Clinical trial results:
A Randomized, Double-blind, Phase 3 Study to Evaluate Safety, Reactogenicity, and Immunogenicity of Co-administration of Ad26.COV2.S and Influenza Vaccines in Healthy Adults 18 Years of Age and Older

Summary

EudraCT number	2021-003953-43
Trial protocol	PL BE
Global end of trial date	15 November 2022

Results information

Result version number	v1
This version publication date	01 December 2023
First version publication date	01 December 2023

Trial information

Trial identification

Sponsor protocol code	VAC31518COV3005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05091307
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Vaccines & Prevention B.V.
Sponsor organisation address	Archimedesweg 4-6, CN 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	15 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 November 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 demonstrate the non-inferiority (NI) of the humoral immune response of the 4 influenza vaccine strains after concomitant administration of the Ad26.COV2.S vaccine and a seasonal quadrivalent standard-dose influenza vaccine versus the administration of a seasonal quadrivalent standard-dose influenza vaccine administered alone; and to demonstrate the NI of the binding antibody response after concomitant administration of Ad26.COV2.S vaccine and a seasonal quadrivalent standard-dose influenza vaccine versus the administration of Ad26.COV2.S vaccine administered alone.

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 99
Country: Number of subjects enrolled	Poland: 114
Country: Number of subjects enrolled	United States: 648
Worldwide total number of subjects	861
EEA total number of subjects	213

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)	674
From 65 to 84 years	186
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 861 subjects were enrolled, of which 715 subjects 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
Arm title	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo

Arm description:

Subjects aged greater than or equal to (>=) 18 years and older received a single intramuscular (IM) injection of Ad26.COV2.S at 5*10^10 viral particles (vp) dose level and a seasonal quadrivalent (Q) standard dose (SD) influenza vaccine with 60 micrograms (mcg) hemagglutinin (HA) on Day 1 followed by a single IM injection of placebo (matched to Ad26.COV2.S) on Day 29.

Arm type	Experimental
Investigational medicinal product name	Ad26.COV2.S
Investigational medicinal product code	
Other name	VAC31518; JNJ-78436735
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single dose of Ad26.COV2.S at 5*10^10 vp dose level on Day 1.

Investigational medicinal product name	Q SD influenza vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a Q SD influenza vaccine with 60 mcg HA on Day 1.

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 a single dose of placebo (matched to Ad26.COV2.S) on Day 29.

Arm title	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S

Arm description:

Subjects aged >=18 years and older received a single IM injection of placebo (matched to Ad26.COV2.S) and a seasonal Q SD influenza vaccine with 60 mcg of HA on Day 1 followed by a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.

Arm type	Experimental

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a single dose of placebo (matched to Ad26.COV2.S) on Day 1.

Investigational medicinal product name	Q SD influenza vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a seasonal Q SD influenza vaccine with 60 mcg of HA on Day 1

Investigational medicinal product name	Ad26.COV2.S
Investigational medicinal product code	
Other name	VAC31518; JNJ-78436735
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a single dose of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.

Arm title	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and Placebo

Arm description:

Subjects aged >=65 years and older received a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level and a seasonal Q high dose (HD) influenza vaccine with 240 mcg HA on Day 1 followed by a single IM injection of placebo (matched to Ad26.COV2.S) on Day 29.

Arm type	Experimental
Investigational medicinal product name	Ad26.COV2.S
Investigational medicinal product code	
Other name	VAC31518; JNJ-78436735
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single dose of Ad26.COV2.S at 5*10^10 vp dose level on Day 1.

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 a single dose of placebo (matched to Ad26.COV2.S) on Day 29.

Investigational medicinal product name	Q HD influenza vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a seasonal Q HD influenza vaccine with 240 mcg HA on Day 1.

Arm title	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S

Arm description:

Subjects aged >=65 years and older received a single IM injection of placebo (matched to Ad26.COV2.S) and a seasonal Q HD influenza vaccine with 240 mcg of HA on Day 1 followed by a single

of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.

Arm type	Experimental
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 a single dose of placebo (matched to Ad26.COV2.S) on Day 1.

Investigational medicinal product name	Q HD influenza vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received a seasonal Q HD influenza vaccine with 240 mcg of HA on Day 1.

Investigational medicinal product name	Ad26.COV2.S
Investigational medicinal product code	
Other name	VAC31518; JNJ-78436735
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single dose of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.

Number of subjects in period 1	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and Placebo
Started	382	386	47
Treated (Vaccinated subjects)	382	384	47
Completed	312	316	43
Not completed	70	70	4
Adverse event, serious fatal	-	-	1
Covid-19 Vaccine/Treatment	14	15	1
Consent withdrawn by subject	16	16	-
Physician decision	1	-	-
Unspecified	4	4	-
Initiated Prohibited Medication	1	-	-
Randomised but not vaccinated	-	2	-
Lost to follow-up	33	33	2
Protocol deviation	1	-	-

Number of subjects in period 1	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Started	46

Treated (Vaccinated subjects)	46
Completed	44
Not completed	2
Adverse event, serious fatal	-
Covid-19 Vaccine/Treatment	1
Consent withdrawn by subject	1
Physician decision	-
Unspecified	-
Initiated Prohibited Medication	-
Randomised but not vaccinated	-
Lost to follow-up	-
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo
Reporting group description:	
Subjects aged greater than or equal to (>=) 18 years and older received a single intramuscular (IM) injection of Ad26.COV2.S at 5*10^10 viral particles (vp) dose level and a seasonal quadrivalent (Q) standard dose (SD) influenza vaccine with 60 micrograms (mcg) hemagglutinin (HA) on Day 1 followed by a single IM injection of placebo (matched to Ad26.COV2.S) on Day 29.	
Reporting group title	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S
Reporting group description:	
Subjects aged >=18 years and older received a single IM injection of placebo (matched to Ad26.COV2.S) and a seasonal Q SD influenza vaccine with 60 mcg of HA on Day 1 followed by a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.	
Reporting group title	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and Placebo
Reporting group description:	
Subjects aged >=65 years and older received a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level and a seasonal Q high dose (HD) influenza vaccine with 240 mcg HA on Day 1 followed by a single IM injection of placebo (matched to Ad26.COV2.S) on Day 29.	
Reporting group title	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Reporting group description:	
Subjects aged >=65 years and older received a single IM injection of placebo (matched to Ad26.COV2.S) and a seasonal Q HD influenza vaccine with 240 mcg of HA on Day 1 followed by a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.	

Reporting group values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and Placebo
Number of subjects	382	386	47
Age Categorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	336	338	0
From 65 to 84 years	46	48	47
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	46.2	45.5	71.1
standard deviation	± 14.92	± 15.25	± 4.58
Sex: Female, Male Units: subjects			
Female	191	178	22
Male	191	208	25

Reporting group values	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S	Total	
Number of subjects	46	861	
Age Categorical Units: subjects			
Children (2-11 years)	0	0	

Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	674	
From 65 to 84 years	45	186	
85 years and over	1	1	
Age Continuous Units: years			
arithmetic mean	71.3		
standard deviation	± 5.29	-	
Sex: Female, Male Units: subjects			
Female	33	424	
Male	13	437	

End points

End points reporting groups

Reporting group title	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo

Reporting group description:

Subjects aged greater than or equal to (>=) 18 years and older received a single intramuscular (IM) injection of Ad26.COV2.S at 5*10^10 viral particles (vp) dose level and a seasonal quadrivalent (Q) standard dose (SD) influenza vaccine with 60 micrograms (mcg) hemagglutinin (HA) on Day 1 followed by a single IM injection of placebo (matched to Ad26.COV2.S) on Day 29.

Reporting group title	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S

Reporting group description:

Subjects aged >=18 years and older received a single IM injection of placebo (matched to Ad26.COV2.S) and a seasonal Q SD influenza vaccine with 60 mcg of HA on Day 1 followed by a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.

Reporting group title	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and Placebo

Reporting group description:

Subjects aged >=65 years and older received a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level and a seasonal Q high dose (HD) influenza vaccine with 240 mcg HA on Day 1 followed by a single IM injection of placebo (matched to Ad26.COV2.S) on Day 29.

Reporting group title	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S

Reporting group description:

Subjects aged >=65 years and older received a single IM injection of placebo (matched to Ad26.COV2.S) and a seasonal Q HD influenza vaccine with 240 mcg of HA on Day 1 followed by a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.

Primary: Groups 1 and 2: Geometric Mean Titers (GMTs) of Hemagglutination Inhibition (HI) Antibodies Against Each of the Four Influenza Vaccine Strains 28 Days after the Administration of a Seasonal Quadrivalent Standard-dose Influenza Vaccine

End point title	Groups 1 and 2: Geometric Mean Titers (GMTs) of Hemagglutination Inhibition (HI) Antibodies Against Each of the Four Influenza Vaccine Strains 28 Days after the Administration of a Seasonal Quadrivalent Standard-dose Influenza Vaccine[1]

End point description:

GMTs of HI antibodies were measured using hemagglutination inhibition (HAI) assay against each of four influenza vaccine strains (A/Victoria [H1N1], A/Cambodia [H3N2], B/Victoria [B/Victoria] and B/Phuket [B/Yamagata]). This endpoint was planned to be analysed for specified arms only. The per-protocol influenza immunogenicity (PPII) set included all randomised subjects who received Ad26.COV2.S vaccine in combination with seasonal influenza vaccine for co-administration group and those who received seasonal influenza vaccine alone for control group, for whom immunogenicity data were available for at least one of influenza strains in vaccine. Subjects with major protocol deviation were excluded from PPII analysis. 'N' (number of subjects analysed)=subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

28 days after vaccination with seasonal quadrivalent standard-dose influenza vaccine (Day 29)

Notes:

[1] - 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: This outcome measure was planned to be analysed for specified arm only.

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	320	333		
Units: Titers				
geometric mean (confidence interval 95%)				
A/Victoria (H1N1)	306 (271 to 346)	393 (348 to 445)		
A/Cambodia (H3N2)	134 (119 to 150)	165 (147 to 186)		
B/Victoria (B/Victoria)	38 (34 to 43)	38 (33 to 43)		
B/Phuket (B/Yamagata)	32 (29 to 36)	33 (30 to 37)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

A/Victoria (H1N1): Based on analysis of variance (ANOVA) models, CIs around the difference (Group 2 [control group] minus Group 1 [CoAd group]) was calculated and back-transformed (by exponentiation: 2^CI) to CIs around a geometric mean ratio (GMR: GMTControl/GMTCoAd).

Comparison groups	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo v Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S
Number of subjects included in analysis	653
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	1.53

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

B/Victoria (B/Victoria): Based on ANOVA models, CIs around the difference (Group 2 [control group] minus Group 1 [CoAd group]) was calculated and back-transformed (by exponentiation: 2^CI) to CIs around a geometric mean ratio (GMR: GMTControl/GMTCoAd).

Comparison groups	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo v Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S

Number of subjects included in analysis	653
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.19

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
B/Phuket (B/Yamagata): Based on ANOVA models, CIs around the difference (Group 2 [control group] minus Group 1 [CoAd group]) was calculated and back-transformed (by exponentiation: 2^CI) to CIs around a geometric mean ratio (GMR: GMTControl/GMTCoAd).	
Comparison groups	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo v Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S
Number of subjects included in analysis	653
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.21

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
A/Cambodia (H3N2): Based on ANOVA models, CIs around the difference (Group 2 [control group] minus Group 1 [CoAd group]) was calculated and back-transformed (by exponentiation: 2^CI) to CIs around a geometric mean ratio (GMR: GMTControl/GMTCoAd).	
Comparison groups	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo v Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S
Number of subjects included in analysis	653
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	1.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	1.45

Primary: Groups 1 and 2: Geometric Mean Concentrations (GMCs) of Antibodies Measured by Spiked-Enzyme-linked Immunosorbent Assay (S-ELISA) 28 Days After Administration of Ad26.COV2.S Vaccine

End point title	Groups 1 and 2: Geometric Mean Concentrations (GMCs) of Antibodies Measured by Spiked-Enzyme-linked Immunosorbent Assay (S-ELISA) 28 Days After Administration of Ad26.COV2.S Vaccine[2]

End point description:

GMCs of antibody titers measured by S-ELISA at 28 days after administration of Ad26.COV2.S vaccine was reported. This endpoint was planned to be analysed for specified arms only. Seronegative subjects (at Day 1) who became serology positive during the study, subjects with positive molecular test for severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) and major protocol deviation were excluded from PPSI analysis. The per protocol SARS-CoV-2 immunogenicity set (PPSI) included all randomised subjects who received Ad26.COV2.S vaccine in combination with seasonal influenza vaccine for co-administration group and Ad26.COV2.S vaccine alone for control group, and for whom immunogenicity data was available. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

28 days after vaccination with Ad26.COV2.S vaccine (Group 1: Day 29, Group 2: Day 57)

Notes:

[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: This outcome measure was planned to be analysed for specified arm only.

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	257	209		
Units: ELISA Unit per millilitre (EU/mL)				
geometric mean (confidence interval 95%)	22531 (20140 to 25205)	25035 (22189 to 28246)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Based on ANOVA models, CIs around the difference (Group 2 [control group] minus Group 1 [CoAd group]) was calculated and back-transformed (by exponentiation: 2^CI) to CIs around a geometric mean ratio (GMR: GMTControl/GMTCoAd).

Comparison groups	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo v Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.26

Secondary: Number of Subjects With Solicited Local Adverse Events (AEs) up to 7 Days After Each Vaccination

End point title	Number of Subjects With Solicited Local Adverse Events (AEs) up to 7 Days After Each Vaccination

End point description:

An AE was any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Solicited local AEs were defined events that subjects were specifically asked about and which were noted by subjects in the diary. Solicited local AEs included erythema, swelling/induration, and pain/tenderness. The full analysis set (FAS) included all randomised subjects with at least 1 documented study vaccine administration. Here, 'n' (number analysed) signifies subjects who were evaluated at each specified category.

End point type	Secondary

End point timeframe:

7 days after first vaccination on Day 1 (up to Day 8); 7 days after second vaccination on Day 29 (up to Day 36)

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	382	384	47	46
Units: Subjects				
After first vaccination (n=382,384,47,46)	261	204	23	21
After second vaccination (n=342,348,46,45)	34	210	3	24

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Unsolicited AEs up to 28 Days After Each Vaccination

End point title	Number of Subjects With Unsolicited AEs up to 28 Days After Each Vaccination

End point description:

An AE was any untoward medical occurrence in a clinical study subjects administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Unsolicited AEs were all AEs for which the subject is not specifically questioned in the subject diary. The FAS included all randomised subjects with at least 1 documented study vaccine administration. Here, 'n' (number analysed) signifies subjects who were evaluated at each specified category.

End point type	Secondary

End point timeframe:

28 days after first vaccination on Day 1 (up to Day 29); 28 days after second vaccination on Day 29 (up to Day 57)

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	382	384	47	46
Units: Subjects				
After first vaccination (n=382,384,47,46)	71	71	10	9
After second vaccination (n=342,348,46,45)	36	50	11	8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Solicited Systemic AEs up to 7 Days After Each Vaccination

End point title	Number of Subjects With Solicited Systemic AEs up to 7 Days After Each Vaccination

End point description:

An AE was any untoward medical occurrence in a clinical study participant administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. Solicited systemic AEs included fever (defined as body temperature of 38.0-degree celsius or higher), headache, fatigue, myalgia, nausea, vomiting were collected within 7 days after each vaccination. The FAS included all randomised subjects with at least 1 documented study vaccine administration. Here, 'n' (number analysed) signifies subjects who were evaluated at each specified category.

End point type	Secondary

End point timeframe:

7 days after first vaccination on Day 1 (up to Day 8); 7 days after second vaccination on Day 29 (up to Day 36)

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	382	384	47	46
Units: Subjects				
After first vaccination (n=382,384,47,46)	256	205	30	26
After second vaccination (n=342,348,46.45)	84	208	8	22

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Medically-attended Adverse Events (MAAEs)

End point title	Number of Subjects With Medically-attended Adverse Events (MAAEs)

End point description:

Number of subjects with MAAEs was reported. MAAEs were defined as AEs with medically-attended visits including hospital, emergency room, urgent care clinic, or other visits to or from medical personnel for any reason. New onset of chronic diseases was collected as part of the MAAEs. The FAS included all randomised subjects with at least 1 documented study vaccine administration.

End point type	Secondary

End point timeframe:

From Day 1 (post-vaccination) to end of the study (up to 12.5 months)

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	382	384	47	46
Units: Subjects	51	51	11	16

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE was any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. SAE was any untoward medical occurrence that at any dose results in any of the following outcomes: death; initial or prolonged inpatient hospitalization; life-threatening experience

(immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly/birth defect; suspected transmission of any infectious agent via a medicinal product or medically important. The FAS included all randomised subjects with at least 1 documented study vaccine administration.

End point type	Secondary

End point timeframe:

From Day 1 (post-vaccination) to end of the study (up to 12.5 months)

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	382	384	47	46
Units: Subjects	9	7	1	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events of Special Interest (AESIs)

End point title	Number of Subjects With Adverse Events of Special Interest (AESIs)

End point description:

Number of subjects with AESIs was 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), a syndrome characterised by a combination of both a thrombotic event and thrombocytopenia, was considered to be an AESI in this study. A suspected TTS case was defined as: Thrombotic events: suspected deep vessel venous or arterial thrombotic events; Thrombocytopenia, defined as platelet count below 150,000/microliter. The FAS included all randomised subjects with at least 1 documented study vaccine administration.

End point type	Secondary

End point timeframe:

From Day 1 (post-vaccination) to end of the study (up to 12.5 months)

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	382	384	47	46
Units: Subjects	8	12	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 3 and 4: GMTs of HI Antibodies Against Each of the Four Influenza Vaccine Strains 28 Days after the Administration of a Seasonal Quadrivalent High-dose Influenza Vaccine

End point title	Groups 3 and 4: GMTs of HI Antibodies Against Each of the Four Influenza Vaccine Strains 28 Days after the Administration of a Seasonal Quadrivalent High-dose Influenza Vaccine[3]

End point description:

GMTs of HI antibodies were measured using hemagglutination inhibition (HAI) assay against each of four influenza vaccine strains (A/Victoria [H1N1], A/Tasmania[H3N2], B/Washington [B/Victoria] and B/Phuket [B/Yamagata]). This endpoint was planned to be analysed for specified arms only. The PPII set included all randomised subjects who received Ad26.COV2.S vaccine in combination with a seasonal influenza vaccine for the coadministration group and those who received a seasonal influenza vaccine alone for the control group, for whom immunogenicity data were available for at least one of the influenza strains in the vaccine. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

28 days after vaccination with seasonal quadrivalent high-dose influenza vaccine (Day 29)

Notes:

[3] - 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: This outcome measure was planned to be analysed for specified arm only.

End point values	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	41		
Units: Titers				
geometric mean (confidence interval 95%)				
A/Victoria (H1N1)	286 (204 to 400)	484 (369 to 636)		
A/Tasmania (H3N2)	284 (200 to 402)	509 (365 to 711)		
B/Washington (B/Victoria)	61 (46 to 81)	75 (53 to 106)		
B/Phuket (B/Yamagata)	38 (29 to 50)	39 (30 to 52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with AEs Leading to Withdrawal from the Study

End point title	Number of Subjects with AEs Leading to Withdrawal from the Study

End point description:

Number of subjects with AE leading to withdrawal from the study was reported. The FAS included all randomised subjects with at least 1 documented study vaccine administration.

End point type	Secondary

End point timeframe:

From Day 1 (post-vaccination) to end of the study (up to 12.5 months)

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	382	384	47	46
Units: Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: GMCs of Antibodies Measured by S-ELISA 28 Days After Administration of Ad26.COV2.S Vaccine in COVID-19 Vaccine Naive Subjects

End point title	GMCs of Antibodies Measured by S-ELISA 28 Days After Administration of Ad26.COV2.S Vaccine in COVID-19 Vaccine Naive Subjects

End point description:

GMCs of antibodies measured by S-ELISA 28 days after administration of Ad26.COV.S vaccine in Covid-19 vaccine naive subjects was reported. In the below data table, '0' in the number analysed field signifies that none of the subjects were evaluable at the specified timepoint. PPSI included all randomised subjects who received Ad26.COV2.S vaccine in combination with seasonal influenza vaccine for co-administration group and Ad26.COV2.S vaccine alone for control group and for whom immunogenicity data was available. Subjects with positive molecular test for SARSCoV-2 were also excluded. Here, 'N' (number of subjects analysed)=who were evaluable for this endpoint, 'n'(number analyzed)=subject who were evaluated at specified timepoint. Here, -99999 and 99999 signifies that lower limit and upper limit of 95% confidence interval could not be estimated as only 1 subject was analysed on Day 57 in Group 4.

End point type	Secondary

End point timeframe:

28 days after the administration of Ad26.COV2.S vaccine (that is, for Groups 1 and 3: Day 29; for Groups 2 and 4: Day 57)

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	40	0[4]	1
Units: EU/mL				
geometric mean (confidence interval 95%)	10340 (6557 to 16306)	14704 (9010 to 23998)	(to)	38905 (-99999 to 99999)

Notes:

[4] - No Subjects were available for analysis on Day 29 in Group 3.

Statistical analyses

No statistical analyses for this end point

Secondary: Group 3 and 4: GMCs of Antibodies Measured by S-ELISA 28 Days After Administration of Ad26.COV2.S Vaccine

End point title	Group 3 and 4: GMCs of Antibodies Measured by S-ELISA 28 Days After Administration of Ad26.COV2.S Vaccine[5]

End point description:

GMCs of antibody titers measured by S-ELISA at 28 days after administration of Ad26.COV2.S vaccine was reported. This endpoint was planned to be analysed for specified arms only. Seronegative subjects (at Day 1) who became serology positive during the study, subjects with positive molecular test for SARSCoV-2 and major protocol deviation were excluded from PPSI analysis. The PPSI included all randomised subjects who received Ad26.COV2.S vaccine in combination with seasonal influenza vaccine for the co-administration group and Ad26.COV2.S vaccine alone for the control group, and for whom immunogenicity data was available. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

28 days after vaccination with Ad26.COV2.S vaccine (Group 3: Day 29, Group 4: Day 57)

Notes:

[5] - 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: This outcome measure was planned to be analysed for specified arm only.

End point values	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	33		
Units: EU/mL				
geometric mean (confidence interval 95%)	17569 (13391 to 23051)	20743 (12732 to 33794)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Seroconversion for each of the 4 Influenza Vaccine Strains at 28 Days After the Administration of a Seasonal Quadrivalent (High-dose and Standard-dose) Influenza Vaccine

End point title	Percentage of Subjects with Seroconversion for each of the 4 Influenza Vaccine Strains at 28 Days After the Administration of a Seasonal Quadrivalent (High-dose and Standard-dose) Influenza Vaccine

End point description:

Seroconversion of 4 influenza vaccine strains (group 1 & 2: A/Victoria [H1N1], A/Cambodia [H3N2], B/Victoria [B/Victoria], B/Phuket [B/Yamagata]; group 3 & 4: A/Victoria [H1N1], B/Phuket (B/Yamagata), A/Tasmania [H3N2], B/Washington [B/Victoria]) at 28 days after administration of seasonal quadrivalent (HD & SD) influenza vaccine: HI titer >=1:40 in subjects with pre-vaccination HI titer of less than(<)1:10 or >=4-fold HI titer increase in subjects with pre-vaccination HI titer of >=1:10.'n=0'&99999: none of subjects were evaluable at specified timepoint. PPII set: all randomised subjects who received Ad26.COV2.S vaccine in combination with seasonal influenza vaccine for co-administration group and those who received seasonal influenza vaccine alone for control group, for whom immunogenicity data were available for at least 1 of influenza strains in vaccine; excluded subjects with major protocol deviation. N (number of subjects analysed)=subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

28 days after the administration of a seasonal quadrivalent influenza vaccine (Day 29)

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	320	333	43	41
Units: Percentage of subjects				
number (confidence interval 95%)				
A/Victoria (H1N1) (n=320,333,43,41)	64.1 (58.5 to 69.3)	70.0 (64.7 to 74.8)	65.1 (49.1 to 79.0)	70.7 (54.5 to 83.9)
A/Cambodia (H3N2) (n=320,333,0,0)	39.1 (33.7 to 44.6)	46.8 (41.4 to 52.4)	99999 (99999 to 99999)	99999 (99999 to 99999)
B/Victoria (B/Victoria) (n=320,333,0,0)	42.8 (37.3 to 48.4)	43.5 (38.1 to 49.1)	99999 (99999 to 99999)	99999 (99999 to 99999)
B/Phuket (B/Yamagata)(n=320,333,43,41)	35.3 (30.1 to 40.8)	36.9 (31.7 to 42.4)	37.2 (23.0 to 53.3)	34.1 (20.1 to 50.6)
A/Tasmania (H3N2)(n=0,0,43,41)	99999 (99999 to 99999)	99999 (99999 to 99999)	72.1 (56.3 to 84.7)	70.7 (54.5 to 83.9)
B/Washington (B/Victoria) (n=0,0,43,41)	99999 (99999 to 99999)	99999 (99999 to 99999)	41.9 (27.0 to 57.9)	53.7 (37.4 to 69.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Seroprotection for each of the 4 Influenza Vaccine Strains as HI titer >= 1:40 at 28 Days After the Administration of a Seasonal Quadrivalent (High-dose and Standard-dose) Influenza Vaccine

End point title	Percentage of Subjects with Seroprotection for each of the 4 Influenza Vaccine Strains as HI titer >= 1:40 at 28 Days After the Administration of a Seasonal Quadrivalent (High-dose and Standard-dose) Influenza Vaccine

End point description:

Seroprotection was defined for each of the 4 influenza vaccine strains (For group 1 and 2: A/Victoria [H1N1], A/Cambodia [H3N2], B/Victoria [B/Victoria], B/Phuket [B/Yamagata]; For group 3 and 4: A/Victoria [H1N1], B/Phuket (B/Yamagata), A/Tasmania [H3N2], B/Washington [B/Victoria]) as HI titer >=1:40 at 28 days after the administration of a seasonal quadrivalent (HD and SD) influenza vaccine. 'n=0' & 99999: signifies that none of the subjects were evaluable at the specified timepoint. The PPII set included all randomized subjects who received Ad26.COV2.S vaccine in combination with seasonal influenza vaccine for coadministration group and those who received seasonal influenza vaccine alone for control group, for whom immunogenicity data were available for at least one of influenza strains in vaccine. Subjects with major protocol deviation were excluded from PPII analysis. 'N' (number of subjects analyzed)= subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

28 days after the administration of a seasonal quadrivalent influenza vaccine (Day 29)

End point values	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	320	333	43	41
Units: Percentage of subjects				
number (confidence interval 95%)				
A/Victoria (H1N1) (n=320,333,43,41)	97.8 (95.5 to 99.1)	97.3 (94.9 to 98.8)	100.0 (91.8 to 100.0)	100.0 (91.4 to 100.0)
A/Cambodia (H3N2) (n=320,333,0,0)	92.8 (89.4 to 95.4)	93.4 (90.2 to 95.8)	99999 (99999 to 99999)	99999 (99999 to 99999)
B/Victoria (B/Victoria) (n=320,333,0,0)	56.9 (51.2 to 62.4)	57.4 (51.8 to 62.7)	99999 (99999 to 99999)	99999 (99999 to 99999)
B/Phuket (B/Yamagata) (n=320,333,43,41)	52.2 (46.6 to 57.8)	55.0 (49.4 to 60.4)	62.8 (46.7 to 77.0)	63.4 (46.9 to 77.9)
A/Tasmania (H3N2) (n=0,0,43,41)	99999 (99999 to 99999)	99999 (99999 to 99999)	97.7 (87.7 to 99.9)	100.0 (91.4 to 100.0)
B/Washington (B/Victoria) (n=0,0,43,41)	99999 (99999 to 99999)	99999 (99999 to 99999)	79.1 (64.0 to 90.0)	82.9 (67.9 to 92.8)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 (post-vaccination) to end of the study (up to 12.5 months)

Adverse event reporting additional description:

The full analysis set (FAS) included all randomised subjects with at least 1 documented study vaccine administration.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo

Reporting group description:

Subjects aged greater than or equal to (>=) 18 years and older received a single intramuscular (IM) injection of Ad26.COV2.S at 5*10^10 viral particles (vp) dose level and a seasonal quadrivalent (Q) standard dose (SD) influenza vaccine with 60 micrograms (mcg) hemagglutinin (HA) on Day 1 followed by a single IM injection of placebo (matched to Ad26.COV2.S) on Day 29.

Reporting group title	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S

Reporting group description:

Subjects aged >=18 years and older received a single IM injection of placebo (matched to Ad26.COV2.S) and a seasonal Q SD influenza vaccine with 60 mcg of HA on Day 1 followed by a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.

Reporting group title	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and Placebo

Reporting group description:

Subjects aged >=18 years and older received a single IM injection of placebo (matched to Ad26.COV2.S) and a seasonal Q SD influenza vaccine with 60 mcg of HA on Day 1 followed by a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.

Reporting group title	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S

Reporting group description:

Subjects aged >=18 years and older received a single IM injection of placebo (matched to Ad26.COV2.S) and a seasonal Q SD influenza vaccine with 60 mcg of HA on Day 1 followed by a single IM injection of Ad26.COV2.S at 5*10^10 vp dose level on Day 29.

Serious adverse events	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 382 (2.36%)	2 / 46 (4.35%)	1 / 47 (2.13%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal Neoplasm			
subjects affected / exposed	0 / 382 (0.00%)	0 / 46 (0.00%)	0 / 47 (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

Polycythaemia Vera			
subjects affected / exposed	1 / 382 (0.26%)	0 / 46 (0.00%)	0 / 47 (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
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	1 / 382 (0.26%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Abnormal Uterine Bleeding			
subjects affected / exposed	1 / 382 (0.26%)	0 / 46 (0.00%)	0 / 47 (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
Respiratory, thoracic and mediastinal disorders			
Pleurisy			
subjects affected / exposed	0 / 382 (0.00%)	0 / 46 (0.00%)	0 / 47 (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 Oedema			
subjects affected / exposed	0 / 382 (0.00%)	0 / 46 (0.00%)	0 / 47 (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 / 382 (0.00%)	0 / 46 (0.00%)	0 / 47 (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
Psychiatric disorders			
Bipolar Disorder			
subjects affected / exposed	1 / 382 (0.26%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Fibula Fracture			
subjects affected / exposed	1 / 382 (0.26%)	0 / 46 (0.00%)	0 / 47 (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
Joint Injury			
subjects affected / exposed	1 / 382 (0.26%)	0 / 46 (0.00%)	0 / 47 (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
Cardiac disorders			
Cardiac Arrest			
subjects affected / exposed	0 / 382 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Chronic Left Ventricular Failure			
subjects affected / exposed	0 / 382 (0.00%)	0 / 46 (0.00%)	0 / 47 (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
Nervous system disorders			
Optic Neuritis			
subjects affected / exposed	0 / 382 (0.00%)	0 / 46 (0.00%)	0 / 47 (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
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 382 (0.26%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary Obstruction			
subjects affected / exposed	1 / 382 (0.26%)	0 / 46 (0.00%)	0 / 47 (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
Skin and subcutaneous tissue disorders			
Skin Ulcer			

subjects affected / exposed	1 / 382 (0.26%)	0 / 46 (0.00%)	0 / 47 (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
Renal and urinary disorders			
Calculus Urinary			
subjects affected / exposed	0 / 382 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 382 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 382 (0.00%)	0 / 46 (0.00%)	0 / 47 (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
Staphylococcal Infection			
subjects affected / exposed	1 / 382 (0.26%)	0 / 46 (0.00%)	0 / 47 (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

Serious adverse events	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 384 (1.82%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal Neoplasm			
subjects affected / exposed	1 / 384 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Polycythaemia Vera			

subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Abnormal Uterine Bleeding			
subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleurisy			
subjects affected / exposed	1 / 384 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary Oedema			
subjects affected / exposed	1 / 384 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary Embolism			
subjects affected / exposed	1 / 384 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Bipolar Disorder			
subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fibula Fracture			

subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint Injury			
subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac Arrest			
subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic Left Ventricular Failure			
subjects affected / exposed	1 / 384 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Optic Neuritis			
subjects affected / exposed	1 / 384 (0.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 384 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary Obstruction			
subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin Ulcer			

subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus Urinary			
subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 384 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Covid-19			
subjects affected / exposed	1 / 384 (0.26%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Staphylococcal Infection			
subjects affected / exposed	0 / 384 (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	Group 1: Ad26.COV2.S + Q SD Influenza Vaccine and Placebo	Group 4: Placebo + Q HD Influenza Vaccine and Ad26.COV2.S	Group 3: Ad26.COV2.S + Q HD Influenza Vaccine and Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 382 (11.78%)	6 / 46 (13.04%)	11 / 47 (23.40%)
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 382 (0.79%)	3 / 46 (6.52%)	2 / 47 (4.26%)
occurrences (all)	3	3	2
Covid-19			

subjects affected / exposed	42 / 382 (10.99%)	5 / 46 (10.87%)	10 / 47 (21.28%)
occurrences (all)	42	5	10

Non-serious adverse events	Group 2: Placebo + Q SD Influenza Vaccine and Ad26.COV2.S		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 384 (11.72%)		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 384 (1.30%)		
occurrences (all)	7		
Covid-19			
subjects affected / exposed	42 / 384 (10.94%)		
occurrences (all)	42		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 February 2022	The purpose of this amendment was to perform a descriptive analysis for the high-dose regimen instead, because it was unlikely that enough subjects greater than or equal to (>=)65 years of age could be recruited in time before the end of the influenza season to power the non-inferiority hypothesis testing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported