Clinical trial results:
A single-site, randomised, controlled, parallel design, open-label investigation of an approved nebulised recombinant human DNase enzyme (dornase alfa) to reduce hyperinflammation in hospitalised participants with COVID-19 (The COVASE trial)

Summary

EudraCT number	2020-001937-11
Trial protocol	GB
Global end of trial date	05 November 2021
Results information	
Result version number	v2 (current)
This version publication date	22 December 2023
First version publication date	04 June 2023
Version creation reason	• Correction of full data set Minor corrections
Summary attachment (see zip file)	CSR COVASE V2.0 (Final CSR COVASE_V2.0.pdf)

Trial information

Trial identification	
Sponsor protocol code	132333
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04359654
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	University College London
Sponsor organisation address	Gower Street, London, United Kingdom, WC1E 6BT
Public contact	Joint Research Office, University College London, ctimps@ucl.ac.uk
Scientific contact	Professor Joanna Porter, University College London, joanna.porter@ucl.ac.uk

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	04 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 November 2021
Global end of trial reached?	Yes
Global end of trial date	05 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of nebulised dornase alpha on C-reactive Protein (CRP) in hospitalised participants with COVID-19

Protection of trial subjects:

The IMP treatment had been in widespread clinical use since the 1960s without side effects Reassured that they could withdraw at any time with no impact on their clinical treatment. Trial team were happy to involve family members if needed for discussions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 June 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	United Kingdom: 41
Worldwide total number of subjects	41
EEA total number of subjects	0

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)	25
From 65 to 84 years	16

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

31 subjects were randomised to BAC + dornase-alfa, with 10 randomised to BAC.
1 subject from the BAC + dornase alfa group withdrew consent prior to treatment and was replaced.
There were 30 evaluable participants in the BAC + dornase-alfa group.
1 subject from the BAC group had a baseline CRP measurement and no more, hence was unevaluable.

Pre-assignment

Screening details:

Inclusion criteria
1. 18 years+
2. Participants who are hospitalised for suspected Coronavirus (SARS-CoV)-2 infection confirmed by polymerase chain reaction (PCR) test or radiological confirmation with chest CT
3. Stable oxygen saturation (>=94%) on supplementary oxygen
4. CRP >= 30 mg/L

All patients admitted with SARS-Cov-2 screened.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable.

Arms

Are arms mutually exclusive?	Yes
Arm title	Dornase Alfa

Arm description:

Nebulised Dornase Alfa (DA) 2.5mg bd for 7 days or until discharge whatever was sooner

Arm type	Experimental
Investigational medicinal product name	Dornase Alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

2.5mg bd

Arm title	Best available care

Arm description:

Standard treatment

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Dornase Alfa	Best available care
Started	31	10
Completed	30	9
Not completed	1	1
Consent withdrawn by subject	1	-
Discharged from hospital before data collected	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	41	41	
Age categorical Units: Subjects			
Adults 18+	39	39	
Not recorded	2	2	
Age continuous Units: years			
median	56		
full range (min-max)	31 to 77	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	30	30	
Not recorded	2	2	

End points

End points reporting groups	
Reporting group title	Dornase Alfa
Reporting group description:	
Nebulised Dornase Alfa (DA) 2.5mg bd for 7 days or until discharge whatever was sooner	
Reporting group title	Best available care
Reporting group description:	
Standard treatment	

Primary: Changes in CRP	
End point title	Changes in CRP
End point description:	
Changes in acute phase reactant (C-Reactive Protein (CRP)) - a clinically important marker of inflammation.	
End point type	Primary
End point timeframe:	
The analysis is conducted at 7 days.	

End point values	Dornase Alfa	Best available care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	9		
Units: mg/L				
number (not applicable)	30	9		

Statistical analyses

Statistical analysis title	Analysis
Statistical analysis description:	
The primary outcome was CRP up to 7 days or at hospital discharge, whichever was sooner, analysed on the log scale. Pre-specified secondary outcomes included days on oxygen; time to hospital discharge; mortality by day 35; and changes in clinically relevant biomarkers including lymphocyte count and D-dimer levels. Efficacy assessments of the primary and secondary outcomes in the modified intention-to-treat population were performed on all randomised participants who had received at least 1 dose	
Comparison groups	Dornase Alfa v Best available care
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [1]
Method	Mixed models analysis
Parameter estimate	least square mean
Point estimate	-0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	-0.02
Variability estimate	Standard error of the mean
Dispersion value	0.23

Notes:

[1] - Mixed models analysis, CRP analysed on log scale

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed by research from randomisation to 35 days follow.

Adverse event reporting additional description:

As per the trial protocol SAEs assessed as anticipated with COVID-19 infection were not reportable to Sponsor. Of the 16 SAEs recorded on the trial database only 6 were reported to Sponsor. All SAEs were assessed as not related to trial IMP.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Best Available Care
Reporting group description: -	
Reporting group title	Dornase Alfa

Reporting group description: -

Serious adverse events	Best Available Care	Dornase Alfa	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 9 (22.22%)	8 / 30 (26.67%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (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			
Pulmonary embolism			
subjects affected / exposed	1 / 9 (11.11%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure type 2			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			

subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure type 1			
subjects affected / exposed	0 / 9 (0.00%)	4 / 30 (13.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (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			
Pyelonephritis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration pneumonia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospital Acquired Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2.5 %

Non-serious adverse events	Best Available Care	Dornase Alfa	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)	16 / 30 (53.33%)	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 9 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	3	
Chest tightness			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Dry nose			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Dysphonia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Emphysema			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Haemoptysis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Hypercapnia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Sputum bloody			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Tachypnoea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Psychiatric disorders			

Confusion aggravated			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Sleep disturbance			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Oxygen saturation decreased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Pericardial Effusion			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Cognitive impairment			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Dizzy spells			

subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Tingling feet/hands			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Blood in stool			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 9 (11.11%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			
subjects affected / exposed	1 / 9 (11.11%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Rectal bleeding			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Tingling mouth			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Ulcerative Colitis relapse			

subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Transaminitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Leg spasm			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Polyarthralgia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Infections and infestations			
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported