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

Submission date
20/05/2020

Recruitment status
No longer recruiting

Registration date
20/05/2020

Overall study status
Completed

Last Edited
09/09/2022

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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?
Insmed 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)

Contact information

Type(s)
Public

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Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-001643-13

Integrated Research Application System (IRAS)
281986

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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 (0131 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

Study type(s)
Treatment

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

Key secondary outcome(s))
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 ≤ 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

Completion date
28/02/2021

Eligibility

Key inclusion criteria
Current inclusion criteria as of 10/11/2020:

1. Aged ≥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 (SpO2) ≤94% on room air prior to randomization OR
4.4. Requiring supplemental oxygen OR
4.5. Lymphocyte count <1 x 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.

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Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

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 x 109 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

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Date of first enrolment
20/05/2020

Date of final enrolment
31/01/2021

Locations

Countries of recruitment
United Kingdom

England

Scotland

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
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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
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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

ROR
https://ror.org/03h2bxq36

Organisation

NHS Tayside

Funder(s)

Funder type
Industry

Funder Name
Insmed Incorporated

Results and Publications

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?
Results article		02/09/2022	09/09/2022	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes