Clinical trial results:
A randomised, double-blind, placebo-controlled, Phase III trial to determine the efficacy and safety of inhaled SNG001 for the treatment of patients hospitalised due to moderate COVID-19

Summary

EudraCT number	2020-004743-83
Trial protocol	GB BE PT FR NL IT DE RO ES
Global end of trial date	10 February 2022

Results information

Result version number	v1 (current)
This version publication date	25 February 2023
First version publication date	25 February 2023

Trial information

Trial identification

Sponsor protocol code	SG018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04732949
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Synairgen Research Ltd
Sponsor organisation address	Tremona Road, Southampton, United Kingdom, SO16 6YD
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Scientific contact	Brooke Clarke, Synairgen Research Ltd, 02 380512800, Brooke.Clarke@synairgen.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 February 2022
Is this the analysis of the primary completion data?	No

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

Notes:

General information about the trial

Main objective of the trial:

To evaluate recovery in patients with moderate Coronavirus disease 2019 (COVID-19) after administration of SNG001 compared to placebo.

Protection of trial subjects:

This trial was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines, and other local applicable laws and regulations. After the trial had been fully explained and the patient had been given ample time to read the patient information sheet (PIS)/ICF, consider the trial, and discuss it in detail, informed consent was gained. The method of obtaining and documenting informed consent and the contents of the consent was discussed and agreed with the appropriate competent authorities. For this study, methods included both written and video consent with only sites in India implementing the audio-video process as per their local guidelines. Each method was discussed and approved by the, applicable IEC/IRB before the site obtained the first consent. Informed consent was always obtained from the patient before any trial related procedures were performed, irrespective of the method used. Patients were informed that their participation was voluntary.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 January 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	Netherlands: 11
Country: Number of subjects enrolled	Portugal: 26
Country: Number of subjects enrolled	Romania: 14
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	United Kingdom: 176
Country: Number of subjects enrolled	Belgium: 19
Country: Number of subjects enrolled	France: 41
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Italy: 41
Country: Number of subjects enrolled	Brazil: 18
Country: Number of subjects enrolled	India: 72
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Mexico: 32

Country: Number of subjects enrolled	Serbia: 81
Country: Number of subjects enrolled	United States: 19
Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	Colombia: 9
Worldwide total number of subjects	623
EEA total number of subjects	201

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)	483
From 65 to 84 years	133
85 years and over	7

Subject disposition

Recruitment

Recruitment details:

This trial was conducted at 112 centers which included 623 patients across 17 countries. The trial began on 12 January 2021 (first patient consented) and was completed on 10 Feb 2022.

Pre-assignment

Screening details:

The pre-treatment assessments were performed on Day 0 prior to the first dose preferably. All the study assessments were performed as per the schedule of assessments.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The patient and investigator-blinded with regard to SNG001 or placebo but not the dose.

Arms

Are arms mutually exclusive?	Yes
Arm title	SNG001

Arm description:

Patients received SNG001 via inhalation using nebuliser, once a day for 14 days

Arm type	Experimental
Investigational medicinal product name	SNG001
Investigational medicinal product code	SNG001
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

The SNG001 nebuliser (study medication) solution delivered using the nebuliser. The study medication was taken once daily at approximately the same time of day for 14 consecutive days. There was a gap of at least 8 hours between doses.

Arm title	Placebo

Arm description:

Patients received Placebo via inhalation using nebuliser, once a day for 14 days

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

The Placebo delivered using the nebuliser. The Placebo was taken once daily at approximately the same time of day for 14 consecutive days. There was a gap of at least 8 hours between doses.

Number of subjects in period 1	SNG001	Placebo
Started	309	314
Completed	233	231
Not completed	76	83
Adverse event, serious fatal	16	18
Consent withdrawn by subject	23	27
Physician decision	2	1
Adverse event, non-fatal	2	1
Other	6	3
Non-serious adverse event	1	3
Non-compliance	-	2
Lost to follow-up	26	27
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	SNG001
Reporting group description:	
Patients received SNG001 via inhalation using nebuliser, once a day for 14 days	
Reporting group title	Placebo
Reporting group description:	
Patients received Placebo via inhalation using nebuliser, once a day for 14 days	

Reporting group values	SNG001	Placebo	Total
Number of subjects	309	314	623
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	52	53.7	
standard deviation	± 15.19	± 14.42	-
Gender categorical			
Units: Subjects			
Female	203	208	411
Male	106	106	212

End points

End points reporting groups	
Reporting group title	SNG001
Reporting group description:	
Patients received SNG001 via inhalation using nebuliser, once a day for 14 days	
Reporting group title	Placebo
Reporting group description:	
Patients received Placebo via inhalation using nebuliser, once a day for 14 days	

Primary: Time to Hospital Discharge	
End point title	Time to Hospital Discharge
End point description:	
The time to hospital discharge in patients with moderate COVID-19 after administration of SNG001 compared to placebo was evaluated. The Intent-to-Treat (ITT) analysis population consisted of all randomised patients.	
End point type	Primary
End point timeframe:	
Day 28	

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	314		
Units: day				
median (full range (min-max))	7.0 (7.0 to 8.0)	8.0 (7.0 to 9.0)		

Statistical analyses

Statistical analysis title	SNG001 vs Placebo
Statistical analysis description:	
Hazard Ratio for time to hospital discharge	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.509
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.27

Primary: Time to Recovery

End point title	Time to Recovery

End point description:

Recovery in patients with moderate COVID-19 after administration of SNG001 compared to placebo by time to recovery was evaluated.
The ITT analysis population consisted of all randomised patients.

Here, the arbitrary value 9999.9999 indicates not calculable. The upper limit was not calculable due to Insufficient number of participants with events

End point type	Primary

End point timeframe:

Day 28

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	314		
Units: day				
median (full range (min-max))	25.0 (22.0 to 9999.9999)	25.0 (22.0 to 9999.9999)		

Statistical analyses

Statistical analysis title	SNG001 vs Placebo
Statistical analysis description:	
Hazard Ratio for time to OSCI recovery	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.888
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.28

Secondary: Number of Patients Who Progressed to Severe Disease or Death

End point title	Number of Patients Who Progressed to Severe Disease or Death

End point description:

The efficacy of SNG001 compared to placebo in patients with moderate COVID-19 by assessing progression to severe disease or death was evaluated. Severe disease was defined by the Ordinal Scale for Clinical Improvement (OSCI) as a score between 5 and 7. Death was defined by an OSCI score of 8. The ITT analysis population consisted of all randomised patients. Here, the number of participants analyzed signifies the participants with available data that were analyzed for this outcome measure.

End point type	Secondary

End point timeframe:

Until Day 35

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	308	312		
Units: participants	33	45		

Statistical analyses

Statistical analysis title	SNG001 vs Placebo

Statistical analysis description:

Odds Ratio for progression to severe disease or death

Comparison groups	Placebo v SNG001
Number of subjects included in analysis	620
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.161
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	1.15

Secondary: Number of Patients Who Were Intubated or Who Died

End point title	Number of Patients Who Were Intubated or Who Died

End point description:

The efficacy of SNG001 compared to placebo in patients with moderate COVID-19 by assessing progression to intubation or death was evaluated. Intubation was defined by the OSCI as a score

between 6 and 7. Death was defined by an OSCI score of 8.
The ITT analysis population consisted of all randomised patients.

End point type	Secondary

End point timeframe:

Until Day 35

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	314		
Units: participants	20	23		

Statistical analyses

Statistical analysis title	SNG001 vs Placebo
Statistical analysis description:	
Odds Ratio for intubation or death	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.61
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.61

Secondary: Number of Patients Who Died Within 35 Days of First Dose

End point title	Number of Patients Who Died Within 35 Days of First Dose

End point description:

Patients who died within 35 days of first dose of study intervention were calculated.
The ITT analysis population consisted of all randomised patients.

End point type	Secondary

End point timeframe:

Until Day 35 of first dose

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	314		
Units: participants	14	17		

Statistical analyses

Statistical analysis title	SNG001 vs Placebo
Statistical analysis description: Odds Ratio for death	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.544
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1.67

Secondary: Cumulative Number of Patients Who Were Discharged From Hospital

End point title	Cumulative Number of Patients Who Were Discharged From Hospital

End point description:

The efficacy of SNG001 compared to placebo in patients with moderate COVID-19 was assessed by hospital dischargen on given days.
The ITT analysis population consisted of all randomised patients.

End point type	Secondary

End point timeframe:

Days 7, 14, 21 and 28

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	314		
Units: participants				
Day 7	154	141		
Day 14	231	223		
Day 21	245	249		
Day 28	249	255		

Statistical analyses

Statistical analysis title	SNG001 vs Placebo (Day 7)
Statistical analysis description: Odds Ratio for hospital discharge (Day 7)	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.323
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.64

Statistical analysis title	SNG001 vs Placebo (Day 14)
Statistical analysis description: Odds Ratio for hospital discharge (Day 14)	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.406
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.7

Statistical analysis title	SNG001 vs Placebo (Day 21)
Statistical analysis description: Odds Ratio for hospital discharge (Day 21)	
Comparison groups	Placebo v SNG001

Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.828
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.43

Statistical analysis title	SNG001 vs Placebo (Day 28)
Statistical analysis description:	
Odds Ratio for hospital discharge (Day 28)	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.706
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.4

Secondary: Cumulative Number of Patients With Recovery

End point title	Cumulative Number of Patients With Recovery

End point description:

The efficacy of SNG001 compared to placebo in patients with moderate COVID-19 by assessing recovery was evaluated. Recovery is defined as no limitation of activities according to the Ordinal Scale of Clinical Improvement (OSCI), with no rebound at subsequent assessments.
The ITT analysis population consisted of all randomised patients.

End point type	Secondary

End point timeframe:

Days 7, 14, 21 and 28

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	314		
Units: participants				
Day 7	28	17		
Day 14	75	73		
Day 21	117	118		
Day 28	145	151		

Statistical analyses

Statistical analysis title	SNG001 vs Placebo (Day 7)
Statistical analysis description: Odds Ratio for OSCI recovery (Day 7)	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.101
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	3.22

Statistical analysis title	SNG001 vs Placebo (Day 14)
Statistical analysis description: Odds Ratio for OSCI recovery (Day 14)	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.942
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.45

Statistical analysis title	SNG001 vs Placebo (Day 21)
Statistical analysis description: Odds Ratio for OSCI recovery (Day 21)	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.824
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.35

Statistical analysis title	SNG001 vs Placebo (Day 28)
Statistical analysis description: Odds Ratio for OSCI recovery (Day 28)	
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.613
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.28

Secondary: Improvement Based on Entire WHO OSCI Score

End point title	Improvement Based on Entire WHO OSCI Score

End point description:

The efficacy of SNG001 compared to placebo in patients with moderate COVID-19 by assessing improvement across the entire WHO OSCI were evaluated. Improvement in clinical status is based on the 9-point OSCI score. The score ranges from 0 to 8, where lower score of 0 represents no clinical or virological evidence of infection and higher score of 8 represents death. Higher scores indicated worse outcome.
The ITT analysis population consisted of all randomised patients.

End point type	Secondary

End point timeframe:
Until Day 35

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	314		
Units: participants				
Baseline, 0 = No clinical or virological evidence	0	0		
Baseline, 1 = No limitations of activities	0	0		
Baseline, 2 = Limitation of activities	1	0		
Baseline, 3 = Hospitalised - no oxygen therapy	3	8		
Baseline, 4 = Oxygen by mask, or nasal prongs	304	304		
Baseline, 5 = Non-invasive ventilation	1	2		
Baseline, 6 = Intubation & mechanical ventilation	0	0		
Baseline, 7 = Ventilation + organ support	0	0		
Baseline, 8 = Death	0	0		
Missing	0	0		
Day 7, 0 = No clinical or virological evidence	20	14		
Day 7, 1 = No limitations of activities	18	12		
Day 7, 2 = Limitation of activities	115	114		
Day 7, 3 = Hospitalised - no oxygen therapy	42	42		
Day 7, 4 = Oxygen by mask, or nasal prongs	53	69		
Day 7, 5 = Non-invasive ventilation	18	26		
Day 7, 6 = Intubation & mechanical ventilation	2	2		
Day 7, 7 = Ventilation + organ support	3	3		
Day 7, 8 = Death	4	0		
Day 7, Missing	34	32		
Day 14, 0 = No clinical or virological evidence	62	57		
Day 14, 1 = No limitations of activities	24	30		
Day 14, 2 = Limitation of activities	135	127		
Day 14, 3 = Hospitalised - no oxygen therapy	11	18		
Day 14, 4 = Oxygen by mask, or nasal prongs	13	15		
Day 14, 5 = Non-invasive ventilation	2	4		
Day 14, 6 = Intubation & mechanical ventilation	3	1		
Day 14, 7 = Ventilation + organ support	3	9		
Day 14, 8 = Death	9	7		
Day 14, Missing	47	46		
Day 21, 0 = No clinical or virological evidence	89	94		
Day 21, 1 = No limitations of activities	32	23		

Day 21, 2 = Limitation of activities	109	114		
Day 21, 3 = Hospitalised - no oxygen therapy	3	4		
Day 21, 4 = Oxygen by mask, or nasal prongs	7	4		
Day 21, 5 = Non-invasive ventilation	1	0		
Day 21, 6 = Intubation & mechanical ventilation	2	1		
Day 21, 7 = Ventilation + organ support	2	8		
Day 21, 8 = Death	12	9		
Day 21, Missing	52	57		
Day 28, 0 = No clinical or virological evidence	123	134		
Day 28, 1 = No limitations of activities	23	13		
Day 28, 2 = Limitation of activities	85	95		
Day 28, 3 = Hospitalised - no oxygen therapy	0	0		
Day 28, 4 = Oxygen by mask, or nasal prongs	3	2		
Day 28, 5 = Non-invasive ventilation	4	0		
Day 28, 6 = Intubation & mechanical ventilation	0	1		
Day 28, 7 = Ventilation + organ support	1	3		
Day 28, 8 = Death	14	14		
Day 28, Missing	56	52		
Day 35, 0 = No clinical or virological evidence	147	153		
Day 35, 1 = No limitations of activities	10	16		
Day 35, 2 = Limitation of activities	71	73		
Day 35, 3 = Hospitalised - no oxygen therapy	0	0		
Day 35, 4 = Oxygen by mask, or nasal prongs	2	1		
Day 35, 5 = Non-invasive ventilation	1	0		
Day 35, 6 = Intubation & mechanical ventilation	2	1		
Day 35, 7 = Ventilation + organ support	1	1		
Day 35, 8 = Death	14	17		
Day 35, Missing	61	52		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Score According to the Breathlessness, Cough and Sputum Scale (BCSS)

End point title	Change From Baseline in Total Score According to the Breathlessness, Cough and Sputum Scale (BCSS)

End point description:

The efficacy of SNG001 compared with placebo in patients with moderate COVID-19 by assessing changes in daily breathlessness, cough and sputum scores on a scale of 0 (no symptoms) up to 4 (severe symptoms) was evaluated. The BCSS is a daily patient-reported outcome measure that was designed as a daily diary in which patients were asked to record the severity of three symptoms: breathlessness, cough and sputum. Each symptom is represented by a single item which is evaluated on a 5-point scale ranging from 0-4, with higher scores indicating more severe symptoms. Breathing

difficulty: 0=None, 1=Mild, 2=Moderate, 3=Marked, 4=Severe; Cough: 0=No cough, 2=Occasional, 3=Frequent, 4=Almost constant; Sputum: 0=None, 1=Mild, 2=Moderate, 3=Marked, 4=Severe.
A mean decline of 1 point on the BCSS total scale signifies a substantial reduction in symptom severity.

The ITT analysis population consisted of all randomised patients.

End point type	Secondary
End point timeframe:	
Baseline to Day 15	

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	314		
Units: Score on a scale				
least squares mean (standard error)	-2.1 (± 0.09)	-2.2 (± 0.09)		

Statistical analyses

Statistical analysis title	SNG001 vs Placebo
Comparison groups	SNG001 v Placebo
Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.41
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.12

Secondary: Change From Baseline in National Early Warning Score (NEWS2) During the Hospitalisation Period

End point title	Change From Baseline in National Early Warning Score (NEWS2) During the Hospitalisation Period

End point description:

The efficacy of SNG001 compared to placebo in patients with moderate COVID-19 by assessing changes in NEWS2 during hospitalisation period was evaluated. The NEWS2 is a tool which is used in detection and response to clinical deterioration in adult patients and is a key element of patient safety and improving patient outcomes. The NEWS2 score was calculated using Six physiological parameters such as: respiration rate, oxygen saturation, systolic blood pressure, pulse rate, level of consciousness or new confusion and temperature. Each parameter was assigned a score between 0 and 3 and the NEWS2 score was calculated as the sum of the individual parameter scores. NEWS2 score between 0 and 4: Low, Score of any individual parameter of 3: Low-medium, NEWS2 score of 5 or 6: Medium, NEWS2

score of 7 or more: High.
Higher scores indicates high clinical risk.
The ITT analysis population consisted of all randomised patients.

End point type	Secondary

End point timeframe:

Day 1 until Day 28

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	87		
Units: Score on a scale				
least squares mean (standard error)				
Day 7 (n= 75, 87)	-0.7 (± 3.08)	-0.7 (± 2.55)		
Day 14 (n= 17, 30)	0.2 (± 3.83)	-0.3 (± 3.32)		
Day 21 (n= 10, 12)	2.8 (± 3.16)	2.3 (± 3.62)		
Day 28 (n= 4, 6)	-0.5 (± 2.08)	4.5 (± 4.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With Presence of COVID-19 Symptoms Based on Daily Assessment

End point title	Number of Patients With Presence of COVID-19 Symptoms Based on Daily Assessment

End point description:

The efficacy of SNG001 compared to placebo in patients with moderate COVID-19 by daily assessment of COVID-19 symptoms was evaluated. The presence of COVID-19 symptoms were assessed. Individual symptoms related to COVID-19/SARS-CoV-2 infection such as fever, breathlessness, and fatigue were assessed.
The ITT analysis population consisted of all randomised patients.

End point type	Secondary

End point timeframe:

Day 1 until Day 90

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	314		
Units: participants				
Baseline (n= 309, 314)	306	310		
Day 7 (n= 264, 271)	221	234		
Day 14 (n= 247, 251)	169	162		
Day 21 (n= 243, 238)	154	139		
Day 28 (n= 236, 243)	122	117		
Day 35 (n= 164, 171)	61	69		

Day 60 (n= 166, 171)	44	57		
Day 90 (n= 176, 176)	41	51		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With Limitations of Usual Activities Based on Daily Assessment

End point title	Number of Patients With Limitations of Usual Activities Based on Daily Assessment

End point description:

The efficacy of SNG001 compared to placebo in patients with moderate COVID-19 by daily assessment of limitation of usual activities was evaluated. The patients with limitations of usual activities were the patients who were unable to do usual activities (work, study, housework, family or leisure activities). The ITT analysis population consisted of all randomised patients.

End point type	Secondary

End point timeframe:

Day 1 until Day 35

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	314		
Units: participants				
Day 1 (n= 309, 314)	0	1		
Day 7 (n= 275, 283)	115	114		
Day 14 (n= 262, 268)	135	127		
Day 21 (n= 257, 257)	109	114		
Day 28 (n= 253, 262)	85	95		
Day 35 (n= 248, 262)	71	73		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Measured Using EuroQol 5-dimension 5-level (EQ-5D-5L)

End point title	Quality of Life Measured Using EuroQol 5-dimension 5-level (EQ-5D-5L)

End point description:

The efficacy of SNG001 compared to placebo in patients with moderate COVID-19 by using EQ-5D-5L was evaluated. The EQ-5D-5L provides a simple descriptive profile and a single index value for health status. The EQ-5D-5L self-rated questionnaire includes a visual analogue scale, which records the respondent's self-rated health status on a graduated (0–100) scale, with higher scores for higher health-related quality of life. It also includes the EQ-5D-5L descriptive system, which comprises 5 dimensions of health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The responses record five levels of severity (no problems/slight problems/moderate problems/severe

problems/extreme problems) within a particular EQ-5D dimension. Here, 100 means the best health and 0 means the worst health.
The ITT analysis population consisted of all randomised patients.

End point type	Secondary

End point timeframe:

Day 0, Day 7, Day 15, Day 28, Day 60 and Day 90

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302	311		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 0 (n= 302, 311)	56.4 (± 21.72)	56.9 (± 20.95)		
Day 7 (n= 259, 264)	72.6 (± 18.39)	71.1 (± 20.44)		
Day 15 (n= 241, 251)	79.5 (± 18.25)	79.0 (± 16.51)		
Day 28 (n= 234, 242)	83.3 (± 16.00)	83.5 (± 14.90)		
Day 60 (n= 230, 232)	88.9 (± 14.16)	88.0 (± 13.56)		
Day 90 (n= 233, 229)	90.3 (± 12.65)	89.9 (± 13.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: General Anxiety Disorder 7 Questionnaire (GAD-7) Total Score

End point title	General Anxiety Disorder 7 Questionnaire (GAD-7) Total Score

End point description:

The efficacy of SNG001 compared to placebo in patients with moderate COVID-19 by assessing long-COVID-19 symptoms was evaluated. Assessment of long-COVID-19 symptoms based on GAD-7 scale. GAD-7 scores seven individual item scales by assigning scores of 0, 1, 2, and 3, to the response categories of "not at all", "several days", "more than half the days", and "nearly every day", respectively. The GAD-7 total score is calculated by summing the individual item scales to give a total score between 0 and 21. Higher score indicates severe anxiety.
The ITT analysis population consisted of all randomised patients.

End point type	Secondary

End point timeframe:

Day 15, Day 28, Day 60 and Day 90

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	249		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 15 (n=238, 249)	3.3 (± 4.08)	3.5 (± 4.30)		
Day 28 (n= 231, 240)	2.2 (± 3.67)	1.9 (± 3.29)		
Day 60 (n= 229, 231)	1.4 (± 3.06)	1.7 (± 3.38)		

Day 90 (n= 228, 227)	1.0 (± 2.41)	1.6 (± 3.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-FS [Version 4]) Total Score

End point title	Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-FS [Version 4]) Total Score

End point description:

Long-COVID-19 symptoms based on FACIT Fatigue Scale (Version 4) were evaluated. The FACIT Fatigue Scale (Version 4) included statements for patients such as: I feel fatigued; I feel weak all over; I feel listless ("washed out"); I feel tired; I have trouble starting things because I am tired; I have trouble finishing things because I am tired; I have energy; I am able to do my usual activities; I need to sleep during the day; I am too tired to eat; I need help doing my usual activities; and I am frustrated by being too tired to do the things I want to do. Based on responses on above statements, scoring was done and scores ranges from 0 to 4, where 0 represents not at all bothered by any of the above problems and 4 indicates very much bothered every day by any of the above problems. Total scores will be calculated as per the algorithm to give a total score on a scale between 0 and 52, where a higher total score indicates lower level of fatigue.

End point type	Secondary

End point timeframe:

Day 15, Day 28, Day 60 and Day 90

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	248		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 15 (n= 239, 248)	39.1 (± 9.79)	38.7 (± 10.31)		
Day 28 (n= 233, 237)	42.5 (± 10.19)	42.8 (± 8.98)		
Day 60 (n= 228, 230)	46.4 (± 8.22)	45.5 (± 7.96)		
Day 90 (n= 230, 229)	46.9 (± 8.01)	46.3 (± 7.78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Health Questionnaire-9 (PHQ-9) Total Score

End point title	Patient Health Questionnaire-9 (PHQ-9) Total Score

End point description:

Long-COVID-19 symptoms based on PHQ-9 were evaluated. Patient Health Questionnaire-9 (PHQ-9) scores nine individual item scales by assigning scores of 0, 1, 2, and 3, to the response categories of

“not at all”, “several days”, “more than half the days”, and “nearly every day”, respectively. PHQ-9 total scores are calculated by summing the individual item scales to give a total score between 0 and 27. Higher scores indicated worse outcome.
The ITT analysis population consisted of all randomised patients.

End point type	Secondary
End point timeframe:	
Day 15, Day 28, Day 60 and Day 90	

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237	245		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 15 (n= 237, 245)	4.6 (± 4.47)	5.0 (± 4.71)		
Day 28 (n= 232, 238)	3.2 (± 4.15)	3.1 (± 4.02)		
Day 60 (n= 228, 229)	1.7 (± 3.23)	2.1 (± 3.85)		
Day 90 (n= 229, 228)	1.5 (± 3.05)	2.0 (± 3.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Pain Severity as Measured by Brief Pain Inventory Composite Scores

End point title	Overall Pain Severity as Measured by Brief Pain Inventory Composite Scores

End point description:

Brief Pain Inventory Composite Scores is a self administered questionnaire that assesses pain interference. Overall pain severity score is calculated as the mean of questions of the brief pain inventory. The overall pain severity score is the average pain, on a scale from 0 to 10 of the worst pain, least pain and average pain in the last 24 hours and pain right now scores. Here, 0 indicates "No pain" and 10 indicates "Worst pain".

End point type	Secondary
End point timeframe:	
Day 15, Day 28, Day 60 and Day 90	

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	55		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Day 15 (n= 50, 55)	3.4 (± 2.13)	3.3 (± 1.98)		
Day 28 (n= 34, 38)	3.2 (± 1.98)	3.2 (± 1.77)		
Day 60 (n= 21, 20)	4.1 (± 1.54)	3.3 (± 1.94)		
Day 90 (n= 21, 21)	4.5 (± 2.14)	3.5 (± 2.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Patients With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

The general safety and tolerability of SNG001 compared to placebo when administered to patients with moderate COVID-19 by assessing number of patients with AEs was assessed.
The Safety analysis population included all patients in the ITT population who receive at least one dose of study drug.

LTD: leading to discontinuation

End point type	Secondary

End point timeframe:

From the day informed consent is obtained until 28 days after the last administration of the study medication (Day 90)

End point values	SNG001	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301	303		
Units: participants				
Any Treatment-emergent adverse event (TEAE)	251	251		
Any serious TEAE	38	55		
Any serious related TEAE	3	3		
Any fatal TEAE	16	16		
Any fatal TEAE related to study treatment	0	0		
Any TEAE related to study treatment	68	77		
Any TEAE LTD of study treatment	24	23		
Any Adverse Events of Note	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the day informed consent is obtained until 28 days after the last administration of the study medication (Day 90)

Adverse event reporting additional description:

There were two patients randomised to placebo, one of which was never dosed and the other was dosed but the fatal Adverse Event (AE) started before dosing (i.e. not treatment emergent). For adverse event reporting, safety population was used.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	SNG001

Reporting group description:

Patients received SNG001 via inhalation using nebuliser, once a day for 14 days.

Reporting group title	Placebo

Reporting group description:

Patients received Placebo via inhalation using nebuliser, once a day for 14 days.

Serious adverse events	SNG001	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 301 (12.62%)	55 / 303 (18.15%)	
number of deaths (all causes)	16	18	
number of deaths resulting from adverse events	16	16	
Investigations			
Anticoagulation drug level above therapeutic			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen consumption increased			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation decreased			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	2 / 301 (0.66%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	2 / 2	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 301 (0.33%)	2 / 303 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	2 / 2	
Cardiac failure			
subjects affected / exposed	1 / 301 (0.33%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Myocardial ischaemia			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Myocardial infarction			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Coronary artery disease			

subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dysaesthesia			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 301 (0.33%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
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			
Blood disorder			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (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			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	9 / 301 (2.99%)	9 / 303 (2.97%)	
occurrences causally related to treatment / all	1 / 9	0 / 9	
deaths causally related to treatment / all	2 / 2	2 / 2	
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 301 (0.66%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Acute respiratory failure			
subjects affected / exposed	1 / 301 (0.33%)	7 / 303 (2.31%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	2 / 2	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 301 (0.33%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pneumomediastinum			

subjects affected / exposed	1 / 301 (0.33%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngospasm			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 301 (0.00%)	5 / 303 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 301 (0.00%)	2 / 303 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary tract disorder			

subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 301 (1.00%)	2 / 303 (0.66%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 301 (0.33%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Disorientation			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric decompensation			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	11 / 301 (3.65%)	8 / 303 (2.64%)	
occurrences causally related to treatment / all	0 / 11	0 / 8	
deaths causally related to treatment / all	5 / 5	3 / 3	
COVID-19 pneumonia			
subjects affected / exposed	8 / 301 (2.66%)	8 / 303 (2.64%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	4 / 4	2 / 2	

Pneumonia			
subjects affected / exposed	3 / 301 (1.00%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 301 (0.33%)	0 / 303 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia acinetobacter			
subjects affected / exposed	1 / 301 (0.33%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Lower respiratory tract infection			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia haemophilus			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 301 (0.00%)	1 / 303 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	

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

Non-serious adverse events	SNG001	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	250 / 301 (83.06%)	248 / 303 (81.85%)	
Nervous system disorders			
Headache			
subjects affected / exposed	71 / 301 (23.59%)	61 / 303 (20.13%)	
occurrences (all)	84	76	
Anosmia			
subjects affected / exposed	18 / 301 (5.98%)	20 / 303 (6.60%)	
occurrences (all)	18	20	
Ageusia			
subjects affected / exposed	13 / 301 (4.32%)	18 / 303 (5.94%)	
occurrences (all)	13	19	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	39 / 301 (12.96%)	40 / 303 (13.20%)	
occurrences (all)	40	43	
Chest pain			
subjects affected / exposed	36 / 301 (11.96%)	52 / 303 (17.16%)	
occurrences (all)	37	54	
Pyrexia			
subjects affected / exposed	23 / 301 (7.64%)	30 / 303 (9.90%)	
occurrences (all)	25	34	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	25 / 301 (8.31%)	9 / 303 (2.97%)	
occurrences (all)	26	9	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	22 / 301 (7.31%)	26 / 303 (8.58%)	
occurrences (all)	23	31	
Constipation			
subjects affected / exposed	21 / 301 (6.98%)	22 / 303 (7.26%)	
occurrences (all)	23	27	

Vomiting			
subjects affected / exposed	21 / 301 (6.98%)	23 / 303 (7.59%)	
occurrences (all)	22	26	
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	70 / 301 (23.26%)	72 / 303 (23.76%)	
occurrences (all)	78	85	
Rhinorrhoea			
subjects affected / exposed	58 / 301 (19.27%)	54 / 303 (17.82%)	
occurrences (all)	62	55	
Oropharyngeal pain			
subjects affected / exposed	55 / 301 (18.27%)	47 / 303 (15.51%)	
occurrences (all)	57	50	
Wheezing			
subjects affected / exposed	45 / 301 (14.95%)	35 / 303 (11.55%)	
occurrences (all)	54	45	
Cough			
subjects affected / exposed	39 / 301 (12.96%)	28 / 303 (9.24%)	
occurrences (all)	46	32	
Dyspnoea			
subjects affected / exposed	30 / 301 (9.97%)	41 / 303 (13.53%)	
occurrences (all)	35	46	
Haemoptysis			
subjects affected / exposed	16 / 301 (5.32%)	22 / 303 (7.26%)	
occurrences (all)	16	22	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	60 / 301 (19.93%)	60 / 303 (19.80%)	
occurrences (all)	62	65	
Arthralgia			
subjects affected / exposed	54 / 301 (17.94%)	54 / 303 (17.82%)	
occurrences (all)	62	62	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 December 2020	Amendment 2: Recruitment commenced on this version of the protocol. Changes were made following interactions with key regulatory agencies- Key secondary efficacy endpoint 'Time to hospital discharge, defined by the OSCI score of 2 or below, with no rebound at subsequent assessments' to a primary efficacy endpoint; Secondary efficacy endpoints 'Progression to intubation or death, defined by the OSCI score of 6 or above within 28 days of first dose.' and 'death within 28 days of first dose.' to key secondary efficacy endpoints; Addition of the following secondary endpoint: 'daily assessment of COVID-19 symptoms and limitation of usual activities'.
22 February 2021	Amendment 4: Removed exclusion criteria number 12 that excluded patients who had received a prior SARS-CoV-2 vaccination; Included PK sampling schedule based on agreed FDA requirements

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported