



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 intramuscular 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

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

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|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

Reporting groups

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|-----------------------|------|
| 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 | 12 / 200 (6.00%) | | |
| occurrences (all) | 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: