Clinical trial results:
A Randomized, Double-blind, Placebo-controlled Phase 3 Study to Evaluate the Safety and Immunogenicity of an Ad26.RSV.preF-based Vaccine in Adults Aged 18 to 59-years, Including Those at High-risk for Severe RSV

Summary

EudraCT number	2021-001909-77
Trial protocol	DE BE ES
Global end of trial date	12 August 2022

Results information

Result version number	v1 (current)
This version publication date	27 August 2023
First version publication date	27 August 2023

Trial information

Trial identification

Sponsor protocol code	CR109038

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05070546
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Vaccines & Prevention B.V
Sponsor organisation address	4-6, Archimedesweg, Leiden, Netherlands, 2333
Public contact	Clinical Registry Group, Janssen Vaccines & Prevention B.V, clinicaltrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Vaccines & 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	12 August 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate safety and reactogenicity of adenovirus serotype 26 pre-fusion conformation-stabilized F protein (Ad26.RSV.preF) based respiratory syncytial virus (RSV) vaccine in healthy and high-risk adults aged 18 to 59 years; to demonstrate the non-inferiority of the humoral response to the administration of Ad26.RSV.preF-based vaccine in adults aged 18 to 59 years versus in adults aged 65 years and older and If non-inferiority was demonstrated in adults: to demonstrate the non-inferiority of the humoral response to the administration of Ad26.RSV.preF-based vaccine in high-risk adults aged 18 to 59 years versus in adults aged 65 years and older in whom efficacy of the vaccine was demonstrated.

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	29 September 2021
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	Belgium: 278
Country: Number of subjects enrolled	Germany: 312
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Sweden: 277
Country: Number of subjects enrolled	United States: 231
Worldwide total number of subjects	1118
EEA total number of subjects	887

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)	775
From 65 to 84 years	342
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 1124 subjects were enrolled and randomized. Of these, 6 subjects discontinued the study prior to receiving study vaccination. Therefore, 1118 subjects were included in the analysis.

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	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein

Arm description:

Healthy adult subjects aged 18 to 59 years received a single intramuscular (IM) injection containing mixture of adenovirus serotype 26 respiratory syncytial virus pre-fusion conformation-stabilized F protein (Ad26.RSV.preF) 1*10^11 viral particles (vp) and RSV preF protein 150 micrograms (mcg) on Day 1.

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

Dosage and administration details:

Subjects received mixture of adenovirus serotype 26 pre-fusion conformation-stabilized F protein (Ad26.RSV.preF) 1*10^11 viral particles (vp) and respiratory syncytial virus preF virus prefusion F protein (RSV preF protein) 150 micrograms (mcg) on Day 1.

Arm title	Group 2 (Cohort 1): Placebo

Arm description:

Healthy adult subjects aged 18 to 59 years received a single IM injection of matching placebo on Day 1.

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 matching placebo on Day 1.

Arm title	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein

Arm description:

High-risk adult subjects aged 18 to 59 years received a single IM injection containing mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

Arm type	Experimental

Investigational medicinal product name	Ad26.RSV.preF and RSV preF protein
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

Arm title	Group 4 (Cohort 2): Placebo

Arm description:

High-risk adult subjects aged 18 to 59 years received a single IM injection of matching placebo on Day 1.

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 matching placebo on Day 1.

Arm title	Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein

Arm description:

Adult subjects aged 65 years and older received a single IM injection containing mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

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

Dosage and administration details:

Subjects received mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

Arm title	Group 6 (Cohort 3): Placebo

Arm description:

Adult subjects aged 65 years and older received a single IM injection of matching placebo on Day 1.

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 matching placebo on Day 1.

Number of subjects in period 1	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein	Group 2 (Cohort 1): Placebo	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein
Started	319	68	319
Completed	310	65	309
Not completed	9	3	10
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	1	1	3
Unspecified	-	-	-
Lost to follow-up	8	2	7

Number of subjects in period 1	Group 4 (Cohort 2): Placebo	Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein	Group 6 (Cohort 3): Placebo
Started	69	313	30
Completed	68	308	29
Not completed	1	5	1
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	-	-	-
Unspecified	-	3	-
Lost to follow-up	1	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein
Reporting group description:	
Healthy adult subjects aged 18 to 59 years received a single intramuscular (IM) injection containing mixture of adenovirus serotype 26 respiratory syncytial virus pre-fusion conformation-stabilized F protein (Ad26.RSV.preF) 1*10^11 viral particles (vp) and RSV preF protein 150 micrograms (mcg) on Day 1.	
Reporting group title	Group 2 (Cohort 1): Placebo
Reporting group description:	
Healthy adult subjects aged 18 to 59 years received a single IM injection of matching placebo on Day 1.	
Reporting group title	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein
Reporting group description:	
High-risk adult subjects aged 18 to 59 years received a single IM injection containing mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.	
Reporting group title	Group 4 (Cohort 2): Placebo
Reporting group description:	
High-risk adult subjects aged 18 to 59 years received a single IM injection of matching placebo on Day 1.	
Reporting group title	Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein
Reporting group description:	
Adult subjects aged 65 years and older received a single IM injection containing mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.	
Reporting group title	Group 6 (Cohort 3): Placebo
Reporting group description:	
Adult subjects aged 65 years and older received a single IM injection of matching placebo on Day 1.	

Reporting group values	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein	Group 2 (Cohort 1): Placebo	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein
Number of subjects	319	68	319
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	319	68	319
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	38.8	38.4	44.4
standard deviation	± 12.33	± 12.34	± 11.81
Sex: Female, Male Units: subjects			
Female	193	40	174

Male	126	28	145

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	1	0	2
Black or African American	24	4	7
Native Hawaiian or Other Pacific Islander	0	0	1
White	289	64	308
More than one race	4	0	0
Unknown or Not Reported	1	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	42	10	40
Not Hispanic or Latino	274	57	276
Unknown or Not Reported	3	1	3
Region of Enrollment Units: Subjects			
BELGIUM	178	36	38
GERMANY	0	0	175
SPAIN	0	0	15
SWEDEN	33	8	50
UNITED STATES	108	24	41
AgeContinuous Units: years			
arithmetic mean	38.8	38.4	44.4
standard deviation	± 12.33	± 12.34	± 11.81

Reporting group values	Group 4 (Cohort 2): Placebo	Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein	Group 6 (Cohort 3): Placebo
Number of subjects	69	313	30
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	69	0	0
From 65-84 years	0	312	30
85 years and over	0	1	0
Age continuous Units: years			
arithmetic mean	44.6	71.1	71.2
standard deviation	± 11.58	± 4.74	± 5.1

Sex: Female, Male Units: subjects			
Female	39	181	21
Male	30	132	9
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Black or African American	1	9	0
Native Hawaiian or Other Pacific Islander	0	1	0
White	68	303	29
More than one race	0	0	1
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	9	19	2
Not Hispanic or Latino	60	289	28
Unknown or Not Reported	0	5	0
Region of Enrollment Units: Subjects			
BELGIUM	5	18	3
GERMANY	38	88	11
SPAIN	5	0	0
SWEDEN	15	160	11
UNITED STATES	6	47	5
AgeContinuous Units: years			
arithmetic mean	44.6	71.1	71.2
standard deviation	± 11.58	± 4.74	± 5.1

Reporting group values	Total		
Number of subjects	1118		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	775		
From 65-84 years	342		
85 years and over	1		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		

Sex: Female, Male Units: subjects			
Female	648		
Male	470		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1		
Asian	3		
Black or African American	45		
Native Hawaiian or Other Pacific Islander	2		
White	1061		
More than one race	5		
Unknown or Not Reported	1		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	122		
Not Hispanic or Latino	984		
Unknown or Not Reported	12		
Region of Enrollment Units: Subjects			
BELGIUM	278		
GERMANY	312		
SPAIN	20		
SWEDEN	277		
UNITED STATES	231		
AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein

Reporting group description:

Healthy adult subjects aged 18 to 59 years received a single intramuscular (IM) injection containing mixture of adenovirus serotype 26 respiratory syncytial virus pre-fusion conformation-stabilized F protein (Ad26.RSV.preF) 1*10^11 viral particles (vp) and RSV preF protein 150 micrograms (mcg) on Day 1.

Reporting group title	Group 2 (Cohort 1): Placebo

Reporting group description:

Healthy adult subjects aged 18 to 59 years received a single IM injection of matching placebo on Day 1.

Reporting group title	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein

Reporting group description:

High-risk adult subjects aged 18 to 59 years received a single IM injection containing mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

Reporting group title	Group 4 (Cohort 2): Placebo

Reporting group description:

High-risk adult subjects aged 18 to 59 years received a single IM injection of matching placebo on Day 1.

Reporting group title	Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein

Reporting group description:

Adult subjects aged 65 years and older received a single IM injection containing mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

Reporting group title	Group 6 (Cohort 3): Placebo

Reporting group description:

Adult subjects aged 65 years and older received a single IM injection of matching placebo on Day 1.

Subject analysis set title	Groups 1&3: Ad26.RSV.preF and RSV preF protein
Subject analysis set type	Per protocol

Subject analysis set description:

Healthy (Group 1) and high-risk adult (Group 3) subjects aged 18 to 59 years received intramuscular (IM) injection containing mixture of adenovirus serotype 26 pre-fusion conformation-stabilized F protein (Ad26.RSV.preF) 1*10^11 viral particles (vp) and respiratory syncytial virus prefusion Fprotein (RSV preF protein) 150 micrograms (mcg) on Day 1.

Subject analysis set title	Arm: Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein
Subject analysis set type	Per protocol

Subject analysis set description:

Adult subjects aged 65 years and older received a single IM injection containing mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

Subject analysis set title	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein
Subject analysis set type	Per protocol

Subject analysis set description:

High-risk adult subjects aged 18 to 59 years received a single IM injection containing mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

Primary: Cohorts 1 and 2: Number of Subjects with Solicited Local Adverse Events (AEs)

End point title	Cohorts 1 and 2: Number of Subjects with Solicited Local Adverse Events (AEs)[1][2]

End point description:

Number of subjects with solicited local AEs at 7 days post-vaccination in Cohorts 1 and 2 were reported. An AE is any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Solicited local AEs were predefined local events (at the injection site: erythema, pain/tenderness and swelling) that were by definition considered as related to the study vaccine and collected within 7 days after vaccination. Full analysis set (FAS) included all subjects who received study vaccine, regardless of the

occurrence of protocol deviations and vaccine type (study vaccine or placebo). Here 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint. This endpoint was planned to be analysed for specified cohorts only.

End point type	Primary

End point timeframe:

7 days after vaccination on Day 1 (Day 8)

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: Endpoint was planned to be analyzed for specified arms only.

[2] - 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: Endpoint was planned to be analyzed for specified arms only.

End point values	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein	Group 2 (Cohort 1): Placebo	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein	Group 4 (Cohort 2): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	316	68	318	68
Units: subjects	273	10	276	15

Statistical analyses

No statistical analyses for this end point

Primary: Cohorts 1 and 2: Number of Subjects with Solicited Systemic AEs

End point title	Cohorts 1 and 2: Number of Subjects with Solicited Systemic AEs[3][4]

End point description:

Number of subjects with solicited systemic AEs at 7 days post-vaccination in Cohorts 1 and 2 were reported. An AE is any untoward medical occurrence in a subjects participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Solicited systemic AEs including pyrexia, headache, fatigue, myalgia and nausea were collected within 7 days after vaccination. FAS included all subjects who received study vaccine, regardless of the occurrence of protocol deviations and vaccine type (study vaccine or placebo). Here 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint. This endpoint was planned to be analysed for specified cohorts only.

End point type	Primary

End point timeframe:

7 days after vaccination on Day 1 (Day 8)

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: Endpoint was planned to be analyzed for specified arms only.

[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: Endpoint was planned to be analyzed for specified arms only.

End point values	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein	Group 2 (Cohort 1): Placebo	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein	Group 4 (Cohort 2): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	316	68	318	68
Units: subjects	277	33	275	40

Statistical analyses

No statistical analyses for this end point

Primary: Cohorts 1 and 2: Number of Subjects with Unsolicited AEs

End point title	Cohorts 1 and 2: Number of Subjects with Unsolicited AEs[5][6]

End point description:

Number of subjects with unsolicited AEs post-vaccination in Cohorts 1 and 2 were reported. An AE was defined as any untoward medical occurrence in a subject participating in a clinical study that did not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Unsolicited AEs were defined as all AEs for which the subject was not specifically questioned in the subject diary. FAS included all subjects who received study vaccine, regardless of the occurrence of protocol deviations and vaccine type (study vaccine or placebo). This endpoint was planned to be analysed for specified cohorts only.

End point type	Primary

End point timeframe:

28 days after vaccination on Day 1 (Day 29)

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: Endpoint was planned to be analyzed for specified arms only.

[6] - 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: Endpoint was planned to be analyzed for specified arms only.

End point values	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein	Group 2 (Cohort 1): Placebo	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein	Group 4 (Cohort 2): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	319	68	319	69
Units: subjects	111	13	85	12

Statistical analyses

No statistical analyses for this end point

Primary: Cohorts 1 and 2: Number of Subjects with Serious Adverse Events (SAEs)

End point title	Cohorts 1 and 2: Number of Subjects with Serious Adverse Events (SAEs)[7]

End point description:

Number of subjects with SAEs post-vaccination were reported. An AE was defined as any untoward

medical event that occurred in a subject administered an investigational product, and it did not necessarily indicated only events with clear causal relationship with the relevant investigational product. SAE was defined as any AE that resulted in: death, persistent or significant disability/incapacity, required inpatient hospitalization or prolongation of existing hospitalization, was life-threatening experience, was a congenital anomaly/birth defect and would jeopardize subject and/or required medical or surgical intervention to prevent one of the outcomes listed above. FAS included all subjects who received study vaccine, regardless of the occurrence of protocol deviations and vaccine type (study vaccine or placebo).

End point type	Primary

End point timeframe:

6 months after vaccination on Day 1 (Day 183)

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: Endpoint was planned to be analyzed for specified arms only.

End point values	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein	Group 2 (Cohort 1): Placebo	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein	Group 4 (Cohort 2): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	319	68	319	69
Units: subjects	1	1	10	0

End point values	Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein	Group 6 (Cohort 3): Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313	30		
Units: subjects	13	1		

Statistical analyses

No statistical analyses for this end point

Primary: Cohorts 1 and 2: Number of Subjects with Adverse Events of Special Interest (AESI)

End point title	Cohorts 1 and 2: Number of Subjects with Adverse Events of Special Interest (AESI)[8]

End point description:

Number of subjects with AESI post-vaccination were reported. AESIs were significant AEs that were judged to be of special interest because of clinical importance, known or suspected class effects, or based on nonclinical signals. Thrombosis with thrombocytopenia syndrome (TTS) was considered as an AESI. FAS included all subjects who received study vaccine, regardless of the occurrence of protocol deviations and vaccine type (study vaccine or placebo).

End point type	Primary

End point timeframe:

6 months after vaccination on Day 1 (Day 183)

Notes:

[8] - 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: Endpoint was planned to be analyzed for specified arms only.

End point values	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein	Group 2 (Cohort 1): Placebo	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein	Group 4 (Cohort 2): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	319	68	319	69
Units: subjects	0	0	0	0

End point values	Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein	Group 6 (Cohort 3): Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313	30		
Units: subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Cohorts 1 (Group 1), 2 (Group 3), and 3 (Group 5): Respiratory Syncytial Virus (RSV) A2 Strain Neutralizing Antibody Titers

End point title	Cohorts 1 (Group 1), 2 (Group 3), and 3 (Group 5): Respiratory Syncytial Virus (RSV) A2 Strain Neutralizing Antibody Titers

End point description:

RSV A2 strain neutralizing antibody titers of the vaccine-induced immune response was assessed through virus neutralization assay and were expressed as 50% inhibitory concentration (IC50) units. The Per-protocol Immunogenicity (PPI) set included all randomized subjects on Day 15 who received study vaccine and for whom immunogenicity data were available. Here 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint. This endpoint was planned to be analysed for specified arms only. As planned, combined data of subjects aged 18-59 years (in Cohort 1 (group 1) and Cohort 2 (group 3) has been reported.

End point type	Primary

End point timeframe:

14 days after vaccination on Day 1 (Day 15)

End point values	Groups 1&3: Ad26.RSV.preF and RSV preF protein	Arm: Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	602	290	301	
Units: Titers				
geometric mean (confidence interval 95%)	6491 (5847 to 7206)	4596 (4059 to 5204)	7095 (6261 to 8042)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Non-inferiority of Cohort 3 (Group 5) versus Cohorts 1 (Group 1) and 2 (Group 3) in terms of RSV A2 Strain neutralizing antibody titers against 14 days after vaccination, using a non-inferiority margin of 0.67 for the GMT ratio (Cohort 3 [Group 5]/Cohort 1[Group1] and 2 [Group 3]).	
Comparison groups	Arm: Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein v Groups 1&3: Ad26.RSV.preF and RSV preF protein
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Geometric Mean Ratio
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	1.6

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Non-inferiority of Cohort 3 (Group 5) versus Cohort 2 (Group 3 in terms of RSV A2 Strain neutralizing antibody titers against 14 days after vaccination, using a non-inferiority margin of 0.67 for the GMT ratio (Cohort 3 [Group 5]/Cohort 2 [Group 3]).	
Comparison groups	Arm: Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein v Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Geometric Mean Ratio
Point estimate	1.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.34
upper limit	1.78

Primary: Cohorts 1 (Group 1), 2 (Group 3), and 3 (Group 5): Percentage of Subjects with Seroresponse as Assessed by Virus Neutralizing Assay (VNA-A2)	
End point title	Cohorts 1 (Group 1), 2 (Group 3), and 3 (Group 5): Percentage of Subjects with Seroresponse as Assessed by Virus Neutralizing Assay (VNA-A2)

End point description:

Percentage of subjects with seroresponse as assessed by VNA A2 strain were reported. Seroresponse was defined as a 4-fold increase from baseline in Day 15 VNA-A2 antibody titers. PPI set included all randomized subjects on Day 15 who received study vaccine and for whom immunogenicity data were available. Here 'N' (number of subjects analysed) signifies number of subjects who were evaluable for this endpoint. This endpoint was planned to be analysed for specified arms only. As planned, combined data of subjects aged 18-59 years (in Cohort 1 (group 1) and Cohort 2 (group 3) has been reported.

End point type	Primary

End point timeframe:

14 days after vaccination on Day 1 (Day 15)

End point values	Groups 1&3: Ad26.RSV.preF and RSV preF protein	Arm: Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	602	290	300	
Units: percentage of subjects				
number (not applicable)	89.37	82.41	88	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Non-inferiority of Cohort 3 (Group 5) versus Cohorts 1 (Group 1) and 2 (Group 3) in terms of RSV A2 Strain neutralizing antibody titers against 14 days after vaccination, using a non-inferiority margin of -10% for the GMT ratio (Cohort 3 [Group 5]/Cohort 1[Group1] and 2 [Group 3]).

Comparison groups	Groups 1&3: Ad26.RSV.preF and RSV preF protein v Arm: Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein
Number of subjects included in analysis	892
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Difference in Seroresponse rate
Parameter estimate	Difference in Seroresponse rate
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	10.9

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Non-inferiority of Cohort 3 (Group 5) versus Cohorts 1 (Group 1) and 2 (Group 3) in terms of RSV A2 Strain neutralizing antibody titers against 14 days after vaccination, using a non-inferiority margin of -10% for the GMT ratio (Cohort 3 [Group 5]/Cohort 2 [Group 3]).	
Comparison groups	Arm: Group 5 (Cohort 3): Ad26.RSV.preF and RSV preF protein v Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein
Number of subjects included in analysis	590
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in Seroresponse rate
Point estimate	4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	10.5

Secondary: Cohorts 1, 2, and 3: Geomteric Mean Titers (GMTs) of RSV Fusion Protein (F-protein) Antibodies as assessed by Enzyme-linked Immunosorbent Assay (ELISA)- Pre-Fusion

End point title	Cohorts 1, 2, and 3: Geomteric Mean Titers (GMTs) of RSV Fusion Protein (F-protein) Antibodies as assessed by Enzyme-linked Immunosorbent Assay (ELISA)- Pre-Fusion
End point description:	
GMTs of RSV Fusion Protein (PreF) antibodies as assessed by ELISA-Pre-Fusion at Day 15 were reported. PPI set included all randomized subjects on Day 15 who received study vaccine and for whom immunogenicity data were available.	
End point type	Secondary
End point timeframe:	
14 days after vaccination on Day 1 (Day 15)	

End point values	Group 1 (Cohort 1): Ad26.RSV.preF and RSV preF protein	Group 2 (Cohort 1): Placebo	Group 3 (Cohort 2): Ad26.RSV.preF and RSV preF protein	Group 4 (Cohort 2): Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	302	64	301	61
Units: ELISA Units/Litre (EU/L)				
geometric mean (confidence interval 95%)	4662 (4350 to 4997)	246 (214 to 284)	5175 (4808 to 5569)	283 (246 to 326)

End point values	Group 5	Group 6		

	(Cohort 3): Ad26.RSV.preF and RSV preF protein	(Cohort 3): Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	29		
Units: ELISA Units/Litre (EU/L)				
geometric mean (confidence interval 95%)	3864 (3559 to 4196)	240 (203 to 285)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 183

Adverse event reporting additional description:

Full analysis set included all subjects who received study vaccine, regardless of the occurrence of protocol deviations and vaccine type (study vaccine or placebo).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Cohort 1: Ad26.RSV.preF and RSV preF protein (Group 1)

Reporting group description:

Healthy adult subjects aged 18 to 59 years received intramuscular (IM) injection containing mixture of adenovirus serotype 26 pre-fusion conformation-stabilized F protein (Ad26.RSV.preF) 1*10^11 viral particles (vp) and respiratory syncytial virus prefusion Fprotein (RSV preF protein) 150 micrograms (mcg) on Day 1.

Reporting group title	Cohort 1: Placebo (Group 2)

Reporting group description:

Healthy adult subjects aged 18 to 59 years received IM injection of matching placebo on Day 1.

Reporting group title	Cohort 3: Placebo (Group 6)

Reporting group description:

Adult subjects aged 65 years and older received IM injection of matching placebo on Day 1 of vaccination.

Reporting group title	Cohort 2: Placebo (Group 4)

Reporting group description:

High-risk adult subjects aged 18 to 59 years received IM injection of matching placebo on Day 1.

Reporting group title	Cohort 3: Ad26.RSV.preF and RSV preF protein (Group 5)

Reporting group description:

Adult subjects aged 65 years and older received IM injection containing mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

Reporting group title	Cohort 2: Ad26.RSV.preF and RSV preF protein (Group 3)

Reporting group description:

High-risk adult subjects aged 18 to 59 years received IM injection containing mixture of Ad26.RSV.preF 1*10^11 vp and RSV preF protein 150 mcg on Day 1.

Serious adverse events	Cohort 1: Ad26.RSV.preF and RSV preF protein	Cohort 1: Placebo (Group 2)	Cohort 3: Placebo (Group 6)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 319 (0.31%)	1 / 68 (1.47%)	1 / 30 (3.33%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder Cancer Stage 0, with Cancer in Situ			

subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Her2 Positive Breast Cancer			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Injury, poisoning and procedural complications			
Radius Fracture			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Thermal Burn			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Traumatic Fracture			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Hypertensive Crisis			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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

Aortic Valve Stenosis			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Atrial Fibrillation			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Cardiogenic Shock			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Myocardial Infarction			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Facial Paresis			
subjects affected / exposed	1 / 319 (0.31%)	0 / 68 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Reproductive system and breast disorders			
Testicular Torsion			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Pulmonary Embolism			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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			
Gastroenteritis Viral			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Haemorrhagic Fever with Renal Syndrome			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Herpes Zoster			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Mastitis			

subjects affected / exposed	0 / 319 (0.00%)	1 / 68 (1.47%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis Aseptic			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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
Pneumonia			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	0 / 30 (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

Serious adverse events	Cohort 2: Placebo (Group 4)	Cohort 3: Ad26.RSV.preF and RSV preF protein	Cohort 2: Ad26.RSV.preF and RSV preF protein
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 69 (0.00%)	13 / 313 (4.15%)	10 / 319 (3.13%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder Cancer Stage 0, with Cancer in Situ			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Her2 Positive Breast Cancer			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Radius Fracture			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal Burn			

subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic Fracture			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Crisis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic Valve Stenosis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic Shock			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			

subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial Infarction			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Facial Paresis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	0 / 319 (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
Syncope			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Testicular Torsion			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	0 / 69 (0.00%)	2 / 313 (0.64%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Ureterolithiasis			

subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis Viral			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic Fever with Renal Syndrome			
subjects affected / exposed	0 / 69 (0.00%)	1 / 313 (0.32%)	0 / 319 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Zoster			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	0 / 319 (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
Meningitis Aseptic			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Cohort 1: Ad26.RSV.preF and RSV preF protein	Cohort 1: Placebo (Group 2)	Cohort 3: Placebo (Group 6)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 319 (24.14%)	5 / 68 (7.35%)	5 / 30 (16.67%)
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 319 (1.25%)	4 / 68 (5.88%)	0 / 30 (0.00%)
occurrences (all)	4	4	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	60 / 319 (18.81%)	1 / 68 (1.47%)	0 / 30 (0.00%)
occurrences (all)	60	1	0
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 319 (0.63%)	1 / 68 (1.47%)	1 / 30 (3.33%)
occurrences (all)	2	1	1
Vomiting			
subjects affected / exposed	8 / 319 (2.51%)	0 / 68 (0.00%)	0 / 30 (0.00%)
occurrences (all)	8	0	0
Skin and subcutaneous tissue disorders			
Night Sweats			
subjects affected / exposed	8 / 319 (2.51%)	0 / 68 (0.00%)	0 / 30 (0.00%)
occurrences (all)	8	0	0
Musculoskeletal and connective tissue disorders			
Muscle Spasms			
subjects affected / exposed	0 / 319 (0.00%)	0 / 68 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1

Infections and infestations			
Covid-19			
subjects affected / exposed	8 / 319 (2.51%)	1 / 68 (1.47%)	1 / 30 (3.33%)
occurrences (all)	8	1	1
Nasopharyngitis			
subjects affected / exposed	1 / 319 (0.31%)	0 / 68 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 319 (0.94%)	0 / 68 (0.00%)	1 / 30 (3.33%)
occurrences (all)	3	0	1
Sinusitis			
subjects affected / exposed	7 / 319 (2.19%)	0 / 68 (0.00%)	1 / 30 (3.33%)
occurrences (all)	7	0	1

Non-serious adverse events	Cohort 2: Placebo (Group 4)	Cohort 3: Ad26.RSV.preF and RSV preF protein	Cohort 2: Ad26.RSV.preF and RSV preF protein
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 69 (11.59%)	32 / 313 (10.22%)	50 / 319 (15.67%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 69 (0.00%)	2 / 313 (0.64%)	2 / 319 (0.63%)
occurrences (all)	0	2	2
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 69 (1.45%)	15 / 313 (4.79%)	31 / 319 (9.72%)
occurrences (all)	1	15	31
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	0 / 319 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 69 (0.00%)	2 / 313 (0.64%)	2 / 319 (0.63%)
occurrences (all)	0	2	2
Vomiting			
subjects affected / exposed	0 / 69 (0.00%)	2 / 313 (0.64%)	2 / 319 (0.63%)
occurrences (all)	0	2	2
Skin and subcutaneous tissue disorders			

Night Sweats			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Muscle Spasms			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences (all)	0	0	1
Infections and infestations			
Covid-19			
subjects affected / exposed	3 / 69 (4.35%)	2 / 313 (0.64%)	4 / 319 (1.25%)
occurrences (all)	3	2	4
Nasopharyngitis			
subjects affected / exposed	3 / 69 (4.35%)	9 / 313 (2.88%)	9 / 319 (2.82%)
occurrences (all)	3	9	9
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 69 (4.35%)	1 / 313 (0.32%)	1 / 319 (0.31%)
occurrences (all)	3	1	1
Sinusitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 313 (0.00%)	1 / 319 (0.31%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 August 2021	The purpose of this amendment was to include the addition of seroresponse rates in addition to neutralizing antibody geoemtric mean titers (GMTs) as primary endpoints to evaluate non-inferiority of immune responses. The primary immunogenicity endpoint was also modified from respiratory syncytial virus prefusion Fprotein (RSV preF protein) imuunoglobulin (IgG) (by enzyme-linked immunosorbent assay [ELISA]) to a functional immune marker (anti-RSV virus neutralizing antibodies). The statistical hypotheses and success criteria were revised accordingly, resulting also in a change in sample size and randomization ratios.
30 November 2021	The purpose of this amendment was to include provision of additional guidance in the appendix to the protocol for inclusion of participants in Cohort 2, with examples of chronic cardiac and pulmonary comorbidities eligible for participation in this cohort. Furthermore, additional language referring to laboratory diagnostic tests for the follow-up and assessment of potential adverse event of special interests (AESIs) was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported