



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 | <ul style="list-style-type: none">• Correction of full data setMinor 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 ($\geq 94\%$) 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 occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 30 (0.00%) 0 | |
| Depression subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Sleep disturbance subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Investigations Blood glucose increased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Oxygen saturation decreased subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 30 (0.00%) 0 | |
| Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Cardiac disorders Bradycardia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 30 (3.33%) 1 | |
| Pericardial Effusion subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Nervous system disorders Cognitive impairment subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Dizzy spells | | | |

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

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