Clinical trial results:
A Phase 3, Single-Arm, Open-label Clinical Study to Evaluate the Safety and Immunogenicity of 4 doses of V114 Administered to Healthy Infants in South Korea.

Summary

EudraCT number	2020-003181-39
Trial protocol	Outside EU/EEA
Global end of trial date	07 December 2022

Results information

Result version number	v1 (current)
This version publication date	18 May 2023
First version publication date	18 May 2023

Trial information

Trial identification

Sponsor protocol code	V114-036

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04633226
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, 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	04 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2022
Global end of trial reached?	Yes
Global end of trial date	07 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of this phase 3, single-arm, open-label study is to evaluate the safety and immunogenicity of a 4-dose regimen of V114 administered to healthy infants in South Korea.

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	10 February 2021
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	Korea, Republic of: 58
Worldwide total number of subjects	58
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)	58
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study enrolled healthy South Korean infants, approximately 2 months of age, from 42 days to 90 days inclusive.

Pre-assignment

Screening details:

58 infants (42 days to 90 days of age) were enrolled to receive V114. One participant was enrolled in error (participant had received previous administration of Prevenar 13™) and was discontinued from the study without receipt of V114.

Period 1

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

Arms

Arm title	V114

Arm description:

Participants received 4 total doses of V114, administered at approximately 2, 4, 6, and 12 to 15 months of age.

Arm type	Experimental
Investigational medicinal product name	V114
Investigational medicinal product code	
Other name	VAXNEUVANCE™, Pneumococcal 15-valent Conjugate Vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

15-valent pneumococcal conjugate vaccine (PCV) containing 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) present in Prevnar 13™ plus 2 additional serotypes (22F, 33F) in each 0.5 mL dose

Number of subjects in period 1	V114
Started	58
Vaccination 1 (~2 months of age)	57
Vaccination 2 (~4 months of age)	56
Vaccination 3 (~6 months of age)	55
Vaccination 4 (~12 to 15 months of age)	50 [1]
Completed	53
Not completed	5
Randomized by mistake without study treatment	1
Withdrawal by parent/guardian	4

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants could have been considered to complete the study without receipt of Vaccination 4 (~12 to 15 months of age).

Baseline characteristics

Reporting groups	
Reporting group title	V114
Reporting group description:	
Participants received 4 total doses of V114, administered at approximately 2, 4, 6, and 12 to 15 months of age.	

Reporting group values	V114	Total	
Number of subjects	58	58	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	58	58	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: weeks			
arithmetic mean	8.7		
standard deviation	± 1.2	-	
Gender Categorical Units: Subjects			
Female	33	33	
Male	25	25	
Race Units: Subjects			
Asian	58	58	
Ethnicity Units: Subjects			
Not Hispanic or Latino	57	57	
Not Reported	1	1	

End points

End points reporting groups

Reporting group title	V114

Reporting group description:

Participants received 4 total doses of V114, administered at approximately 2, 4, 6, and 12 to 15 months of age.

Primary: Percentage of participants with ≥1 solicited injection-site adverse events (AEs)

End point title	Percentage of participants with ≥1 solicited injection-site adverse events (AEs)[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Following any of the doses of V114, the percentage of participants with solicited injection-site AEs was assessed. The solicited injection-site AEs consist of redness/erythema, hard lump/induration, tenderness/pain, and swelling. All randomized participants who received at least 1 dose of study vaccination were analyzed.

End point type	Primary

End point timeframe:

Up to 7 days after any vaccination, up to a total of ~ 13 months

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 statistical analyses were planned for this endpoint.

End point values	V114			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Percentage of Participants				
number (not applicable)				
Injection site erythema	54.4			
Injection site induration	57.9			
Injection site pain	50.9			
Injection site swelling	59.6			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with ≥1 solicited systemic AE

End point title	Percentage of participants with ≥1 solicited systemic AE[2]

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Following any of the doses of V114, the percentage of participants with solicited systemic AEs was assessed. The solicited systemic AEs consist of appetite lost/decreased appetite, irritability, drowsiness/somnolence, and hives or welts/urticaria. All randomized participants who received at least 1

dose of study vaccination were analyzed.

End point type	Primary

End point timeframe:

Up to 7 days after any vaccination, up to a total of ~ 13 months

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 statistical analyses were planned for this endpoint.

End point values	V114			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Percentage of Participants				
number (not applicable)				
Decreased appetite	71.9			
Irritability	89.5			
Somnolence	82.5			
Urticaria	8.8			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with ≥1 vaccine-related serious adverse events (SAEs)

End point title	Percentage of participants with ≥1 vaccine-related serious adverse events (SAEs)[3]

End point description:

A serious adverse event (SAE) is an AE that is life-threatening, requires or prolongs an existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is another important medical event deemed such by medical or scientific judgment. The percentage of participants with a vaccine-related SAE following any dose of V114 was reported. Vaccine-related SAEs were counted starting after vaccine dose 1 through completion of study. All randomized participants who received at least 1 dose of study vaccination were analyzed.

End point type	Primary

End point timeframe:

Up to approximately 14.5 months

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 statistical analyses were planned for this endpoint.

End point values	V114			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Percentage of Participants				
number (confidence interval 95%)	0.0 (0.0 to 6.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants discontinuing study therapy due to AE(s)

End point title	Percentage of participants discontinuing study therapy due to AE(s)[4]

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The percentage of participants who discontinued study treatment due to an AE is reported. The analysis population consisted of all participants who received at least 1 dose of study vaccination.

End point type	Primary

End point timeframe:

Up to approximately 13 months

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 statistical analyses were planned for this endpoint.

End point values	V114			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Percentage of Participants				
number (confidence interval 95%)	0.0 (0.0 to 6.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with anti-pneumococcal polysaccharides (PnPs) serotype-specific immunoglobulin G (IgG) ≥0.35 µg/mL

End point title	Percentage of participants with anti-pneumococcal polysaccharides (PnPs) serotype-specific immunoglobulin G (IgG) ≥0.35 µg/mL[5]

End point description:

The percentage of participants with IgG threshold values of ≥0.35 µg/mL for the 15 serotypes contained in V114 (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F) at 30 days postdose 3 is reported. The multiplex, pneumococcal electrochemiluminescence (PnECL) v2.0 assay was used to quantify IgG serotype-specific antibodies. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed.

End point type	Primary

End point timeframe:

30 days after vaccination 3 (Up to a total of ~5 months)

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 statistical analyses were planned for this endpoint.

End point values	V114			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: Percentage of Participants				
number (confidence interval 95%)				
Serotype 1 (n=47)	100.0 (92.5 to 100.0)			
Serotype 3 (n=47)	100.0 (92.5 to 100.0)			
Serotype 4 (n=47)	100.0 (92.5 to 100.0)			
Serotype 5 (n=47)	100.0 (92.5 to 100.0)			
Serotype 6A (n=47)	100.0 (92.5 to 100.0)			
Serotype 6B (n=47)	95.7 (85.5 to 99.5)			
Serotype 7F (n=47)	100.0 (92.5 to 100.0)			
Serotype 9V (n=47)	100.0 (92.5 to 100.0)			
Serotype 14 (n=47)	100.0 (92.5 to 100.0)			
Serotype 18C (n=47)	97.9 (88.7 to 99.9)			
Serotype 19A (n=47)	97.9 (88.7 to 99.9)			
Serotype 19F (n=47)	100.0 (92.5 to 100.0)			
Serotype 22F (n=47)	100.0 (92.5 to 100.0)			
Serotype 23F (n=47)	100.0 (92.5 to 100.0)			
Serotype 33F (n=47)	97.9 (88.7 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Geometric mean concentrations (GMCs) of anti-PnPs serotype-specific IgG at 30 days postdose 3

End point title	Geometric mean concentrations (GMCs) of anti-PnPs serotype-specific IgG at 30 days postdose 3[6]

End point description:

The anti-PnPs serotype-specific IgG Geometric Mean Concentrations (GMCs) at 30 days postdose 3 for each serotype-specific were reported. The multiplex, ECL-based PnECL v2.0 assay was used. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed.

End point type	Primary

End point timeframe:

30 days after vaccination 3 (Up to a total of ~5 months)

Notes:

[6] - 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 statistical analyses were planned for this endpoint.

End point values	V114			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (n=47)	1.69 (1.46 to 1.94)			
Serotype 3 (n=47)	1.70 (1.41 to 2.06)			
Serotype 4 (n=47)	1.87 (1.49 to 2.34)			
Serotype 5 (n=47)	2.14 (1.74 to 2.63)			
Serotype 6A (n=47)	2.16 (1.74 to 2.67)			
Serotype 6B (n=47)	2.53 (1.93 to 3.32)			
Serotype 7F (n=47)	2.80 (2.35 to 3.32)			
Serotype 9V (n=47)	2.01 (1.63 to 2.47)			
Serotype 14 (n=47)	7.47 (5.98 to 9.32)			
Serotype 18C (n=47)	1.90 (1.47 to 2.46)			
Serotype 19A (n=47)	2.20 (1.76 to 2.76)			
Serotype 19F (n=47)	3.04 (2.55 to 3.63)			
Serotype 22F (n=47)	5.97 (4.83 to 7.37)			
Serotype 23F (n=47)	1.71 (1.37 to 2.15)			
Serotype 33F (n=47)	2.41 (1.84 to 3.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean concentrations (GMCs) of anti-PnPs serotype-specific IgG at 30 days postdose 4

End point title	Geometric mean concentrations (GMCs) of anti-PnPs serotype-specific IgG at 30 days postdose 4

End point description:

The anti-PnPs serotype-specific IgG Geometric Mean Concentrations (GMCs) at 30 days postdose 4 for each serotype-specific were reported. The multiplex, ECL-based PnECL v2.0 assay was used. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed.

End point type	Secondary

End point timeframe:

30 days after vaccination 4 (Up to a total of ~14 months)

End point values	V114			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (n=49)	2.24 (1.77 to 2.83)			
Serotype 3 (n=49)	1.32 (1.07 to 1.62)			
Serotype 4 (n=49)	1.86 (1.39 to 2.49)			
Serotype 5 (n=49)	3.27 (2.57 to 4.17)			
Serotype 6A (n=49)	5.77 (4.38 to 7.60)			
Serotype 6B (n=49)	6.80 (5.28 to 8.76)			
Serotype 7F (n=49)	5.17 (3.92 to 6.81)			
Serotype 9V (n=49)	3.27 (2.50 to 4.28)			
Serotype 14 (n=49)	9.04 (7.22 to 11.31)			
Serotype 18C (n=49)	3.81 (2.97 to 4.88)			
Serotype 19A (n=49)	4.91 (4.03 to 5.97)			
Serotype 19F (n=49)	5.41 (4.40 to 6.65)			
Serotype 22F (n=49)	9.20 (7.19 to 11.79)			
Serotype 23F (n=49)	2.82 (2.14 to 3.73)			
Serotype 33F (n=49)	6.21 (5.05 to 7.63)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to ~14.5 months

Adverse event reporting additional description:

The analysis population for Number of Deaths (all causes) included all randomized participants (N=58). The analysis population for AEs included all randomized participants who received at least 1 dose of study vaccination.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	V114

Reporting group description:

Participants received 4 total doses of V114, administered at approximately 2, 4, 6, and 12 to 15 months of age.

Serious adverse events	V114		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 57 (7.02%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Asymptomatic COVID-19			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis norovirus			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection bacterial			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	V114		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 57 (98.25%)		
Nervous system disorders			
Somnolence			
subjects affected / exposed	47 / 57 (82.46%)		
occurrences (all)	108		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	31 / 57 (54.39%)		
occurrences (all)	64		
Pyrexia			
subjects affected / exposed	19 / 57 (33.33%)		
occurrences (all)	27		
Injection site urticaria			
subjects affected / exposed	9 / 57 (15.79%)		
occurrences (all)	13		
Injection site swelling			
subjects affected / exposed	34 / 57 (59.65%)		
occurrences (all)	72		
Injection site pain			
subjects affected / exposed	29 / 57 (50.88%)		
occurrences (all)	73		
Injection site induration			

subjects affected / exposed occurrences (all)	33 / 57 (57.89%) 70		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 3 / 57 (5.26%) 5		
Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all)	 3 / 57 (5.26%) 3		
Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all)	 5 / 57 (8.77%) 7		
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	 51 / 57 (89.47%) 138		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 5 / 57 (8.77%) 7		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 41 / 57 (71.93%) 65		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 December 2021	Amendment 01: Primary reason for amendment was to reduce the number of participants in the study due to the enrollment challenges primarily related to the COVID-19 pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported