



Clinical trial results:

A Randomized, Double-blind, Phase 3 Study to Evaluate 6 Dose Levels of Ad26.COVS Administered As a Two-Dose Schedule in Healthy Adults

Summary

EudraCT number	2020-005801-14
Trial protocol	DE PL
Global end of trial date	10 July 2023

Results information

Result version number	v1
This version publication date	07 February 2024
First version publication date	07 February 2024

Trial information

Trial identification

Sponsor protocol code	VAC31518COV3003
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04908722
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	17 August 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 July 2023
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 6 dose levels of Ad26.COV2.S administered as a 2-dose schedule in healthy adults and demonstrate non-inferiority of each dose level comparing with the release titer.

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	18 June 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	Brazil: 811
Country: Number of subjects enrolled	Germany: 368
Country: Number of subjects enrolled	United States: 292
Country: Number of subjects enrolled	South Africa: 122
Worldwide total number of subjects	1593
EEA total number of subjects	368

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)	1593

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study involves Main study:1321 subjects were enrolled, of which 1080 completed the main study and Sub study:272 subjects were enrolled of which 231 completed the sub study. As planned, the Subject disposition, Baseline characteristics, Outcome measures data, and Adverse events data were analysed and reported combined for the Main and sub-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 9x10 ¹⁰ vp

Arm description:

Subjects in the main study and sub study received intramuscular (IM) injection of Ad26.COV2.S 9x10¹⁰ viral particles (vp) on Days 1 and 57.

Arm type	Experimental
Investigational medicinal product name	Ad26.COV2.S
Investigational medicinal product code	VAC31518
Other name	JNJ-78436735 Ad26COVS1
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects in the received Ad26.COV2.S 9X10¹⁰ vp on Days 1 and 57.

Arm title	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp
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Arm description:

Subjects in the main study received IM injection of Ad26.COV2.S 7x10¹⁰ vp on Days 1 and 57.

Arm type	Experimental
Investigational medicinal product name	Ad26.COV2.S
Investigational medicinal product code	VAC31518
Other name	JNJ-78436735 Ad26COVS1
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received Ad26.COV2.S 7x10¹⁰ vp on Days 1 and 57.

Arm title	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp
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Arm description:

Subjects in the main study and sub study received IM injection of Ad26.COV2.S 5x10¹⁰ vp on Days 1 and 57.

Arm type	Experimental
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Investigational medicinal product name	Ad26.COV2.S
Investigational medicinal product code	VAC31518
Other name	JNJ-78436735 Ad26COVS1
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received Ad26.COV2.S 5x10 ¹⁰ vp on Days 1 and 57.	
Arm title	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Arm description:	
Subjects in the main study received IM injection of Ad26.COV2.S 3.5x10 ¹⁰ vp on Days 1 and 57.	
Arm type	Experimental
Investigational medicinal product name	Ad26.COV2.S
Investigational medicinal product code	VAC31518
Other name	JNJ-78436735 Ad26COVS1
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received Ad26.COV2.S 3.5x10 ¹⁰ vp on Days 1 and 57.	
Arm title	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp
Arm description:	
Subjects in the main study and sub study received IM injection of Ad26.COV2.S 2.5x10 ¹⁰ vp on Days 1 and 57.	
Arm type	Experimental
Investigational medicinal product name	Ad26.COV2.S
Investigational medicinal product code	VAC31518
Other name	JNJ-78436735 Ad26COVS1
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received Ad26.COV2.S 2.5x10 ¹⁰ vp on Days 1 and 57.	
Arm title	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp
Arm description:	
Subjects in the main study and sub study received IM injection of Ad26.COV2.S 1.25x10 ¹⁰ vp on Days 1 and 57.	
Arm type	Experimental
Investigational medicinal product name	Ad26.COV2.S
Investigational medicinal product code	VAC31518
Other name	JNJ-78436735 Ad26COVS1
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received Ad26.COV2.S 1.25x10 ¹⁰ vp on Days 1 and 57.	

Number of subjects in period 1	Group 1: Ad26.COV2.S	Group 2: Ad26.COV2.S	Group 3: Ad26.COV2.S
Started	288	221	291
Main Study	220 ^[1]	221	222 ^[2]
Sub Study	68 ^[3]	0 ^[4]	69 ^[5]
Per protocol immunogenicity (PPI) set	276	212	282
Completed	237	178	244
Not completed	51	43	47
Adverse event, serious fatal	1	-	-
Physician decision	1	1	1
Initiated prohibited medication	-	-	-
Protocol deviation	1	-	-
Unspecified	3	1	3
Lost to follow-up	33	33	36
Withdrawal by subject	12	8	7

Number of subjects in period 1	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp
Started	220	288	285
Main Study	220	219 ^[6]	219 ^[7]
Sub Study	0 ^[8]	69 ^[9]	66 ^[10]
Per protocol immunogenicity (PPI) set	212	277	271
Completed	179	240	233
Not completed	41	48	52
Adverse event, serious fatal	-	-	1
Physician decision	2	-	-
Initiated prohibited medication	1	-	1
Protocol deviation	-	-	1
Unspecified	2	4	1
Lost to follow-up	30	32	34
Withdrawal by subject	6	12	14

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only reported subjects were included in main study.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only reported subjects were included in sub study.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only reported subjects were included in sub study.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only reported subjects were included in sub study.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only reported subjects were included in main study.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only reported subjects were included in sub study.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only reported subjects were included in sub study.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only reported subjects were included in main study.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only reported subjects were included in main study.

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Only reported subjects were included in main study.

Baseline characteristics

Reporting groups

Reporting group title	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp
Reporting group description: Subjects in the main study and sub study received intramuscular (IM) injection of Ad26.COV2.S 9x10 ¹⁰ viral particles (vp) on Days 1 and 57.	
Reporting group title	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp
Reporting group description: Subjects in the main study received IM injection of Ad26.COV2.S 7x10 ¹⁰ vp on Days 1 and 57.	
Reporting group title	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp
Reporting group description: Subjects in the main study and sub study received IM injection of Ad26.COV2.S 5x10 ¹⁰ vp on Days 1 and 57.	
Reporting group title	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Reporting group description: Subjects in the main study received IM injection of Ad26.COV2.S 3.5x10 ¹⁰ vp on Days 1 and 57.	
Reporting group title	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp
Reporting group description: Subjects in the main study and sub study received IM injection of Ad26.COV2.S 2.5x10 ¹⁰ vp on Days 1 and 57.	
Reporting group title	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp
Reporting group description: Subjects in the main study and sub study received IM injection of Ad26.COV2.S 1.25x10 ¹⁰ vp on Days 1 and 57.	

Reporting group values	Group 1: Ad26.COV2.S	Group 2: Ad26.COV2.S	Group 3: Ad26.COV2.S
Number of subjects	288	221	291
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	288	221	291
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	35.6	35.2	34.8
standard deviation	± 10.21	± 9.87	± 9.82
Title for Gender Units: subjects			
Female	117	73	119
Male	170	148	172
Undifferentiated	1	0	0

Reporting group values	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp
Number of subjects	220	288	285

Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	220	288	285
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	34.7	34.5	33.4
standard deviation	± 9.36	± 9.81	± 9.63
Title for Gender Units: subjects			
Female	72	106	103
Male	148	182	182
Undifferentiated	0	0	0

Reporting group values	Total		
Number of subjects	1593		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	1593		
From 65 to 84 years	0		
85 years and over	0		
Title for AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		
Title for Gender Units: subjects			
Female	590		
Male	1002		
Undifferentiated	1		

End points

End points reporting groups

Reporting group title	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp
Reporting group description: Subjects in the main study and sub study received intramuscular (IM) injection of Ad26.COV2.S 9x10 ¹⁰ viral particles (vp) on Days 1 and 57.	
Reporting group title	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp
Reporting group description: Subjects in the main study received IM injection of Ad26.COV2.S 7x10 ¹⁰ vp on Days 1 and 57.	
Reporting group title	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp
Reporting group description: Subjects in the main study and sub study received IM injection of Ad26.COV2.S 5x10 ¹⁰ vp on Days 1 and 57.	
Reporting group title	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Reporting group description: Subjects in the main study received IM injection of Ad26.COV2.S 3.5x10 ¹⁰ vp on Days 1 and 57.	
Reporting group title	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp
Reporting group description: Subjects in the main study and sub study received IM injection of Ad26.COV2.S 2.5x10 ¹⁰ vp on Days 1 and 57.	
Reporting group title	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp
Reporting group description: Subjects in the main study and sub study received IM injection of Ad26.COV2.S 1.25x10 ¹⁰ vp on Days 1 and 57.	

Primary: Geometric Mean Concentration of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) S Protein Binding Antibodies Measured by Enzyme-Linked Immunosorbent Assay (ELISA) 28 Days After First Vaccination

End point title	Geometric Mean Concentration of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) S Protein Binding Antibodies Measured by Enzyme-Linked Immunosorbent Assay (ELISA) 28 Days After First Vaccination ^[1]
End point description: Geometric mean concentration of SARS-CoV-2 S protein binding antibodies measured by ELISA were reported. As per planned analysis, the data were analysed and reported combined for the main study and sub-study. The per protocol immunogenicity set included all randomised and vaccinated subjects for whom immunogenicity data were available excluding subjects with major protocol deviations expected to impact the immunogenicity outcomes. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.	
End point type	Primary
End point timeframe: 28 days after first vaccination (at Day 29)	
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: Descriptive statistics was done, no inferential statistical analysis was performed.	

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	191	250	189
Units: ELISA Units per millilitre (EU/mL)				
geometric mean (confidence interval 95%)	2351 (1849 to 2989)	1714 (1305 to 2250)	2189 (1726 to 2775)	1377 (1062 to 1786)

End point values	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	251		
Units: ELISA Units per millilitre (EU/mL)				
geometric mean (confidence interval 95%)	1626 (1255 to 2106)	1976 (1521 to 2566)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Ratio of Antibodies Measured by S-ELISA at 28 Days After First Vaccination

End point title	Geometric Mean Ratio of Antibodies Measured by S-ELISA at 28 Days After First Vaccination ^[2] ^[3]
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End point description:

Geometric mean ratio of antibodies measured by S-ELISA were reported. Geometric mean ratio was calculated as ratio of 1 dose of Ad26.COV2.S 9x10¹⁰ vp, Ad26.COV2.S 7x10¹⁰ vp, Ad26.COV2.S 3.5x10¹⁰, Ad26.COV2.S 2.5x10¹⁰, and Ad26.COV2.S 1.25x10¹⁰ vp divided by 1 dose of Ad26.COV2.S 5x10¹⁰ vp at Day 29. As per planned analysis, the data were analysed and reported combined for the main study and sub-study. The per protocol immunogenicity set included all randomized and vaccinated subjects for whom immunogenicity data were available excluding subjects with major protocol deviations expected to impact the immunogenicity outcomes. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this end point.

End point type	Primary
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End point timeframe:

Day 29 (28 days post dose 1)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics was done, no inferential statistical analysis was performed.

[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: Statistical Analysis was not planned for all the arms of Baseline period.

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	191	189	243
Units: Ratio				
geometric mean (confidence interval 97.5%)	1.15 (0.926 to 1.440)	1.07 (0.844 to 1.356)	0.94 (0.742 to 1.193)	0.80 (0.641 to 1.00)

End point values	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp			
Subject group type	Reporting group			
Number of subjects analysed	251			
Units: Ratio				
geometric mean (confidence interval 97.5%)	0.81 (0.648 to 1.007)			

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentration of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) S Protein Binding Antibodies Measured by Enzyme-Linked Immunosorbent Assay (ELISA) 14 Days After Second Vaccination

End point title	Geometric Mean Concentration of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) S Protein Binding Antibodies Measured by Enzyme-Linked Immunosorbent Assay (ELISA) 14 Days After Second Vaccination ^[4]
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End point description:

Geometric mean concentration of SARS-CoV-2 S protein binding antibodies measured by ELISA were reported. As per planned analysis, the data were analysed and reported combined for the main study and sub-study. The per protocol immunogenicity set included all randomised and vaccinated subjects for whom immunogenicity data were available excluding subjects with major protocol deviations expected to impact the immunogenicity outcomes. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

14 days after second vaccination (at Day 71)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics was done, no inferential statistical analysis was performed.

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	171	130	180	134
Units: ELISA Units per millilitre (EU/mL)				
geometric mean (confidence interval 95%)	4997 (4145 to 6023)	3757 (3030 to 4659)	3855 (3185 to 4666)	3460 (2781 to 4304)

End point values	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	184		
Units: ELISA Units per millilitre (EU/mL)				
geometric mean (confidence interval 95%)	3641 (2969 to 4465)	3905 (3113 to 4897)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Ratio of Antibodies Measured by S-ELISA 14 Days After Second Vaccination

End point title	Geometric Mean Ratio of Antibodies Measured by S-ELISA 14 Days After Second Vaccination ^{[5][6]}
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End point description:

Geometric mean ratio of antibodies measured by S-ELISA were reported. Geometric mean ratio was calculated as ratio of 2 doses on Day 71 dose of Ad26.COV2.S 9x10¹⁰ vp, Ad26.COV2.S 7x10¹⁰ vp, Ad26.COV2.S 3.5x10¹⁰, Ad26.COV2.S 2.5x10¹⁰, and Ad26.COV2.S 1.25x10¹⁰ vp divided by 1 dose of Ad26.COV2.S 5x10¹⁰ vp at Day 29 and values observed at post-vaccination on Day 71 of 2 doses of Ad26.COV2.S 9x10¹⁰ vp, Ad26.COV2.S 7x10¹⁰ vp, Ad26.COV2.S 3.5x10¹⁰, Ad26.COV2.S 2.5x10¹⁰, and Ad26.COV2.S 1.25x10¹⁰ vp divided by 2 doses for Ad26.COV2.S 5x10¹⁰ vp at Day 71. As per planned analysis, the data were analysed and reported combined for the main study and sub-study. The per protocol immunogenicity set included all randomised and vaccinated subjects for whom immunogenicity data were available excluding subjects with major protocol deviations expected to impact the immunogenicity outcomes. N (number of subjects analysed): subjects who were evaluable for this outcome measure.

End point type	Primary
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End point timeframe:

Group 3: 28 days after first vaccination (Day 29), 14 days after second vaccination (Day 71); Groups 1, 2, 4, 5, and 6: 14 days after second vaccination (Day 71)

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: Descriptive statistics was done, no inferential statistical analysis was performed.

[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: Statistical Analysis was not planned for all the arms of Baseline period.

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	171	130	134	172
Units: Ratio				
geometric mean (confidence interval 97.5%)				
2 doses at Day 71/1 dose at Day 29	2.53 (1.992 to 3.207)	2.37 (1.829 to 3.077)	2.20 (1.697 to 2.841)	1.79 (1.408 to 2.265)

2 doses at Day 71/ 2 doses at Day 71	1.41 (1.088 to 1.815)	1.32 (1.000 to 1.739)	1.22 (0.928 to 1.606)	0.99 (0.769 to 1.282)
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End point values	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp			
Subject group type	Reporting group			
Number of subjects analysed	184			
Units: Ratio				
geometric mean (confidence interval 97.5%)				
2 doses at Day 71/1 dose at Day 29	1.70 (1.348 to 2.148)			
2 doses at Day 71/ 2 doses at Day 71	0.95 (0.736 to 1.217)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Serological Response to Vaccination to SARS-COV-2 S Protein as Measured by ELISA

End point title	Percentage of Subjects with Serological Response to Vaccination to SARS-COV-2 S Protein as Measured by ELISA
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End point description:

Percentage of subjects with serological response to vaccination to SARS-COV-2 S Protein as Measured by ELISA were reported. A subject was considered a responder if one or both of the following conditions were satisfied: (1) the baseline (pre-dose 1) sample value was less than or equal to (\leq) lower limit of quantification (LLOQ) and the post-baseline sample was greater than ($>$) LLOQ; (2) the baseline sample (pre-dose 1) value was $>$ LLOQ and the post-baseline sample value represented an at least 4-fold (≥ 4 -fold) increase from the baseline sample value. As per planned analysis, the data were analyzed and reported combined for the main study and sub-study. The per protocol immunogenicity set included all randomised and vaccinated subjects for whom immunogenicity data were available excluding subjects with major protocol deviations expected to impact the immunogenicity outcomes.

End point type	Secondary
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End point timeframe:

Up to Week 60

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	191	250	189
Units: Percentage of subjects				
number (not applicable)				
Day 29 (n=249,191,250,189,243,251)	82.7	90.1	78.8	87.8
Day 57 (n=216,167,217,162,219,220)	81.9	88.6	80.2	92.0
Day 71 (n=171,130,180,134,172,184)	81.9	92.3	79.4	91.8
Week 32 (n=112,86,128,90,121,136)	72.3	83.7	68.0	86.7

Week 60 (n=45,33,42,37,45,52)	68.9	81.8	61.9	83.8
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End point values	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	251		
Units: Percentage of subjects				
number (not applicable)				
Day 29 (n=249,191,250,189,243,251)	80.2	76.1		
Day 57 (n=216,167,217,162,219,220)	81.3	77.7		
Day 71 (n=171,130,180,134,172,184)	80.8	76.1		
Week 32 (n=112,86,128,90,121,136)	68.6	63.2		
Week 60 (n=45,33,42,37,45,52)	60.0	53.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of SARS-CoV-2 S Protein Binding Antibody Measured by ELISA

End point title	Geometric Mean Concentration of SARS-CoV-2 S Protein Binding Antibody Measured by ELISA
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End point description:

Geometric mean concentration of SARS-CoV-2 S protein binding antibody measured by ELISA were reported. As per planned analysis, the data were analyzed and reported combined for the main study and sub-study. The per protocol immunogenicity set included all randomised and vaccinated subjects for whom immunogenicity data were available excluding subjects with major protocol deviations expected to impact the immunogenicity outcomes. Here, 'N' (number of subjects analysed) signifies subjects who were evaluable for this end point.

End point type	Secondary
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End point timeframe:

Up to Week 60

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	249	191	250	189
Units: ELISA Unit (EU)/mL				
geometric mean (confidence interval 95%)				
Day 29 (n=249,191,250,189,243,251)	2351 (1849 to 2989)	1714 (1305 to 2250)	2189 (1726 to 2775)	1377 (1062 to 1786)
Day 57 (n=216,167,217,162,219,220)	2722 (2156 to 3438)	1842 (1404 to 2417)	2089 (1651 to 2643)	1622 (1233 to 2134)
Day 71 (n=171,130,180,134,172,184)	4997 (4145 to 6023)	3757 (3030 to 4659)	3855 (3185 to 4666)	3460 (2781 to 4304)

Week 32 (n=112,86,128,90,121,136)	3331 (2499 to 4438)	2903 (2706 to 4058)	2616 (2001 to 3420)	2059 (1470 to 2885)
Week 60 (n=45,33,42,37,45,52)	4968 (3119 to 7915)	5010 (3146 to 7981)	2363 (1448 to 3857)	2191 (1224 to 3921)

End point values	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	251		
Units: ELISA Unit (EU)/mL				
geometric mean (confidence interval 95%)				
Day 29 (n=249,191,250,189,243,251)	1626 (1255 to 2106)	1976 (1521 to 2566)		
Day 57 (n=216,167,217,162,219,220)	1919 (1481 to 2486)	2293 (1766 to 2978)		
Day 71 (n=171,130,180,134,172,184)	3641 (2969 to 4465)	3905 (3113 to 4897)		
Week 32 (n=112,86,128,90,121,136)	3067 (2268 to 4148)	2707 (2000 to 3662)		
Week 60 (n=45,33,42,37,45,52)	2769 (1776 to 4317)	3664 (2169 to 6190)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Solicited Local Adverse Events (AEs) for 7 Days After Each Vaccination

End point title	Number of Subjects with Solicited Local Adverse Events (AEs) for 7 Days After Each Vaccination
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End point description:

An AE was 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 pre-defined local (at the injection site) AEs for which subjects were specifically questioned and which were noted by subject in their e-diary for 7 days after each vaccination. Solicited local AEs included injection site pain/tenderness, erythema and swelling at the study vaccine injection site. As per planned analysis, the data were analyzed and reported combined for the main study and sub-study. Full analysis set included all subjects with at least one vaccine administration documented. Here, 'n' (number of subjects analysed) signifies number of subjects evaluable for this timepoint.

End point type	Secondary
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End point timeframe:

7 days after each vaccination (first [1st] vaccination [at Day 8], second [2nd] vaccination [at Day 64])

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	288	221	291	220
Units: Subjects				
After 1st vaccination (n=288,221,291,220,288,285)	179	143	162	137
After 2nd vaccination (n=264,200,269,199,270,258)	130	100	124	95

End point values	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	285		
Units: Subjects				
After 1st vaccination (n=288,221,291,220,288,285)	155	133		
After 2nd vaccination (n=264,200,269,199,270,258)	111	104		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Solicited Systemic AEs for 7 Days After Each Vaccination

End point title	Number of Subjects with Solicited Systemic AEs for 7 Days After Each Vaccination
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End point description:

An AE was 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 systemic AEs (include body temperature, fatigue, headache, nausea, myalgia) were noted in the subject diary after 7 days of each vaccination. As per planned analysis, the data were analyzed and reported combined for the main study and sub-study. Full analysis set included all subjects with at least one vaccine administration documented. Here, 'n' (number of subjects analysed) signifies number of subjects evaluable for this timepoint.

End point type	Secondary
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End point timeframe:

7 days after each vaccination (1st vaccination [at Day 8], 2nd vaccination [at Day 64])

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	288	221	291	220
Units: Subjects				

After 1st vaccination (n=288,221,291,220,288,285)	204	156	173	135
After 2nd vaccination (n=264,200,269,199,270,258)	144	98	111	91

End point values	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	285		
Units: Subjects				
After 1st vaccination (n=288,221,291,220,288,285)	156	152		
After 2nd vaccination (n=264,200,269,199,270,258)	105	109		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Unsolicited AEs for 28 Days After Each Vaccination

End point title	Number of Subjects with Unsolicited AEs for 28 Days After Each Vaccination
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End point description:

Unsolicited AEs were all AEs for which the subject was not specifically questioned in the subject diary. As per planned analysis, the data were analyzed and reported combined for the main study and sub-study. Full analysis set included all subjects with at least one vaccine administration documented. Here, 'n' (number of subjects analysed) signifies number of subjects evaluable for this timepoint.

End point type	Secondary
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End point timeframe:

28 days after each vaccination (1st vaccination [at Day 29], 2nd vaccination [at Day 85])

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	288	221	291	220
Units: Subjects				
After 1st vaccination (n=288,221,291,220,288,285)	78	60	55	58
After 2nd vaccination (n=264,200,269,199,270,258)	55	28	49	39

End point values	Group 5: Ad26.COV2.S	Group 6: Ad26.COV2.S		
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	x10 ¹⁰ vp	x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	285		
Units: Subjects				
After 1st vaccination (n=288,221,291,220,288,285)	69	59		
After 2nd vaccination (n=264,200,269,199,270,258)	53	50		

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)
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End point description:

SAE was any untoward medical occurrence that at any dose may resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a suspected transmission of any infectious agent via a medicinal product. As per planned analysis, the data were analyzed and reported combined for the main study and sub-study. Full analysis set included all subjects with at least one vaccine administration documented.

End point type	Secondary
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End point timeframe:

From Day 1 (post-vaccination) up to end of the study (up to 60 weeks)

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	288	221	291	220
Units: Subjects	13	3	4	4

End point values	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	285		
Units: Subjects	3	5		

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)
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End point description:

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 were considered to be an AESI. As per planned analysis, the data were analyzed and reported combined for the main study and sub-study. Full analysis set included all subjects with at least one vaccine administration documented.

End point type	Secondary
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End point timeframe:

From Day 1 (post-vaccination) up to end of the study (up to 60 weeks)

End point values	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	288	221	291	220
Units: Subjects	0	0	0	0

End point values	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	285		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with AEs Leading to Study Discontinuation

End point title	Number of Subjects with AEs Leading to Study Discontinuation
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End point description:

Number of subjects with AEs leading to study discontinuation were reported. Full analysis set included all subjects with at least one vaccine administration documented.

End point type	Secondary
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End point timeframe:

Up to 60 weeks

End point values	Group 1: Ad26.COVS.S 9x10 ¹⁰ vp	Group 2: Ad26.COVS.S 7x10 ¹⁰ vp	Group 3: Ad26.COVS.S 5x10 ¹⁰ vp	Group 4: Ad26.COVS.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	288	221	291	220
Units: Subjects	0	0	0	0

End point values	Group 5: Ad26.COVS.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COVS.S 1.25x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	285		
Units: Subjects	0	0		

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)
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End point description:

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. Routine study visits were not considered medically-attended visits. New onset of chronic diseases were collected as part of the MAAEs. As per planned analysis, the data were analyzed and reported combined for the main study and sub-study. Full analysis set included all subjects with at least one vaccine administration documented.

End point type	Secondary
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End point timeframe:

6 months after second vaccination (up to 32 weeks)

End point values	Group 1: Ad26.COVS.S 9x10 ¹⁰ vp	Group 2: Ad26.COVS.S 7x10 ¹⁰ vp	Group 3: Ad26.COVS.S 5x10 ¹⁰ vp	Group 4: Ad26.COVS.S 3.5x10 ¹⁰ vp
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	288	221	281	220
Units: Subjects	54	34	50	35

End point values	Group 5: Ad26.COVS.S 2.5x10 ¹⁰ vp	Group 6: Ad26.COVS.S 1.25x10 ¹⁰ vp		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	285		
Units: Subjects	48	35		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 (post-vaccination) up to end of the study (i.e. up to 60 weeks)

Adverse event reporting additional description:

Full analysis set included all subjects with at least one vaccine administration documented. As per planned analysis, the data were analyzed and reported combined for the main study and sub-study.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Group 1: Ad26.COV2.S 9x10 ¹⁰ vp
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Reporting group description:

Subjects in the main and sub study received a single dose of IM injection of Ad26.COV2.S 9x10¹⁰ vp on Days 1 and 57.

Reporting group title	Group 2: Ad26.COV2.S 7x10 ¹⁰ vp
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Reporting group description:

Subjects in the main study received a single dose of IM injection of Ad26.COV2.S 7x10¹⁰ vp on Days 1 and 57.

Reporting group title	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp
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Reporting group description:

Subjects in the main and sub study received a single dose of IM injection of Ad26.COV2.S 1.25x10¹⁰ vp on Days 1 and 57.

Reporting group title	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp
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Reporting group description:

Subjects in the main received a single dose of IM injection of Ad26.COV2.S 3.5x10¹⁰ vp on Days 1 and 57.

Reporting group title	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp
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Reporting group description:

Subjects in the main and sub study received a single dose of IM injection of Ad26.COV2.S 2.5x10¹⁰ vp on Days 1 and 57.

Reporting group title	Group 3: Ad26.COV2.S 5x10 ¹⁰ vp
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Reporting group description:

Subjects in the main and sub study received a single dose of IM injection of Ad26.COV2.S 5x10¹⁰ vp on Days 1 and 57.

Serious adverse events	Group 1: Ad26.COV2.S	Group 2: Ad26.COV2.S	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 288 (4.51%)	3 / 221 (1.36%)	5 / 285 (1.75%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tongue Neoplasm Malignant Stage Unspecified			

subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Gestational Diabetes			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Drowning			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Reproductive system and breast disorders			
Hydrosalpinx			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Ovarian Cyst Torsion			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian Disorder			

subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal Haemorrhage			
subjects affected / exposed	0 / 288 (0.00%)	1 / 221 (0.45%)	0 / 285 (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
Respiratory, thoracic and mediastinal disorders			
Pleural Effusion			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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			
Anxiety Disorder			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Depression			
subjects affected / exposed	0 / 288 (0.00%)	1 / 221 (0.45%)	0 / 285 (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
Psychotic Disorder			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Suicide Attempt			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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			
Ankle Fracture			
subjects affected / exposed	0 / 288 (0.00%)	1 / 221 (0.45%)	0 / 285 (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
Gun Shot Wound			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Stab Wound			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Cardiac disorders			
Myopericarditis			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Nervous system disorders			
Carotid Artery Dissection			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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
Paraesthesia			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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
Myasthenia Gravis			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Syncope			

subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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			
Anaemia			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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
Anal Fistula			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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			
Nephrolithiasis			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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			
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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			
Appendicitis			

subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Cellulitis			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Pelvic Abscess			
subjects affected / exposed	1 / 288 (0.35%)	0 / 221 (0.00%)	0 / 285 (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
Pyelonephritis			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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
Pyelonephritis Acute			
subjects affected / exposed	0 / 288 (0.00%)	0 / 221 (0.00%)	0 / 285 (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	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 3: Ad26.COV2.S
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 220 (1.82%)	3 / 288 (1.04%)	4 / 291 (1.37%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tongue Neoplasm Malignant Stage Unspecified			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			

subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gestational Diabetes			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
General disorders and administration site conditions			
Drowning			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Death			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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			
Hydrosalpinx			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Ovarian Cyst Torsion			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Ovarian Disorder			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Vaginal Haemorrhage			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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			
Pleural Effusion			
subjects affected / exposed	0 / 220 (0.00%)	1 / 288 (0.35%)	0 / 291 (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
Psychiatric disorders			
Anxiety Disorder			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Anxiety			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Depression			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Psychotic Disorder			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Suicide Attempt			
subjects affected / exposed	0 / 220 (0.00%)	1 / 288 (0.35%)	0 / 291 (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			
Ankle Fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Gun Shot Wound			

subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Stab Wound			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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			
Myopericarditis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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			
Carotid Artery Dissection			
subjects affected / exposed	1 / 220 (0.45%)	0 / 288 (0.00%)	0 / 291 (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
Paraesthesia			
subjects affected / exposed	0 / 220 (0.00%)	1 / 288 (0.35%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia Gravis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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 / 220 (0.00%)	0 / 288 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal Fistula			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 220 (0.45%)	0 / 288 (0.00%)	0 / 291 (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
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	1 / 220 (0.45%)	0 / 288 (0.00%)	0 / 291 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Cellulitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Pelvic Abscess			

subjects affected / exposed	0 / 220 (0.00%)	0 / 288 (0.00%)	0 / 291 (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
Pyelonephritis			
subjects affected / exposed	1 / 220 (0.45%)	0 / 288 (0.00%)	0 / 291 (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
Pyelonephritis Acute			
subjects affected / exposed	1 / 220 (0.45%)	0 / 288 (0.00%)	0 / 291 (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

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

Non-serious adverse events	Group 1: Ad26.COV2.S	Group 2: Ad26.COV2.S	Group 6: Ad26.COV2.S 1.25x10 ¹⁰ vp
Total subjects affected by non-serious adverse events			
subjects affected / exposed	245 / 288 (85.07%)	187 / 221 (84.62%)	217 / 285 (76.14%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 288 (2.08%)	0 / 221 (0.00%)	0 / 285 (0.00%)
occurrences (all)	9	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	26 / 288 (9.03%)	14 / 221 (6.33%)	22 / 285 (7.72%)
occurrences (all)	28	20	28
Headache(Solicited)			
subjects affected / exposed	184 / 288 (63.89%)	139 / 221 (62.90%)	123 / 285 (43.16%)
occurrences (all)	260	202	165
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 288 (1.74%)	1 / 221 (0.45%)	0 / 285 (0.00%)
occurrences (all)	5	1	0
Thrombocytopenia			
subjects affected / exposed	8 / 288 (2.78%)	5 / 221 (2.26%)	9 / 285 (3.16%)
occurrences (all)	8	6	15

General disorders and administration site conditions			
Chills			
subjects affected / exposed	11 / 288 (3.82%)	5 / 221 (2.26%)	0 / 285 (0.00%)
occurrences (all)	13	5	0
Fatigue			
subjects affected / exposed	15 / 288 (5.21%)	11 / 221 (4.98%)	15 / 285 (5.26%)
occurrences (all)	19	14	22
Fatigue(Solicited)			
subjects affected / exposed	171 / 288 (59.38%)	140 / 221 (63.35%)	132 / 285 (46.32%)
occurrences (all)	248	202	178
Pyrexia			
subjects affected / exposed	9 / 288 (3.13%)	10 / 221 (4.52%)	7 / 285 (2.46%)
occurrences (all)	14	14	7
Vaccination Site Erythema(Solicited)			
subjects affected / exposed	3 / 288 (1.04%)	5 / 221 (2.26%)	5 / 285 (1.75%)
occurrences (all)	3	5	5
Pyrexia(Solicited)			
subjects affected / exposed	68 / 288 (23.61%)	41 / 221 (18.55%)	16 / 285 (5.61%)
occurrences (all)	77	42	17
Vaccination Site Pain			
subjects affected / exposed	7 / 288 (2.43%)	8 / 221 (3.62%)	8 / 285 (2.81%)
occurrences (all)	8	12	10
Vaccination Site Swelling(Solicited)			
subjects affected / exposed	8 / 288 (2.78%)	9 / 221 (4.07%)	8 / 285 (2.81%)
occurrences (all)	8	9	9
Vaccination Site Pain(Solicited)			
subjects affected / exposed	198 / 288 (68.75%)	156 / 221 (70.59%)	160 / 285 (56.14%)
occurrences (all)	306	242	234
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 288 (2.08%)	3 / 221 (1.36%)	2 / 285 (0.70%)
occurrences (all)	6	3	3
Nausea			
subjects affected / exposed	6 / 288 (2.08%)	5 / 221 (2.26%)	5 / 285 (1.75%)
occurrences (all)	7	6	6
Nausea(Solicited)			

subjects affected / exposed occurrences (all)	95 / 288 (32.99%) 123	78 / 221 (35.29%) 99	65 / 285 (22.81%) 80
Odynophagia subjects affected / exposed occurrences (all)	3 / 288 (1.04%) 3	5 / 221 (2.26%) 7	5 / 285 (1.75%) 7
Vomiting subjects affected / exposed occurrences (all)	4 / 288 (1.39%) 4	1 / 221 (0.45%) 1	2 / 285 (0.70%) 3
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	7 / 288 (2.43%) 9	5 / 221 (2.26%) 7	4 / 285 (1.40%) 5
Dyspnoea subjects affected / exposed occurrences (all)	6 / 288 (2.08%) 6	0 / 221 (0.00%) 0	1 / 285 (0.35%) 1
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	10 / 288 (3.47%) 12	12 / 221 (5.43%) 17	18 / 285 (6.32%) 20
Myalgia(Solicited) subjects affected / exposed occurrences (all)	183 / 288 (63.54%) 260	126 / 221 (57.01%) 175	111 / 285 (38.95%) 151
Infections and infestations Influenza subjects affected / exposed occurrences (all)	35 / 288 (12.15%) 57	26 / 221 (11.76%) 31	25 / 285 (8.77%) 35
Covid-19 subjects affected / exposed occurrences (all)	9 / 288 (3.13%) 14	21 / 221 (9.50%) 30	13 / 285 (4.56%) 19
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 288 (1.04%) 3	7 / 221 (3.17%) 7	12 / 285 (4.21%) 13
Rhinitis subjects affected / exposed occurrences (all)	8 / 288 (2.78%) 9	6 / 221 (2.71%) 8	2 / 285 (0.70%) 2

Non-serious adverse events	Group 4: Ad26.COV2.S 3.5x10 ¹⁰ vp	Group 5: Ad26.COV2.S 2.5x10 ¹⁰ vp	Group 3: Ad26.COV2.S
Total subjects affected by non-serious adverse events			
subjects affected / exposed	188 / 220 (85.45%)	228 / 288 (79.17%)	236 / 291 (81.10%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 220 (1.82%)	0 / 288 (0.00%)	3 / 291 (1.03%)
occurrences (all)	4	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	21 / 220 (9.55%)	23 / 288 (7.99%)	11 / 291 (3.78%)
occurrences (all)	25	26	12
Headache(Solicited)			
subjects affected / exposed	109 / 220 (49.55%)	133 / 288 (46.18%)	146 / 291 (50.17%)
occurrences (all)	150	175	195
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 220 (0.00%)	6 / 288 (2.08%)	8 / 291 (2.75%)
occurrences (all)	0	7	9
Thrombocytopenia			
subjects affected / exposed	7 / 220 (3.18%)	4 / 288 (1.39%)	1 / 291 (0.34%)
occurrences (all)	8	5	1
General disorders and administration site conditions			
Chills			
subjects affected / exposed	5 / 220 (2.27%)	4 / 288 (1.39%)	2 / 291 (0.69%)
occurrences (all)	6	4	2
Fatigue			
subjects affected / exposed	9 / 220 (4.09%)	5 / 288 (1.74%)	7 / 291 (2.41%)
occurrences (all)	9	5	9
Fatigue(Solicited)			
subjects affected / exposed	113 / 220 (51.36%)	124 / 288 (43.06%)	144 / 291 (49.48%)
occurrences (all)	164	173	207
Pyrexia			
subjects affected / exposed	4 / 220 (1.82%)	4 / 288 (1.39%)	5 / 291 (1.72%)
occurrences (all)	4	4	7
Vaccination Site Erythema(Solicited)			

subjects affected / exposed occurrences (all)	4 / 220 (1.82%) 4	2 / 288 (0.69%) 2	9 / 291 (3.09%) 9
Pyrexia(Solicited) subjects affected / exposed occurrences (all)	27 / 220 (12.27%) 27	22 / 288 (7.64%) 25	33 / 291 (11.34%) 37
Vaccination Site Pain subjects affected / exposed occurrences (all)	3 / 220 (1.36%) 4	6 / 288 (2.08%) 6	4 / 291 (1.37%) 6
Vaccination Site Swelling(Solicited) subjects affected / exposed occurrences (all)	3 / 220 (1.36%) 3	3 / 288 (1.04%) 3	9 / 291 (3.09%) 12
Vaccination Site Pain(Solicited) subjects affected / exposed occurrences (all)	153 / 220 (69.55%) 231	175 / 288 (60.76%) 265	190 / 291 (65.29%) 284
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	3 / 220 (1.36%) 5	2 / 288 (0.69%) 2	3 / 291 (1.03%) 4
Nausea subjects affected / exposed occurrences (all)	5 / 220 (2.27%) 5	5 / 288 (1.74%) 5	2 / 291 (0.69%) 2
Nausea(Solicited) subjects affected / exposed occurrences (all)	58 / 220 (26.36%) 71	64 / 288 (22.22%) 78	67 / 291 (23.02%) 79
Odynophagia subjects affected / exposed occurrences (all)	1 / 220 (0.45%) 1	2 / 288 (0.69%) 3	3 / 291 (1.03%) 3
Vomiting subjects affected / exposed occurrences (all)	1 / 220 (0.45%) 1	1 / 288 (0.35%) 1	6 / 291 (2.06%) 6
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	7 / 220 (3.18%) 7	7 / 288 (2.43%) 8	3 / 291 (1.03%) 4
Dyspnoea			

subjects affected / exposed occurrences (all)	1 / 220 (0.45%) 2	2 / 288 (0.69%) 2	2 / 291 (0.69%) 3
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	12 / 220 (5.45%)	7 / 288 (2.43%)	6 / 291 (2.06%)
occurrences (all)	15	7	8
Myalgia(Solicited)			
subjects affected / exposed	115 / 220 (52.27%)	118 / 288 (40.97%)	144 / 291 (49.48%)
occurrences (all)	159	159	188
Infections and infestations			
Influenza			
subjects affected / exposed	26 / 220 (11.82%)	37 / 288 (12.85%)	38 / 291 (13.06%)
occurrences (all)	41	52	50
Covid-19			
subjects affected / exposed	20 / 220 (9.09%)	22 / 288 (7.64%)	20 / 291 (6.87%)
occurrences (all)	29	35	28
Nasopharyngitis			
subjects affected / exposed	6 / 220 (2.73%)	8 / 288 (2.78%)	7 / 291 (2.41%)
occurrences (all)	8	13	8
Rhinitis			
subjects affected / exposed	4 / 220 (1.82%)	10 / 288 (3.47%)	1 / 291 (0.34%)
occurrences (all)	4	11	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 March 2021	The purpose of this amendment was to remove the placebo arms of the study for ethical reasons. Furthermore, after consideration of additional COV2001 study results, dose groups of 9×10^{10} vp, 7×10^{10} vp, and 3.5×10^{10} vp Ad26.COV2.S were added and the 1-dose regimen was removed, resulting in 6 dose-groups, each receiving 2 doses.
10 May 2021	The purpose of this amendment was to include additional safety measures due to reports of adverse events following use of the Ad26.COV2.S vaccine under emergency use authorisation in the United States (US), suggesting an increased risk of thrombosis combined with thrombocytopenia. Based on this, thrombosis with thrombocytopenia syndrome (TTS), which was a very rare event, followed in this protocol as adverse event of special interest (AESI) that needed to be reported to the sponsor within 24 hours of awareness. In addition, the protocol had been adjusted to align with the latest vaccine risk language.
23 June 2021	The main purpose of this amendment was to move the Day 85 sampling timepoint (28 days post-dose 2) to Day 71 (14 days post-dose 2) in order to align across VAC31518COVID studies. This amendment also updated the amount of blood volume needed (from 12 millilitre [mL] to 15 mL) to be collected at baseline and for AESI evaluations due to the increased volume of blood needed to isolate serum/plasma for the coagulation related assays in the study. An additional exclusion criterion for subjects with a history of capillary leak syndrome was added.
03 August 2021	The purpose of this amendment was to include the mechanism for the rare thrombosis with TTS events that was reported after vaccination with Johnson & Johnson's Ad26.COV2.S vaccine was not known.
30 November 2021	The purpose of this amendment was to clarify that hematology assessment was assessed pre- and post-vaccination in all of the subjects in both the main and sub study. In addition, exploratory endpoints were updated or added in both the main and sub study to include analysis against emerging variants due to the evolving nature of the corona virus-2019 (COVID-19) virus.
01 June 2022	The purpose of this amendment was to allow flexibility to stop enrollment in the sub-study of seronegative subjects earlier due to the increasing challenges of recruiting seronegative subjects into the sub study. The amendment also removed the interim analysis after the first vaccination at 28 days post dose 1 of the main study.
16 September 2022	The purpose of this amendment was to modify the order of the sequential non-inferiority assessment hypothesis testing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported