Clinical trial results:
A Phase III, Open-Label Clinical Trial to Study the Safety and Immunogenicity of V110 in Subjects 50 Years of Age and Older and in Subjects 2 to 49 Years of Age at Increased Risk for Pneumococcal Disease, from the Russian Population

Summary

EudraCT number	2015-001656-29
Trial protocol	Outside EU/EEA
Global end of trial date	22 October 2013

Results information

Result version number	v1 (current)
This version publication date	10 February 2016
First version publication date	17 July 2015

Trial information

Trial identification

Sponsor protocol code	V110-018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01734239
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 October 2013
Global end of trial reached?	Yes
Global end of trial date	22 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine if Pneumovax™ 23 (V110) is safe and immunogenic in participants from the Russian population who are 50 years of age and older or 2 to 49 years of age and at increased risk for pneumococcal disease.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 June 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Russian Federation: 102
Worldwide total number of subjects	102
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	18
Adolescents (12-17 years)	7
Adults (18-64 years)	61
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study enrolled participants >=50 years of age and participants 2 to 49 years of age who have increased risk for pneumococcal disease. Additional inclusion and exclusion criteria applied.

Pre-assignment

Screening details:

A total of 102 participants were screened and enrolled.

Period 1

Period 1 title	Vaccination and Follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Pneumovax™ 23

Arm description:

Participants between 2 and 49 years of age with increased risk for pneumococcal disease received a single, 0.5-mL intramuscular injection of Pneumovax™ 23 on Day 1. Follow-up was to Day 28.

Arm type	Experimental
Investigational medicinal product name	Pneumovax™ 23
Investigational medicinal product code	
Other name	V110
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a single, 0.5-mL intramuscular injection of Pneumovax™ 23 on Day 1. Vaccine contains 25 µg of each of the 23 pneumococcal polysaccharides serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F.

Number of subjects in period 1	Pneumovax™ 23
Started	102
Completed	102

Baseline characteristics

Reporting groups	
Reporting group title	Pneumovax™ 23
Reporting group description:	
Participants between 2 and 49 years of age with increased risk for pneumococcal disease received a single, 0.5-mL intramuscular injection of Pneumovax™ 23 on Day 1. Follow-up was to Day 28.	

Reporting group values	Pneumovax™ 23	Total	
Number of subjects	102	102	
Age categorical Units: Subjects			
2 to 49 years	52	52	
>=50 years	50	50	
Age continuous Units: years			
arithmetic mean	40.4		
standard deviation	± 23.1	-	
Gender categorical Units: Subjects			
Female	37	37	
Male	65	65	

End points

End points reporting groups

Reporting group title	Pneumovax™ 23

Reporting group description:

Participants between 2 and 49 years of age with increased risk for pneumococcal disease received a single, 0.5-mL intramuscular injection of Pneumovax™ 23 on Day 1. Follow-up was to Day 28.

Primary: Geometric Mean Concentration of Antibodies to Pneumococcal Serotypes Contained in the Vaccine

End point title	Geometric Mean Concentration of Antibodies to Pneumococcal Serotypes Contained in the Vaccine[1]

End point description:

Serum antibodies to pneumococcal serotypes were measured by enzyme-linked immunosorbent assays. Per protocol, pneumococcal serotypes 1, 6B, 14, 19F, and 23F were assessed. The per protocol immunogenicity population included all enrolled participants except 2 who were excluded because blood samples were collected outside the allowable day range.

End point type	Primary

End point timeframe:

Prevaccination and Day 28 after vaccination

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypotheses were tested in this study.

End point values	Pneumovax™ 23			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 prevaccination	0.2 (0.2 to 0.3)			
Serotype 1 Day 28 postvaccination	3.2 (2.5 to 4.2)			
Serotype 6B prevaccination	0.6 (0.4 to 0.7)			
Serotype 6B Day 28 postvaccination	3.7 (2.8 to 5)			
Serotype 14 prevaccination	2.1 (1.6 to 2.9)			
Serotype 14 Day 28 postvaccination	20.4 (15.3 to 27.3)			
Serotype 19F prevaccination	1.5 (1.2 to 1.9)			
Serotype 19F Day 28 postvaccination	11.3 (8.8 to 14.3)			
Serotype 23F prevaccination	0.8 (0.6 to 1.1)			
Serotype 23F Day 28 postvaccination	6.5 (4.9 to 8.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with >=2-fold Increase from Prevaccination to Postvaccination in Antibodies to Pneumococcal Serotypes Contained in the Vaccine

End point title	Percentage of Participants with >=2-fold Increase from Prevaccination to Postvaccination in Antibodies to Pneumococcal Serotypes Contained in the Vaccine[2]

End point description:

Serum antibodies to pneumococcal serotypes were measured by enzyme-linked immunosorbent assays. A >=2-fold increase in serum antibody is a marker for serologic response to pneumococcal vaccination in adults. Per protocol, pneumococcal serotypes 1, 6B, 14, 19F, and 23F were assessed. The per protocol immunogenicity population included all enrolled participants except 2 who were excluded because blood samples were collected outside the allowable day range.

End point type	Primary

End point timeframe:

Day 28 postvaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypotheses were tested in this study.

End point values	Pneumovax™ 23			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Percentage of participants				
number (confidence interval 95%)				
Serotype 1	92 (84.8 to 96.5)			
Serotype 6B	83 (74.2 to 89.8)			
Serotype 14	89 (81.2 to 94.4)			
Serotype 19F	81 (71.9 to 88.2)			
Serotype 23F	84 (75.3 to 90.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Elevated Body Temperature (>=37.6 °C Axillary/ >=38.0 °C Oral or Equivalent)

End point title	Number of Participants with Elevated Body Temperature (>=37.6 °C Axillary/ >=38.0 °C Oral or Equivalent)[3]

End point description:

The All Subjects as Treated population included all enrolled participants.

End point type	Primary

End point timeframe:

Up to 5 days postvaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypotheses were tested in this study.

End point values	Pneumovax™ 23			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: Number of participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Reporting an Injection-site or Systemic Adverse Experience that was Reported by >=4 Participants

End point title	Number of Participants Reporting an Injection-site or Systemic Adverse Experience that was Reported by >=4 Participants[4]

End point 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 sponsor's product, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the sponsor's product, is also an AE. Injection-site or systemic AEs that occurred in >=4 participants were reported for this endpoint. The All Subjects as Treated population included all enrolled participants.

End point type	Primary

End point timeframe:

Up to Day 14 postvaccination

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypotheses were tested in this study.

End point values	Pneumovax™ 23			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: Number of participants	21			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Reporting Serious Adverse Experiences

End point title	Number of Participants Reporting Serious Adverse

End point description:

A serious adverse event is an AE that 1) results in death, 2) is life threatening, 3) results in a persistent or significant disability or incapacity, 4) results in or prolongs an existing inpatient hospitalization, 5) is a congenital anomaly or birth defect, 6) is a cancer, 7) is an overdose, or 8) is another important medical event which, based on appropriate medical judgment, may jeopardize the participant and may require medical or surgical intervention. The All Subjects as Treated population included all enrolled participants.

End point type	Primary

End point timeframe:

Up to Day 28 postvaccination

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal hypotheses were tested in this study.

End point values	Pneumovax™ 23			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: Number of participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse experiences were collected through Day 14 postvaccination; serious adverse experiences were collected through Day 28 postvaccination.

Adverse event reporting additional description:

Participants received a single, 0.5-mL intramuscular injection of Pneumovax™ 23 on Day 1. Follow-up was to Day 28.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Pneumovax™ 23: All Participants

Reporting group description: -

Serious adverse events	Pneumovax™ 23: All Participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 102 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Pneumovax™ 23: All Participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 102 (13.73%)		
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	14 / 102 (13.73%)		
occurrences (all)	14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 February 2013	Protocol Amendment V110-018-01 included the following changes: 1) added urinalysis, complete blood count (CBC) and blood chemistry laboratory test procedures prior to vaccination at Visit 1 (Day 1) and at Visit 2 (Day 28) for all subjects, 2) created a new protocol section to add the urinalysis procedure prior to vaccination at Visit 1 (Day 1) and at Visit 2 (Day 28) for all subjects, 3) changed Section title from "Serum Collection" to "Blood Sample Collection", added text to state that 2 mL whole blood will be collected to perform CBC prior to vaccination at Visit 1 (Day 1) and at Visit 2 (Day 28) for all subjects, added text to state that 2 mL serum will be collected to perform blood chemistry prior to vaccination at Visit 1 (Day 1) and at Visit 2 (Day 28) for all subjects, and 4) added text to state that results of the urinalysis, CBC and blood chemistry prior to vaccination at Visit 1 (Day 1) and at Visit 2 (Day 28) will be summarized.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported