Clinical trial results:
A Randomized, Controlled, Observer-Blind, Phase 1/2a Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of Ad26.RSV.Pref In RSV-Seronegative Toddlers 12 to 24 Months Of Age

Summary

EudraCT number	2017-003859-36
Trial protocol	SE DE GB FI ES Outside EU/EEA PL
Global end of trial date	02 November 2021

Results information

Result version number	v1 (current)
This version publication date	15 May 2022
First version publication date	15 May 2022

Trial information

Trial identification

Sponsor protocol code	VAC18194RSV2002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03606512
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Vaccines and Prevention B.V.
Sponsor organisation address	Archimedesweg 4-6, Leiden, Netherlands, 2333 CN
Public contact	Clinical Registry Group, Janssen Vaccines and Prevention B.V., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Vaccines and Prevention B.V., ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002172-PIP02-17
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to assess the safety and reactogenicity of an intramuscular regimen of 3 doses of 2.5*10^10 viral particles (vp) of adenovirus serotype 26 based respiratory syncytial virus pre-fusion protein (Ad26.RSV.preF) vaccine in RSV-seronegative toddlers aged 12 to 24 months.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 14
Country: Number of subjects enrolled	Brazil: 5
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Finland: 11
Country: Number of subjects enrolled	Poland: 3
Worldwide total number of subjects	38
EEA total number of subjects	14

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)	38
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: -

Pre-assignment

Screening details:

Total 38 subjects (20 subjects in adenovirus serotype 26 based respiratory syncytial virus pre-fusion protein [Ad26.RSV.preF] and 18 subjects in Placebo/Nimenrix arm) were randomised and received at least 1 dose of study vaccine. Out of 38, 36 subjects completed the study (18 subjects Ad26.RSV.preF and 18 subjects in Placebo/Nimenrix arms).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo or Nimenrix

Arm description:

Subjects received placebo by intramuscular (IM) injection on Days 1, 29 and 57. Placebo could be replaced with Nimenrix on Day 57 in countries where the commercial vaccine Nimenrix is licensed.

Arm type	Placebo
Investigational medicinal product name	Nimenrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Nimenrix was administered as 0.5 mL solution for IM injection on Day 57.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Placebo was administered as an IM injection on Days 1, 29 and 57.

Arm title	Ad26.RSV.preF (2.5*10^10 vp)

Arm description:

Subjects received IM injection of 2.5*10^10 viral particles (vp) of an Ad26.RSV.preF on Days 1, 29, and 57.

Arm type	Experimental
Investigational medicinal product name	Ad26.RSV.preF
Investigational medicinal product code	
Other name	JNJ-64400141
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Ad26.RSV.preF was administered as an IM injection at a dose of 2.5*10^10 vp on Days 1, 29, and 57.

Number of subjects in period 1	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)
Started	18	20
Subjects who received Nimenrix on Day 57	12 [1]	0 [2]
Subjects who received Placebo on Day 57	6 [3]	0 [4]
Completed	18	18
Not completed	0	2
Unspecified	-	1
Lost to follow-up	-	1

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: Placebo was replaced with Nimenrix for 12 subjects, on Day 57 in countries where the commercial vaccine Nimenrix is licensed.

[2] - 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: Placebo was replaced with Nimenrix for 12 subjects, on Day 57 in countries where the commercial vaccine Nimenrix is licensed.

[3] - 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: Placebo was replaced with Nimenrix for 12 subjects, on Day 57 in countries where the commercial vaccine Nimenrix is licensed.

[4] - 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: Placebo was replaced with Nimenrix for 12 subjects, on Day 57 in countries where the commercial vaccine Nimenrix is licensed.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo or Nimenrix
Reporting group description:	
Subjects received placebo by intramuscular (IM) injection on Days 1, 29 and 57. Placebo could be replaced with Nimenrix on Day 57 in countries where the commercial vaccine Nimenrix is licensed.	
Reporting group title	Ad26.RSV.preF (2.5*10^10 vp)
Reporting group description:	
Subjects received IM injection of 2.5*10^10 viral particles (vp) of an Ad26.RSV.preF on Days 1, 29, and 57.	

Reporting group values	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)	Total
Number of subjects	18	20	38
Title for AgeCategorical			
Units: subjects			
Infants and toddlers (28 days-23 months)	18	20	38
Title for AgeContinuous			
Units: months			
arithmetic mean	17.8	16.2	
standard deviation	± 2.94	± 3.17	-
Title for Gender			
Units: subjects			
Female	11	11	22
Male	7	9	16

End points

End points reporting groups

Reporting group title	Placebo or Nimenrix
Reporting group description:	
Subjects received placebo by intramuscular (IM) injection on Days 1, 29 and 57. Placebo could be replaced with Nimenrix on Day 57 in countries where the commercial vaccine Nimenrix is licensed.	
Reporting group title	Ad26.RSV.preF (2.5*10^10 vp)
Reporting group description:	
Subjects received IM injection of 2.5*10^10 viral particles (vp) of an Ad26.RSV.preF on Days 1, 29, and 57.	
Subject analysis set title	Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received placebo by intramuscular (IM) injection on Days 1, 29 and 57.	
Subject analysis set title	Nimenrix
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received Nimenrix by IM injection on Day 57 in countries where the commercial vaccine Nimenrix is licensed.	

Primary: Number of Subjects with Solicited Local and Systemic Adverse Events (AEs) for 7 Days After First Vaccination

End point title	Number of Subjects with Solicited Local and Systemic Adverse Events (AEs) for 7 Days After First Vaccination[1]
End point description:	
An AE is any untoward medical event that occurs in a subjects administered an investigational product, and it does not necessarily indicate only events with a clear causal relationship with the relevant investigational product. Solicited local/systemic AEs were precisely defined events that subjects were specifically asked about and which were noted by subjects in the diary. Solicited local AEs included injection-site pain/tenderness, injection-site erythema and injection-site swelling/induration. Solicited systemic AEs included fatigue, headache, nausea, myalgia and fever. The Full Analysis set (FAS) included all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations.	
End point type	Primary
End point timeframe:	
Up to Day 8 (7 days after first vaccination on Day 1)	

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: Only descriptive statistics were reported. No inferential statistics was planned for the primary endpoints.

End point values	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Subjects				
Solicited Local AEs	2	6		
Solicited Systemic AEs	11	17		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Solicited Local and Systemic AEs for 7 Days After Second Vaccination

End point title	Number of Subjects with Solicited Local and Systemic AEs for 7 Days After Second Vaccination[2]

End point description:

An AE is any untoward medical event that occurs in a subjects administered an investigational product, and it does not necessarily indicate only events with a clear causal relationship with the relevant investigational product. Solicited local/systemic AEs were precisely defined events that subjects were specifically asked about and which were noted by subjects in the diary. Solicited local AEs included injection-site pain/tenderness, injection-site erythema and injection-site swelling/induration. Solicited systemic AEs included fatigue, headache, nausea, myalgia and fever. The FAS included all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations.

End point type	Primary

End point timeframe:

Up to Day 36 (7 days after second vaccination on Day 29)

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: Only descriptive statistics were reported. No inferential statistics was planned for the primary endpoints.

End point values	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Subjects				
Solicited Local AEs	1	9		
Solicited Systemic AEs	9	11		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Solicited Local and Systemic AEs for 7 Days After Third Vaccination

End point title	Number of Subjects with Solicited Local and Systemic AEs for 7 Days After Third Vaccination[3][4]

End point description:

An AE is any untoward medical event that occurs in a subjects administered an investigational product, and it does not necessarily indicate only events with a clear causal relationship with the relevant investigational product. Solicited local/systemic AEs were precisely defined events that subjects were specifically asked about and which were noted by subjects in the diary. Solicited local AEs included injection-site pain/tenderness, injection-site erythema and injection-site swelling/induration. Solicited systemic AEs included fatigue, headache, nausea, myalgia and fever. The FAS included all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations. Here, 'N' (Number of subjects analyzed) included all subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Up to Day 64 (7 days after third vaccination on Day 57)

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: Only descriptive statistics were reported. No inferential statistics was planned for the primary endpoints.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned, the endpoint is not reporting statistics for any of the arms of baseline period.

End point values	Ad26.RSV.preF (2.5*10^10 vp)	Placebo	Nimenrix	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	6	12	
Units: Subjects				
Solicited Local AEs	7	1	4	
Solicited Systemic AEs	12	3	4	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Unsolicited AEs for 28 Days After First Vaccination

End point title	Number of Subjects with Unsolicited AEs for 28 Days After First Vaccination[5]

End point description:

An AE is any untoward medical event that occurs in a subject administered an investigational product, and it does not necessarily indicate only events with a clear causal relationship with the relevant investigational product. Unsolicited AEs were precisely defined events that participants were not asked about and which were not noted by participants in the diary. The FAS included all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations.

End point type	Primary

End point timeframe:

Up to Day 29 (28 days after first vaccination on Day 1)

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: Only descriptive statistics were reported. No inferential statistics was planned for the primary endpoints.

End point values	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Subjects	5	9		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Unsolicited AEs for 28 Days After Second Vaccination

End point title	Number of Subjects with Unsolicited AEs for 28 Days After Second Vaccination[6]

End point description:

An AE is any untoward medical event that occurs in a subjects administered an investigational product, and it does not necessarily indicate only events with a clear causal relationship with the relevant investigational product. Unsolicited AEs were precisely defined events that participants were not asked about and which were not noted by participants in the diary. The FAS included all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations.

End point type	Primary

End point timeframe:

Up to Day 57 (28 days after second vaccination on Day 29)

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: Only descriptive statistics were reported. No inferential statistics was planned for the primary endpoints.

End point values	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	20		
Units: Subjects	7	9		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Unsolicited AEs for 28 Days After Third Vaccination

End point title	Number of Subjects with Unsolicited AEs for 28 Days After Third Vaccination[7][8]

End point description:

An AE is any untoward medical event that occurs in a subjects administered an investigational product, and it does not necessarily indicate only events with a clear causal relationship with the relevant investigational product. Unsolicited AEs were precisely defined events that participants were not asked about and which were not noted by participants in the diary. The FAS included all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations. Here, 'N' (Number of subjects analyzed) included all subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Up to Day 85 (28 days after third vaccination on Day 57)

Notes:

[7] - 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: Only descriptive statistics were reported. No inferential statistics was planned for the primary endpoints.
[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned, the endpoint is not reporting statistics for any of the arms of baseline period.

End point values	Ad26.RSV.preF (2.5*10^10 vp)	Placebo	Nimenrix	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	19	6	12	
Units: Subjects	7	3	3	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Serious Adverse Events (SAEs)

End point title	Number of Subjects with Serious Adverse Events (SAEs)[9][10]

End point description:

Number of participants with SAEs were reported. SAE is any AE that results in: death, persistent or significant disability/incapacity, requires inpatient hospitalization or prolongation of existing hospitalization, is life-threatening experience, is a congenital anomaly/birth defect and may jeopardize participant and/or may require medical or surgical intervention to prevent one of the outcomes listed above. The FAS included all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations.

End point type	Primary

End point timeframe:

Up to 1 year and 9 months

Notes:

[9] - 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: Only descriptive statistics were reported. No inferential statistics was planned for the primary endpoints.
[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As planned, the endpoint is not reporting statistics for any of the arms of baseline period.

End point values	Ad26.RSV.preF (2.5*10^10 vp)	Placebo	Nimenrix	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	6	12	
Units: Subjects	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of Neutralizing Antibodies to Respiratory Syncytial Virus (RSV) A2 Strain

End point title	Titers of Neutralizing Antibodies to Respiratory Syncytial Virus (RSV) A2 Strain

End point description:

Neutralizing antibody titers assessed by virus neutralizing antibodies (VNA) against the RSV A2 strain were expressed as 50% inhibitory concentration (IC50) units. The seropositivity cut-off for this assay is an IC50 of 42.7 for RSV A2. The Per-protocol Immunogenicity (PPI) analysis set included all randomized

and vaccinated subjects for whom immunogenicity data are available, excluding subjects with major protocol deviations expecting to impact the immunogenicity outcomes. Here, 'n' (number analyzed) is defined as subjects analyzed for specified time points. Here, values below the seropositivity cut-off (less than [<] 42.7) were imputed with zero.

End point type	Secondary

End point timeframe:

Days 1, 8, 85, and 267 (End of first RSV season)

End point values	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	19		
Units: Titers				
geometric mean (confidence interval 95%)				
Day 1 (n=18,19)	0 (0 to 0)	0 (0 to 0)		
Day 8 (n=17,18)	0 (0 to 0)	0 (0 to 52)		
Day 85 (n=16,14)	0 (0 to 45)	293 (240 to 358)		
Day 267 (End of first RSV season) (n=15,9)	0 (0 to 46)	269 (115 to 632)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-Fusion A Immunoglobulin G (IgG) Serum Antibody Response as Assessed by Enzyme-linked Immunosorbent Assay (ELISA)

End point title	Pre-Fusion A Immunoglobulin G (IgG) Serum Antibody Response as Assessed by Enzyme-linked Immunosorbent Assay (ELISA)

End point description:

Pre-fusion A IgG serum antibody response was assessed by ELISA. The PPI analysis set included all randomized and vaccinated subjects for whom immunogenicity data are available, excluding subjects with major protocol deviations expecting to impact the immunogenicity outcomes. Here, 'n' (number analyzed) is defined as subjects analyzed for specified time points. Here, 99999 signifies that data point could not be calculated since all values were below the cut-off value. Here, values below the seropositivity cut-off (<16.1) were imputed with zero.

End point type	Secondary

End point timeframe:

Days 1, 8, 85, and 267 (End of first RSV season)

End point values	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	19		
Units: ELISA units per liter (EU/L)				
geometric mean (confidence interval 95%)				
Day 1 (n=18,19)	0 (-99999 to 99999)	0 (-99999 to 99999)		
Day 8 (n=17,19)	0 (-99999 to 99999)	0 (0 to 0)		
Day 85 (n=16,14)	0 (0 to 0)	236 (187 to 299)		
Day 267 (End of first RSV season) (n=15,9)	0 (0 to 27)	212 (79 to 571)		

Statistical analyses

No statistical analyses for this end point

Secondary: Post-Fusion A IgG Serum Antibody Response as Assessed by ELISA

End point title	Post-Fusion A IgG Serum Antibody Response as Assessed by ELISA

End point description:

Post-fusion A IgG serum antibody response as assessed by ELISA was reported. The PPI analysis set included all randomized and vaccinated subjects for whom immunogenicity data are available, excluding subjects with major protocol deviations expecting to impact the immunogenicity outcomes. Here, 'n' (number analyzed) is defined as subjects analyzed for specified time points. Here, 99999 signifies that data point could not be calculated, since all values were below the cut-off value. Here, values below the seropositivity cut-off (<17.0) were imputed with zero.

End point type	Secondary

End point timeframe:

Days 1, 8, 85, and 267 (End of first RSV season)

End point values	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	19		
Units: EU/L				
geometric mean (confidence interval 95%)				
Day 1 (n=18,19)	0 (-99999 to 99999)	0 (-99999 to 99999)		
Day 8 (n=16,19)	0 (-99999 to 99999)	0 (0 to 0)		
Day 85 (n=16,14)	0 (0 to 0)	47 (40 to 54)		
Day 267 (End of first RSV season) (n=15,9)	0 (0 to 30)	58 (22 to 153)		

Statistical analyses

No statistical analyses for this end point

Secondary: T-cell Response (Percent [%]) to RSV F Peptides for T-helper (Th) 1 and Th2 Subtyping as Measured by Flow Cytometry

End point title	T-cell Response (Percent [%]) to RSV F Peptides for T-helper (Th) 1 and Th2 Subtyping as Measured by Flow Cytometry

End point description:

T-cell response (%) to RSV F peptides for T-helper Th1 and Th2 subtyping as measured by flow cytometry was assessed. Th1(% of CD4+ interferon gamma [IFN-g]+T cells; LLOQ=0.05%) and Th2 (% of CD4+ interleukin [IL]-4+/IL-13+ and CD40L+T cells; LLOQ=0.07%) responses were determined by intracellular cytokines after RSV F peptide stimulation. PPI analysis set included all randomized and vaccinated subjects for whom immunogenicity data are available, excluding subjects with major protocol deviations expecting to impact the immunogenicity outcomes. Here 'N' (Number analyzed) included all subjects evaluable for this endpoint and 'n' (number analyzed) defined as subjects analyzed for specified timepoints. Here 99999 refer that due to low number of viable PBMCs, the positive control in the ICS assay (Staphylococcal enterotoxin B [SEB]) could not be performed for all samples and an analysis was thought not to be informative on such a limited amount of datapoints so no conclusions can be drawn.

End point type	Secondary

End point timeframe:

Baseline and Day 85

End point values	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	16		
Units: % CD4+ T-cells				
median (inter-quartile range (Q1-Q3))				
CD4: Th1: IFN-gamma: Baseline (n=13,16)	99999 (99999 to 99999)	99999 (99999 to 99999)		
CD4: Th1: IFN-gamma: Day 85 (n=9,8)	99999 (99999 to 99999)	99999 (99999 to 99999)		
CD4: Th2: IL4/IL13 and CD40L: Baseline (n=13,16)	99999 (99999 to 99999)	99999 (99999 to 99999)		
CD4: Th2: IL4/IL13 and CD40L Day 85 (n=9,8)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Severe RSV-lower Respiratory Tract Infection (LRTI)

End point title	Number of Subjects with Severe RSV-lower Respiratory Tract Infection (LRTI)

End point description:

Number of subjects with severe RSV-LRTI were reported. The Modified Intent-to-treat (mITT) analysis set is defined as a subset of the FAS excluding subjects who are seronegative at screening but for whom there is an anamnestic response at Day 8.

End point type	Secondary

End point timeframe:

Up to 1 year 9 months

End point values	Placebo or Nimenrix	Ad26.RSV.preF (2.5*10^10 vp)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	19		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 1 year 9 months	
Adverse event reporting additional description:	
The Full Analysis set (FAS) included all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Ad26.RSV.preF (2.5*10^10 vp)
Reporting group description:	
Subjects received IM injection of 2.5*10^10 viral particles (vp) of an Ad26.RSV.preF on Days 1, 29, and 57.	
Reporting group title	Placebo or Nimenrix
Reporting group description:	
Subjects received placebo by intramuscular (IM) injection on Days 1, 29 and 57. Placebo could be replaced with Nimenrix on Day 57 in countries where the commercial vaccine Nimenrix is licensed.	

Serious adverse events	Ad26.RSV.preF (2.5*10^10 vp)	Placebo or Nimenrix	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Ad26.RSV.preF (2.5*10^10 vp)	Placebo or Nimenrix	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 20 (75.00%)	14 / 18 (77.78%)	
Injury, poisoning and procedural complications			

Arthropod Bite			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Skin Abrasion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Skin Laceration			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Thermal Burn			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Drooling			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Injection Site Bruising			
subjects affected / exposed	1 / 20 (5.00%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Tenderness			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Middle Ear Effusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	

Immune system disorders			
Allergy to Arthropod Bite			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 20 (5.00%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Abdominal Pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Teething			
subjects affected / exposed	4 / 20 (20.00%)	0 / 18 (0.00%)	
occurrences (all)	4	0	
Respiratory, thoracic and mediastinal disorders			
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 20 (5.00%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Nasal Congestion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash Macular			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	2	
Miliaria			

subjects affected / exposed	1 / 20 (5.00%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Dry Skin			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Dermatitis Diaper			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	2 / 20 (10.00%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Irritability			
subjects affected / exposed	1 / 20 (5.00%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Croup Infectious			
subjects affected / exposed	2 / 20 (10.00%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Exanthema Subitum			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Hand-Foot-And-Mouth Disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 20 (5.00%)	2 / 18 (11.11%)	
occurrences (all)	1	3	
Oral Viral Infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Otitis Media			

subjects affected / exposed	0 / 20 (0.00%)	3 / 18 (16.67%)	
occurrences (all)	0	4	
Otitis Media Acute			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	2	
Rhinitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Respiratory Tract Infection			
subjects affected / exposed	4 / 20 (20.00%)	5 / 18 (27.78%)	
occurrences (all)	5	5	
Pharyngitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Rhinovirus Infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 20 (20.00%)	2 / 18 (11.11%)	
occurrences (all)	17	5	
Viral Infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 20 (10.00%)	1 / 18 (5.56%)	
occurrences (all)	6	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2018	The protocol amendment was made to remove seropositive subjects from the study so that seronegative toddlers can be evaluated independent of any findings that might occur in seropositive toddlers at the 1*10^11 viral particles (vp) dose level.
13 July 2018	The protocol amendment was made to reduce the dose of adenovirus serotype 26 based respiratory syncytial virus pre-fusion protein (Ad26.RSV.preF) from 5*10^10 vp to 2.5*10^10 vp.
07 November 2018	The protocol amendment was made to incorporate vaccination with Nimenrix as an alternative for the Day 57 vaccination with placebo (0.9 percent [%] saline) for subjects in the control group (in accordance with the local label and local regulations, and unless contra-indicated).
08 April 2019	To introduce more active follow-up of ongoing respiratory tract infection (RTIs)/otitis media cases to capture the potential worsening of RTI/otitis media cases that are reported as not severe during the initial RTI visit and to clarify the responsibilities of the clinical endpoint committee (CEC) in terms of evaluation of RTI cases and severity grading of RTIs.
05 July 2019	This amendment was made to align the global protocol with changes made requests from the German Health Authority.
25 May 2020	This protocol amendment was made primarily to reduce the overall number of RSV-seronegative toddlers in the study from 48 to 36.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported