

# STOP-COVID19: Superiority Trial Of Protease inhibition in COVID-19 (coronavirus infection)

<b>Submission date</b> 20/05/2020	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 20/05/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 09/09/2022	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. People who have developed the condition may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe.

In 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. As of March 2020, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.

Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions (such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.

There is currently no vaccine to prevent infection with SARS-CoV-2 and no therapeutic agent to treat COVID-19. This clinical trial is designed to evaluate the potential of brensocatib (INS1007) as a novel therapy for the treatment of adult patients hospitalized with COVID-19.

### Who can participate?

Persons over 16 years who have been admitted to hospital as an inpatient, and have laboratory-confirmed SARS-CoV-2 infection (COVID-19).

### What does the study involve?

Participants will be randomised to receive brensocatib or placebo 25mg orally once daily for 28 days.

What are the possible benefits and risks of participating?

Brensocatib is an un-licensed medicine but it's already been used in clinical trials. Trials with healthy people and those with lung conditions (with over 250 people involved) showed that the medicine was generally well tolerated by people in the trial. The most common side effects reported were cough, increased phlegm, headache and breathlessness. These are common symptoms for people with lung conditions and they were also reported frequently by people taking the placebo tablets. Two side effects that we know are possible with this medicine are thickening of the skin and inflammation of the gums, both of which happen rarely. (added 21/05/2020)

Where is the study run from?

Ninewells Hospital and Medical School (UK)

When is the study starting and how long is it expected to run for?

March 2020 to February 2021 (updated 21/01/2021, previously: January 2021 (updated 10/11/2020, previously: December 2020))

Who is funding the study?

Insmmed Incorporated (USA)

Who is the main contact?

Unfortunately, this study is not recruiting public volunteers at this time. This is because the research isn't ready for volunteers yet or the researchers are directly identifying volunteers in certain areas or hospitals. Please do not contact the research team as they will not be able to respond. For more information about COVID-19 research, visit the Be Part of Research homepage. (added 21/05/2020)

### **Study website**

<https://stop-covid19.org.uk/>

## **Contact information**

### **Type(s)**

Public

### **Contact name**

Mrs Margaret Band

### **Contact details**

Taydside Clinical Trials Unit

TASC

Level 3

Ninewells Hospital and Medical School

Dundee

United Kingdom

DD1 9SY

+44 (0)1382 383097

m.band@dundee.ac.uk

### **Type(s)**

Scientific

**Contact name**

Prof James Chalmers

**Contact details**

Division of Cardiovascular Medicine  
Level 5  
Ninewells Hospital and Medical School  
Dundee  
United Kingdom  
DD1 9SY  
+44 (0)1382 383642  
j.chalmers@dundee.ac.uk

**Additional identifiers****EudraCT/CTIS number**

2020-001643-13

**IRAS number**

281986

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

01.01.20, IRAS 281986, CPMS 45682

**Study information****Scientific Title**

A randomised double-blind placebo-controlled trial of brensocatib (INS1007) in patients with severe COVID-19

**Acronym**

STOP-COVID19

**Study objectives**

Treatment with brensocatib in addition to standard care will be superior to standard care alone in achieving improved clinical status in patients initially hospitalised with COVID-19.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 20/05/2020, Scotland A Research Ethics Committee (Research Ethics Service, 2nd Floor Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, UK; +44 (0)131 465 5680; Manx. Neill@nhslothian.scot.nhs.uk), ref: 20/SS/0057

**Study design**

Multi-centre randomized double-blind placebo-controlled parallel-group trial

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

### **Participant information sheet**

<https://stop-covid19.org.uk/>

### **Health condition(s) or problem(s) studied**

COVID-19 (SARS-CoV-2 infection)

### **Interventions**

Participants will be randomised to receive brensocatib or placebo 25 mg orally once daily for 28 days.

Randomisation performed using an interactive web-based randomisation system (added 21/05/2020).

### **Intervention Type**

Drug

### **Phase**

Phase III

### **Drug/device/biological/vaccine name(s)**

Brensocatib (INS1007)

### **Primary outcome measure**

Participant clinical status (on a 7-point ordinal scale); up to day 29

### **Secondary outcome measures**

1. Clinical Severity: Time to an improvement of one category from admission using 7-point ordinal scale; daily whilst in hospital
2. Participant clinical status on 7-point ordinal scale; Days 3, 5, 8, 11, 15 and 29
3. Mean change in the 7-point ordinal scale; Baseline to days 3, 5, 8, 11, 15 and 29
4. National Early Warning Score (NEWS): Time to discharge or to a NEWS of  $\leq 2$  and maintained for 24 hours, whichever occurs first; Daily whilst hospitalised. Change from baseline; Days 8, 15, 29
5. Oxygenation: Oxygen free days; 0-29 days. Incidence and duration of new oxygen use during the trial; 0 - 29 days
6. Mechanical Ventilation: Ventilator free days; 0-29 days. Incidence and duration of new mechanical ventilation use during the trial; 0-29 days

7. Hospitalisation: Duration of hospitalisation (days); Date of admission and discharge
8. Mortality: 28-day mortality; date of death
9. Safety:
  - 9.1. Cumulative incidence of SAEs; 0-29 days
  - 9.2. Discontinuation or temporary suspension of treatment; 0 - 29 days
  - 9.3. Changes in white cell count, haemoglobin, platelets, creatinine, total bilirubin, ALT, and AST over time (hospitalised participants only); Days 0, 3, 5, 8, 11, 15, 29
  - 9.4. Adverse events of special interest- hyperkeratosis, infections and dental complications; 0-29 days
10. Virologic efficacy (Tayside participants only):
  - 10.1. Percent of participants with SARS-CoV-2 detectable in nasopharyngeal (NP) sample; Day 15 and day 29
  - 10.2. Quantitative SARS-CoV-2 virus in NP samples; Day 15 and day 29
  - 10.3. Neutrophil elastase and heparin binding protein measurement in blood; Days 0, 8, 15, 29
  - 10.4. Neutrophil functional studies (NET formation, phagocytosis, elastase release, neutrophil proteomics; Days 0, 15, 29
11. Quality of life: EQ-5D-5L administered via telephone (if at home) or in person if still in hospital; day 29

### **Overall study start date**

30/03/2020

### **Completion date**

28/02/2021

## **Eligibility**

### **Key inclusion criteria**

Current inclusion criteria as of 10/11/2020:

1. Aged  $\geq 16$  years
2. SARS-CoV-2 infection (clinically suspected+ or laboratory confirmed\*).
3. Admitted to hospital as in-patient less than 96 hours prior to randomisation^
4. Illness of any duration, and at least one of the following:
  - 4.1. Radiographic infiltrates by imaging (e.g. chest x-ray, computed tomography (CT) scan) OR
  - 4.2. Evidence of rales/crackles on physical examination OR
  - 4.3. Peripheral capillary oxygen saturation (SpO<sub>2</sub>)  $\leq 94\%$  on room air prior to randomization OR
  - 4.4. Requiring supplemental oxygen OR
  - 4.5. Lymphocyte count  $< 1 \times 10^9$  cells/l
5. Participant (or legally authorized representative) provides written informed consent
6. Able to take oral medication
7. Participant (or legally authorised representative) understands and agrees to comply with planned trial procedures

\*Laboratory-confirmed: SARS-CoV-2 infection as determined by polymerase chain reaction (PCR), or other commercial or public health assay in any specimen < 96 hours prior to randomization.

+Clinically suspected: in general, SARS-CoV-2 infection should be suspected when a patient presents with (i) typical symptoms (e.g. influenza-like illness with fever and muscle pain, or respiratory illness with cough and shortness of breath); and (ii) compatible chest X-ray findings (consolidation or ground-glass shadowing); and (iii) alternative causes have been considered unlikely or excluded (e.g. heart failure, influenza). However, the diagnosis remains a clinical one

based on the opinion of the managing doctor.

^Where a patient has been admitted to hospital for a non COVID-19 reason and develops COVID19 symptoms whilst an in-patient, randomisation may occur up to 96 hours from onset of symptoms.

---

#### Previous inclusion criteria:

1. Aged  $\geq 16$  years
2. Laboratory-confirmed SARS-CoV-2 infection as determined by polymerase chain reaction (PCR), or other commercial or public health assay in any specimen < 96 h prior to randomization
3. Admitted to hospital as in-patient
4. Illness of any duration, and at least one of the following:
  - 4.1. Radiographic infiltrates by imaging (e.g. chest x-ray, computed tomography (CT) scan) OR
  - 4.2. Evidence of rales/crackles on physical examination OR
  - 4.3. Peripheral capillary oxygen saturation (SpO<sub>2</sub>)  $\leq 94\%$  on room air prior to randomization OR
  - 4.4. Requiring supplemental oxygen OR
  - 4.5. Lymphocyte count  $< 1 \times 10^9$  cells/l
5. Participant (or legally authorized representative) provides written informed consent
6. Able to take oral medication
7. Participant (or legally authorised representative) understands and agrees to comply with planned trial procedures

#### Participant type(s)

Patient

#### Age group

Adult

#### Sex

Both

#### Target number of participants

400

#### Total final enrolment

406

#### Key exclusion criteria

Current exclusion criteria as of 21/01/2021:

1. Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) > 5 times the upper limit of normal, result within 72 hours of randomization (the result closest to randomization should be used if several results are available).
2. History of severe liver disease
3. Stage 4 severe chronic kidney disease or requiring dialysis (i.e. eGFR < 30), result within 72 hours of randomization (the result closest to randomization should be used if several results are available)
4. Absolute neutrophil count less than  $1.0 \times 10^9$  cells per L within 72 hours of randomization (the result closest to randomization should be used if several results are available)

5. Current treatments with potent Cyp3A4 inducers/inhibitors (e.g Itraconazole, Ketoconazole, diltiazem, verapamil, phenytoin or rifampicin)
6. HIV treatments - current treatment with protease/integrase inhibitors or non-nucleoside reverse transcriptase inhibitors\*
7. Pregnant or breast feeding
8. Anticipated transfer to another hospital which is not a trial site within 24 hours
9. Allergy to Brensocatib
10. Use of any investigational drug within five times of the elimination half-life after the last trial dose or within 30 days, whichever is longer. Co-enrolment with COVID-19 trials is allowed as per co-enrolment agreements and/or individual decision by the CI
11. Women of child-bearing potential must be willing to have pregnancy testing prior to trial entry.

\*The Liverpool HIV checker (<https://www.hiv-druginteractions.org/checker>) should be used to check for any HIV drug interactions. Simvastatin could be used as a surrogate for Brensocatib as it metabolised similarly by CYP 3A4 pathway

---

Previous exclusion criteria as of 10/11/2020:

1. Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) >5x the upper limit of normal, result within 72 h of randomization (the result closest to randomization should be used if several results are available)
2. History of severe liver disease
3. Stage 4 severe chronic kidney disease or requiring dialysis (i.e. eGFR <30), result within 72 h of randomization (the result closest to randomization should be used if several results are available)
4. Absolute neutrophil count less than  $1.0 \times 10^9$  cells/l within 72 h of randomization (the result closest to randomization should be used if several results are available)
5. Current treatment with Itraconazole, Ketoconazole, diltiazem, verapamil, phenytoin or rifampicin
6. HIV treatments - current treatment with protease/integrase inhibitors or non-nucleoside reverse transcriptase inhibitors\*
7. Pregnant or breast feeding
8. Anticipated transfer to another hospital which is not a trial site within 24 hours
9. Allergy to brensocatib
10. Use of any investigational drug within 5 times the elimination half-life after the last trial dose or within 30 days, whichever is longer

\*The Liverpool HIV checker (<https://www.hiv-druginteractions.org/checker>) should be used to check for any HIV drug interactions. Simvastatin could be used as a surrogate for Brensocatib as it metabolised similarly by CYP 3A4 pathway.

---

Previous exclusion criteria:

1. Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) >5x the upper limit of normal, result within 72 h of randomization (the result closest to randomization should be used if several results are available)
2. History of severe liver disease
3. Stage 4 severe chronic kidney disease or requiring dialysis (i.e. eGFR <30), result within 72 h of randomization (the result closest to randomization should be used if several results are available)
4. Absolute neutrophil count less than  $1.0 \times 10^9$  cells/l within 72 h of randomization (the result

closest to randomization should be used if several results are available)  
5. Current treatment with itraconazole, ketoconazole, diltiazem or verapamil  
6. Pregnant or breast feeding  
7. Anticipated transfer to another hospital which is not a trial site within 24 hours  
8. Allergy to brensocatib  
9. Use of any investigational drug within 5 times the elimination half-life after the last trial dose or within 30 days, whichever is longer

**Date of first enrolment**

20/05/2020

**Date of final enrolment**

31/01/2021

## **Locations**

**Countries of recruitment**

England

Scotland

United Kingdom

Wales

**Study participating centre**

**Ninewells Hospital and Medical School**

NHS Tayside

Dundee

United Kingdom

DD1 9SY

**Study participating centre**

**Wishaw Hosptial**

NHS Lanarkshire

Wishaw

United Kingdom

ML2 0PD

**Study participating centre**

**Raigmore Hospital**

NHS Highland

Inverness

United Kingdom

IV2 3UJ



**Study participating centre**

**Aberdeen Royal Infirmary**

NHS Grampian  
Aberdeen  
United Kingdom  
AB25 2ZN

**Study participating centre**

**Queen Elizabeth Hospital Birmingham**

University Hospitals Birmingham NHS Foundation Trust  
Mindelsohn Way  
Edgbaston  
Birmingham  
United Kingdom  
B15 2GW

**Study participating centre**

**Cardiff and Vale University Health Board**

Cardiff and Vale UHB Headquarters  
University Hospital of Wales (UHW)  
Heath Park  
Cardiff  
United Kingdom  
CF14 4XW

**Study participating centre**

**Forth Valley Royal Hospital**

NHS Forth Valley  
Stirling Rd  
Larbert  
United Kingdom  
FK5 4WR

**Study participating centre**

**NHS Fife**

Kirkcaldy  
United Kingdom  
KY12 0SU

**Study participating centre**

**Queen Alexandra Hospital**

Portsmouth Hospitals NHS Trust

Southwick Hill Road

Portsmouth

United Kingdom

PO6 3LY

**Study participating centre**

**Glenfield Hospital**

University Hospitals of Leicester NHS Trust

Groby Road

Leicester

United Kingdom

LE3 9QP

**Study participating centre**

**Royal United Hospital**

Royal United Hospitals Bath NHS Foundation Trust

Bath

United Kingdom

BA1 3NG

**Study participating centre**

**University Hospitals North Midlands NHS Trust**

Stoke on Trent

United Kingdom

ST4 6QG

**Study participating centre**

**Sheffield Teaching Hospitals NHS Foundation Trust**

Sheffield

United Kingdom

S10 2JF

**Study participating centre**

**Princess Alexandra Hospital NHS Trust**

Harlow

United Kingdom

CM20 1QX

# Sponsor information

## Organisation

University of Dundee

## Sponsor details

TASC

Level 3

Ninewells Hospital and Medical School

Dundee

Scotland

United Kingdom

DD1 9SY

+44 (0)1382 383900

TASCgovernance@dundee.ac.uk

## Sponsor type

University/education

## Website

<http://www.dundee.ac.uk/>

## ROR

<https://ror.org/03h2bxq36>

## Organisation

NHS Tayside

## Sponsor details

TASC

Level 3

Ninewells Hospital and Medical School

Dundee

Scotland

United Kingdom

DD1 9SY

+44 (0)1382 383900

TASCgovernance@dundee.ac.uk

## Sponsor type

Hospital/treatment centre

## Website

<http://www.nhstayside.scot.nhs.uk/index.htm>

# Funder(s)

## Funder type

Industry

## Funder Name

Insmmed Incorporated

# Results and Publications

## Publication and dissemination plan

Publication will include:

Peer reviewed scientific journals

Conference presentations

Publication on website

Dissemination to participants and public

## Intention to publish date

28/02/2022

## Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication.

## IPD sharing plan summary

Other

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		02/09/2022	09/09/2022	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No