Clinical trial results:
COVID-19: A Phase 2b/3, Randomized, Observer-Blinded, Placebo-Controlled, Multicenter Clinical Study Evaluating the Efficacy and Safety of Investigational SARS-CoV-2 mRNA Vaccine CVnCoV in Adults 18 Years of Age and Older

Summary

EudraCT number	2020-003998-22
Trial protocol	BE DE NL
Global end of trial date	10 June 2022

Results information

Result version number	v1 (current)
This version publication date	28 December 2022
First version publication date	28 December 2022

Trial information

Trial identification

Sponsor protocol code	CV-NCOV-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04652102
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CureVac SE
Sponsor organisation address	Schumannstr 27, Frankfurt, Germany, 60325
Public contact	Clinical Trial Information, CureVac SE, 0049 6976805870, clinicaltrials@curevac.com
Scientific contact	Clinical Trial Information, CureVac SE, 0049 6976805870, clinicaltrials@curevac.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	10 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Efficacy Objectives:
• To demonstrate the efficacy of a 2-dose schedule of CVnCoV in the prevention of first episodes of virologically-confirmed cases of COVID-19 of any severity in Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) naïve participants.

Primary Safety Objectives
• To evaluate the safety of CVnCoV administered as a 2-dose schedule to participants 18 years of age and older.
• To evaluate the reactogenicity of CVnCoV administered as a 2-dose schedule to participants 18 years of age and older participating in Phase 2b of the trial.

Protection of trial subjects:

This trial was conducted in compliance with Good Clinical Practice (GCP), including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 December 2020
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	Peru: 7452
Country: Number of subjects enrolled	Argentina: 6762
Country: Number of subjects enrolled	Mexico: 6293
Country: Number of subjects enrolled	Colombia: 4356
Country: Number of subjects enrolled	Panama: 3005
Country: Number of subjects enrolled	Dominican Republic: 1767
Country: Number of subjects enrolled	Spain: 2917
Country: Number of subjects enrolled	Germany: 2811
Country: Number of subjects enrolled	Netherlands: 2160
Country: Number of subjects enrolled	Belgium: 2157
Worldwide total number of subjects	39680
EEA total number of subjects	10045

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)	36740
From 65 to 84 years	2906
85 years and over	34

Subject disposition

Recruitment

Recruitment details:

This trial was performed in Argentina, Belgium, Colombia, the Dominican Republic, Germany, Mexico, the Netherlands, Panama, Peru and Spain between 11 December 2020 and 10 June 2022.

Pre-assignment

Screening details:

Of the 39680 participants who were randomized, 39540 participants received at least one dose vaccine.

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

Blinding implementation details:

The trial was converted to an open-label design as of protocol amendment v4 (25 November 2021).

Arms

Are arms mutually exclusive?	Yes
Arm title	CVnCoV 12 µg Vaccine

Arm description:

Participants in the Phase 2b and Phase 3 periods were vaccinated with CVnCoV 12 µg as an intramuscular injection by needle in the deltoid area, preferably in the non-dominant arm, on Day 1 and Day 29.

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

Dosage and administration details:

CVnCoV 12 µg administered as an intramuscular injection.

Arm title	Placebo

Arm description:

Participants in the Phase 2b and Phase 3 periods were vaccinated with matching placebo as an intramuscular injection by needle in the deltoid area, preferably in the non-dominant arm, on Day 1 and Day 29.

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

Dosage and administration details:

Matching placebo administered as an intramuscular injection.

Number of subjects in period 1[1]	CVnCoV 12 µg Vaccine	Placebo
Started	19787	19753
Phase 2b Participants	2007 [2]	1987 [3]
Phase 3 Participants	17780	17766
Rolled Over to Open Label Phase	8513 [4]	0 [5]
Completed	11451	4161
Not completed	8336	15592
Physician decision	78	40
Consent withdrawn by subject	4625	5594
Adverse event, non-fatal	14	13
Miscellaneous	80	64
Protocol Specified Withdrawal Criterion Met	49	2230
Participant Received Alternate Authorised Vaccine	1407	6552
Study Terminated by Sponsor	64	17
Lost to follow-up	2019	1082

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of participants in the baseline period included only participants randomized into Phase 2b or 3 who received at least one dose of CVnCoV or placebo.

[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: The milestones include Phase 2b and Phase 3 participants as well as participants who rolled over to the Open Label Phase.

[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: The milestones include Phase 2b and Phase 3 participants as well as participants who rolled over to the Open Label Phase.

[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: The milestones include Phase 2b and Phase 3 participants as well as participants who rolled over to the Open Label Phase.

[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: The milestones include Phase 2b and Phase 3 participants as well as participants who rolled over to the Open Label Phase.

Baseline characteristics

Reporting groups	
Reporting group title	CVnCoV 12 µg Vaccine
Reporting group description:	
Participants in the Phase 2b and Phase 3 periods were vaccinated with CVnCoV 12 µg as an intramuscular injection by needle in the deltoid area, preferably in the non-dominant arm, on Day 1 and Day 29.	
Reporting group title	Placebo
Reporting group description:	
Participants in the Phase 2b and Phase 3 periods were vaccinated with matching placebo as an intramuscular injection by needle in the deltoid area, preferably in the non-dominant arm, on Day 1 and Day 29.	

Reporting group values	CVnCoV 12 µg Vaccine	Placebo	Total
Number of subjects	19787	19753	39540
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	18316	18295	36611
From 65-84 years	1453	1442	2895
85 years and over	18	16	34
Age continuous Units: years			
arithmetic mean	43.0	43.0	
standard deviation	± 14.49	± 14.50	-
Gender categorical Units: Subjects			
Female	8935	8936	17871
Male	10852	10817	21669
Ethnicity Units: Subjects			
Hispanic or Latino	14732	14740	29472
Not Hispanic or Latino	4960	4932	9892
Unknown or Not Reported	95	81	176
Race/Ethnicity Units: Subjects			
White	9012	8989	18001
Black or African American	383	356	739
Asian Indian	18	10	28
Chinese	21	22	43
Filipino	1	3	4
Japanese	5	0	5

Korean	0	2	2
Vietnamese	9	9	18
American Indian or Alaska Native	2492	2485	4977
Other	7797	7812	15609
Not Reported	34	44	78
Unknown	15	21	36

End points

End points reporting groups

Reporting group title	CVnCoV 12 µg Vaccine
Reporting group description:	
Participants in the Phase 2b and Phase 3 periods were vaccinated with CVnCoV 12 µg as an intramuscular injection by needle in the deltoid area, preferably in the non-dominant arm, on Day 1 and Day 29.	
Reporting group title	Placebo
Reporting group description:	
Participants in the Phase 2b and Phase 3 periods were vaccinated with matching placebo as an intramuscular injection by needle in the deltoid area, preferably in the non-dominant arm, on Day 1 and Day 29.	

Primary: Number of Participants Who Experienced a First Episode of Virologically-confirmed {Reverse Transcription Polymerase Chain Reaction (RT-PCR) Positive} Case of COVID-19 of Any Severity

End point title	Number of Participants Who Experienced a First Episode of Virologically-confirmed {Reverse Transcription Polymerase Chain Reaction (RT-PCR) Positive} Case of COVID-19 of Any Severity

End point description:

A case of COVID-19 meeting the definition for primary efficacy analysis was defined as:
• Virologically-confirmed case of COVID-19 (of any severity) defined as a positive SARS-CoV-2 specific RT-PCR test in a person with clinically symptomatic COVID-19.
• Symptom onset ≥ 15 days after second trial vaccination.
• First episode of virologically-confirmed COVID-19, i.e. the participant must not have had a history of virologically confirmed COVID-19 illness at enrollment or have had developed a case of virologically-confirmed COVID-19 before 15 days after the second trial vaccination.
• Participant was SARS-CoV-2 naïve at baseline & Day 43 (defined as seronegative to N protein in the blood samples collected at baseline and Day 43).
• Primary efficacy cases were confirmed by an Adjudication Committee.

The analysis set used was the efficacy analysis set (EAS). Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine.

End point type	Primary

End point timeframe:

Day 44 to Day 393

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12851	12211		
Units: participants	83	145		

Statistical analyses

Statistical analysis title	CVnCoV 12 µg Vaccine Versus Placebo

Statistical analysis description:

Proportion of cases coming from the CVnCoV group among all cases.

Comparison groups	Placebo v CVnCoV 12 µg Vaccine
Number of subjects included in analysis	25062
Analysis specification	Pre-specified
Analysis type	superiority[1]
Parameter estimate	Proportion
Point estimate	0.364
Confidence interval	
level	95.83 %
sides	2-sided
lower limit	0.299
upper limit	0.433

Notes:

[1] - Derived from an exact 2-sided 95.826% Pearson-Clopper confidence interval (CI) on proportion of cases coming from the CVnCoV group among all cases.

Statistical analysis title	CVnCoV 12 µg Vaccine Versus Placebo

Statistical analysis description:

Vaccine efficacy (VE) calculated as VE = 1 – p/(1-p) *1/r where p represents the proportion of cases coming from the CVnCoV group among all cases and r represents the ratio of total follow-up time of subjects in the CVnCoV group over the total follow-up time of participants in the placebo group.

Comparison groups	CVnCoV 12 µg Vaccine v Placebo
Number of subjects included in analysis	25062
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.016 [3]
Method	Exact Binomial Test
Parameter estimate	Vaccine Efficacy
Point estimate	48.2
Confidence interval	
level	95.83 %
sides	2-sided
lower limit	31
upper limit	61.4

Notes:

[2] - 2-sided 95.826% CI on VE, derived from the exact 2-sided 95.826% Pearson-Clopper CI on proportion of cases coming from the CVnCoV group among all cases.

[3] - 1-sided p-value from the exact binomial test on proportion of cases coming from the CVnCoV group among all cases (equivalent to a test on VE with H0: VE ≤30%). Statistically significant if lower than 0.02087.

Primary: Number of Participants Who Experienced One or More Medically-attended Adverse Events (AE)

End point title	Number of Participants Who Experienced One or More Medically-attended Adverse Events (AE)[4]

End point description:

Medically-attended AEs were defined as AEs with medically-attended visits that were not routine visits for physical examination or vaccination, such as visits for hospitalization, an emergency room visit, or an otherwise unscheduled visit to or from medical personnel (medical doctor) for any reason. Clinic visits for COVID-19 testing resulting in negative test results were not considered as medically attended visits, if there is no confirmed diagnosis and no prescribed concomitant medication.

The Investigator assessed the relationship between trial vaccine and occurrence of each AE.

The analysis set used was the safety analysis set (SAS). Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Primary

End point timeframe:

Day 1 to Day 211

Notes:

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

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19787	19753		
Units: participants				
Any Medically-attended AE	2555	2084		
Any Related Medically-attended AE	505	138		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced One or More Serious AE (SAE)

End point title	Number of Participants Who Experienced One or More Serious AE (SAE)[5]

End point description:

An SAE was defined as any untoward medical occurrence that, at any dose:
• Resulted in death.
• Was life-threatening.
• Required inpatient hospitalization or prolongation of existing hospitalization.
• Resulted in persistent disability/incapacity.
• Was a congenital anomaly/birth defect in the offspring of the participant.
• Was an important medical event.

The Investigator assessed the relationship between trial vaccine and occurrence of each SAE.

The analysis set used was the SAS. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Primary

End point timeframe:

Day 1 to Day 393

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: No comparative statistical analyses were planned.

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19787	19753		
Units: participants				
Any SAE	149	111		
Any Related SAE	8	1		

Statistical analyses

No statistical analyses for this end point

Primary: Intensity of SAEs as Per Investigator Assessment

End point title	Intensity of SAEs as Per Investigator Assessment[6]

End point description:

An SAE was defined as any untoward medical occurrence that, at any dose:
• Resulted in death.
• Was life-threatening.
• Required inpatient hospitalization or prolongation of existing hospitalization.
• Resulted in persistent disability/incapacity.
• Was a congenital anomaly/birth defect in the offspring of the participant.
• Was an important medical event.

The Investigator made an assessment of intensity of each SAE reported during the trial. Each SAE was graded from Mild (Grade 1) to Severe (Grade 3), where higher grades indicated a worse outcome.

The analysis set used was the SAS including only participants who experienced SAEs. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Primary

End point timeframe:

Day 1 to Day 393

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative statistical analyses were planned.

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	111		
Units: participants				
Mild (Grade 1)	21	10		
Moderate (Grade 2)	50	35		
Severe (Grade 3)	74	66		
Missing	4	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced One or More Adverse Event of Special Interest (AESI)

End point title	Number of Participants Who Experienced One or More Adverse Event of Special Interest (AESI)[7]

End point description:

AESIs included:
• AEs with a suspected immune-medicated etiology.
• Other AEs relevant to SARS-CoV-2 vaccine development or the target disease.

The Investigator assessed the relationship between trial vaccine and occurrence of each AESI.

The analysis set used was the SAS. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Primary

End point timeframe:

Day 1 to Day 393

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative statistical analyses were planned.

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19787	19753		
Units: participants				
Any AESI	64	47		
Any Related AESI	19	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced a Fatal SAE

End point title	Number of Participants Who Experienced a Fatal SAE[8]

End point description:

A fatal SAE was defined as an SAE that resulted in death.

The analysis set used was the SAS. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Primary

End point timeframe:

Day 1 to Day 393

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative statistical analyses were planned.

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19787	19753		
Units: participants	11	12		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2b Participants Only: Number of Participants Who Experienced One or More Solicited AE

End point title	Phase 2b Participants Only: Number of Participants Who Experienced One or More Solicited AE[9]

End point description:

Solicited local AEs (injection site pain, redness, swelling, and itching) and solicited systemic AEs (fever, headache, fatigue, chills, myalgia, arthralgia, nausea/vomiting, and diarrhea) were recorded on the day of vaccination and the following 7 days using an eDiary.

The analysis set used was the SASsol. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Primary

End point timeframe:

Up to 7 days after vaccination (Days 1 to 7 and Days 29 to 36)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative statistical analyses were planned.

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2003	1978		
Units: participants				
Any Solicited Local AE	1699	477		
Any Solicited Systemic AE	1881	1255		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2b Participants Only: Intensity of Solicited AEs as Per Investigator Assessment

End point title	Phase 2b Participants Only: Intensity of Solicited AEs as Per Investigator Assessment[10]

End point description:

Solicited local AEs (injection site pain, redness, swelling, and itching) and solicited systemic AEs (fever, headache, fatigue, chills, myalgia, arthralgia, nausea/vomiting, and diarrhea) were recorded on the day of vaccination and the following 7 days using an eDiary.

The Investigator made an assessment of intensity of each solicited AE reported during the trial. Each solicited AE was graded from Mild (Grade 1) to Severe (Grade 3), where higher grades indicated a worse outcome.

The analysis set used was the SASsol including only participants who experienced solicited AEs. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Primary

End point timeframe:

Up to 7 days after vaccination (Days 1 to 7 and Days 29 to 36)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative statistical analyses were planned.

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2003[11]	1978[12]		
Units: participants				
Any Solicited Local AEs - Mild (Grade 1)	1226	452		
Any Solicited Local AEs - Moderate (Grade 2)	448	24		
Any Solicited Local AEs - Severe (Grade 3)	25	1		
Any Solicited Systemic AEs - Mild (Grade 1)	376	708		
Any Solicited Systemic AEs - Moderate (Grade 2)	969	487		
Any Solicited Systemic AEs - Severe (Grade 3)	536	60		

Notes:

[11] - Any Solicited Local AEs (Mild, Moderate and Severe) - N = 1699

[12] - Any Solicited Local AEs (Mild, Moderate and Severe) - N = 477

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2b Participants Only: Number of Participants Who Experienced One or More Unsolicited AE

End point title	Phase 2b Participants Only: Number of Participants Who Experienced One or More Unsolicited AE[13]

End point description:

eDiaries were used for collection of unsolicited AEs on each vaccination day and the following 28 days. In addition, participants received a prompt (by e.g., a phone call or text message) to verify whether the participants had any health concerns since the last visit. The Investigator assessed the relationship between trial vaccine and each occurrence of each AE.

The analysis set used was the SAS 2. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Primary

End point timeframe:

Up to 28 days after vaccination (Days 1 to 29 and Days 29 to 57)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative statistical analyses were planned.

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2007	1987		
Units: participants				
Any Unsolicited AE	1016	911		
Any Related Unsolicited AE	511	269		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2b Participants Only: Intensity of Unsolicited AEs as Per Investigator Assessment

End point title	Phase 2b Participants Only: Intensity of Unsolicited AEs as Per Investigator Assessment[14]

End point description:

eDiaries were used for collection of unsolicited AEs on each vaccination day and the following 28 days. In addition, participants received a prompt (by e.g., a phone call or text message) to verify whether the participants had any health concerns since the last visit.

The Investigator made an assessment of intensity of each unsolicited AE reported during the trial. Each unsolicited AE was graded from Mild (Grade 1) to Severe (Grade 3), where higher grades indicated a worse outcome.

The analysis set used was the SAS 2. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Primary

End point timeframe:

Up to 28 days after vaccination (Days 1 to 29 and Days 29 to 57)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative statistical analyses were planned.

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1016	911		
Units: participants				
Mild (Grade 1)	712	641		
Moderate (Grade 2)	259	225		
Severe (Grade 3)	44	38		
Missing	1	7		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Experienced One or More AEs Leading to Vaccine Withdrawal or Trial Discontinuation

End point title	Number of Participants Who Experienced One or More AEs Leading to Vaccine Withdrawal or Trial Discontinuation[15]

End point description:

The analysis set used was the SAS. Participants were censored at the first day after unblinding or at the

day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Primary

End point timeframe:

Day 1 to Day 393

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative statistical analyses were planned.

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19787	19753		
Units: participants				
Any AE Leading to Vaccine Withdrawal	32	33		
Any AE Leading to Withdrawal From Trial	17	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2b Participants Only: Duration of Solicited AEs

End point title	Phase 2b Participants Only: Duration of Solicited AEs

End point description:

Solicited local AEs (injection site pain, redness, swelling, and itching) and solicited systemic AEs (fever, headache, fatigue, chills, myalgia, arthralgia, nausea/vomiting, and diarrhea) were recorded on the day of vaccination and the following 7 days using an eDiary. Duration is calculated as consecutive days with a respective solicited AE regardless of the grade of the AE. AEs ongoing after Day 8 are included. In each case only the longest consecutive duration is displayed.

Solicited local AEs (CVnCoV 12 µg Vaccine, Placebo):
- Injection site pain N = 1674, 417
- Redness N = 89, 25
- Swelling N = 149, 17
- Itching N = 141, 93

Solicited systemic AEs (CVnCoV 12 µg Vaccine, Placebo):
- Fever N = 617, 13
- Headache N = 1541, 806
- Fatigue N = 1603, 845
- Chills N = 1011, 162
- Myalgia N = 1327, 378
- Arthralgia N = 578, 148
- Nausea/Vomiting N = 414, 151
- Diarrhea N = 376, 224

End point type	Secondary

End point timeframe:

Up to 7 days after vaccination (Days 1 to 7 and Days 29 to 36)

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2003	1978		
Units: days				
arithmetic mean (standard deviation)				
Solicited Local AEs - Injection Site Pain	2.3 (± 1.24)	1.5 (± 1.24)		
Solicited Local AEs - Redness	2.2 (± 2.32)	2.1 (± 1.99)		
Solicited Local AEs - Swelling	1.7 (± 0.97)	0.2 (± 0.56)		
Solicited Local AEs - Itching	1.6 (± 1.20)	1.4 (± 1.42)		
Solicited Systemic AEs - Fever	1.3 (± 0.52)	1.0 (± 0.00)		
Solicited Systemic AEs - Headache	2.0 (± 1.41)	1.8 (± 2.45)		
Solicited Systemic AEs - Fatigue	2.3 (± 2.84)	2.0 (± 2.25)		
Solicited Systemic AEs - Chills	1.3 (± 0.67)	1.4 (± 0.83)		
Solicited Systemic AEs - Myalgia	1.8 (± 1.08)	1.6 (± 1.13)		
Solicited Systemic AEs - Arthralgia	1.6 (± 0.98)	1.6 (± 1.19)		
Solicited Systemic AEs - Nausea/Vomiting	1.5 (± 0.97)	1.3 (± 0.82)		
Solicited Systemic AEs - Diarrhea	1.4 (± 0.95)	1.3 (± 0.90)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Experienced a First Episode of Virologically-confirmed (RT-PCR Positive) Moderate to Severe Case of COVID-19

End point title	Number of Participants Who Experienced a First Episode of Virologically-confirmed (RT-PCR Positive) Moderate to Severe Case of COVID-19

End point description:

Moderate COVID-19 cases were defined by any one of the following:
• Shortness of breath or difficulty breathing.
• Respiratory rate ≥ 20 to < 30 breaths per minute.
• Abnormal SpO2 but still > 93% on room air at sea level.
• Clinical or radiographic evidence of lower respiratory tract disease.
• Radiologic evidence of deep vein thrombosis (DVT).

Severe COVID-19 cases were defined by any one of the following:
• Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥ 30 breaths per minute, heart rate ≥ 125 per minute, SpO2 ≤ 93% on room air at sea level or PaO2/FIO2 < 300 mm Hg).
• Respiratory failure (defined as needing high flow-oxygen, noninvasive ventilation, mechanical ventilation or ECMO).
• Evidence of shock (SBP < 90mm Hg, DBP < 60 mmHg, or requiring vasopressors).
• Significant renal, hepatic, or neurologic dysfunction
• Admission to intensive care unit (ICU).
• Death.

The analysis set used was the EAS.

End point type	Secondary

End point timeframe:

Day 44 to Day 393

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12851	12211		
Units: participants	12	37		

Statistical analyses

Statistical analysis title	CVnCoV 12 µg Vaccine Versus Placebo

Statistical analysis description:

Proportion of cases coming from the CVnCoV group among all cases.

Comparison groups	Placebo v CVnCoV 12 µg Vaccine
Number of subjects included in analysis	25062
Analysis specification	Pre-specified
Analysis type	superiority[16]
Parameter estimate	Proportion
Point estimate	0.245
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.133
upper limit	0.389

Notes:

[16] - Derived from an exact 2-sided 95% Pearson-Clopper CI on proportion of cases coming from the CVnCoV group among all cases.

Statistical analysis title	CVnCoV 12 µg Vaccine Versus Placebo

Statistical analysis description:

VE calculated as VE = 1 - p/(1-p) *1/r where p represents the proportion of cases coming from the CVnCoV group among all cases and r represents the ratio of total follow-up time of participants in the CVnCoV group over the total follow-up time of participants in the placebo group.

Comparison groups	CVnCoV 12 µg Vaccine v Placebo
Number of subjects included in analysis	25062
Analysis specification	Pre-specified
Analysis type	superiority[17]
Parameter estimate	Vaccine Efficacy
Point estimate	70.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	42.5
upper limit	86.1

Notes:

[17] - 2-sided 95% CI on VE, derived from the exact 2-sided 95% Pearson-Clopper CI on proportion of cases coming from the CVnCoV group among all cases.

Secondary: Number of Participants Who Experienced a First Episode of Virologically-confirmed (RT-PCR Positive) Severe Case of COVID-19

End point title	Number of Participants Who Experienced a First Episode of Virologically-confirmed (RT-PCR Positive) Severe Case of COVID-19

End point description:

Severe COVID-19 cases were defined by any one of the following:
• Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥ 30 breaths per minute, heart rate ≥ 125 per minute, SpO2 ≤ 93% on room air at sea level or PaO2/FIO2 < 300 mm Hg).
• Respiratory failure (defined as needing high flow-oxygen, noninvasive ventilation, mechanical ventilation or ECMO).
• Evidence of shock (SBP < 90mm Hg, DBP < 60 mmHg, or requiring vasopressors).
• Significant renal, hepatic, or neurologic dysfunction
• Admission to intensive care unit (ICU).
• Death.

The analysis set used was the EAS. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Secondary

End point timeframe:

Day 44 to Day 393

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12851	12211		
Units: participants	4	10		

Statistical analyses

Statistical analysis title	CVnCoV 12 µg Vaccine Versus Placebo

Statistical analysis description:

Proportion of cases coming from the CVnCoV group among all cases.

Comparison groups	CVnCoV 12 µg Vaccine v Placebo
Number of subjects included in analysis	25062
Analysis specification	Post-hoc
Analysis type	superiority[18]
Parameter estimate	Proportion
Point estimate	0.286
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.084
upper limit	0.581

Notes:

[18] - Derived from an exact 2-sided 95% Pearson-Clopper CI on proportion of cases coming from the CVnCoV group among all cases.

Statistical analysis title	CVnCoV 12 µg Vaccine Versus Placebo

Statistical analysis description:

VE calculated as VE = 1 - p/(1-p) *1/r where p represents the proportion of cases coming from the CVnCoV group among all cases and r represents the ratio of total follow-up time of participants in the CVnCoV group over the total follow-up time of participants in the placebo group.

Comparison groups	CVnCoV 12 µg Vaccine v Placebo

Number of subjects included in analysis	25062
Analysis specification	Pre-specified
Analysis type	superiority[19]
Parameter estimate	Vaccine Efficacy
Point estimate	63.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.5
upper limit	91.7

Notes:

[19] - 2-sided 95% CI on VE, derived from the exact 2-sided 95% Pearson-Clopper CI on proportion of cases coming from the CVnCoV group among all cases.

Secondary: Number of Participants Who Experienced a First Episode of Virologically-confirmed (RT-PCR Positive) Case of COVID-19 of Any Severity Due to Infection With "Wild Type" and "Alpha" SARS-CoV-2 Strains in SARS-CoV-2 Naïve Participants

End point title	Number of Participants Who Experienced a First Episode of Virologically-confirmed (RT-PCR Positive) Case of COVID-19 of Any Severity Due to Infection With "Wild Type" and "Alpha" SARS-CoV-2 Strains in SARS-CoV-2 Naïve Participants

End point description:

The characterization of SARS-CoV-2 variants were implemented by viral whole genome sequencing of nasopharyngeal swab samples of participants followed by comparison with previously sequenced and typified genomes.
The following phylogenetic clustering was applied:

1. "Wild type" virus: WT/D614G, lineages A.1/B.1 without the variant of concerns (VOCs) (i.e., without B.1.1.7 [Alpha], B.1.351 [Beta], B.1.429 [Epsilon]).
2. "UK" VOC: B.1.1.7 (Alpha).

A case of COVID-19 was defined as follows:
• Virologically-confirmed case of COVID-19 defined as a positive SARS-CoV-2 specific RT-PCR test in a person with clinically symptomatic COVID-19.
• Symptom onset ≥ 15 days after second vaccination.
• First episode of virologically-confirmed COVID-19.
• Participant was SARS-CoV-2 naïve at baseline and Day 43.

The analysis set used was the EAS. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlie

End point type	Secondary

End point timeframe:

Day 44 to Day 393

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12851	12211		
Units: participants	29	56		

Statistical analyses

Statistical analysis title	CVnCoV 12 µg Vaccine Versus Placebo

Statistical analysis description:

Proportion of cases coming from the CVnCoV group among all cases.

Comparison groups	CVnCoV 12 µg Vaccine v Placebo
Number of subjects included in analysis	25062
Analysis specification	Pre-specified
Analysis type	superiority[20]
Parameter estimate	Proportion
Point estimate	0.341
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.242
upper limit	0.452

Notes:

[20] - Derived from an exact 2-sided 95% Pearson-Clopper CI on proportion of cases coming from the CVnCoV group among all cases.

Statistical analysis title	CVnCoV 12 µg Vaccine Versus Placebo

Statistical analysis description:

VE calculated as VE = 1 - p/(1-p) *1/r where p represents the proportion of cases coming from the CVnCoV group among all cases and r represents the ratio of total follow-up time of participants in the CVnCoV group over the total follow-up time of participants in the placebo group.

Comparison groups	CVnCoV 12 µg Vaccine v Placebo
Number of subjects included in analysis	25062
Analysis specification	Pre-specified
Analysis type	superiority[21]
Parameter estimate	Vaccine Efficacy
Point estimate	53.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.4
upper limit	71.2

Notes:

[21] - 2-sided 95% CI on VE, derived from the exact 2-sided 95% Pearson-Clopper CI on proportion of cases coming from the CVnCoV group among all cases.

Secondary: Number of Participants Aged ≥ 61 Who Experienced a First Episode of Virologically-confirmed (RT-PCR Positive) Case of COVID-19 of Any Severity

End point title	Number of Participants Aged ≥ 61 Who Experienced a First Episode of Virologically-confirmed (RT-PCR Positive) Case of COVID-19 of Any Severity

End point description:

A case of COVID-19 was defined as follows:
• Virologically-confirmed case of COVID-19 (of any severity) defined as a positive SARS-CoV-2 specific RT-PCR test in a person with clinically symptomatic COVID-19.
• Symptom onset ≥ 15 days after second trial vaccination.
• First episode of virologically-confirmed COVID-19, i.e. the participant must not have had a history of virologically-confirmed COVID-19 illness at enrollment or have had developed a case of virologically-confirmed COVID-19 before 15 days after the second trial vaccination.
• Participant was SARS-CoV-2 naïve at baseline and Day 43 (defined as seronegative to N protein in the blood samples collected at baseline and Day 43).

The analysis set used was the EA including only participants who were aged ≥ 61. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Secondary
End point timeframe:	
Day 44 to Day 393	

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1319	1180		
Units: participants	12	9		

Statistical analyses

Statistical analysis title	CVnCoV 12 µg Vaccine Versus Placebo
Statistical analysis description:	
Proportion of cases coming from the CVnCoV group among all cases.	
Comparison groups	CVnCoV 12 µg Vaccine v Placebo
Number of subjects included in analysis	2499
Analysis specification	Pre-specified
Analysis type	superiority[22]
Parameter estimate	Proportion
Point estimate	0.571
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.782

Notes:

[22] - Derived from an exact 2-sided 95% Pearson-Clopper CI on proportion of cases coming from the CVnCoV group among all cases.

Statistical analysis title	CVnCoV 12 µg Vaccine Versus Placebo
Statistical analysis description:	
VE calculated as VE = 1 - p/(1-p) *1/r where p represents the proportion of cases coming from the CVnCoV group among all cases and r represents the ratio of total follow-up time of participants in the CVnCoV group over the total follow-up time of participants in the placebo group.	
Comparison groups	CVnCoV 12 µg Vaccine v Placebo
Number of subjects included in analysis	2499
Analysis specification	Pre-specified
Analysis type	superiority[23]
Parameter estimate	Vaccine Efficacy
Point estimate	-11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-200.5
upper limit	56.7

Notes:

[23] - 2-sided 95% CI on VE, derived from the exact 2-sided 95% Pearson-Clopper CI on proportion of cases coming from the CVnCoV group among all cases.

Secondary: Burden of Disease (BoD) Score #1 Based on First Episodes of Virologically-confirmed (RT-PCR Positive) Cases of COVID-19

End point title	Burden of Disease (BoD) Score #1 Based on First Episodes of Virologically-confirmed (RT-PCR Positive) Cases of COVID-19

End point description:

Score #1 was defined as no disease (not infected or asymptomatic infection) = 0; mild or moderate disease = 1; severe disease = 2.

The analysis set used was the EAS. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Secondary

End point timeframe:

Day 44 to Day 393

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12851	12211		
Units: participants				
0 - No Disease	12768	12066		
1 - Mild or Moderate Disease	79	135		
2 - Severe Disease	4	10		

Statistical analyses

No statistical analyses for this end point

Secondary: BoD Score #2 Based on First Episodes of Virologically-confirmed (RT-PCR Positive) Cases of COVID-19

End point title	BoD Score #2 Based on First Episodes of Virologically-confirmed (RT-PCR Positive) Cases of COVID-19

End point description:

Score #2 was defined as no disease (not infected or asymptomatic infection) = 0; disease without hospitalization = 1; disease with hospitalization = 2; death = 3.

The analysis set used was the EAS. Participants were censored at the first day after unblinding or at the day after receiving the authorized/licensed vaccine, whichever was earlier.

End point type	Secondary

End point timeframe:

Day 44 to Day 393

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12851	12211		
Units: participants				
0 - No Disease	12768	12066		
1 - Disease Without Hospitalization	82	143		
2 - Disease With Hospitalization	0	2		
3 - Death	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Experienced a Virologically-confirmed (RT-PCR Positive) Case of COVID-19 of Any Severity With Symptom Onset at Any Time After the First Study Vaccination

End point title	Number of Participants Who Experienced a Virologically-confirmed (RT-PCR Positive) Case of COVID-19 of Any Severity With Symptom Onset at Any Time After the First Study Vaccination

End point description:

case of COVID-19 was defined as follows:
• Virologically-confirmed case of COVID-19 (of any severity) defined as a positive SARS-CoV-2 specific RT-PCR test in a person with clinically symptomatic COVID-19.
• Symptom onset ≥ 15 days after second trial vaccination.
• First episode of virologically-confirmed COVID-19, i.e. the participant must not have had a history of virologically-confirmed COVID-19 illness at enrollment or have had developed a case of virologically-confirmed COVID-19 before 15 days after the second trial vaccination.
• Participant was SARS-CoV-2 naïve at baseline and Day 43 (defined as seronegative to N protein in the blood samples collected at baseline and Day 43).

This analysis was not completed as different definitions of COVID-19 cases used during blinding, open-label and after implementation of an urgent safety measures letter led to biases that did not permit analysis of COVID-19 cases at the end of the trial.

End point type	Secondary

End point timeframe:

Post vaccination on Day 1 up to Day 393

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[24]	0[25]		
Units: participants				

Notes:

[24] - Data were not analyzed for this endpoint.

[25] - Data were not analyzed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: SARS-CoV-2 receptor binding domain (RBD) of Spike (S) Protein Antibody Levels on Days 1, 29, 43, 120 and 211

End point title	SARS-CoV-2 receptor binding domain (RBD) of Spike (S) Protein Antibody Levels on Days 1, 29, 43, 120 and 211

End point description:

Titers of IgG antibodies directed against the SARS-CoV-2 RBD of Spike Protein antigen were measured by ELISA and expressed as GMTs with 95% CI. Participants who have tested positive for SARS-CoV-2 via PCR or N-protein antibodies have their data included up to the point of positive test result or symptom onset. Participants who received a licensed/authorized vaccine were censored at the day after receiving the licensed/authorized vaccine.

Per Protocol Immunogenicity (PPI) Set: Included all Phase 2b participants from the Immunogenicity Subset who were seronegative at baseline, received both doses as randomized and within the specified windows, had no important protocol deviations that impacted immunogenicity outcomes, did not receive medical treatments that interfered with the proposed immunogenicity measurements and had at least 1 blood sample collected at baseline and starting at 14 days post-second vaccination available for analysis.

End point type	Secondary

End point timeframe:

Days 1 (baseline), 29, 43, 120 and 211

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	544[26]	525[27]		
Units: titers				
geometric mean (confidence interval 95%)				
Day 1	50.791 (50.151 to 51.439)	50.763 (50.079 to 51.456)		
Day 29	54.090 (52.213 to 56.034)	50.734 (50.074 to 51.403)		
Day 43	734.657 (645.552 to 836.061)	50.902 (50.082 to 51.737)		
Day 120	227.439 (203.647 to 254.011)	57.357 (52.843 to 62.257)		
Day 211	371.341 (161.098 to 855.966)	107.556 (23.919 to 483.648)		

Notes:

[26] - Day 1 - N = 544
Day 29 - N = 536
Day 43 - N = 518
Day 120 - N = 432
Day 211 - N = 27

[27] - Day 1 - N = 525
Day 29 - N = 516
Day 43 - N = 498
Day 120 - N = 245
Day 211 - N = 7

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Seroconverting to SARS-CoV-2 RBD of S Protein antibodies on Days 29, 43, 120 and 211

End point title	Percentage of Participants Seroconverting to SARS-CoV-2 RBD of S Protein antibodies on Days 29, 43, 120 and 211

End point description:

Titers of IgG antibodies directed against the SARS-CoV-2 RBD of Spike Protein antigen were measured by ELISA. Percentage with 95% CI of participants for whom a seroconversion was observed is presented by group. In participants who tested seronegative to the N protein for SARS-CoV-2 at baseline, seroconversion was defined as a fold increase above 1 in antibody titer against SARS-CoV-2 RBD of S protein. Participants who tested positive for SARS-CoV-2 via PCR or N-protein antibodies had their data included up to the point of positive test result or symptom onset. Participants who received a licensed/authorized vaccine were censored at the day after receiving the licensed/authorized vaccine.

The analysis set used was the PPI Set.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Days 29, 43, 120 and 211

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	536[28]	516[29]		
Units: percentage of participants				
number (confidence interval 95%)				
Day 29	4.3 (2.7 to 6.4)	0.4 (0.0 to 1.4)		
Day 43	87.1 (83.9 to 89.8)	0.6 (0.1 to 1.8)		
Day 120	72.2 (67.7 to 76.4)	4.9 (2.6 to 8.4)		
Day 211	66.7 (46.0 to 83.5)	28.6 (3.7 to 71.0)		

Notes:

[28] - Day 29 - N = 536
Day 43 - N = 518
Day 120 - N = 432
Day 211 - N = 27
[29] - Day 29 - N = 516
Day 43 - N = 498
Day 120 - N = 245
Day 211 - N = 7

Statistical analyses

No statistical analyses for this end point

Secondary: SARS-CoV-2 viral neutralizing antibody levels on Days 1, 29, 43, 120 and 211

End point title	SARS-CoV-2 viral neutralizing antibody levels on Days 1, 29, 43, 120 and 211

End point description:

Titers of viral neutralizing antibodies were determined by an activity assay and expressed as GMTs with 95% CI. Participants who have tested positive for SARS-CoV-2 via PCR or N-protein antibodies have their data included up to the point of positive test result or symptom onset. Participants who received a licensed/authorized vaccine were censored at the day after receiving the licensed/authorized vaccine. The analysis set used was the PPI Set.

End point type	Secondary

End point timeframe:

Days 1 (baseline), 29, 43, 120 and 211

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	544[30]	525[31]		
Units: titers				
geometric mean (confidence interval 95%)				
Day 1	5.016 (4.993 to 5.039)	5.007 (4.994 to 5.020)		
Day 29	5.141 (5.022 to 5.263)	5.030 (4.995 to 5.066)		
Day 43	18.211 (16.394 to 20.230)	5.049 (5.003 to 5.096)		
Day 120	7.105 (6.640 to 7.603)	5.136 (5.008 to 5.267)		
Day 211	14.325 (7.183 to 28.565)	6.729 (4.209 to 10.757)		

Notes:

[30] - Day 1 - N = 544
Day 29 - N = 536
Day 43 - N = 518
Day 120 - N = 432
Day 211 - N = 27
[31] - Day 1 - N = 525
Day 29 - N = 516
Day 43 - N = 498
Day 120 - N = 245
Day 211 - N = 7

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Seroconverting to SARS-CoV-2 Viral Neutralizing Antibodies on Days 29, 43, 120 and 211

End point title	Percentage of Participants Seroconverting to SARS-CoV-2 Viral Neutralizing Antibodies on Days 29, 43, 120 and 211

End point description:

Titers of viral neutralizing antibodies were determined by an activity assay. Percentage with 95% CI of participants for whom a seroconversion was observed is presented by group.. In participants who tested seronegative to the N protein for SARS-CoV-2 at baseline, seroconversion was defined as a fold increase above 1 in antibody titer against SARS-CoV-2 neutralizing antibody titer. Participants who have been tested positive for SARS-CoV-2 via PCR or N-protein antibodies have their data included up to the point of positive test result or symptom onset. Participants who received a licensed/authorized vaccine were censored at the day after receiving the licensed/authorized vaccine.

The analysis set used was the PPI Set.

End point type	Secondary

End point timeframe:

Baseline and Days 29, 43, 120 and 211

End point values	CVnCoV 12 µg Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	536[32]	516[33]		
Units: percentage of participants				
number (confidence interval 95%)				
Day 29	1.5 (0.6 to 2.9)	0.6 (0.1 to 1.7)		
Day 43	65.1 (60.8 to 69.2)	1.0 (0.3 to 2.3)		
Day 120	24.8 (20.8 to 29.1)	2.0 (0.7 to 4.7)		
Day 211	33.3 (16.5 to 54.0)	28.6 (3.7 to 71.0)		

Notes:

[32] - Day 29 - N = 536
Day 43 - N = 518
Day 120 - N = 432
Day 211 - N = 27

[33] - Day 29 - N = 516
Day 43 - N = 498
Day 120 - N = 245
Day 211 - N = 7

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Occurring on the Day of Vaccination and the following 28 Days after any dose (Days 1 to 29 and Days 29 to 57)

Adverse event reporting additional description:

Participants who became unblinded and/or received a licensed/authorized vaccine were censored at the day after unblinding or at the day after receiving the licensed/authorized vaccine, whichever is earlier.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants in the Phase 2b and Phase 3 periods were vaccinated with matching placebo as an intramuscular injection by needle in the deltoid area, preferably in the non-dominant arm, on Day 1 and Day 29.

Reporting group title	CVnCoV 12 µg Vaccine

Reporting group description:

Participants in the Phase 2b and Phase 3 periods were vaccinated with CVnCoV 12 µg as an intramuscular injection by needle in the deltoid area, preferably in the non-dominant arm, on Day 1 and Day 29.

Serious adverse events	Placebo	CVnCoV 12 µg Vaccine	
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 19753 (0.27%)	71 / 19787 (0.36%)	
number of deaths (all causes)	14	17	
number of deaths resulting from adverse events	8	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma	Additional description: Basal cell carcinoma		
subjects affected / exposed	0 / 19753 (0.00%)	3 / 19787 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer	Additional description: Breast cancer		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma stage 0	Additional description: Cervix carcinoma stage 0		

subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma	Additional description: Clear cell renal cell carcinoma		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma	Additional description: Glioblastoma		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic malignant melanoma	Additional description: Metastatic malignant melanoma		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer	Additional description: Papillary thyroid cancer		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phaeochromocytoma	Additional description: Phaeochromocytoma		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer	Additional description: Prostate cancer		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma	Additional description: Squamous cell carcinoma		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-cell lymphoma	Additional description: T-cell lymphoma		

subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid adenoma	Additional description: Thyroid adenoma		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superficial vein thrombosis	Additional description: Superficial vein thrombosis		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb	Additional description: Venous thrombosis limb		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy on oral contraceptive	Additional description: Pregnancy on oral contraceptive		
subjects affected / exposed	0 / 19753 (0.00%)	2 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy with injectable contraceptive	Additional description: Pregnancy with injectable contraceptive		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain	Additional description: Chest pain		

subjects affected / exposed	1 / 19753 (0.01%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Fallopian tube cyst	Additional description: Fallopian tube cyst		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrosalpinx	Additional description: Hydrosalpinx		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema	Additional description: Acute pulmonary oedema		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atelectasis	Additional description: Atelectasis		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion	Additional description: Pleural effusion		

subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	1 / 19753 (0.01%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Psychiatric disorders			
Attention deficit hyperactivity disorder	Additional description: Attention deficit hyperactivity disorder		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression	Additional description: Depression		
subjects affected / exposed	3 / 19753 (0.02%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression	Additional description: Major depression		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mixed anxiety and depressive disorder	Additional description: Mixed anxiety and depressive disorder		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation	Additional description: Suicidal ideation		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

HIV test positive	Additional description: HIV test positive		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accident	Additional description: Accident		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ankle fracture	Additional description: Ankle fracture		
subjects affected / exposed	1 / 19753 (0.01%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cartilage injury	Additional description: Cartilage injury		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury	Additional description: Chest injury		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture	Additional description: Clavicle fracture		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury	Additional description: Craniocerebral injury		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epicondylitis	Additional description: Epicondylitis		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fibula fracture	Additional description: Fibula fracture		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hand fracture	Additional description: Hand fracture		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Humerus fracture	Additional description: Humerus fracture		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Joint dislocation	Additional description: Joint dislocation		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ligament rupture	Additional description: Ligament rupture		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Meniscus injury	Additional description: Meniscus injury		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Radius fracture	Additional description: Radius fracture		
subjects affected / exposed	1 / 19753 (0.01%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Rib fracture	Additional description: Rib fracture		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skin laceration	Additional description: Skin laceration

subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fractured base	Additional description: Skull fractured base		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma	Additional description: Subdural haematoma		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture	Additional description: Tendon rupture		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture	Additional description: Tibia fracture		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture	Additional description: Ulna fracture		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access site haematoma	Additional description: Vascular access site haematoma		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction	Additional description: Acute myocardial infarction		
subjects affected / exposed	1 / 19753 (0.01%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angina unstable	Additional description: Angina unstable		

subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery	Additional description: Arteriosclerosis coronary artery		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia	Additional description: Bradycardia		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute	Additional description: Cardiac failure acute		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive	Additional description: Cardiac failure congestive		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest	Additional description: Cardio-respiratory arrest		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery disease	Additional description: Coronary artery disease		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia	Additional description: Myocardial ischaemia		

subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Silent myocardial infarction	Additional description: Silent myocardial infarction		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid sinus syndrome	Additional description: Carotid sinus syndrome		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multifocal motor neuropathy	Additional description: Multifocal motor neuropathy		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis	Additional description: Multiple sclerosis		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure	Additional description: Seizure		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage	Additional description: Subarachnoid haemorrhage		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamic infarction	Additional description: Thalamic infarction		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack	Additional description: Transient ischaemic attack		

subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Normocytic anaemia	Additional description: Normocytic anaemia		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness neurosensory	Additional description: Deafness neurosensory		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional	Additional description: Vertigo positional		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Keratitis	Additional description: Keratitis		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic nerve disorder	Additional description: Optic nerve disorder		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis	Additional description: Colitis		

subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis microscopic	Additional description: Colitis microscopic		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric perforation	Additional description: Gastric perforation		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia	Additional description: Inguinal hernia		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute	Additional description: Pancreatitis acute		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer haemorrhage	Additional description: Peptic ulcer haemorrhage		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone	Additional description: Bile duct stone		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis	Additional description: Cholecystitis		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute	Additional description: Cholecystitis acute		

subjects affected / exposed	0 / 19753 (0.00%)	2 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis	Additional description: Cholelithiasis		
subjects affected / exposed	1 / 19753 (0.01%)	2 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema	Additional description: Angioedema		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
IgA nephropathy	Additional description: IgA nephropathy		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis	Additional description: Nephrolithiasis		
subjects affected / exposed	2 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention	Additional description: Urinary retention		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Autoimmune thyroiditis	Additional description: Autoimmune thyroiditis		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Bursitis	Additional description: Bursitis		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion	Additional description: Intervertebral disc protrusion		
subjects affected / exposed	1 / 19753 (0.01%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plica syndrome	Additional description: Plica syndrome		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis	Additional description: Synovitis		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess	Additional description: Abscess		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis	Additional description: Appendicitis		
subjects affected / exposed	1 / 19753 (0.01%)	4 / 19787 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial	Additional description: Arthritis bacterial		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bartholin's abscess	Additional description: Bartholin's abscess		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

COVID-19	Additional description: COVID-19		
subjects affected / exposed	2 / 19753 (0.01%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	

COVID-19 pneumonia	Additional description: COVID-19 pneumonia		
subjects affected / exposed	4 / 19753 (0.02%)	3 / 19787 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 4	0 / 3	

Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	1 / 19753 (0.01%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Complicated appendicitis	Additional description: Complicated appendicitis		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hantaviral infection	Additional description: Hantaviral infection		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Herpes simplex	Additional description: Herpes simplex		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Liver abscess	Additional description: Liver abscess		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Localised infection	Additional description: Localised infection		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Meningitis bacterial	Additional description: Meningitis bacterial

subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oophoritis	Additional description: Oophoritis		
subjects affected / exposed	0 / 19753 (0.00%)	1 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic inflammatory disease	Additional description: Pelvic inflammatory disease		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis	Additional description: Pyelonephritis		
subjects affected / exposed	2 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingitis	Additional description: Salpingitis		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis	Additional description: Sepsis		
subjects affected / exposed	1 / 19753 (0.01%)	0 / 19787 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	0 / 19753 (0.00%)	2 / 19787 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	CVnCoV 12 µg Vaccine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3285 / 19753 (16.63%)	4355 / 19787 (22.01%)	
Nervous system disorders			
Headache	Additional description: Headache		
subjects affected / exposed	1225 / 19753 (6.20%)	2310 / 19787 (11.67%)	
occurrences (all)	1805	3911	
General disorders and administration site conditions			
Chills	Additional description: Chills		
subjects affected / exposed	240 / 19753 (1.22%)	1439 / 19787 (7.27%)	
occurrences (all)	286	2065	
Fatigue	Additional description: Fatigue		
subjects affected / exposed	1019 / 19753 (5.16%)	1893 / 19787 (9.57%)	
occurrences (all)	1483	3200	
Injection site pain	Additional description: Injection site pain		
subjects affected / exposed	537 / 19753 (2.72%)	2008 / 19787 (10.15%)	
occurrences (all)	644	3231	
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	95 / 19753 (0.48%)	1305 / 19787 (6.60%)	
occurrences (all)	102	1700	
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Myalgia		
subjects affected / exposed	509 / 19753 (2.58%)	1728 / 19787 (8.73%)	
occurrences (all)	634	2588	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 February 2021	The following changes were made: • The planned extension study was removed from the protocol for this trial and was submitted as a separate protocol. • Several COVID-19 vaccines have been authorized for emergency use since the original protocol and guidance was added on the handling of participant participation and data from participants who request to be unblinded due to being eligible to receive an authorized/licensed vaccine to prevent COVID-19. • The secondary safety objective was reclassified as a primary objective. • Instructions added that gene sequencing should be performed in participants with a positive RT PCR test to identify mutations in the S protein. • Samples for CMI and genomic biomarkers could also be taken in Phase 3 and not only in the Phase 2b immunogenicity subset. • It was clarified throughout the protocol that: - COVID-19 is not to be reported as an AE. - Different types of AEs, and any concomitant medication used for the treatment therefore, should only be collected during the specified reporting periods. - Participants may receive the second dose if they develop COVID 19 between the first and second doses (after being symptom-free for 2 weeks).
29 March 2021	The following changes were made: • The co-primary objective (and corresponding endpoint) regarding the efficacy of CVnCoV in the prevention of moderate to severe COVID 19 was changed to a key secondary objective. Subsequently, the corresponding statistical calculations were also updated. • Various strains have been identified since the original protocol and therefore a key secondary efficacy objective was added to demonstrate the efficacy of CVnCoV in the prevention of COVID 19 caused by the "wild type" (ie, WT/D614G lineages A.1/B.1 without VOC B.1.1.7, B.1.351, B.1.429) and "UK" (B.1.1.7) strains. An exploratory objective was added to demonstrate the efficacy on any other strains was also added. • The number of participants with exploratory immunogenicity assessment decreased from 400 to 200.
25 November 2021	The following changes were made: • To unblind all remaining blinded participants and inform them of the treatment received. • To monitor safety of the following participants remaining in the open-label phase after unblinding: - Participants who had received CVnCoV and received/would receive an AV through their national vaccination program. - Participants who had received CVnCoV and continued follow-up in the trial as initially planned, without receiving an AV.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported