ZOSTAVAX™ Administered Concomitantly With PNEUMOVAX™ 23 (V211-012)(COMPLETED)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

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

ClinicalTrials.gov Identifier:
NCT00535730

First received: September 21, 2007
Last updated: April 1, 2015
Last verified: April 2015
History of Changes

Purpose

The purpose of this study is to determine whether Zoster Vaccine Live and Pneumococcal Vaccine, polyvalent are as well tolerated and immunogenic when the vaccines are given together (in different body sites), as when they are given alone, in adults 60 years of age and older.

Condition	Intervention	Phase
Herpes Zoster Pneumococcal Infection	Biological: Zoster Vaccine, Live, (Oka-Merck), ZOSTAVAX™ Biological: Comparator: placebo (concomitant-vaccine matched) Biological: Pneumococcal Vaccine, Polyvalent (23-valent), PNEUMOVAX™ 23	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator)
Primary Purpose: Prevention

Official Title: A Phase III Double-Blind, Randomized, Multicenter Study to Evaluate the Safety, Tolerability, and Immunogenicity of ZOSTAVAX™ Administered Concomitantly Versus Nonconcomitantly With PNEUMOVAX™ 23 in Subjects 60 Years of Age and Older

Resource links provided by NLM:

MedlinePlus related topics: Pneumococcal Infections Shingles

Drug Information available for: Heptavalent pneumococcal conjugate vaccine Herpes Zoster Vaccine Pneumococcal Vaccines

U.S. FDA Resources

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

Primary Outcome Measures:

- Geometric Mean Titer (GMT) of Varicella-zoster Virus (VZV) Antibody Responses at 4 Weeks Postvaccination [Time Frame: 4 weeks postvaccination] [Designated as safety issue: No]

  GMT of the VZV antibody responses at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 and those who receive ZOSTAVAX™ and PNEUMOVAX™ 23 nonconcomitantly. *gpELISA = glycoprotein enzyme-linked immunosorbent assay

- Geometric Mean Fold Rise (GMFR) of the Varicella-zoster Virus (VZV) Antibody Responses From Day 1 to 4 Weeks Postvaccination. [Time Frame: Four weeks postvaccination] [Designated as safety issue: No]

  GMFR of the VZV antibody response from prevaccination to Week 4 postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23. gpELISA = glycoprotein enzyme-linked immunosorbent assay.

- Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 3 Antibody Response at 4 Weeks Postvaccination. [Time Frame: Four weeks postvaccination] [Designated as safety issue: No]

  GMT of the PnPs serotype 3 antibody response at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 and those who receive ZOSTAVAX™ and PNEUMOVAX™ 23 nonconcomitantly.

- Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 14 Antibody Response at 4 Weeks Postvaccination. [Time Frame: Four weeks postvaccination] [Designated as safety issue: No]

  GMT of the PnPs serotype 14 antibody response at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 and those who receive ZOSTAVAX™ and PNEUMOVAX™ 23 nonconcomitantly.

- Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 19A Antibody Response at 4 Weeks Postvaccination. [Time Frame: Four weeks postvaccination] [Designated as safety issue: No]

  GMT of the PnPs serotype 19A antibody response at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 and those who receive ZOSTAVAX™ and PNEUMOVAX™ 23 nonconcomitantly.

- Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 22F Antibody Response at 4 Weeks Postvaccination. [Time Frame: Four weeks postvaccination] [Designated as safety issue: No]

  GMT of the PnPs serotype 22F antibody response at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 and those who receive ZOSTAVAX™ and PNEUMOVAX™ 23 nonconcomitantly.

Secondary Outcome Measures:

- Safety and Tolerability of Both Vaccines When Administered Concomitantly. [Time Frame: Eight weeks postvaccination] [Designated as safety issue: Yes]

  All adverse events were analyzed including serious adverse events; injection-site adverse events; Vaccination Report Card prompted systemic adverse events, including varicella-like rashes or herpes zoster-like rashes; all other systemic adverse events.

Enrollment:	473
Study Start Date:	June 2007
Study Completion Date:	February 2008
Primary Completion Date:	February 2008 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Placebo Comparator: 1 Placebo Comparator	Biological: Zoster Vaccine, Live, (Oka-Merck), ZOSTAVAX™ 0.65 mL injection Zoster Vaccine, Live, (Oka-Merck) over 4 week vaccination period Other Name: ZOSTAVAX™ Biological: Comparator: placebo (concomitant-vaccine matched) Pneumococcal Vaccine, Polyvalent (23-valent) 0.5 mL Placebo injection over 4 week vaccination period.
Experimental: 2 vaccine	Biological: Zoster Vaccine, Live, (Oka-Merck), ZOSTAVAX™ 0.65 mL injection Zoster Vaccine, Live, (Oka-Merck) over 4 week vaccination period Other Name: ZOSTAVAX™ Biological: Pneumococcal Vaccine, Polyvalent (23-valent), PNEUMOVAX™ 23

	Pneumococcal Vaccine, Polyvalent (23-valent) 0.5 mL injection over 4 week vaccination period. Other Name: PNEUMOVAX™ 23

Eligibility

Ages Eligible for Study: 60 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: Yes

Criteria

Inclusion Criteria:

- 60 years of age or older
- Stable underlying conditions
- Postmenopausal if female
- Afebrile

Exclusion Criteria:

- Previously vaccinated with either vaccine
- Immune deficiency
- History of allergy to components in either vaccine
- Concomitant antiviral therapy

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: NCT00535730

Sponsors and Collaborators

Merck Sharp & Dohme Corp.

Investigators

Study Director: Medical Monitor Merck Sharp & Dohme Corp.

More Information

Publications:

MacIntyre CR, Egerton T, McCaughey M, Parrino J, Campbell BV, Su SC, Pagnoni MF, Stek JE, Xu J, Annunziato PW, Chan IS, Silber JL. Concomitant administration of zoster and pneumococcal vaccines in adults ≥60 years old. Hum Vaccin. 2010 Nov;6(11):894-902. Epub 2010 Nov 1.

Responsible Party: Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier: NCT00535730 History of Changes
Other Study ID Numbers: V211-012 2007_592
Study First Received: September 21, 2007
Results First Received: January 21, 2009
Last Updated: April 1, 2015
Health Authority: Germany: Federal Institute for Drugs and Medical Devices

Additional relevant MeSH terms:

Herpes Zoster
Pneumococcal Infections
Gram-Positive Bacterial Infections
Herpesviridae Infections

Bacterial Infections
DNA Virus Infections
Streptococcal Infections
Virus Diseases

ClinicalTrials.gov processed this record on April 20, 2016

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ClinicalTrials.gov Identifier:
NCT00535730

First received: September 21, 2007
Last updated: April 1, 2015
Last verified: April 2015
History of Changes

Results First Received: January 21, 2009

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Prevention
Conditions:	Herpes Zoster Pneumococcal Infection
Interventions:	Biological: Zoster Vaccine, Live, (Oka-Merck), ZOSTAVAX™ Biological: Comparator: placebo (concomitant-vaccine matched) Biological: Pneumococcal Vaccine, Polyvalent (23-valent), PNEUMOVAX™ 23

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

Phase III

First subject enrolled on 18-Jun-2007.

Last subject enrolled on 05-Dec-2007.

The last subject's last visit was 11-Feb-2008.

The study was conducted at 18 study centers throughout Canada, Australia, and Europe.

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
Nonconcomitant Group	Subjects were administered PNEUMOVAX™ 23 intramuscularly on Day 1 followed by ZOSTAVAX™ subcutaneously on Week 4
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1

Participant Flow: Overall Study

	Nonconcomitant Group	Concomitant Group
STARTED	**236**	**237** [1]
COMPLETED	**234**	**230**
NOT COMPLETED	**2**	**7**
Adverse Event	**1**	**1**
Lost to Follow-up	**0**	**1**
Physician Decision	**0**	**1**
Protocol Violation	**1**	**0**
Withdrawal by Subject	**0**	**4**

[1] Two subjects were allocated but not vaccinated making the number of subjects vaccinated 235

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
Nonconcomitant Group	Subjects were administered PNEUMOVAX™ 23 intramuscularly on Day 1 followed by ZOSTAVAX™ subcutaneously on Week 4
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1
Total	Total of all reporting groups

Baseline Measures

	Nonconcomitant Group	Concomitant Group	Total
Number of Participants			

[units: participants]	**236**	**235**	**471**
Age [units: years] Mean (Standard Deviation)	**66.0 (5.6)**	**66.3 (5.6)**	**66.2 (5.6)**
Gender [units: participants]			
Female	**135**	**138**	**273**
Male	**101**	**97**	**198**
Race/Ethnicity, Customized [units: participants]			
Asian	**1**	**1**	**2**
Black or African American	**0**	**1**	**1**
White	**235**	**233**	**468**

Outcome Measures

Hide All Outcome Measures

1. Primary: Geometric Mean Titer (GMT) of Varicella-zoster Virus (VZV) Antibody Responses at 4 Weeks Postvaccination [Time Frame: 4 weeks postvaccination]

Measure Type	Primary
Measure Title	Geometric Mean Titer (GMT) of Varicella-zoster Virus (VZV) Antibody Responses at 4 Weeks Postvaccination
Measure Description	GMT of the VZV antibody responses at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 and those who receive ZOSTAVAX™ and PNEUMOVAX™ 23 nonconcomitantly. *gpELISA = glycoprotein enzyme-linked immunosorbent assay
Time Frame	4 weeks postvaccination
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.
Analysis was per protocol. The following protocol violations resulted in exclusion of subjects from analysis: receipt of prohibited medications; vaccine temperature compromised prior to administration; excluded medical condition; samples collected outside of Statistical Analysis Plan specified time window; exposure to herpes zoster (HZ) or VZV.

Reporting Groups

	Description
Nonconcomitant Group	Subjects were administered PNEUMOVAX™ 23 intramuscularly on Day 1 followed by ZOSTAVAX™ subcutaneously on Week 4
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1

Measured Values

	Nonconcomitant	**Concomitant**

	Group	Group
Number of Participants Analyzed [units: participants]	**225**	**217**
Geometric Mean Titer (GMT) of Varicella-zoster Virus (VZV) Antibody Responses at 4 Weeks Postvaccination [units: gpELISA units*/mL] Geometric Mean (95% Confidence Interval)	**448.5 (400.3 to 502.4)**	**371.6 (328.7 to 420.0)**

Statistical Analysis 1 for Geometric Mean Titer (GMT) of Varicella-zoster Virus (VZV) Antibody Responses at 4 Weeks Postvaccination

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	longitudinal regression model
P Value [4]	0.244

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	The hypothesis was that the GMT of the VZV antibody responses at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 will be noninferior to that in subjects who receive ZOSTAVAX™ nonconcomitantly
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	The power for the noninferiority hypothesis of VZV antibody titers is 92%. The noninferiority margin is the lower bound of the two-sided 95% confidence interval on the VZV antibody GMT ratio[concomitant/nonconcomitant] being >0.67.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	Week 4 postvac, estimated responses, GMT ratio, 95% CI, p-value based on a longitudinal regression model adjusting for prevac titers and age (years)
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	The threshold for statistical significance is 0.025. There is no adjustment for multiple comparisons.

2. Primary: Geometric Mean Fold Rise (GMFR) of the Varicella-zoster Virus (VZV) Antibody Responses From Day 1 to 4 Weeks Postvaccination. [Time Frame: Four weeks postvaccination]

Measure Type	Primary
Measure Title	Geometric Mean Fold Rise (GMFR) of the Varicella-zoster Virus (VZV) Antibody Responses From Day 1 to 4 Weeks Postvaccination.
Measure Description	GMFR of the VZV antibody response from prevaccination to Week 4 postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23. gpELISA = glycoprotein enzyme-linked immunosorbent assay.
Time Frame	Four weeks postvaccination
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.

Analysis was per protocol. The following protocol violations resulted in exclusion of subjects from analysis: receipt of prohibited medications; vaccine temperature compromised prior to administration; excluded medical condition; samples collected outside of Statistical Analysis Plan specified time window; exposure to herpes zoster (HZ) or VZV.

Reporting Groups

	Description
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1

Measured Values

	Concomitant Group
Number of Participants Analyzed [units: participants]	**217**
Geometric Mean Fold Rise (GMFR) of the Varicella-zoster Virus (VZV) Antibody Responses From Day 1 to 4 Weeks Postvaccination. [units: gpELISA units/mL] Geometric Mean (95% Confidence Interval)	**1.9 (1.7 to 2.1)**

Statistical Analysis 1 for Geometric Mean Fold Rise (GMFR) of the Varicella-zoster Virus (VZV) Antibody Responses From Day 1 to 4 Weeks Postvaccination.

Groups [1]	Concomitant Group
Method [2]	t-test, 1 sided
P Value [3]	<0.001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	The hypothesis was that ZOSTAVAX™ elicits an acceptable VZV antibody response when administered concomitantly with PNEUMOVAX™ 23.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	The one-sided p-value for testing acceptability for GMFR is computed based on t-test. CI is computed based on the t distribution
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	The threshold for statistical significance is 0.025. There is no adjustment for multiple comparisons.

3. Primary: Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 3 Antibody Response at 4 Weeks Postvaccination. [Time Frame: Four weeks postvaccination]

Measure Type	Primary
Measure Title	Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 3 Antibody Response at 4 Weeks Postvaccination.
Measure Description	GMT of the PnPs serotype 3 antibody response at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 and those who receive ZOSTAVAX™ and PNEUMOVAX™ 23 nonconcomitantly.
Time Frame	Four weeks postvaccination

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.
Analysis was per protocol. The following protocol violations resulted in exclusion of subjects from analysis: prior receipt of a pneumococcal vaccine; receipt of prohibited medications; vaccine temperature compromised prior to administration; excluded medical condition; samples collected outside of Statistical Analysis Plan specified time window.

Reporting Groups

	Description
Nonconcomitant Group	Subjects were administered PNEUMOVAX™ 23 intramuscularly on Day 1 followed by ZOSTAVAX™ subcutaneously on Week 4
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1

Measured Values

	Nonconcomitant Group	**Concomitant Group**
Number of Participants Analyzed [units: participants]	**228**	**219**
Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 3 Antibody Response at 4 Weeks Postvaccination. [units: micrograms/mL] Geometric Mean (95% Confidence Interval)	**1.2 (1.1 to 1.4)**	**1.1 (1.0 to 1.2)**

Statistical Analysis 1 for Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 3 Antibody Response at 4 Weeks Postvaccination.

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

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	The hypothesis was that the GMT of the PnPs antibody response to serotype 3 at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 will be noninferior to those in subjects who receive ZOSTAVAX™ nonconcomitantly.
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	The power for the noninferiority hypothesis regarding PnPs antibody titer is ~99%. The noninferiority margin is the lower bound of the two-sided 95% confidence interval (CI) on the PnPs antibody GMT ratio [concomitant/nonconcomitant] being >05.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	Week 4 postvac, estimated responses, GMT ratio, 95% CI, p-value based on a longitudinal regression model adjusting for prevac titers and age (years)
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

The threshold for statistical significance is 0.025. There is no adjustment for multiple comparisons.

4. Primary: Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 14 Antibody Response at 4 Weeks Postvaccination. [Time Frame: Four weeks postvaccination]

Measure Type	Primary
Measure Title	Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 14 Antibody Response at 4 Weeks Postvaccination.
Measure Description	GMT of the PnPs serotype 14 antibody response at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 and those who receive ZOSTAVAX™ and PNEUMOVAX™ 23 nonconcomitantly.
Time Frame	Four weeks postvaccination
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.
Analysis was per protocol. The following protocol violations resulted in exclusion of subjects from analysis: prior receipt of a pneumococcal vaccine; receipt of prohibited medications; vaccine temperature compromised prior to administration; excluded medical condition; samples collected outside of Statistical Analysis Plan specified time window.

Reporting Groups

	Description
Nonconcomitant Group	Subjects were administered PNEUMOVAX™ 23 intramuscularly on Day 1 followed by ZOSTAVAX™ subcutaneously on Week 4
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1

Measured Values

	Nonconcomitant Group	**Concomitant Group**
Number of Participants Analyzed [units: participants]	**228**	**219**
Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 14 Antibody Response at 4 Weeks Postvaccination. [units: micrograms/mL] Geometric Mean (95% Confidence Interval)	**26.5 (22.9 to 30.8)**	**25.7 (21.8 to 30.3)**

Statistical Analysis 1 for Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 14 Antibody Response at 4 Weeks Postvaccination.

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

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	The hypothesis was that the GMT of the PnPs antibody responses to serotype 14 at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 will be noninferior to those in subjects who receive ZOSTAVAX™ nonconcomitantly.
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	The power for the noninferiority hypothesis regarding PnPs antibody titer is ~99%. The noninferiority margin is the lower bound of the two-sided 95% confidence interval (CI) on the PnPs antibody GMT ratio [concomitant/nonconcomitant] being >05.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	Week 4 postvac, estimated responses, GMT ratio, 95% CI, p-value based on a longitudinal regression model adjusting for prevac titers and age (years)
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	The threshold for statistical significance is 0.025. There is no adjustment for multiple comparisons.

5. Primary: Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 19A Antibody Response at 4 Weeks Postvaccination. [Time Frame: Four weeks postvaccination]

Measure Type	Primary
Measure Title	Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 19A Antibody Response at 4 Weeks Postvaccination.
Measure Description	GMT of the PnPs serotype 19A antibody response at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 and those who receive ZOSTAVAX™ and PNEUMOVAX™ 23 nonconcomitantly.
Time Frame	Four weeks postvaccination
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.
Analysis was per protocol. The following protocol violations resulted in exclusion of subjects from analysis: prior receipt of a pneumococcal vaccine; receipt of prohibited medications; vaccine temperature compromised prior to administration; excluded medical condition; samples collected outside of Statistical Analysis Plan specified time window.

Reporting Groups

	Description
Nonconcomitant Group	Subjects were administered PNEUMOVAX™ 23 intramuscularly on Day 1 followed by ZOSTAVAX™ subcutaneously on Week 4
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1

Measured Values

	Nonconcomitant Group	**Concomitant Group**
Number of Participants Analyzed [units: participants]	**228**	**219**

Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 19A Antibody Response at 4 Weeks Postvaccination. [units: micrograms/mL] Geometric Mean (95% Confidence Interval)	**10.5 (8.7 to 12.6)**	**10.5 (8.7 to 12.7)**

Statistical Analysis 1 for Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 19A Antibody Response at 4 Weeks Postvaccination.

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

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	The hypothesis was that the GMT of the PnPs antibody responses to serotype 19A at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 will be noninferior to those in subjects who receive ZOSTAVAX™ nonconcomitantly.
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	The power for the noninferiority hypothesis regarding PnPs antibody titer is ~99%. The noninferiority margin is the lower bound of the two-sided 95% confidence interval (CI) on the PnPs antibody GMT ratio [concomitant/nonconcomitant] being >05.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	Week 4 postvac, estimated responses, GMT ratio, 95% CI, p-value based on a longitudinal regression model adjusting for prevac titers and age (years)
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	The threshold for statistical significance is 0.025. There is no adjustment for multiple comparisons.

6. Primary: Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 22F Antibody Response at 4 Weeks Postvaccination. [Time Frame: Four weeks postvaccination]

Measure Type	Primary
Measure Title	Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 22F Antibody Response at 4 Weeks Postvaccination.
Measure Description	GMT of the PnPs serotype 22F antibody response at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 and those who receive ZOSTAVAX™ and PNEUMOVAX™ 23 nonconcomitantly.
Time Frame	Four weeks postvaccination
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.
Analysis was per protocol. The following protocol violations resulted in exclusion of subjects from analysis: prior receipt of a pneumococcal vaccine; receipt of prohibited medications; vaccine temperature compromised prior to administration; excluded medical condition; samples collected outside of Statistical Analysis Plan specified time window.

Reporting Groups

	Description
Nonconcomitant Group	Subjects were administered PNEUMOVAX™ 23 intramuscularly on Day 1 followed by ZOSTAVAX™ subcutaneously on Week 4
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1

Measured Values

	Nonconcomitant Group	Concomitant Group
Number of Participants Analyzed [units: participants]	**228**	**219**
Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 22F Antibody Response at 4 Weeks Postvaccination. [units: micrograms/mL] Geometric Mean (95% Confidence Interval)	**2.8 (2.3 to 3.3)**	**2.5 (2.1 to 3.0)**

Statistical Analysis 1 for Geometric Mean Titer (GMT) of the Pneumococcal Polysaccharide (PnPs) Serotype 22F Antibody Response at 4 Weeks Postvaccination.

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

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	The hypothesis was that the GMT of the PnPs antibody responses to serotype 22F at 4 weeks postvaccination in subjects who receive ZOSTAVAX™ concomitantly with PNEUMOVAX™ 23 will be noninferior to those in subjects who receive ZOSTAVAX™ nonconcomitantly.
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	The power for the noninferiority hypothesis regarding PnPs antibody titer is ~99%. The noninferiority margin is the lower bound of the two-sided 95% confidence interval (CI) on the PnPs antibody GMT ratio [concomitant/nonconcomitant] being >05.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	Week 4 postvac, estimated responses, GMT ratio, 95% CI, p-value based on a longitudinal regression model adjusting for prevac titers and age (years)
[4]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	The threshold for statistical significance is 0.025. There is no adjustment for multiple comparisons.

7. Secondary: Safety and Tolerability of Both Vaccines When Administered Concomitantly. [Time Frame: Eight weeks postvaccination]

Measure Type	Secondary
Measure Title	Safety and Tolerability of Both Vaccines When Administered Concomitantly.

Measure Description	All adverse events were analyzed including serious adverse events; injection-site adverse events; Vaccination Report Card prompted systemic adverse events, including varicella-like rashes or herpes zoster-like rashes; all other systemic adverse events.
Time Frame	Eight weeks postvaccination
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.
All subjects who received at least one vaccination

Reporting Groups

	Description
Nonconcomitant Group	Subjects were administered PNEUMOVAX™ 23 intramuscularly on Day 1 followed by ZOSTAVAX™ subcutaneously on Week 4
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1

Measured Values

	Nonconcomitant Group	**Concomitant Group**
Number of Participants Analyzed [units: participants]	**236**	**235**
Safety and Tolerability of Both Vaccines When Administered Concomitantly. [units: Participants]		
Injection site AEs	**141**	**136**
Systemic AEs	**74**	**70**
Serious AEs	**4**	**2**
Varicella-like Rash	**3**	**2**
Zoster-like Rash	**1**	**1**

No statistical analysis provided for Safety and Tolerability of Both Vaccines When Administered Concomitantly.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description

Nonconcomitant Group	Subjects were administered PNEUMOVAX™ 23 intramuscularly on Day 1 followed by ZOSTAVAX™ subcutaneously on Week 4
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1

Serious Adverse Events

	Nonconcomitant Group	Concomitant Group
Total, serious adverse events		
# participants affected	**4**	**2**
Ear and labyrinth disorders		
Vertigo * 1		
# participants affected / at risk	**0/236 (0.00%)**	**1/235 (0.43%)**
Infections and infestations		
Diverticulitis * 1		
# participants affected / at risk	**1/236 (0.42%)**	**0/235 (0.00%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Non-Hodgkin's Lymphoma * 1		
# participants affected / at risk	**1/236 (0.42%)**	**0/235 (0.00%)**
Nervous system disorders		
Global amnesia * 1		
# participants affected / at risk	**1/236 (0.42%)**	**0/235 (0.00%)**
Respiratory, thoracic and mediastinal disorders		
Chronic obstructive pulmonary disease * 1		
# participants affected / at risk	**1/236 (0.42%)**	**0/235 (0.00%)**
Skin and subcutaneous tissue disorders		
Dermatitis contact * 1		
# participants affected / at risk	**0/236 (0.00%)**	**1/235 (0.43%)**
Vascular disorders		
Haematoma * 1		
# participants affected / at risk	**1/236 (0.42%)**	**0/235 (0.00%)**

* Events were collected by non-systematic assessment

1 Term from vocabulary, MedDRA 11.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	1%

Reporting Groups

	Description
Nonconcomitant Group	Subjects were administered PNEUMOVAX™ 23 intramuscularly on Day 1 followed by ZOSTAVAX™ subcutaneously on Week 4
Concomitant Group	Subjects were administered ZOSTAVAX™ subcutaneously concomitantly with PNEUMOVAX™ 23 intramuscularly at separate injection sites at Day 1

Other Adverse Events

	Nonconcomitant Group	Concomitant Group
Total, other (not including serious) adverse events		
# participants affected	**154**	**143**
Gastrointestinal disorders		
Nausea [* 1]		
# participants affected / at risk	**3/236 (1.27%)**	**2/235 (0.85%)**
Stomach discomfort [* 1]		
# participants affected / at risk	**0/236 (0.00%)**	**3/235 (1.28%)**
Vomiting [* 1]		
# participants affected / at risk	**3/236 (1.27%)**	**0/235 (0.00%)**
General disorders		
Fatigue [* 1]		
# participants affected / at risk	**3/236 (1.27%)**	**1/235 (0.43%)**
Malaise [* 1]		
# participants affected / at risk	**0/236 (0.00%)**	**3/235 (1.28%)**
Pyrexia [* 1]		
# participants affected / at risk	**1/236 (0.42%)**	**5/235 (2.13%)**
Erythema (ZOSTAVAX™ injection site) [† 1]		
# participants affected / at risk	**70/236 (29.66%)**	**72/235 (30.64%)**
Erythema (PNEUMOVAX™ 23 injection site) [† 1]		
# participants affected / at risk	**30/236 (12.71%)**	**46/235 (19.57%)**
Erythema (Placebo injection site) [† 1]		
# participants affected / at risk	**7/236 (2.97%)**	**1/235 (0.43%)**
Induration (ZOSTAVAX™ injection site) [† 1]		
# participants affected / at risk	**3/236 (1.27%)**	**2/235 (0.85%)**
Pain (ZOSTAVAX™ injection site) [† 1]		
# participants affected / at risk	**68/236 (28.81%)**	**74/235 (31.49%)**
Pain (PNEUMOVAX™ 23 injection site) [† 1]		
# participants affected / at risk	**82/236 (34.75%)**	**95/235 (40.43%)**

Pain (Placebo injection site) † [1]		
# participants affected / at risk	21/236 (8.90%)	8/235 (3.40%)
Pruritus (ZOSTAVAX™ injection site) † [1]		
# participants affected / at risk	8/236 (3.39%)	11/235 (4.68%)
Swelling (ZOSTAVAX™ injection site) † [1]		
# participants affected / at risk	63/236 (26.69%)	67/235 (28.51%)
Swelling (PNEUMOVAX™ 23 injection site) † [1]		
# participants affected / at risk	30/236 (12.71%)	49/235 (20.85%)
Swelling (Placebo injection site) † [1]		
# participants affected / at risk	5/236 (2.12%)	3/235 (1.28%)
Infections and infestations		
Nasopharyngitis * [1]		
# participants affected / at risk	5/236 (2.12%)	9/235 (3.83%)
Upper respiratory tract infection * [1]		
# participants affected / at risk	1/236 (0.42%)	5/235 (2.13%)
Urinary tract infection * [1]		
# participants affected / at risk	4/236 (1.69%)	3/235 (1.28%)
Musculoskeletal and connective tissue disorders		
Arthralgia * [1]		
# participants affected / at risk	3/236 (1.27%)	1/235 (0.43%)
Back pain * [1]		
# participants affected / at risk	5/236 (2.12%)	3/235 (1.28%)
Musculoskeletal pain * [1]		
# participants affected / at risk	3/236 (1.27%)	1/235 (0.43%)
Myalgia * [1]		
# participants affected / at risk	4/236 (1.69%)	4/235 (1.70%)
Pain in extremity * [1]		
# participants affected / at risk	4/236 (1.69%)	2/235 (0.85%)
Nervous system disorders		
Headache * [1]		
# participants affected / at risk	4/236 (1.69%)	13/235 (5.53%)
Respiratory, thoracic and mediastinal disorders		
Cough * [1]		
# participants affected / at risk	0/236 (0.00%)	3/235 (1.28%)
Pharyngolaryngeal pain * [1]		
# participants affected / at risk	4/236 (1.69%)	5/235 (2.13%)
Skin and subcutaneous tissue disorders		
Erythema * [1]		
# participants affected / at risk	3/236 (1.27%)	3/235 (1.28%)
Pruritus * [1]		
# participants affected / at risk	3/236 (1.27%)	2/235 (0.85%)

Rash * 1		
# participants affected / at risk	**6/236 (2.54%)**	**1/235 (0.43%)**
Rash Vesicular * 1		
# participants affected / at risk	**4/236 (1.69%)**	**3/235 (1.28%)**

† Events were collected by systematic assessment
* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA 11.0

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: Merck agreements may vary with individual investigators, but will not prohibit any investigator from publishing. Merck supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Results Point of Contact:

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Publications of Results:

MacIntyre CR, Egerton T, McCaughey M, Parrino J, Campbell BV, Su SC, Pagnoni MF, Stek JE, Xu J, Annunziato PW, Chan IS, Silber JL. Concomitant administration of zoster and pneumococcal vaccines in adults ≥60 years old. Hum Vaccin. 2010 Nov;6(11):894-902. Epub 2010 Nov 1.

Responsible Party: Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:	NCT00535730 History of Changes
Other Study ID Numbers:	V211-012 2007_592
Study First Received:	September 21, 2007
Results First Received:	January 21, 2009
Last Updated:	April 1, 2015
Health Authority:	Germany: Federal Institute for Drugs and Medical Devices

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