A Study of V503 Vaccine Given Concomitantly With REPEVAX™ in 11 to 15 Year Olds (V503-007)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT01073293

First received: February 19, 2010
Last updated: May 11, 2015
Last verified: May 2015
History of Changes

Purpose

This study will evaluate whether co-administration of the first dose of V503 and REPEVAX™ is well tolerated and causes a non-inferior immune response when compared to administration of REPEVAX™ one month following the first dose of V503.

Condition	Intervention	Phase
Papillomavirus Infections	Biological: V503 Vaccine Biological: REPEVAX™ (Concomitant) Biological: REPEVAX™ (Non-concomitant)	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Prevention

Official Title: A Phase III Open-Label Clinical Trial to Study the Immunogenicity and Tolerability of V503, a Multivalent Human Papillomavirus (HPV) L1 Virus-Like Particle (VLP) Vaccine, Given Concomitantly With REPEVAX™ in Preadolescents and Adolescents (11 to 15 Year Olds)

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503
  [Time Frame: 4 weeks following Month 6 vaccination] [Designated as safety issue: No]

  Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 were measured using a competitive Luminex immunoassay. Titers are reported in milli Merck Units/mL.

Percentage of Participants With a V503 Injection-site Adverse Experience [Time Frame: Day 1 through Day 5 following Day 1 vaccination] [Designated as safety issue: Yes]

An adverse experience (AE) is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the vaccine. Any worsening of a preexisting condition which is temporally associated with the use of the vaccine is also an AE. Only injection-site AEs in the arm that received V503 vaccination were reported for this endpoint.

- Percentage of Participants With a Repevax™ Injection-site Adverse Experience [Time Frame: Day 1 through Day 5 following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination] [Designated as safety issue: Yes]

  For the Concomitant Vaccination group, injection-site AEs are reported following Day 1 vaccination; for the Non-concomitant Vaccination group, injection-site AEs are reported following Month 1 vaccination. An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the vaccine. Any worsening of a preexisting condition which is temporally associated with the use of the vaccine is also an AE. Only injection-site AEs in the arm that received Repevax™ vaccination were reported for this endpoint.

- Percentage of Participants With Maximum Temperature >=37.8 °C (>=100.0 °F) (Oral or Oral Equivalent) [Time Frame: Up to 5 days following the Day 1 and Month 1 vaccination / visit] [Designated as safety issue: Yes]

  For the Concomitant Vaccination group, temperatures were collected after the Day 1 vaccination and the Month 1 visit; for the Non-concomitant Vaccination group, temperatures were collected after the Day 1 vaccination and the Month 1 vaccination.

- Percentage of Participants With a Systemic Adverse Experience [Time Frame: Up to 15 days following the Day 1 and Month 1 vaccination / visit] [Designated as safety issue: Yes]

  For the Concomitant Vaccination group, systemic AEs were collected after the Day 1 vaccination and the Month 1 visit; for the Non-concomitant Vaccination group, systemic AEs were collected after the Day 1 vaccination and the Month 1 vaccination. An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body that is temporally associated with the use of the study vaccine, whether or not considered related to the use of the vaccine. Any worsening of a preexisting condition which is temporally associated with the use of the vaccine is also an adverse experience. A systemic AE was an AE that was not associated with the injection site.

- Percentage of Participants Who Achieve Acceptable Titers of Anti-Diphtheria and Anti-Tetanus Antibody [Time Frame: 4 weeks following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination] [Designated as safety issue: No]

  For the Concomitant Vaccination group, serum samples were collected 4 weeks after the Day 1 vaccination; for the Non-concomitant Vaccination group, serum samples were collected 4 weeks after the Month 1 vaccination. Titers of neutralizing antibody to diphtheria toxin were measured using a cell-based Diphtheria Micrometabolic Inhibition assay. Serum titers of neutralizing antibody to tetanus toxin were measured using an enzyme immunoassay. The lower limits of quantitation of the assays was 0.01 International Units (IU)/mL and 0.04 IU/mL, respectively. Acceptable titers refer to the World Health Organization-defined protective titer of >=0.1 IU/mL.

- Geometric Mean Titers of Pertussis Antibody Responses [Time Frame: 4 weeks following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination] [Designated as safety issue: No]

  For the Concomitant Vaccination group, serum samples were collected 4 weeks after the Day 1 vaccination; for the Non-concomitant Vaccination group, serum samples were collected 4 weeks after the Month 1 vaccination. Titers of anti-pertussis toxin (PT), anti-filamentous hemagglutinin (FHA), anti-pertactin (PRN), and anti-fimbriae 2/3 (FM 2/3) antibodies were measured using enzyme-linked immunosorbent assays. Titers are expressed as enzyme-linked immunoassay units/mL (ELU/mL).

- Percentage of Participants Who Achieve Acceptable Titers of Anti-Poliovirus Antibody [Time Frame: 4 weeks following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination] [Designated as safety issue: No]

  For the Concomitant Vaccination group, serum samples were collected 4 weeks after the Day 1 vaccination; for the Non-concomitant Vaccination group, serum samples were collected 4 weeks after the Month 1 vaccination. Titers of neutralizing antibody to poliovirus type 1, 2, and 3 were measured using a microneutralization assay. Serial dilutions of sera were incubated with type-specific standard poliovirus and sensitive cells. Neutralization of the virus was measured by cell staining. Acceptable titers were defined as neutralization at >=1:8 dilution of serum.

Secondary Outcome Measures:

- Percentage of Participants Who Seroconvert for Each of the HPV Types [Time Frame: Month 7] [Designated as safety issue: No]

  Blood was drawn at Month 7 and assayed to determine whether or not a participant had achieved seroconversion for the HPV types. The lower limit of the titer (milli Merck U/mL) considered seropositive was as follows: HPV Type 6: >=30, HPV Type 11: >=16; HPV Type 16: >=20, HPV Type 18: >=24, HPV Type 31: >=10, HPV Type 33: >=8, HPV Type 45: >=8, HPV Type 52: >=8, and HPV Type 58: >=8.

Enrollment:	1054
Study Start Date:	April 2010
Study Completion Date:	June 2011
Primary Completion Date:	June 2011 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Concomitant Vaccination V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1	Biological: V503 Vaccine V503 (Multivalent HPV L1 VLP vaccine) given as a 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 Biological: REPEVAX™ (Concomitant) REPEVAX™ given as a single 0.5 mL intramuscular injection at Day 1
Experimental: Non-concomitant Vaccination V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1	Biological: V503 Vaccine V503 (Multivalent HPV L1 VLP vaccine) given as a 0.5 mL intramuscular injection at Day 1, Month 2, and Month 6 Biological: REPEVAX™ (Non-concomitant) REPEVAX™ given as a single 0.5 mL intramuscular injection at Month 1

Eligibility

Ages Eligible for Study:	11 Years to 15 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	Yes

Criteria

Inclusion criteria:

- Participant is in good health
- Participant's parent/legal guardian can read, understand, and complete the vaccination report card
- Participant is not sexually active and does not plan on becoming sexually active during the study
- Participant has received a documented full primary immunization series against diphtheria, tetanus, pertussis, and poliovirus (inactivated and/or oral poliovirus), but not in the last 5 years. There must be a 5-year interval from a prior vaccination containing any one of these vaccine antigens.

Exclusion Criteria:

- Participant has a known allergy to any vaccine component of V503 or REPEVAX™
- Participant has had a severe reaction affecting the brain (e.g., evolving encephalopathy) within 7 days after a previous dose of a pertussis-containing vaccine
- Participant has had a progressive severe illness affecting the brain after a previous dose of tetanus, diphtheria, poliovirus or a component pertussis combination (acellular and whole cell) vaccine
- Participant ever had Guillain-Barré syndrome or brachial neuritis following a previous dose of a tetanus-containing vaccine
- Participant has a condition that is a contraindication to vaccination as indicated in the most up to date package inserts of REPEVAX™
- Participant has a history of severe allergic reaction that required medical intervention
- Participant has hemophilia, thrombocytopenia, is receiving anticoagulation therapy and/or has any coagulation disorder that would contraindicate intramuscular injections
- Participant is concurrently enrolled in clinical studies of investigational agents
- Female participant is pregnant
- Participant has donated blood within 1 week prior to first study vaccination, or intends to donate during the study
- Participant is immunocompromised, immunodeficient, or has an autoimmune condition
- Participant has had a splenectomy
- Participant has received immunosuppressive therapies in the prior year

- Participant has received immune globulin product or blood-derived product in the last 3 months
- Participant has received inactivated vaccine(s) within 14 days or live vaccine(s) within 21 days of first study vaccination
- Participant has received a marketed HPV vaccine or has participated in an HPV vaccine trial
- Participant has received a tetanus, diphtheria, pertussis, or poliovirus (inactivated and/or oral poliovirus) vaccination within the last 5 years
- Participant has a fever ≥100°F within 24 hours of vaccination
- Participant has any history or current condition, therapy, lab abnormality, or other circumstance such that it is not in the best interest of the participant to participate
- Participant and parent/legal guardian are unable to give assent/consent
- Participant is unlikely to adhere to the study procedures or is planning to relocate during the study
- Participant has recent history of illicit drug or alcohol abuse
- Participant has a history of HPV

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT01073293

Sponsors and Collaborators

Merck Sharp & Dohme Corp.

Investigators

Study Director: Medical Director Merck Sharp & Dohme Corp.

More Information

Publications:

Kosalaraksa P, Mehlsen J, Vesikari T, Forstén A, Helm K, Van Damme P, Joura EA, Ciprero K, Maansson R, Luxembourg A, Sobanjo-ter Meulen A. An open-label, randomized study of a 9-valent human papillomavirus vaccine given concomitantly with diphtheria, tetanus, pertussis and poliomyelitis vaccines to healthy adolescents 11-15 years of age. Pediatr Infect Dis J. 2015 Jun;34(6):627-34. doi: 10.1097/INF.0000000000000694.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT01073293 History of Changes
Other Study ID Numbers:	V503-007 2010_512
Study First Received:	February 19, 2010
Results First Received:	December 12, 2014
Last Updated:	May 11, 2015
Health Authority:	Belgium: Federal Agency for Medicines and Health Products, FAMHP

Additional relevant MeSH terms:
Papillomavirus Infections
DNA Virus Infections
Tumor Virus Infections
Virus Diseases

ClinicalTrials.gov processed this record on April 20, 2016

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First received: February 19, 2010
Last updated: May 11, 2015
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History of Changes

Results First Received: December 12, 2014

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Prevention
Condition:	Papillomavirus Infections
Interventions:	Biological: V503 Vaccine Biological: REPEVAX™ (Concomitant) Biological: REPEVAX™ (Non-concomitant)

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description

Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Participant Flow: Overall Study

	Concomitant Vaccination	Non-concomitant Vaccination
STARTED	**526**	**528**
COMPLETED	**521**	**517**
NOT COMPLETED	**5**	**11**
Lost to Follow-up	**0**	**1**
Withdrawal by Subject	**5**	**10**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1
Total	Total of all reporting groups

Baseline Measures

	Concomitant Vaccination	Non-concomitant Vaccination	Total
Number of Participants [units: participants]	**526**	**528**	**1054**
Age [units: Years] Mean (Standard Deviation)	**12.4 (1.2)**	**12.4 (1.2)**	**12.4 (1.2)**
Gender [units: Participants]			
Female	**264**	**264**	**528**

Male	**262**	**264**	**526**

Outcome Measures

Hide All Outcome Measures

1. Primary: Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503 [Time Frame: 4 weeks following Month 6 vaccination]

Measure Type	Primary
Measure Title	Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503
Measure Description	Serum antibody titers for HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 were measured using a competitive Luminex immunoassay. Titers are reported in milli Merck Units/mL.
Time Frame	4 weeks following Month 6 vaccination
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The per-protocol population included participants who received all study vaccinations, were seronegative to HPV on Day 1, and had serum samples available for evaluation of the endpoint

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Measured Values

	Concomitant Vaccination	**Non-concomitant Vaccination**
Number of Participants Analyzed [units: participants]	**525**	**528**
Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503 [units: milli Merck Units/mL] Geometric Mean (Full Range)		
Anti-HPV 6: n=477, 461	**1637.9 (8.0 to 24405.0)**	**1725.0 (173.0 to 12040.0)**
Anti-HPV 11: n=479, 462	**1170.3 (84.0 to 13438.0)**	**1212.6 (153.0 to 9816.0)**
Anti-HPV 16: n=489, 479	**6529.4 (689.0 to 76781.0)**	**6940.6 (841.0 to 49390.0)**

Anti-HPV18: n=486, 475	**1854.1 (81.0 to 38887.0)**	**1954.8 (49.0 to 15582.0)**
Anti-HPV 31: n=485, 473	**1646.2 (88.0 to 22848.0)**	**1750.6 (118.0 to 32822.0)**
Anti-HPV 33: n=487, 478	**823.8 (54.0 to 6563.0)**	**915.5 (110.0 to 7058.0)**
Anti-HPV 45: n=489, 478	**658.2 (28.0 to 14131.0)**	**675.6 (29.0 to 8725.0)**
Anti-HPV 52: n=490, 479	**965.4 (45.0 to 11730.0)**	**1015.3 (79.0 to 14392.0)**
Anti-HPV 58: n=484, 469	**1188.8 (102.0 to 13681.0)**	**1334.8 (106.0 to 14752.0)**

Statistical Analysis 1 for Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Fold difference in GMT [5]	0.95
95% Confidence Interval	0.86 to 1.05

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-HPV 6
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.5
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001

Fold difference in GMT [5]	0.97
95% Confidence Interval	0.87 to 1.07

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-HPV 11
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.5
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Fold difference in GMT [5]	0.94
95% Confidence Interval	0.85 to 1.04

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-HPV 16
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.5
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 4 for Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Fold difference in GMT [5]	0.95
95% Confidence Interval	0.84 to 1.07

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-HPV 18
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.5
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 5 for Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Fold difference in GMT [5]	0.94
95% Confidence Interval	0.84 to 1.06

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-HPV 31
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.5
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:

	No text entered.

Statistical Analysis 6 for Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Fold difference in GMT [5]	0.90
95% Confidence Interval	0.81 to 1.00

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-HPV 33
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.5
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 7 for Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Fold difference in GMT [5]	0.97
95% Confidence Interval	0.86 to 1.11

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-HPV 45
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.5
[3]	Other relevant method information, such as adjustments or degrees of freedom:

	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 8 for Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Fold difference in GMT [5]	0.95
95% Confidence Interval	0.85 to 1.06

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-HPV 52
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.5
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 9 for Geometric Mean Titers (GMTs) of the Antibody Response to Each of the Human Papillomavirus (HPV) Types Contained in V503

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Fold difference in GMT [5]	0.89
95% Confidence Interval	0.80 to 0.99

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-HPV 58

[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.5
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

2. Primary: Percentage of Participants With a V503 Injection-site Adverse Experience [Time Frame: Day 1 through Day 5 following Day 1 vaccination]

Measure Type	Primary
Measure Title	Percentage of Participants With a V503 Injection-site Adverse Experience
Measure Description	An adverse experience (AE) is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the vaccine. Any worsening of a preexisting condition which is temporally associated with the use of the vaccine is also an AE. Only injection-site AEs in the arm that received V503 vaccination were reported for this endpoint.
Time Frame	Day 1 through Day 5 following Day 1 vaccination
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The population analyzed included all vaccinated participants with follow-up

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Measured Values

	Concomitant Vaccination	**Non-concomitant Vaccination**
Number of Participants Analyzed [units: participants]	**524**	**527**
Percentage of Participants With a V503 Injection-site Adverse Experience [units: Percentage of participants]	**63.4**	**62.8**

No statistical analysis provided for Percentage of Participants With a V503 Injection-site Adverse Experience

3. Primary: Percentage of Participants With a Repevax™ Injection-site Adverse Experience [Time Frame: Day 1 through Day 5 following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination]

Measure Type	Primary
Measure Title	Percentage of Participants With a Repevax™ Injection-site Adverse Experience
Measure Description	For the Concomitant Vaccination group, injection-site AEs are reported following Day 1 vaccination; for the Non-concomitant Vaccination group, injection-site AEs are reported following Month 1 vaccination. An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the vaccine. Any worsening of a preexisting condition which is temporally associated with the use of the vaccine is also an AE. Only injection-site AEs in the arm that received Repevax™ vaccination were reported for this endpoint.
Time Frame	Day 1 through Day 5 following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The population analyzed included all vaccinated participants with follow-up

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Measured Values

	Concomitant Vaccination	**Non-concomitant Vaccination**
Number of Participants Analyzed [units: participants]	**525**	**520**
Percentage of Participants With a Repevax™ Injection-site Adverse Experience [units: Percentage of participants]	**88.0**	**84.6**

No statistical analysis provided for Percentage of Participants With a Repevax™ Injection-site Adverse Experience

4. Primary: Percentage of Participants With Maximum Temperature >=37.8 °C (>=100.0 °F) (Oral or Oral Equivalent) [Time Frame: Up to 5 days following the Day 1 and Month 1 vaccination / visit]

Measure Type	Primary
Measure Title	Percentage of Participants With Maximum Temperature >=37.8 °C (>=100.0 °F) (Oral or Oral Equivalent)

Measure Description	For the Concomitant Vaccination group, temperatures were collected after the Day 1 vaccination and the Month 1 visit; for the Non-concomitant Vaccination group, temperatures were collected after the Day 1 vaccination and the Month 1 vaccination.
Time Frame	Up to 5 days following the Day 1 and Month 1 vaccination / visit
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The population analyzed included all vaccinated participants with follow-up

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Measured Values

	Concomitant Vaccination	**Non-concomitant Vaccination**
Number of Participants Analyzed [units: participants]	**524**	**525**
Percentage of Participants With Maximum Temperature >=37.8 °C (>=100.0 °F) (Oral or Oral Equivalent) [units: Percentage of participants]	**8.8**	**8.4**

No statistical analysis provided for Percentage of Participants With Maximum Temperature >=37.8 °C (>=100.0 °F) (Oral or Oral Equivalent)

5. Primary: Percentage of Participants With a Systemic Adverse Experience [Time Frame: Up to 15 days following the Day 1 and Month 1 vaccination / visit]

Measure Type	Primary
Measure Title	Percentage of Participants With a Systemic Adverse Experience
Measure Description	For the Concomitant Vaccination group, systemic AEs were collected after the Day 1 vaccination and the Month 1 visit; for the Non-concomitant Vaccination group, systemic AEs were collected after the Day 1 vaccination and the Month 1 vaccination. An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body that is temporally associated with the use of the study vaccine, whether or not considered related to the use of the vaccine. Any worsening of a preexisting condition which is temporally associated with the use of the vaccine is also an adverse experience. A systemic AE was an AE that was not associated with the injection site.
Time Frame	Up to 15 days following the Day 1 and Month 1 vaccination / visit
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or

another method. Also provides relevant details such as imputation technique, as appropriate.
The population analyzed included all vaccinated participants with follow-up

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Measured Values

	Concomitant Vaccination	**Non-concomitant Vaccination**
Number of Participants Analyzed [units: participants]	**525**	**527**
Percentage of Participants With a Systemic Adverse Experience [units: Percentage of participants]	**48.6**	**48.6**

No statistical analysis provided for Percentage of Participants With a Systemic Adverse Experience

6. Primary: Percentage of Participants Who Achieve Acceptable Titers of Anti-Diphtheria and Anti-Tetanus Antibody [Time Frame: 4 weeks following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination]

Measure Type	Primary
Measure Title	Percentage of Participants Who Achieve Acceptable Titers of Anti-Diphtheria and Anti-Tetanus Antibody
Measure Description	For the Concomitant Vaccination group, serum samples were collected 4 weeks after the Day 1 vaccination; for the Non-concomitant Vaccination group, serum samples were collected 4 weeks after the Month 1 vaccination. Titers of neutralizing antibody to diphtheria toxin were measured using a cell-based Diphtheria Micrometabolic Inhibition assay. Serum titers of neutralizing antibody to tetanus toxin were measured using an enzyme immunoassay. The lower limits of quantitation of the assays was 0.01 International Units (IU)/mL and 0.04 IU/mL, respectively. Acceptable titers refer to the World Health Organization-defined protective titer of >=0.1 IU/mL.
Time Frame	4 weeks following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The per-protocol population included participants who received vaccination and had serum samples available for evaluation of the endpoint

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1

Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Measured Values

	Concomitant Vaccination	Non-concomitant Vaccination
Number of Participants Analyzed [units: participants]	**525**	**528**
Percentage of Participants Who Achieve Acceptable Titers of Anti-Diphtheria and Anti-Tetanus Antibody [units: Percentage of participants] Number (95% Confidence Interval)		
Anti-diphtheria titer >=0.1 IU/mL: n=505, 474	**99.8 (98.9 to 100)**	**99.6 (98.5 to 99.9)**
Anti-tetanus titer >=0.1 IU/mL: n=504, 472	**99.6 (98.6 to 100)**	**99.6 (98.5 to 99.9)**

Statistical Analysis 1 for Percentage of Participants Who Achieve Acceptable Titers of Anti-Diphtheria and Anti-Tetanus Antibody

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	Miettinen and Nurminen
P Value [4]	<0.001
Difference in percentage [5]	0.2
95% Confidence Interval	-0.7 to 1.4

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-diphtheria titer >=0.1 IU/mL
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the percentage difference is greater than -10
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percentage of Participants Who Achieve Acceptable Titers of Anti-Diphtheria and Anti-Tetanus Antibody

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes

Method [3]	Miettinen and Nurminen
P Value [4]	<0.001
Difference in percentage [5]	0.0
95% Confidence Interval	-1.1 to 1.2

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-tetanus titer >=0.1 IU/mL
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the percentage difference is greater than -10
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

7. Primary: Geometric Mean Titers of Pertussis Antibody Responses [Time Frame: 4 weeks following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination]

Measure Type	Primary
Measure Title	Geometric Mean Titers of Pertussis Antibody Responses
Measure Description	For the Concomitant Vaccination group, serum samples were collected 4 weeks after the Day 1 vaccination; for the Non-concomitant Vaccination group, serum samples were collected 4 weeks after the Month 1 vaccination. Titers of anti-pertussis toxin (PT), anti-filamentous hemagglutinin (FHA), anti-pertactin (PRN), and anti-fimbriae 2/3 (FM 2/3) antibodies were measured using enzyme-linked immunosorbent assays. Titers are expressed as enzyme-linked immunoassay units/mL (ELU/mL).
Time Frame	4 weeks following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The per-protocol population included participants who received vaccination and had serum samples available for evaluation of the endpoint

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant

	arm at Month 1

Measured Values

	Concomitant Vaccination	Non-concomitant Vaccination
Number of Participants Analyzed [units: participants]	**525**	**528**
Geometric Mean Titers of Pertussis Antibody Responses [units: ELU/mL] Geometric Mean (95% Confidence Interval)		
Anti-PT: n=505, 473	**41.5 (38.4 to 44.9)**	**43.8 (40.4 to 47.5)**
Anti-FHA: n=505, 474	**188.1 (176.2 to 200.8)**	**190.6 (178.1 to 203.9)**
Anti-PRN: n=505, 474	**372.9 (334.8 to 415.2)**	**398.2 (356.3 to 445.0)**
Anti-FIM 2/3: n=505, 474	**378.2 (324.4 to 440.9)**	**423.6 (361.5 to 496.2)**

Statistical Analysis 1 for Geometric Mean Titers of Pertussis Antibody Responses

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Fold difference in GMT [5]	0.95
95% Confidence Interval	0.85 to 1.06

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-PT
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.67
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Geometric Mean Titers of Pertussis Antibody Responses

Groups [1]	All groups

Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Fold difference in GMT [5]	0.99
95% Confidence Interval	0.90 to 1.08

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-FHA
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.67
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Geometric Mean Titers of Pertussis Antibody Responses

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	<0.001
Difference in GMT [5]	0.94
95% Confidence Interval	0.80 to 1.09

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-PRN
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.67
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 4 for Geometric Mean Titers of Pertussis Antibody Responses

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	ANOVA
P Value [4]	0.005
Difference in GMT [5]	0.89
95% Confidence Interval	0.72 to 1.11

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Anti-FIM 2/3
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the lower limit of the 95% confidence interval for the fold difference is >0.67
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

8. Primary: Percentage of Participants Who Achieve Acceptable Titers of Anti-Poliovirus Antibody [Time Frame: 4 weeks following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination]

Measure Type	Primary
Measure Title	Percentage of Participants Who Achieve Acceptable Titers of Anti-Poliovirus Antibody
Measure Description	For the Concomitant Vaccination group, serum samples were collected 4 weeks after the Day 1 vaccination; for the Non-concomitant Vaccination group, serum samples were collected 4 weeks after the Month 1 vaccination. Titers of neutralizing antibody to poliovirus type 1, 2, and 3 were measured using a microneutralization assay. Serial dilutions of sera were incubated with type-specific standard poliovirus and sensitive cells. Neutralization of the virus was measured by cell staining. Acceptable titers were defined as neutralization at >=1:8 dilution of serum.
Time Frame	4 weeks following Day 1 (Concomitant) or Month 1 (Non-concomitant) vaccination
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The per-protocol population included participants who received vaccination and had serum samples available for evaluation of the endpoint

Reporting Groups

	Description

Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Measured Values

	Concomitant Vaccination	Non-concomitant Vaccination
Number of Participants Analyzed [units: participants]	**525**	**528**
Percentage of Participants Who Achieve Acceptable Titers of Anti-Poliovirus Antibody [units: Percentage of participants] Number (95% Confidence Interval)		
Poliovirus type 1: n=505, 474	**99.6 (98.4 to 100)**	**99.8 (98.7 to 100)**
Poliovirus type 2: n=505, 474	**99.6 (98.4 to 100)**	**99.8 (98.7 to 100)**
Poliovirus type 3: n=505, 474	**100 (99.1 to 100)**	**100 (99.1 to 100)**

Statistical Analysis 1 for Percentage of Participants Who Achieve Acceptable Titers of Anti-Poliovirus Antibody

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	Miettinen and Nurminen
P Value [4]	<0.001
Difference in percentage [5]	-0.2
95% Confidence Interval	-1.2 to 0.8

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Poliovirus type 1
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the difference is statistically less than 10 percentage points
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Percentage of Participants Who Achieve Acceptable Titers of Anti-Poliovirus Antibody

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	Miettinen and Nurminen
P Value [4]	<0.001
Difference in percentage [5]	-0.2
95% Confidence Interval	-1.2 to 0.8

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Poliovirus type 2
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the difference is statistically less than 10 percentage points
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[5]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Percentage of Participants Who Achieve Acceptable Titers of Anti-Poliovirus Antibody

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	Miettinen and Nurminen
P Value [4]	<0.001
Difference in percentage [5]	0.0
95% Confidence Interval	-0.8 to 0.8

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Poliovirus type 3
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Noninferiority of concomitant versus non-concomitant vaccination is demonstrated if the difference is statistically less than 10 percentage points
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

[5]	Other relevant estimation information:
	No text entered.

9. Secondary: Percentage of Participants Who Seroconvert for Each of the HPV Types [Time Frame: Month 7]

Measure Type	Secondary
Measure Title	Percentage of Participants Who Seroconvert for Each of the HPV Types
Measure Description	Blood was drawn at Month 7 and assayed to determine whether or not a participant had achieved seroconversion for the HPV types. The lower limit of the titer (milli Merck U/mL) considered seropositive was as follows: HPV Type 6: >=30, HPV Type 11: >=16; HPV Type 16: >=20, HPV Type 18: >=24, HPV Type 31: >=10, HPV Type 33: >=8, HPV Type 45: >=8, HPV Type 52: >=8, and HPV Type 58: >=8.
Time Frame	Month 7
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The per-protocol population included participants who received all study vaccinations, were seronegative to HPV on Day 1, and had serum samples available for evaluation of the endpoint

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm on Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Measured Values

	Concomitant Vaccination	**Non-concomitant Vaccination**
Number of Participants Analyzed [units: participants]	**525**	**528**
Percentage of Participants Who Seroconvert for Each of the HPV Types [units: Percentage of participants]		
Anti-HPV 6: n=477, 461	**99.8**	**100.0**
Anti-HPV 11: n=479, 462	**100.0**	**100.0**
Anti-HPV 16: n=489, 479	**100.0**	**100.0**
Anti-HPV 18: n=486, 475	**100.0**	**100.0**
Anti-HPV 31: n=485, 473	**100.0**	**100.0**
Anti-HPV 33: n=487, 478	**100.0**	**100.0**
Anti-HPV 45: n=489, 478	**100.0**	**100.0**

Anti-HPV 52: n=490, 479	**100.0**	**100.0**
Anti-HPV 58: n=484, 469	**100.0**	**100.0**

No statistical analysis provided for Percentage of Participants Who Seroconvert for Each of the HPV Types

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Serious adverse events: up to Month 7; Other adverse events: Day 1 through Day 5 following any vaccination for injection-site AEs and Day 1 through Day 15 following any vaccination for non-injection-site AEs
Additional Description	Adverse events were collected for all participants who received at least one dose of V503 and Repevax™

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Serious Adverse Events

	Concomitant Vaccination	**Non-concomitant Vaccination**
Total, serious adverse events		
# participants affected / at risk	**9/525 (1.71%)**	**7/527 (1.33%)**
General disorders		
Non-cardiac chest pain		
# participants affected / at risk	**1/525 (0.19%)**	**0/527 (0.00%)**
# events	**1**	**0**
Infections and infestations		
Appendiceal abscess		
# participants affected / at risk	**0/525 (0.00%)**	**1/527 (0.19%)**
# events	**0**	**1**
Appendicitis		
# participants affected / at risk	**1/525 (0.19%)**	**2/527 (0.38%)**
# events	**1**	**2**
Dengue fever		
# participants affected / at risk	**1/525 (0.19%)**	**0/527 (0.00%)**
# events	**1**	**0**
Pyelonephritis		
# participants affected / at risk	**1/525 (0.19%)**	**0/527 (0.00%)**
# events	**1**	**0**
Pyelonephritis acute		

# participants affected / at risk	0/525 (0.00%)	1/527 (0.19%)
# events	0	1
Viral pharyngitis		
# participants affected / at risk	1/525 (0.19%)	0/527 (0.00%)
# events	1	0
Injury, poisoning and procedural complications		
Forearm fracture		
# participants affected / at risk	2/525 (0.38%)	0/527 (0.00%)
# events	2	0
Road traffic accident		
# participants affected / at risk	1/525 (0.19%)	0/527 (0.00%)
# events	1	0
Thermal burn		
# participants affected / at risk	0/525 (0.00%)	1/527 (0.19%)
# events	0	1
Musculoskeletal and connective tissue disorders		
Fibromyalgia		
# participants affected / at risk	1/525 (0.19%)	0/527 (0.00%)
# events	1	0
Nervous system disorders		
Syncope		
# participants affected / at risk	0/525 (0.00%)	1/527 (0.19%)
# events	0	1
Psychiatric disorders		
Eating disorder		
# participants affected / at risk	0/525 (0.00%)	1/527 (0.19%)
# events	0	1

Other Adverse Events

Hide Other Adverse Events

Time Frame	Serious adverse events: up to Month 7; Other adverse events: Day 1 through Day 5 following any vaccination for injection-site AEs and Day 1 through Day 15 following any vaccination for non-injection-site AEs
Additional Description	Adverse events were collected for all participants who received at least one dose of V503 and Repevax™

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month 2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Day 1
Non-concomitant Vaccination	V503 given as a 0.5 mL intramuscular injection in the deltoid muscle of the non-dominant arm on Day 1, Month

	2, and Month 6, and Repevax™ given as a 0.5 mL intramuscular injection in the deltoid muscle of the dominant arm at Month 1

Other Adverse Events

	Concomitant Vaccination	Non-concomitant Vaccination
Total, other (not including serious) adverse events		
# participants affected / at risk	**509/525 (96.95%)**	**505/527 (95.83%)**
Gastrointestinal disorders		
Abdominal pain upper		
# participants affected / at risk	**19/525 (3.62%)**	**28/527 (5.31%)**
# events	**22**	**28**
Nausea		
# participants affected / at risk	**39/525 (7.43%)**	**36/527 (6.83%)**
# events	**42**	**46**
General disorders		
Injection-site erythema		
# participants affected / at risk	**228/525 (43.43%)**	**185/527 (35.10%)**
# events	**351**	**290**
Injection-site pain		
# participants affected / at risk	**501/525 (95.43%)**	**493/527 (93.55%)**
# events	**1500**	**1463**
Injection-site pruritus		
# participants affected / at risk	**28/525 (5.33%)**	**27/527 (5.12%)**
# events	**31**	**36**
Injection-site swelling		
# participants affected / at risk	**295/525 (56.19%)**	**230/527 (43.64%)**
# events	**528**	**403**
Pyrexia		
# participants affected / at risk	**88/525 (16.76%)**	**71/527 (13.47%)**
# events	**105**	**86**
Infections and infestations		
Nasopharyngitis		
# participants affected / at risk	**18/525 (3.43%)**	**32/527 (6.07%)**
# events	**18**	**39**
Upper respiratory tract infection		
# participants affected / at risk	**23/525 (4.38%)**	**27/527 (5.12%)**
# events	**24**	**31**
Nervous system disorders		
Headache		
# participants affected / at risk	**167/525 (31.81%)**	**140/527 (26.57%)**
# events	**265**	**200**
Respiratory, thoracic and mediastinal disorders		
Oropharyngeal pain		
# participants affected / at risk	**23/525 (4.38%)**	**30/527 (5.69%)**

# events	25	32

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☑ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Restriction Description: The sponsor must have the opportunity to review all proposed abstracts, manuscripts, or presentations regarding this study 60 days prior to submission for publication/presentation. Any information identified by the sponsor as confidential must be deleted prior to submission.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme Corp.
phone: 1-800-672-6372
e-mail: ClinicalTrialsDisclosure@merck.com

Publications of Results:

Kosalaraksa P, Mehlsen J, Vesikari T, Forstén A, Helm K, Van Damme P, Joura EA, Ciprero K, Maansson R, Luxembourg A, Sobanjo-ter Meulen A. An open-label, randomized study of a 9-valent human papillomavirus vaccine given concomitantly with diphtheria, tetanus, pertussis and poliomyelitis vaccines to healthy adolescents 11-15 years of age. Pediatr Infect Dis J. 2015 Jun;34(6):627-34. doi: 10.1097/INF.0000000000000694.

Responsible Party: Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier: NCT01073293 History of Changes
Other Study ID Numbers: V503-007
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Study First Received: February 19, 2010
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Health Authority: Belgium: Federal Agency for Medicines and Health Products, FAMHP

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