



Clinical trial results:

A Randomized, Double-blind, Phase 1/2a Study to Evaluate the Safety, Tolerability and Immunogenicity of Ad26.RSV.preF in Adults 18 to 50 Years of Age and RSV-Seropositive Toddlers 12 to 24 Months of Age Summary

EudraCT number	2017-001345-27
Trial protocol	GB FI Outside EU/EEA
Global end of trial date	21 April 2020

Results information

Result version number	v1 (current)
This version publication date	06 November 2020
First version publication date	06 November 2020

Trial information

Trial identification

Sponsor protocol code	VAC18194RSV2001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03303625
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Vaccines and Prevention B.V.
Sponsor organisation address	Newtonweg 1, Leiden, Netherlands, 2333 CM
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)	EMA-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	03 July 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the safety and tolerability of an intramuscular regimen of 2 doses of 1×10^{11} viral particles (vp) of Ad26.RSV.preF in adults aged 18 to 50 years and 2 doses of 5×10^{10} vp of Ad26.RSV.preF in respiratory syncytial virus (RSV)-seropositive 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. Safety Evaluations included adverse events (AEs), including solicited local and systemic AEs, unsolicited AEs, and serious AEs (SAEs), respiratory tract infection (RTIs) (Cohort 1 only), clinical laboratory tests (Cohort 0 only), vital signs, physical examination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 December 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 15
Country: Number of subjects enrolled	United Kingdom: 31
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	48
EEA total number of subjects	46

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)	36

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 48 subjects were randomized out of which 46 completed the study.

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	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
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Arm title	Cohort 0 (18 to 50 years): Ad26.RSV.preF
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Arm description:

Subjects received a single intramuscular (IM) injection of 1×10^{11} viral particles (vp) adenovirus serotype 26 vectored vaccine expressing the pre-fusion F-protein of the respiratory syncytial virus A2 strain (Ad26.RSV.preF) on Day 1 and Day 29.

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

Dosage and administration details:

Ad26.RSV.preF was administered 1×10^{11} vp as 0.5 mL injection for adults.

Arm title	Cohort 0 (18 to 50 years): Placebo
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Arm description:

Subjects received single IM injection of placebo (sterile 0.9% saline) on Day 1 and Day 29.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Placebo was administered as sterile 0.9% saline for injection.

Arm title	Cohort 1 (12 to 24 months): Ad26.RSV.preF
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Arm description:

Subjects (seropositive for respiratory syncytial virus [RSV] within 42 days prior to vaccination) received single IM injection of 5×10^{10} vp Ad26.RSV.preF on Day 1 and Day 29.

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

Dosage and administration details:

Ad26.RSV.preF was administered as 5×10^{10} vp as 0.25 mL injection for toddlers.

Arm title	Cohort 1 (12 to 24 months): Placebo
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Arm description:

Subjects (seropositive for RSV within 42 days prior to vaccination) received single IM injection of placebo (sterile 0.9% saline) on Day 1 and Day 29.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Placebo was administered as sterile 0.9% saline for injection.

Number of subjects in period 1	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF
Started	8	4	24
Completed	6	4	24
Not completed	2	0	0
Withdrawal by subject	2	-	-

Number of subjects in period 1	Cohort 1 (12 to 24 months): Placebo
Started	12
Completed	12
Not completed	0
Withdrawal by subject	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort 0 (18 to 50 years): Ad26.RSV.preF
Reporting group description: Subjects received a single intramuscular (IM) injection of 1×10^{11} viral particles (vp) adenovirus serotype 26 vectored vaccine expressing the pre-fusion F-protein of the respiratory syncytial virus A2 strain (Ad26.RSV.preF) on Day 1 and Day 29.	
Reporting group title	Cohort 0 (18 to 50 years): Placebo
Reporting group description: Subjects received single IM injection of placebo (sterile 0.9% saline) on Day 1 and Day 29.	
Reporting group title	Cohort 1 (12 to 24 months): Ad26.RSV.preF
Reporting group description: Subjects (seropositive for respiratory syncytial virus [RSV] within 42 days prior to vaccination) received single IM injection of 5×10^{10} vp Ad26.RSV.preF on Day 1 and Day 29.	
Reporting group title	Cohort 1 (12 to 24 months): Placebo
Reporting group description: Subjects (seropositive for RSV within 42 days prior to vaccination) received single IM injection of placebo (sterile 0.9% saline) on Day 1 and Day 29.	

Reporting group values	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF
Number of subjects	8	4	24
Title for AgeCategorical Units: subjects			
Infants and toddlers (28 days-23 months)	0	0	24
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	4	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous			
Units: Years (Cohort 0) and Months (Cohort 1)			
Units: years			
median	37.5	32.0	18
full range (min-max)	28 to 47	27 to 41	13 to 23
Title for Gender Units: subjects			
Female	6	2	13
Male	2	2	11

Reporting group values	Cohort 1 (12 to 24 months): Placebo	Total	
Number of subjects	12	48	
Title for AgeCategorical Units: subjects			
Infants and toddlers (28 days-23 months)	12	36	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	

Adults (18-64 years)	0	12	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous			
Units: Years (Cohort 0) and Months (Cohort 1)			
Units: years			
median	17		
full range (min-max)	14 to 23	-	
Title for Gender			
Units: subjects			
Female	8	29	
Male	4	19	

End points

End points reporting groups

Reporting group title	Cohort 0 (18 to 50 years): Ad26.RSV.preF
Reporting group description: Subjects received a single intramuscular (IM) injection of 1×10^{11} viral particles (vp) adenovirus serotype 26 vectored vaccine expressing the pre-fusion F-protein of the respiratory syncytial virus A2 strain (Ad26.RSV.preF) on Day 1 and Day 29.	
Reporting group title	Cohort 0 (18 to 50 years): Placebo
Reporting group description: Subjects received single IM injection of placebo (sterile 0.9% saline) on Day 1 and Day 29.	
Reporting group title	Cohort 1 (12 to 24 months): Ad26.RSV.preF
Reporting group description: Subjects (seropositive for respiratory syncytial virus [RSV] within 42 days prior to vaccination) received single IM injection of 5×10^{10} vp Ad26.RSV.preF on Day 1 and Day 29.	
Reporting group title	Cohort 1 (12 to 24 months): Placebo
Reporting group description: Subjects (seropositive for RSV within 42 days prior to vaccination) received single IM injection of placebo (sterile 0.9% saline) on Day 1 and Day 29.	

Primary: Number of Subjects with at Least one Solicited Local Adverse Events (AEs)

End point title	Number of Subjects with at Least one Solicited Local Adverse Events (AEs) ^[1]
End point description: Solicited local AEs included erythema, swelling/induration, and pain/tenderness. Subjects were instructed to record occurrences of solicited local AEs in a diary from the day of vaccination (Day 1) to Day 8. The Full Analysis (FA) Set included all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations. All safety analyses were based on the FA set. Here, 'n' (number analyzed) signifies the number of subjects evaluable at a specified timepoint.	
End point type	Primary
End point timeframe: 7 days after each vaccination (up to 36 days)	
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 inferential statistics was planned for the primary endpoints.	

End point values	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF	Cohort 1 (12 to 24 months): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	24	12
Units: subjects				
Post Vaccination 1: n=8, 4, 24, 12	8	1	14	4
Post Vaccination 2: n=6, 4, 24, 12	6	0	14	4

Statistical analyses

Primary: Number of Subjects with at Least one Solicited Systemic Adverse Events

End point title	Number of Subjects with at Least one Solicited Systemic Adverse Events ^[2]
End point description:	
Solicited systemic AEs included fatigue/lethargy, headache, nausea/vomiting, myalgia and fever/pyrexia (defined as body temperature 38 degree Celsius or higher and derived from the oral temperature measurement), diarrhea, irritability/crying, loss of appetite. The Full analysis (FA) Set 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 analyzed) signifies the number of subjects evaluable at a specified timepoint. Here, '99999' indicates that the data for the particular category at the specified time-point were not applicable and collected.	
End point type	Primary
End point timeframe:	
7 days after each vaccination (up to 36 days)	

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 inferential statistics was planned for the primary endpoints.

End point values	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF	Cohort 1 (12 to 24 months): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	24	12
Units: subjects				
Arthralgia: Post Vaccination 1: n=8, 4	5	0	99999	99999
Chills: Post Vaccination 1: n=8, 4	4	0	99999	99999
Fatigue: Post Vaccination 1: n=8, 4, 24, 12	6	0	18	6
Headache: Post Vaccination 1: n=8, 4	4	1	99999	99999
Myalgia: Post Vaccination 1: n=8, 4	8	0	99999	99999
Nausea: Post Vaccination 1: n=8, 4, 24, 12	5	0	8	2
Pyrexia: Post Vaccination 1: n=8, 4, 24, 12	4	0	13	1
Arthralgia: Post Vaccination 2: n=6, 4	1	0	99999	99999
Chills: Post Vaccination 2: n=6, 4	1	0	99999	99999
Fatigue: Post Vaccination 2: n=6, 4, 24, 12	2	1	17	4
Headache: Post Vaccination 2: n=6, 4	2	1	99999	99999
Myalgia: Post Vaccination 2: n=6, 4	2	0	99999	99999
Nausea: Post Vaccination 2: n=6, 4, 24, 12	1	0	6	0
Pyrexia: Post Vaccination 2: n=6, 4, 24, 12	0	0	10	2
Diarrhea: Post Vaccination 1: n= 24, 12	99999	99999	3	4
Irritability: Post Vaccination 1: n= 24, 12	99999	99999	19	10
Loss of appetite: Post Vaccination 1: n= 24, 12	99999	99999	19	7
Diarrhea: Post Vaccination 2: n= 24, 12	99999	99999	5	3
Irritability: Post Vaccination 2: n= 24, 12	99999	99999	19	9
Loss of appetite: Post Vaccination 2: n= 24, 12	99999	99999	17	6

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Unsolicited Adverse Events

End point title	Number of Subjects with Unsolicited Adverse Events ^[3]
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End point description:

Unsolicited adverse events included all adverse events for which the subject is not specifically questioned in the participant diary. The Full analysis (FA) Set 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 analyzed) signifies the number of subjects evaluable at a specified timepoint.

End point type	Primary
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End point timeframe:

Up to 28 days after the each vaccination (up to 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: No inferential statistics was planned for the primary endpoints.

End point values	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF	Cohort 1 (12 to 24 months): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	24	12
Units: subjects				
Post Vaccination 1: n=8, 4, 24, 12	5	0	11	8
Post Vaccination 2: n=6, 4, 24, 12	4	1	12	6

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) ^[4]
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End point description:

SAEs are any untoward medical occurrence that at any dose results in death, is life-threatening (the subject was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe), requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect and is medically important, is a suspected transmission of any infectious agent via a medicinal product. The Full analysis (FA) Set included all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations. There were no SAEs reported for Cohort 0.

End point type	Primary
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End point timeframe:

Up to 1 year

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 inferential statistics was planned for the primary endpoints.

End point values	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF	Cohort 1 (12 to 24 months): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	24	12
Units: subjects	0	0	1	2

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titre of Neutralizing Antibodies Against Respiratory Syncytial Virus (RSV) A2 Strain

End point title	Geometric Mean Titre of Neutralizing Antibodies Against Respiratory Syncytial Virus (RSV) A2 Strain
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End point description:

Geometric mean titre of neutralizing antibody against RSV A2 strain were assessed using an RSV neutralization assay. The Per-protocol Immunogenicity (PPI) Set included all randomized and vaccinated subjects for whom immunogenicity data are available, excluding subject samples with major protocol deviations expecting to impact the immunogenicity outcomes. Here, 'n' (number analyzed) signifies the number of subjects evaluable at a specified timepoint.

End point type	Secondary
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End point timeframe:

Days 29, 57 and 211

End point values	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF	Cohort 1 (12 to 24 months): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	24	12
Units: Titers (IC50 units)				
geometric mean (confidence interval 95%)				
Post Vaccination 1 (Day 29): n=6, 3, 17, 7	1089 (483 to 2456)	603 (101 to 3596)	1608 (730 to 3544)	156 (68 to 358)
Post Vaccination 2 (Day 57): n=6, 3, 17, 8	926 (485 to 1769)	566 (114 to 2805)	2235 (1586 to 3150)	198 (89 to 441)
Post Vaccination 2 (Day 211): n=6, 3, 16, 7	704 (325 to 1526)	574 (139 to 2374)	1164 (734 to 1847)	165 (70 to 387)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Cytokine Subsets (CD4, CD8, Th1 and Th2 Cytokines) to Evaluate Total Cytokine Response

End point title	Percentage of Cytokine Subsets (CD4, CD8, Th1 and Th2 Cytokines) to Evaluate Total Cytokine Response
End point description:	
Total cytokine response (CD4, CD8, Th1 and Th2 Cytokines) after in vitro RSV F protein peptide stimulation was reported as the percentage of CD4+ and CD8+ T cells that produce at least 1 of 3 cytokines. The PPI Set included all randomized and vaccinated subjects for whom immunogenicity data are available, excluding subject samples with major protocol deviations expecting to impact the immunogenicity outcomes. Here, 'n' (number analyzed) signifies the number of subjects evaluable at a specified timepoint. Here, '99999' indicates that the data for the particular arm at the specified time-point were not evaluable. Here 'N' (Number of subjects analyzed) included all subjects evaluable for this endpoint.	
End point type	Secondary
End point timeframe:	
Days 29 and 57	

End point values	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF	Cohort 1 (12 to 24 months): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	13	8
Units: Percentage of cytokines subset				
median (inter-quartile range (Q1-Q3))				
CD4: Post Vaccination 1 (Day 29): n=3, 3, 13, 8	0.170 (0.100 to 0.210)	0.060 (0.050 to 0.080)	0.089 (0.062 to 0.131)	0.074 (0.056 to 0.123)
CD4: Post Vaccination 2 (Day 57): n=4, 3	0.150 (0.110 to 0.350)	0.040 (0.020 to 0.120)	99999 (99999 to 99999)	99999 (99999 to 99999)
CD8: Post Vaccination 1 (Day 29): n=3, 3, 14, 8	0.150 (0.080 to 0.230)	0.090 (0.020 to 0.110)	0.077 (0.024 to 0.116)	0.053 (0.016 to 0.110)
CD8: Post Vaccination 2 (Day 57): n=4, 3	0.080 (0.070 to 0.210)	0.060 (0.000 to 0.190)	99999 (99999 to 99999)	99999 (99999 to 99999)
Th1: Post Vaccination 1 (Day 29): n=4, 3, 13, 8	0.098 (0.040 to 0.146)	0.049 (0.037 to 0.057)	0.034 (0.025 to 0.078)	0.028 (0.017 to 0.055)
Th1: Post Vaccination 2 (Day 57): n=4, 3	0.112 (0.083 to 0.302)	0.039 (0.008 to 0.061)	99999 (99999 to 99999)	99999 (99999 to 99999)
Th2: Post Vaccination 1 (Day 29): n=4, 3, 13, 8	0.003 (0.002 to 0.006)	0.001 (0.001 to 0.001)	0.005 (0.001 to 0.007)	0.003 (0.002 to 0.007)
Th2: Post Vaccination 2 (Day 57): n=4, 3	0.003 (0.001 to 0.022)	0.001 (0.001 to 0.001)	99999 (99999 to 99999)	99999 (99999 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Response of RSV Pre- and Post- Fusion Protein (ELISA)

End point title	Antibody Response of RSV Pre- and Post- Fusion Protein (ELISA)
End point description:	
Analysis of antibodies binding to RSV F protein in post-fusion and pre-fusion form was performed using Elisa. The PPI Set included all randomized and vaccinated subjects for whom immunogenicity data are available, excluding subject samples with major protocol deviations expecting to impact the immunogenicity outcomes. Here 'N' (Number of subjects analyzed) included all subjects evaluable for	

this endpoint. Here, 'n' (number analyzed) signifies the number of subjects evaluable at a specified timepoint.

End point type	Secondary
End point timeframe:	
Days 1, 29, 57 and 211	

End point values	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF	Cohort 1 (12 to 24 months): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	17	9
Units: Elisa units per liter (EU/L)				
geometric mean (confidence interval 95%)				
preF: Post Vaccination 1 (Day 1): n=8, 3, 17, 9	197 (132 to 295)	249 (50 to 1234)	59 (36 to 97)	113 (57 to 223)
preF: Post Vaccination 1 (Day 29): n=6, 3, 17, 8	441 (304 to 639)	261 (60 to 1138)	1174 (524 to 2630)	106 (56 to 199)
preF: Post Vaccination 2 (Day 57): n=6, 3, 17, 8	481 (317 to 729)	244 (60 to 992)	1918 (1497 to 2456)	148 (54 to 402)
preF: Post Vaccination 2 (Day 211): n=6, 3, 16, 7	418 (264 to 664)	292 (45 to 1895)	924 (639 to 1334)	120 (39 to 370)
postF: Post Vaccination 2 (Day 1): n=8, 3, 17, 9	196 (112 to 346)	191 (19 to 1879)	77 (48 to 125)	94 (46 to 190)
postF: Post Vaccination 2 (Day 29): n=6, 3, 17, 8	328 (207 to 521)	207 (25 to 1738)	686 (371 to 1268)	86 (47 to 158)
postF: Post Vaccination 2 (Day 57): n=6, 3, 17, 8	341 (198 to 589)	179 (23 to 1370)	863 (630 to 1184)	109 (52 to 232)
postF: Post Vaccination 2 (Day 211): n=6, 3, 16, 7	268 (142 to 507)	181 (18 to 1870)	420 (306 to 576)	91 (33 to 256)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 1 year

Adverse event reporting additional description:

Safety data were analyzed for all subjects who were randomized and received at least 1 dose of study vaccine.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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Reporting groups

Reporting group title	Cohort 0 (18 to 50 years): Ad26.RSV.preF
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Reporting group description:

Subjects received a single intramuscular (IM) injection of 1×10^{11} viral particles (vp) adenovirus serotype 26 vectored vaccine expressing the pre-fusion F-protein of the respiratory syncytial virus A2 strain (Ad26.RSV.preF) on Day 1 and Day 29.

Reporting group title	Cohort 0 (18 to 50 years): Placebo
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Reporting group description:

Subjects received single IM injection of placebo (sterile 0.9% saline) on Day 1 and Day 29.

Reporting group title	Cohort 1 (12 to 24 months): Ad26.RSV.preF
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Reporting group description:

Subjects (seropositive for RSV within 42 days prior to vaccination) received single IM injection of 5×10^{10} vp Ad26.RSV.preF on Day 1 and Day 29.

Reporting group title	Cohort 1 (12 to 24 months): Placebo
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Reporting group description:

Subjects (seropositive for RSV within 42 days prior to vaccination) received single IM injection of placebo (sterile 0.9% saline) on Day 1 and Day 29.

Serious adverse events	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Wheezing			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 1 (12 to 24 months): Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Wheezing			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 0 (18 to 50 years): Ad26.RSV.preF	Cohort 0 (18 to 50 years): Placebo	Cohort 1 (12 to 24 months): Ad26.RSV.preF
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 8 (75.00%)	1 / 4 (25.00%)	19 / 24 (79.17%)
Investigations			
Heart Rate Increased subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Influenza B Virus Test Positive subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Lymphocyte Count Decreased subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Respiratory Syncytial Virus Test Positive subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache subjects affected / exposed	3 / 8 (37.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	3	0	0
Lethargy subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Loss of Consciousness subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy to Animal subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal Discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Odynophagia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Teething			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Rales			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Irritation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 24 (4.17%) 1
Rhonchi subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 24 (0.00%) 0
Skin and subcutaneous tissue disorders Dermatitis Diaper subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 24 (0.00%) 0
Miliaria subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 24 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 4 (25.00%) 1	0 / 24 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	1 / 24 (4.17%) 1
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 24 (0.00%) 0
Irritability subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 4 (0.00%) 0	0 / 24 (0.00%) 0
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 24 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 24 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 4 (0.00%) 0	0 / 24 (0.00%) 0

Myalgia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Pain in Extremity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Infections and infestations			
Anal Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Body Tinea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Enterovirus Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Hand-Foot-And-Mouth Disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Oral Herpes			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Otitis Externa			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Otitis Media			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	4 / 24 (16.67%)
occurrences (all)	0	0	5
Respiratory Tract Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	4 / 24 (16.67%)
occurrences (all)	0	0	4
Rhinitis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Skin Bacterial Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Tinea Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 8 (37.50%)	0 / 4 (0.00%)	8 / 24 (33.33%)
occurrences (all)	3	0	9
Urinary Tract Infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Viral Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Viral Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 4 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 1 (12 to 24 months): Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 12 (83.33%)		
Investigations			
Heart Rate Increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Influenza B Virus Test Positive			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Lymphocyte Count Decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Respiratory Syncytial Virus Test Positive</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>1 / 12 (8.33%)</p> <p>1</p>		
<p>Nervous system disorders</p> <p>Headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Lethargy</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Loss of Consciousness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p>		
<p>General disorders and administration site conditions</p> <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 12 (8.33%)</p> <p>2</p>		
<p>Immune system disorders</p> <p>Allergy to Animal</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 12 (8.33%)</p> <p>1</p>		
<p>Gastrointestinal disorders</p> <p>Abdominal Discomfort</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Constipation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diarrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>2 / 12 (16.67%)</p> <p>2</p>		

Gastritis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Odynophagia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Teething			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rales			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory Tract Irritation			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rhonchi			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dermatitis Diaper			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Miliaria			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 12 (8.33%)</p> <p>1</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p>		
<p>Psychiatric disorders</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Irritability</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 12 (8.33%)</p> <p>1</p> <p>2 / 12 (16.67%)</p> <p>3</p>		
<p>Renal and urinary disorders</p> <p>Dysuria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pollakiuria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Myalgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in Extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p> <p>0 / 12 (0.00%)</p> <p>0</p>		
<p>Infections and infestations</p> <p>Anal Infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 12 (0.00%)</p> <p>0</p>		

Body Tinea			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Enterovirus Infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hand-Foot-And-Mouth Disease			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Oral Herpes			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Otitis Externa			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Otitis Media			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Respiratory Tract Infection			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	5		
Rhinitis			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Skin Bacterial Infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Tinea Infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Urinary Tract Infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Viral Infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Viral Rash subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 January 2018	The second amendment was made to increase the number of seropositive toddlers by 12 to generate additional safety data; to specify postvaccination monitoring time; and to correct minor changes, clarifications, and corrections made throughout the protocol.
14 November 2018	The third amendment was made to change the enzyme immunoassay (EIA) cut-off criterion for seropositivity to titers >10 EIA units and to allow enrollment of respiratory syncytial virus (RSV) seropositive toddlers who have been screened for a different clinical study of the sponsor if RSV seropositivity was determined using the RSV EIA or virus neutralization assay, to potentially aid recruitment in the study.
18 April 2019	The fourth amendment was made to reduce the overall number of RSV-seropositive toddlers in the study from 48 to 36.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Conclusions on the magnitude of the cellular immune response should be drawn with caution considering the small sample size.

Notes: