Clinical trial results:
An Exploratory, Phase 2a, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Prophylactic Efficacy of a Single Immunization of Ad26.RSV.preF Against Respiratory Syncytial Virus Infection in a Virus Challenge Model in Healthy 18 to 50 Year-Old Adults

Summary

EudraCT number	2017-003194-33
Trial protocol	GB
Global end of trial date	27 November 2018

Results information

Result version number	v2 (current)
This version publication date	23 July 2021
First version publication date	18 December 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	VAC18193RSV2002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03334695
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)	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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 November 2018
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 a trend for the prophylactic efficacy of a single dose of 1*10^11 viral particles (vp) of Adenovirus Serotype 26 Based Respiratory Syncytial Virus Pre-fusion F Protein (Ad26.RSV.preF) administered intramuscularly (IM) to adults aged 18 to 50 years in the RSV challenge model in terms of the reduction of nasal wash viral load as measured by the area under the curve (AUC) over time by quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) compared to placebo.

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 Practice and applicable regulatory requirements. Safety was evaluated based on the following variables: adverse events (AEs), clinical laboratory tests (hematology, serum chemistry, and urinalysis), vital signs measurements, physical examinations and electrocardiograms (ECGs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 August 2017
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	United Kingdom: 63
Worldwide total number of subjects	63
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	63
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In total, 64 subjects were screened. Of these, 63 subjects were randomized and received the study vaccine. One subject was randomized in error and did not receive the study vaccine hence not included in the analyses.

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
Arm title	Ad26.RSV.preF (1*10^11 vp)

Arm description:

Subjects received a single intramuscular injection of 1*10^11 viral particles (vp) of Ad26.RSV.preF on Day -28 followed by intranasal challenge with a respiratory syncytial virus (RSV)-A Memphis 37b virus on Day 0.

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 an intramuscular injection.

Arm title	Placebo

Arm description:

Subjects received a single intramuscular injection of matching placebo on Day -28 followed by intranasal challenge with RSV-A Memphis 37b virus on Day 0.

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:

Subjects received an intramuscular injection of matching placebo.

Number of subjects in period 1	Ad26.RSV.preF (1*10^11 vp)	Placebo
Started	31	32
Received Challenge	27	26
Completed	27	26
Not completed	4	6
Physician decision	1	2
Lost to follow-up	3	3
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Ad26.RSV.preF (1*10^11 vp)
Reporting group description:	
Subjects received a single intramuscular injection of 1*10^11 viral particles (vp) of Ad26.RSV.preF on Day -28 followed by intranasal challenge with a respiratory syncytial virus (RSV)-A Memphis 37b virus on Day 0.	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single intramuscular injection of matching placebo on Day -28 followed by intranasal challenge with RSV-A Memphis 37b virus on Day 0.	

Reporting group values	Ad26.RSV.preF (1*10^11 vp)	Placebo	Total
Number of subjects	31	32	63
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	31	32	63
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	25.9	25.9	
standard deviation	± 6.19	± 6.56	-
Title for Gender Units: subjects			
Female	12	6	18
Male	19	26	45

End points

End points reporting groups

Reporting group title	Ad26.RSV.preF (1*10^11 vp)
Reporting group description:	
Subjects received a single intramuscular injection of 1*10^11 viral particles (vp) of Ad26.RSV.preF on Day -28 followed by intranasal challenge with a respiratory syncytial virus (RSV)-A Memphis 37b virus on Day 0.	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single intramuscular injection of matching placebo on Day -28 followed by intranasal challenge with RSV-A Memphis 37b virus on Day 0.	

Primary: Area Under the Viral Load-time Curve (VL-AUC) of RSV by Quantitative Reverse Transcriptase-polymerase Chain Reaction (qRT-PCR)

End point title	Area Under the Viral Load-time Curve (VL-AUC) of RSV by Quantitative Reverse Transcriptase-polymerase Chain Reaction (qRT-PCR)
End point description:	
VL-AUC for RSV was determined by qRT-PCR assay of nasal wash samples. Here, values below the lower limit of quantification (LLOQ) were imputed with zero. The Intent-to-treat-Challenge (ITTc) population is a subset of the Full Analysis Set (FAS) (all subjects who were randomized and received study vaccine, regardless of the occurrence of protocol deviations) including all randomized, vaccinated and challenged subjects.	
End point type	Primary
End point timeframe:	
From Day 2 to Day 12	

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: log10 copies*hour per millilitre (h/mL)				
median (inter-quartile range (Q1-Q3))	0 (0.0 to 268.8)	236 (20.3 to 605.8)		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Ad26.RSV.preF (1*10^11 vp) v Placebo

Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	Wilcoxon Rank Sum test

Secondary: Peak Viral Load of RSV-A Memphis 37b

End point title	Peak Viral Load of RSV-A Memphis 37b

End point description:

Peak viral load of RSV-A Memphis 37b was defined as the maximum viral load by quantitative RT-PCR assay of nasal wash samples. Here, values below the lower limit of quantification (LLOQ) were imputed with zero. The ITTc population is a subset of the Full Analysis Set (FAS) (all subjects who were randomized and received study vaccine, regardless of the occurrence of protocol deviations) including all randomized, vaccinated and challenged subjects.

End point type	Secondary

End point timeframe:

From Day 2 and Day 12

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: log10 copies per mL				
median (inter-quartile range (Q1-Q3))	0.000 (0.000 to 4.539)	5.365 (3.027 to 6.665)		

Statistical analyses

No statistical analyses for this end point

Secondary: Viral Load by Quantitative RT-PCR Assay on Day 6 and 7

End point title	Viral Load by Quantitative RT-PCR Assay on Day 6 and 7

End point description:

Viral load determined by quantitative RT-PCR assay of nasal wash samples on Day 6 and Day 7 were reported. Here, values below the lower limit of quantification (LLOQ) were imputed with zero. The ITTc population is a subset of the FAS (all subjects who were randomized and received study vaccine, regardless of the occurrence of protocol deviations) including all randomized, vaccinated and challenged subjects. Here 'n' (number of subjects analyzed) signifies the number of subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Day 6 (0 hour and 12 hours) and Day 7 (0 hour and 12 hours)

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: log10 copies per mL				
arithmetic mean (standard error)				
Day 6: 0 hour (n=27, 26)	0.821 (± 0.349)	2.898 (± 0.630)		
Day 6: 12 hour (n=26, 26)	1.261 (± 0.433)	2.939 (± 0.604)		
Day 7: 0 hour (n=27, 26)	1.761 (± 0.436)	3.072 (± 0.586)		
Day 7: 12 hour (n=27, 25)	1.552 (± 0.443)	3.025 (± 0.530)		

Statistical analyses

No statistical analyses for this end point

Secondary: VL-AUC of RSV by Quantitative Culture of RSV (Plaque Assay) on Day 6 and 7

End point title	VL-AUC of RSV by Quantitative Culture of RSV (Plaque Assay) on Day 6 and 7

End point description:

VL-AUC of RSV by the quantitative culture of nasal wash samples was determined. pfu*h/mL stands for plaque-forming units hour per millilitre. The ITTc population is a subset of the FAS (all subjects who were randomized and received study vaccine, regardless of the occurrence of protocol deviations) including all randomized, vaccinated and challenged subjects. Here 'n' (number analyzed) signifies the number of subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Day 6 (0 hour and 12 hours) and Day 7 (0 hour and 12 hours)

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: log10 pfu*h/mL				
arithmetic mean (standard error)				
Day 6: 0 hour (n=27, 26)	0.278 (± 0.1936)	1.587 (± 0.4159)		
Day 6: 12 hour (n=27, 26)	0.304 (± 0.2198)	1.737 (± 0.4320)		
Day 7: 0 hour (n=27, 26)	0.101 (± 0.1015)	1.226 (± 0.3505)		
Day 7: 12 hour (n=27, 25)	0.276 (± 0.1931)	1.237 (± 0.3891)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Symptomatic RSV Infections

End point title	Percentage of Subjects with Symptomatic RSV Infections

End point description:

Symptomatic RSV infection is defined in two ways (Conservative and Liberal). Conservative: subjects had 2 or more quantifiable RT-PCR measurements on different samples, with one of following: symptoms of 2 different categories of subject symptom card (SSC) (Upper Respiratory [runny/stuffy nose, sneezing, sore throat, earache], Lower Respiratory [cough, shortness of breath, chest tightness, wheeze], Systemic [malaise, headache, muscle and/or joint ache]) regardless of grade and assessment timepoint or Grade 2 symptom from any category; Liberal (RT-PCR): had 2/more quantifiable RT-PCR measurements, with clinical symptom of any severity. The Intent-to-treat-Challenge (ITTc) population is a subset of the Full Analysis Set (FAS) (all subjects who were randomized and received study vaccine, regardless of the occurrence of protocol deviations) included all randomized, vaccinated and challenged subjects.

End point type	Secondary

End point timeframe:

From Day 2 to Day 12

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Percentage of subjects				
number (not applicable)				
Liberal	33.3	61.5		
Conservative	22.2	46.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Clinical Symptoms Score at Day 6 and 7

End point title	Total Clinical Symptoms Score at Day 6 and 7

End point description:

The total clinical symptom score was determined as the sum of the scores (grades) ranges from 0 (no symptom) to 52 (severe symptoms) of the 13 self-reportable symptoms on the SSC. Clinical symptoms includes runny nose, stuffy nose, sneezing, sore throat, ear ache, malaise, headache, muscle and/or joint ache, chilliness/ feverishness, cough, chest tightness, shortness of breath and wheeze. For every separate symptom, the score ranges from 0 (I have no symptom) to 4 (its quite bothersome most of the times and stop from participating in activities). The ITTc population is a subset of the FAS (all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations) including all randomized, vaccinated and challenged subjects.

End point type	Secondary

End point timeframe:

Day 6 and 7: morning, afternoon and evening

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Units on a scale				
arithmetic mean (standard error)				
Day 6: Evening	0.5 (± 0.28)	2.5 (± 0.65)		
Day 6: Morning	0.6 (± 0.18)	2.6 (± 0.64)		
Day 6: Afternoon	0.4 (± 0.18)	2.8 (± 0.74)		
Day 7: Evening	0.6 (± 0.32)	2.5 (± 0.63)		
Day 7: Morning	0.6 (± 0.23)	2.5 (± 0.70)		
Day 7: Afternoon	0.6 (± 0.32)	2.5 (± 0.70)		

Statistical analyses

No statistical analyses for this end point

Secondary: Weight of Mucus Secretions Over Time

End point title	Weight of Mucus Secretions Over Time

End point description:

The weight mucous over time was determined in grams using eCRF forms. Subjects were given pre-weighed packets of paper tissues. After each tissue was used for nose blowing or sneezing, the subjects should store them in an airtight plastic bag to calculate the weight of mucus from Day 0 to Day 12. All paper tissues used by each subjects were collected for each 24-hour period up to Day 12, to determine daily mucus weight. The ITTc population is a subset of the FAS (all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations) including all randomized, vaccinated and challenged subjects. Here 'n' (number analyzed) signifies the number of subjects analyzed for this endpoint at specified timepoints.

End point type	Secondary

End point timeframe:

Day 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Grams				
arithmetic mean (standard error)				
Day 0 (27, 25)	0.586 (± 0.1883)	0.175 (± 0.0913)		
Day 1 (26, 25)	0.228 (± 0.0621)	0.086 (± 0.0333)		
Day 2 (27, 25)	0.997 (± 0.2350)	0.428 (± 0.1459)		
Day 3 (27, 25)	0.970 (± 0.2176)	0.543 (± 0.1333)		

Day 4 (27, 26)	1.164 (± 0.3535)	0.714 (± 0.2123)		
Day 5 (27, 26)	1.440 (± 0.8609)	1.068 (± 0.3539)		
Day 6 (27, 26)	1.226 (± 0.4925)	3.132 (± 1.0991)		
Day 7 (27, 26)	1.715 (± 0.7201)	5.124 (± 1.3257)		
Day 8 (27, 26)	0.799 (± 0.2960)	3.230 (± 1.1022)		
Day 9 (27, 26)	1.004 (± 0.4147)	1.798 (± 0.4406)		
Day 10 (27, 26)	0.907 (± 0.3457)	1.785 (± 0.4838)		
Day 11 (27, 26)	0.749 (± 0.2430)	1.172 (± 0.3442)		
Day 12 (27, 26)	0.622 (± 0.2647)	0.990 (± 0.3005)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Tissue Count Over Time

End point title	Number of Tissue Count Over Time

End point description:

Number of tissues used by subjects per time point were reported using eCRF forms. Subjects were given pre-weighed packets of paper tissues. After each tissue was used for nose blowing or sneezing, the subjects should store them in an airtight plastic bag to calculate the number of tissues used from Day 0 to Day 12. All paper tissues used by each subjects were collected for each 24-hour period up to Day 12, to determine daily number of tissues used. The ITTc population is a subset of the FAS (all subjects who were randomized and received study vaccine, regardless of the occurrence of protocol deviations) including all randomized, vaccinated and challenged subjects.

End point type	Secondary

End point timeframe:

Day 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Tissues				
arithmetic mean (standard error)				
Day 0	1.8 (± 0.53)	0.7 (± 0.33)		
Day 1	1.7 (± 0.41)	0.7 (± 0.27)		
Day 2	2.9 (± 0.65)	1.2 (± 0.32)		
Day 3	1.9 (± 0.45)	1.3 (± 0.28)		
Day 4	2.3 (± 0.49)	1.5 (± 0.31)		
Day 5	2.1 (± 0.81)	2.3 (± 0.68)		
Day 6	2.4 (± 0.77)	5.1 (± 1.59)		
Day 7	2.8 (± 0.92)	8.1 (± 1.94)		

Day 8	2.0 (± 0.71)	5.2 (± 1.38)		
Day 9	2.3 (± 0.72)	2.8 (± 0.53)		
Day 10	1.8 (± 0.61)	2.7 (± 0.61)		
Day 11	1.6 (± 0.47)	2.0 (± 0.50)		
Day 12	1.4 (± 0.40)	1.7 (± 0.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Unsolicited Adverse Events (AEs)

End point title	Percentage of Subjects With Unsolicited Adverse Events (AEs)

End point description:

Unsolicited AEs are all AEs for which subjects were specifically not questioned in the subject diary. 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. The Full Analysis 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) included all evaluable subjects who were analyzed at specified categories.

End point type	Secondary

End point timeframe:

Up to 28 days post-vaccination and up to 28 days post-challenge

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: Percentage of subjects				
number (not applicable)				
Post-dose (n=31, 32)	35.5	46.9		
Post-challenge (n=27,26)	74.1	69.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Serious Adverse Events (SAEs)

End point title	Percentage of Subjects With Serious Adverse Events (SAEs)

End point description:

An SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/ incapacity; congenital anomaly. The Full Analysis 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) included all evaluable subjects who were analyzed at specified categories.

End point type	Secondary

End point timeframe:

Up to 6 months post-vaccination and up to 6 months post-challenge

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: Percentage of subjects				
number (not applicable)				
Post-vaccination (n=31, 32)	0	0		
Post-challenge (n=27, 26)	3.2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Solicited Local and Systemic AEs

End point title	Percentage of Subjects With Solicited Local and Systemic AEs

End point description:

Solicited local AEs: erythema, swelling/induration, and pain/tenderness. Solicited systemic AEs: fatigue, headache, myalgia, arthralgia, chills, nausea and fever. The Full Analysis Set 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	Secondary

End point timeframe:

7 days post-vaccination (Day -21)

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: Percentage of Subjects				
number (not applicable)				
Solicited local AEs	100.0	18.8		
Solicited systemic AEs	100.0	50.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Vital Signs Abnormalities

End point title	Percentage of Subjects With Vital Signs Abnormalities

End point description:

Percentage of subjects with vital signs abnormalities were reported. Vital signs measurements included body temperature (measured in degree celsius from less than [<] 37.5 to <39.5), respiratory rate, systolic and diastolic blood pressure, and pulse rate, which were graded by FDA Toxicity Grading Scale Grade 0 (=no grade), Grade 1 (=mild), Grade 2 (=moderate), Grade 3 (=severe) and Grade 4 (=potentially life-threatening). The Full Analysis Set included all subjects who were randomized and received study vaccine, regardless of the occurrence of protocol deviations. Here 'n' (number analyzed) included all evaluable subjects who were analyzed at specified categories.

End point type	Secondary

End point timeframe:

Up to Day 28 post-challenge

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: Percentage of subjects				
number (not applicable)				
Post-dose: Temperature (<37.5)	64.5	93.8		
Post-dose: Temperature (37.5-<38.0)	22.6	3.1		
Post-dose: Temperature (38.0-<38.5)	6.5	0		
Post-dose: Temperature (38.5-<39.0)	6.5	3.1		
Post-dose: Bradycardia (pulse): Grade 1	12.9	3.1		
Post-dose: Bradycardia (pulse): Grade 2	6.5	6.3		
Post-dose: Bradycardia (pulse): Grade 3/4	3.2	0		
Post-dose: Hypertension (diastolic): Grade 1	0	3.1		
Post-dose: Hypertension (diastolic): Grade 2	6.5	0		
Post-dose: Hypertension (systolic): Grade 1	3.2	3.1		
Post-dose: Respiratory rate: Grade 1	25.8	18.8		
Post-dose: Tachycardia (pulse): Grade 1	3.2	0		
Post-challenge: Bradycardia (pulse): Grade 1	18.5	11.5		
Post-challenge: Bradycardia (pulse): Grade 2	3.7	3.8		
Post-challenge: Bradycardia (pulse): Grade 3/4	3.7	0		
Post-challenge: Hypertension (diastolic): Grade 1	3.7	0		
Post-challenge: Hypertension (systolic): Grade 1	0	7.7		
Post-challenge: Respiratory rate: Grade 1	25.9	26.9		
Post-challenge: Tachycardia (pulse): Grade 1	3.7	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Electrocardiogram (ECG) Abnormalities

End point title	Percentage of Subjects With Electrocardiogram (ECG) Abnormalities

End point description:

ECG parameters included heart rate, PR, QRS, QTcB, QTcF, and the uncorrected QT interval which were graded by FDA Toxicity Grading Scale Grade 0 (=no grade), Grade 1 (=mild), Grade 2 (=moderate), Grade 3 (=severe) and Grade 4 (=potentially life-threatening). The ITTc population is a subset of the FA (all subjects who were randomized and received at least one dose of study vaccine, regardless of the occurrence of protocol deviations) set including all randomized, vaccinated and challenged subjects.

End point type	Secondary

End point timeframe:

Up to Day 12 post challenge

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Percentage of Subjects				
number (not applicable)				
Heart rate: Abnormally low: Grade 1	0	3.8		
Heart rate: Abnormally low: Grade 2	0	3.8		
QTc Bazett (450 millisecond [ms], 480 ms)	0	3.8		
QTc Bazett (increase from baseline [30; 60] ms)	7.4	11.5		
QTc Fridericia:(increase from baseline[30; 60]ms)	3.7	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Laboratory Abnormalities (Graded)

End point title	Percentage of Subjects With Clinical Laboratory Abnormalities (Graded)

End point description:

Percentage of subjects with clinical laboratory abnormalities were reported. The biochemical and hematological parameters analyzed were- Alanine aminotransferase (AA), Alkaline phosphatase (AP), Aspartate aminotransferase (AsP), Hyperkalemia, Hypernatremia, Hypoglycemia, Hypophosphatemia, Hemoglobin, Neutrophils, White blood cell (WBC) – increase and Urine protein, which were graded by FDA Toxicity Grading Scale Grade 0 (=no grade), Grade 1 (=mild), Grade 2 (=moderate), Grade 3 (=severe) and Grade 4 (=potentially life-threatening). 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	Secondary

End point timeframe:

Up to Day 28 post-challenge

End point values	Ad26.RSV.preF (1*10^11 vp)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: Percentage of subjects				
number (not applicable)				
Post Dose: AA: Grade 1 (n=31, 32)	9.7	0		
Post Dose: AP: Grade 1 (n=31, 32)	0	3.1		
Post Dose: AsA: Grade 1 (n=31, 32)	6.5	0		
Post Dose: AsA: Grade 2 (n=31, 32)	0	3.1		
Post Dose: Hyperkalemia: Grade 2 (n=31, 32)	3.2	0		
Post Dose: Hypernatremia: Grade 2 (n=31, 32)	3.2	0		
Post Dose: Hypoglycemia: Grade 2 (n=31, 32)	0	3.1		
Post Dose: Hypophosphatemia:Grade 1 (n=31, 32)	3.2	0		
Post Dose: Hypophosphatemia:Grade 2 (n=31, 32)	9.7	0		
Post Dose: Hemoglobin: Grade 1 (n=31, 32)	3.2	3.1		
Post Dose: Hemoglobin: Grade 2 (n=31, 32)	3.2	0		
Post Dose: Neutrophils: Grade 1 (n=31, 32)	12.9	6.3		
Post Dose: WBC increase: Grade 1 (n=31, 32)	0	3.1		
Post Dose: Urine Protein: Grade 1 (n=31, 32)	3.2	3.1		
Post Challenge: AA: Grade 1 (n=27, 26)	25.9	15.4		
Post Challenge: AA: Grade 2 (n=27, 26)	7.4	3.8		
Post Challenge: AP: Grade 1 (n=27, 26)	0	3.8		
Post Challenge: AsA: Grade 1 (n=27, 26)	14.8	15.4		
Post Challenge: AsA: Grade 2 (n=27, 26)	3.7	3.8		
Post Challenge: AsA: Grade 4 (n=27, 26)	0	3.8		
Post Challenge: Bilirubin: Grade 2 (n=27, 26)	3.7	0		
Post Challenge: Hyperglycemia: Grade 1 (n=27, 26)	0	3.8		
Post Challenge: Hyperkalemia: Grade 1 (n=27, 26)	3.7	3.8		
Post Challenge: Hypernatremia: Grade 2 (n=27, 26)	3.7	0		
Post Challenge: Hypophosphatemia:Grade 1 (n=27,26)	3.7	0		
Post Challenge: Hypoproteinemia:Grade 1 (n=27, 26)	11.1	0		
Post Challenge: Eosinophils: Grade 1 (n=27, 26)	0	7.7		
Post Challenge: Hemoglobin: Grade 1 (n=27, 26)	7.4	0		

Post Challenge: Neutrophils: Grade 1 (n=27, 26)	7.4	0		
Post Challenge: Platelets: Grade 1 (n=27, 26)	3.7	3.8		
Post Challenge: Platelets: Grade 2 (n=27, 26)	0	3.8		
Post Challenge: WBC increase: Grade 1 (n=27, 26)	3.7	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 6 months post-vaccination and up to 6 months post-challenge	
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	21.0

Reporting groups	
Reporting group title	Post-dose: Ad26.RSV.preF (1x10^11 vp)
Reporting group description:	
Subjects received a single intramuscular injection of 1*10^11 viral particles (vp) of Ad26.RSV.preF on Day -28.	
Reporting group title	Post-dose: Placebo
Reporting group description:	
Subjects received a single intramuscular injection of matching placebo on Day -28.	
Reporting group title	Post-challenge: Challenge After Ad26.RSV.preF
Reporting group description:	
Subjects undergone intranasal challenge with RSV-A Memphis 37b virus on Day 0, after receiving single intramuscular doses of 1x1011 vp of Ad26.RSV.preF on Day -28.	
Reporting group title	Post-challenge: Challenge After Placebo
Reporting group description:	
Subjects undergone intranasal challenge with RSV-A Memphis 37b virus on Day 0, after receiving single intramuscular doses of placebo on Day -28.	

Serious adverse events	Post-dose: Ad26.RSV.preF (1x10^11 vp)	Post-dose: Placebo	Post-challenge: Challenge After Ad26.RSV.preF
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 27 (3.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Reproductive system and breast disorders			
Ovarian Cyst			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 27 (3.70%)
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	Post-challenge: Challenge After Placebo		
Total subjects affected by serious			

adverse events			
subjects affected / exposed	0 / 26 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Reproductive system and breast disorders			
Ovarian Cyst			
subjects affected / exposed	0 / 26 (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: 5 %

Non-serious adverse events	Post-dose: Ad26.RSV.preF (1x10^11 vp)	Post-dose: Placebo	Post-challenge: Challenge After Ad26.RSV.preF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 31 (12.90%)	9 / 32 (28.13%)	16 / 27 (59.26%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	7 / 27 (25.93%)
occurrences (all)	2	0	7
Aspartate Aminotransferase Increased			
subjects affected / exposed	2 / 31 (6.45%)	1 / 32 (3.13%)	2 / 27 (7.41%)
occurrences (all)	2	1	2
Troponin T Increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	0 / 31 (0.00%)	2 / 32 (6.25%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 31 (3.23%)	4 / 32 (12.50%)	2 / 27 (7.41%)
occurrences (all)	1	4	2
Blood and lymphatic system disorders			

Lymphadenopathy			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	6 / 27 (22.22%)
occurrences (all)	0	0	6
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	1 / 27 (3.70%)
occurrences (all)	0	0	1
Oropharyngeal Pain			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	0 / 27 (0.00%)
occurrences (all)	1	1	0
Epistaxis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dry Skin			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	3 / 27 (11.11%)
occurrences (all)	1	1	3
Infections and infestations			
Pharyngitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	3 / 27 (11.11%)
occurrences (all)	0	0	3

Non-serious adverse events	Post-challenge: Challenge After Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 26 (61.54%)		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	3 / 26 (11.54%)		
occurrences (all)	3		
Aspartate Aminotransferase Increased			
subjects affected / exposed	2 / 26 (7.69%)		
occurrences (all)	2		

Troponin T Increased subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2		
Injury, poisoning and procedural complications Sunburn subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2		
Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all) Oropharyngeal Pain subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 4 2 / 26 (7.69%) 2 3 / 26 (11.54%) 3		
Skin and subcutaneous tissue disorders Dry Skin subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2		
Infections and infestations Pharyngitis subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2018	Issued to update the secondary endpoints. The power calculations for the present study were based on the AUC results observed in the placebo group in a historical RSV study (53718678RSV2001). The RT-PCR assay, used to measure VL-AUC for the primary endpoint in study 53718678RSV2001, was a different assay than the assay used in the current study. Due to the explorative nature of the present study, the statistical assumptions were monitored by an unblinded monitor throughout the study. It was shown that the assay used in the historical study gave more granularity in the lower range compared to the assay used in the current study. As peak viral load should be less sensitive to the difference in the assays compared to the AUC, this parameter was added as a secondary endpoint. The study objectives and efficacy analysis section were updated accordingly.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported