secondary

End point timeframe:

Up to 5 days after any vaccination

End point values	9vHPV Vaccine-Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	200			
Units: Percentage of Participants				
number (confidence interval 95%)	45 (38.0 to 52.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Solicited Systemic Adverse Event

End point title	Percentage of Participants with a Solicited Systemic Adverse Event

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant which did not necessarily have a causal relationship with study vaccine. An AE could therefore be any unfavourable and unintended sign, symptom, or disease temporally associated with the use of study vaccine or a protocol-specified procedure, whether or not considered related to the study vaccine or protocol-specified procedure. Any worsening of a preexisting condition that was temporally associated with the study vaccine or protocol-specified procedure was also an AE. The participant or the parent/guardian of

the participant will be asked to record the participant's oral temperature in the evening after each study vaccination and daily for 4 days after each study vaccination on VRC. The percentage of participants that had an AE due to an elevated oral temperature [(≥ 37.8 °C (100.0 °F)] was summarized.

End point type	Secondary

End point timeframe:

Up to 5 days after any vaccination

End point values	9vHPV Vaccine-Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	200			
Units: Percentage of Participants				
number (not applicable)	0.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Vaccine-related Serious Adverse Event

End point title	Percentage of Participants with a Vaccine-related Serious Adverse Event

End point description:

A serious adverse event (SAE) is an AE that is life-threatening, requires or prolongs an existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is another important medical event deemed such by medical or scientific judgment. The percentage of participants that experience at least SAE that was reported as at least possibly related to the study vaccine was summarized.

End point type	Secondary

End point timeframe:

Up to 4 weeks postdose 3 (Month 7)

End point values	9vHPV Vaccine-Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	200			
Units: Percentage of Participants				
number (not applicable)	0.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers of Geometric Mean Titers of Antibodies to HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 7

End point title	Geometric Mean Titers of Geometric Mean Titers of Antibodies to HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Month 7

End point description:

Anti-HPV Type 6, 11, 16, 18, 31, 33, 45, 52, and 58 antibodies are measured using a Competitive Luminex Immunoassay. Titers are reported in mMU/mL.

End point type	Secondary

End point timeframe:

4 weeks postdose 3 (Month 7)

End point values	9vHPV Vaccine-Immunogenicity			
Subject group type	Subject analysis set			
Number of subjects analysed	200			
Units: mMU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV 6 (n=190)	1008.2 (921.9 to 1102.6)			
Anti-HPV 11 (n=190)	796.3 (722.2 to 878.0)			
Anti-HPV 16 (n=187)	4605.4 (4163.7 to 5093.9)			
Anti-HPV 18 (n=190)	1621.6 (1441.2 to 1824.5)			
Anti-HPV 31 (n=188)	1137.9 (1017.2 to 1273.0)			
Anti-HPV 33 (n=194)	507.8 (458.5 to 562.4)			
Anti-HPV 45 (n=193)	579.2 (511.7 to 655.6)			
Anti-HPV 52 (n=192)	500.8 (450.5 to 556.7)			
Anti-HPV 58 (n=190)	701.8 (628.5 to 783.7)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 4 weeks postdose 3 (Month 7)

Adverse event reporting additional description:

Population included all participants that received at least 1 vaccination with V503 and provided safety data at any time during the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	V503

Reporting group description: -

Serious adverse events	V503		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 200 (0.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Subcutaneous abscess			
subjects affected / exposed	1 / 200 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	V503		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	90 / 200 (45.00%)		
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	89 / 200 (44.50%)		
occurrences (all)	138		
Injection site swelling			

subjects affected / exposed occurrences (all)	12 / 200 (6.00%) 16		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 December 2017	Amendment 1: Primary reason for the amendment was to remove sections and text pertaining to Future Biomedical Research samples.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to limitations in the EudraCT reporting system, the Predose GMTs could not be reported as planned. Almost all titers were < the lower limit of quantification. The results for this endpoint will be posted on ClinicalTrials.gov (NCT03546842).

Notes: