



Clinical trial results:

A Phase IV Open-label, Descriptive Study to Evaluate the Safety and Effectiveness on the Incidence of HPV 6, 11, 16 and 18 Related CIN 2/3 or worse of the Quadrivalent HPV (Types 6, 11, 16, 18) L1 Virus-Like Particle (VLP) Vaccine in 16- to 26-Year-Old Japanese Women

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2015-002932-42 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 01 December 2016 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 13 May 2017 |
| First version publication date | 13 May 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | V501-110 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01544478 |
| 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 | 27 August 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 December 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the long term safety of quadrivalent Human Papillomavirus (HPV) types 6, 11, 16, 18 vaccine (V501) and its effectiveness in the prevention of cervical intraepithelial neoplasia (CIN), adenocarcinoma in situ, and cervical cancer related to HPV in Japanese women.

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 | 22 November 2011 |
| 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: 1030 |
| Worldwide total number of subjects | 1030 |
| 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) | 0 |
| Adolescents (12-17 years) | 2 |
| Adults (18-64 years) | 1028 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Study participants were healthy Japanese females 16 to 26 years of age.

Pre-assignment

Screening details:

A total of 1036 participants were screened and 1030 were enrolled in the study.

Period 1

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

Arms

| | |
|-----------|------|
| Arm title | V501 |
|-----------|------|

Arm description:

Participants received a 0.5 mL vaccination by intramuscular injection of V501 on Day 1, Month 2, and Month 6

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | V501 |
| Investigational medicinal product code | |
| Other name | Gardasil™ Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

A 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6

| Number of subjects in period 1 | V501 |
|--------------------------------|------|
| Started | 1030 |
| Vaccination 1 | 1030 |
| Vaccination 2 | 1026 |
| Vaccination 3 | 1019 |
| Completed | 912 |
| Not completed | 118 |
| Physician decision | 15 |
| Consent withdrawn by subject | 52 |
| Adverse event, non-fatal | 1 |
| Death | 1 |
| Pregnancy | 1 |
| Lost to follow-up | 48 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall Study |
|-----------------------|---------------|

Reporting group description:

Participants received a 0.5 mL vaccination by intramuscular injection of V501 on Day 1, Month 2, and Month 6

| Reporting group values | Overall Study | Total | |
|---------------------------------------|---------------|-------|--|
| Number of subjects | 1030 | 1030 | |
| Age Categorical Units: Subjects | | | |
| Adolescents (12-17 years) | 2 | 2 | |
| Adults (18-64 years) | 1028 | 1028 | |
| Age Continuous Units: years | | | |
| arithmetic mean | 22.9 | | |
| standard deviation | ± 2.2 | - | |
| Gender Categorical Units: Subjects | | | |
| Female | 1030 | 1030 | |
| Male | 0 | 0 | |
| Race Units: Subjects | | | |
| Asian | 1030 | 1030 | |

End points

End points reporting groups

| | |
|--|------|
| Reporting group title | V501 |
| Reporting group description: | |
| Participants received a 0.5 mL vaccination by intramuscular injection of V501 on Day 1, Month 2, and Month 6 | |

Primary: Combined incidence of Cervical Intraepithelial Neoplasia (CIN) 2/3 or worse related to HPV type 6, 11, 16, or 18

| | |
|-----------------|---|
| End point title | Combined incidence of Cervical Intraepithelial Neoplasia (CIN) 2/3 or worse related to HPV type 6, 11, 16, or 18 ^[1] |
|-----------------|---|

End point description:

The endpoint included pathology panel consensus diagnosis of CIN 2 or 3, adenocarcinoma in situ, invasive squamous cervical carcinoma, or invasive adenocarcinoma of the cervix, and HPV type 6, 11, 16, or 18 detected in an adjacent section from the same tissue block. The population analyzed included participants who received the full vaccination series, had at least 1 visit after Month 7, had no general protocol violations, and were seronegative at Baseline and polymerase chain reaction-negative from Baseline through Month 7 for the relevant HPV type. The point estimates and exact 95% confidence intervals for incidence rate were based on the Poisson distribution.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to Month 48

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: No hypothesis testing was planned or conducted for this endpoint

| End point values | V501 | | | |
|---|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 967 ^[2] | | | |
| Units: Cases per 100 person-years at risk | | | | |
| number (confidence interval 95%) | 0 (0 to 0.1) | | | |

Notes:

[2] - A total of 3034.6 person-years was evaluated

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Month 48

Adverse event reporting additional description:

Participants at risk included all who received at least 1 vaccination and had safety follow-up.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------|
| Reporting group title | V501 |
|-----------------------|------|

Reporting group description:

Participants received a 0.5 mL vaccination by intramuscular injection of V501 on Day 1, Month 2, and Month 6

| Serious adverse events | V501 | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 1029 (0.78%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 1 / 1029 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 4 / 1029 (0.39%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 1 / 1029 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Foetal malpresentation | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1029 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations Peritonsillitis subjects affected / exposed | 1 / 1029 (0.10%) | | |
| 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 | V501 | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 169 / 1029 (16.42%) | | |
| General disorders and administration site conditions | | | |
| Injection site pain | | | |
| subjects affected / exposed | 118 / 1029 (11.47%) | | |
| occurrences (all) | 168 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 61 / 1029 (5.93%) | | |
| occurrences (all) | 67 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 14 February 2013 | Amendment 1: change in the handling of relocated participants, and minor changes to the Regimen for Triage: Investigator Aids for Colposcopy and Definitive Therapy |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported