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Trial of inhaled anti-viral (SNG001) for SARS-CoV-2 (COVID-19) infection

Submission date
06/07/2020

Recruitment status
No longer recruiting

Registration date
21/07/2020

Overall study status
Completed

Last Edited
30/01/2024

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The aim of this study is to test SNG001 (the study medication). SNG001 is an inhaled drug that contains interferon-beta, an antiviral protein that occurs naturally in the body. Interferon-beta has been given as an injection to thousands of patients for other diseases (such as multiple sclerosis), this study is about giving SNG001 by inhalation. By administering SNG001 as an aerosol through a nebuliser directly to the lungs it is hoped that the interferon-beta can boost the lungs' antiviral defences and reduce the severity of illness caused by viruses. Recent research has suggested that interferon-beta if given by inhalation might protect the cells in the lungs from cold and flu viruses in vulnerable patients e.g. patient in hospital and those of advanced age and people with some chronic illnesses.
SARS-CoV-2 is a new type of coronavirus that appeared in China in 2019 that causes COVID-19, an acute lung disease. There are currently no drug treatments proven to help patients who have COVID-19. Due to the nature of the disease and how easily it is spread, it is a global threat and there is a need to assess new treatments which could prevent and effectively treat COVID-19.
It is possible that SNG001 could be given as a treatment to patients with confirmed COVID-19 in order to prevent/limit the worsening of lower respiratory tract illness. Researchers first need to test the study medication to see if it can 'switch on' the antiviral defences in the lungs in a way which would help them to fight viruses. The study medication would be given in addition to the normal medical care that patients should receive.

Who can participate?
1. Patients aged 18 or over who have a confirmed SARS-CoV-2 infection which has caused admission to hospital
2. Patients aged over 65 years old or aged 50 and above and have other illnesses which makes them more susceptible to complications of COVID-19, with a confirmed SARS-CoV-2 infection

What does the study involve?
Between 100 and 600 patients with a confirmed SARS-CoV-2 infection will be enrolled into this study. A study doctor will confirm that patients are eligible to enter the study. Eligible patients, who consent to take part in the study, will be randomly put into one of two treatment groups: one group will be given SNG001 and the other group will be given a placebo (a 'dummy treatment', which looks like the study medicine but does not contain Interferon-beta). The study

medication will be given using a handheld nebuliser once a day for 14 days. Several tests (such as checking temperature) and questionnaires will be conducted by a study nurse throughout the 14 days to assess the effects of the study medication. Once the patient has finished taking the study medication, they will be followed up by the study team the following day and also 14 days after the final treatment dose.
For patients taking part in the study at home, all visits with doctors and nurses will take place in their own home and completed by video call. To take part patients will need to have access to video calling technology such as a laptop, tablet, or mobile phone. If a swab test is required, a testing kit will be sent to the patient's home (if they live in the Southampton area) and guidance on how to carry out a self-swab test will be given by a study nurse.
For patients who live outside the Southampton area, they need to have had a recent positive swab result already which confirms a SARS-CoV-2 infection.
A pulse oximeter (a small device which clips on the patient's finger to measure heart rate and oxygen levels in the blood) and a thermometer will be sent to the patient's home. Daily video calls will take place where a healthcare professional will supervise patients taking the study medication and measuring their pulse, oxygen levels in the blood and temperature. They will also ask patients questions about how they are feeling.
The following will be carried out at different times when the patient sees the study staff:
1. Medical history - the doctor/nurse will ask a number of questions about the patient's health problems
2. SARS-CoV-2 infection history – the doctor/nurse will ask a number of questions about the coronavirus infection the patient currently has
3. Demographics – patient's age, date of birth, sex and race
4. Physical examination (hospital setting only) – the doctor will conduct a full physical examination at least once during the study. Sometimes the doctor may only examine the patient' s chest
5. Questionnaires – there will be several questions that either the doctor/nurse or study staff will ask the patient, or the patient will be asked to complete themselves. These will be about the patient's current health status and how they are feeling
6. Vital signs –temperature, pulse, blood oxygen levels, and in the hospital setting only blood pressure and breathing rate
7. 12-lead ECG (hospital setting only) – a 12-lead ECG will be performed to ensure that the rate and rhythm of the heart is normal
8. Chest x-ray (hospital setting only) – only if assessed as necessary by the doctor

What are the possible benefits and risks of participating?
The potential benefits of taking part in this study are that the information that is gained from this study may lead to the advancement of a treatment for the SARS-CoV-2 (COVID 19) infection, not just in the UK but potentially worldwide. In a research study like this one, every risk or side effect cannot be predicted. Each person's reaction to a test, medication, or procedure may be different. The design of the study has taken into consideration all of the known risks; however, participants may have a side effect or be at risk of symptoms, illnesses and/or complications that could not be predicted by the researchers.
The risks of interferon-beta when given by injection are well known, but the full risks of inhaling interferon-β are not known. However, no safety concerns have been raised in previous studies when this drug was inhaled by asthmatics either in a stable state or when they had a cold. Some of the study medication will go through the lungs into the bloodstream, this is normal but the blood levels would be much lower (about one-tenth) than those found after injection, and this will reduce the chance of some of the side effects listed below for interferon-beta given by injection.
Very common effects (at least 1 in 10 people are affected):
1. Flu-like symptoms - headache, muscle aches, chills or a fever

2. Headache
Common effects (less than 1 in 10 people are affected):
1. Loss of appetite
2. Feeling weak and tired
3. Difficulty sleeping
4. Depression
5. Flushing
6. Runny nose
7. Diarrhoea (loose stools)
8. Feeling or being sick (nausea or vomiting)
9. Numbness or tingling of skin
10. Rash, bruising of the skin
11. Increased sweating, night sweats
12. Pain in your muscles, joints, arms, legs or neck
13. Muscles cramps, stiffness in the joints and muscles
14. Changes to blood tests. Symptoms you might notice are tiredness, repeated infection, unexplained bruising or bleeding.
Uncommon effects (less than 1 in 100 people affected):
1. Hair loss
2. Changes to your monthly period
3. Rare effects (less than 1 in 1,000 people affected)
4. Difficulty breathing

Where is the study run from?
Synairgen Research Ltd (UK)

When is the study starting and how long is it expected to run for?
March 2020 to May 2021

Who is funding the study?
Synairgen Research Ltd (UK)

Who is the main contact?
Southampton Clinical Trials Unit
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Contact information

Type(s)
Public

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Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT04385095

Clinical Trials Information System (CTIS)
2020-001023-14

Integrated Research Application System (IRAS)
281317

Protocol serial number
SG016

Study information

Scientific Title
A randomised double-blind placebo-controlled trial to determine the safety and efficacy of inhaled SNG001 (IFNβ-1a for nebulisation) for the treatment of patients with confirmed SARS-CoV-2 infection

Study objectives
SARS-CoV-2 is a global threat and there is a need to assess new treatments which will prevent and effectively treat severe lower respiratory tract (LRT) illness caused by the SARS-CoV-2. Interferon-beta (IFN-β) driven anti-viral responses have been shown to be compromised /deficient in older people and those with chronic airways diseases. These and other patient groups are at high risk of developing severe LRT illness which can be fatal. The IFN-β deficiency

can be overcome or boosted through the administration of exogenous IFN-β. This has been shown both in vitro, using cells from patients, and in clinical trials using SNG001 (an inhaled IFN-β1a formulation for nebulisation) delivered via a breath-actuated nebuliser. It is believed that SNG001 will rectify the deficiency in the lungs in at-risk patients and prevent worsening or accelerate the recovery of severe LRT illness in COVID-19 patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/03/2010, North West - Haydock Research Ethics Committee (3rd Floor - Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8012; haydock.rec@hra.nhs.uk), ref: 20/NW/0168

Primary study design
Interventional

Study design
Multicentre interventional double-blinded randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
Patients in the hospital setting will be randomised to one of two treatment groups (SNG001 or placebo) in a 1:1 ratio according to a pre-specified randomisation schedule in addition to standard of care. In the home setting, the device will also be included within the randomisation schedule and the patients will be randomised to one of four groups (Ultra/ SNG001, Ultra /placebo, I-neb/SNG001 or I-neb/placebo) in a 1:1:1:1 ratio.

SNG001 nebuliser solution is presented in glass syringes containing 0.65 ml of drug product solution containing 12 MIU/ml of IFN-β1a. The I-neb nebuliser is fitted with a 0.53 ml chamber is filled with the contents of one syringe. The Ultra device is filled with the contents of two syringes. Patients inhale one dose per day for 14 days.

The placebo will be the same formulation as the study medication but without IFN-β1a (i.e. only the excipients of the SNG001 solution) and will be administered once daily via the I-neb or Ultra nebuliser.

Patients are followed up for 14 days (+/- 3 days) after the patient's last dose or when the last dose of study medication would have been administered if dosing was stopped (for example if the patient was ventilated).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Interferon beta-1a

Primary outcome(s)
Change in condition measured using the Ordinal Scale for Clinical Improvement during the dosing period - minimum of 0 (patient is well) to a maximum of 8 (death). Time Frame: day 1 to day 15 daily and on day 28

Key secondary outcome(s)
1. Progression to pneumonia as diagnosed by chest x-ray, if no pneumonia is present at time of enrolment (hospital setting only). Time Frame: Day 1 and Day 15 only if the site has the capabilities to perform a chest x-ray, then this should only also be done when required based on clinical judgement
2. Evolution of pneumonia, as diagnosed by chest x-ray, if pneumonia is present at time of enrolment (optional, hospital setting only). Time Frame: Day 1 and Day 15 only if the site has the capabilities to perform a chest x-ray, then this should only also be done when required based on clinical judgement
3. Time to clinical improvement (hospital setting only), defined as:
3.1. Hospital discharge OR
3.2. National Early Warning Score (NEWS)2 of ≤2 maintained for 24 hours, assessed daily until Day 15 or earlier if discharged
4. Time to clinical improvement (home setting only), Assessed daily up to Day 15 and on Day 28, defined as:
4.1. Temperature ≤37.8 °C AND
4.2. COVID-19 symptoms (breathing, cough, sputum, muscle aches, headache, fatigue, sore throat, loss or change to sense of smell and taste, rhinorrhoea and anorexia) all rated as absent or mild. Measured on a 5-point scale (0=none; 1=mild; 2=moderate; 3=marked; 4=severe)
5. Proportion of patients with clinical improvement as defined in 4 above on Day 7 and End of Treatment (hospital and home setting)
6. NEWS2 assessment of acute-illness severity (hospital setting only). Time Frame: Assessed daily up to Day 15 or earlier if discharged
7. Time to improvement of COVID-19 symptoms (fever, breathing, cough, sputum, muscle aches, headache, fatigue, sore throat, loss or change to sense of smell and/or taste, rhinorrhoea and anorexia) (home setting only). Measured on a 5-point scale (0=none; 1=mild; 2=moderate; 3=marked; 4=severe). Time Frame: Daily up to Day 15 and on Day 28
8. Time to self-reported recovery (home setting only). Yes/No answer to question “Do you feel recovered today?” Time Frame: Daily from Day 2 to Day 15 and on Day 28
9 Self-reported daily rating of overall feeling of wellness (home setting only) using a 10-point scale answer to the question “How well are you feeling today?” (1 is the worst and 10 the best the patient can imagine). Time Frame: Daily until Day 15 and on Day 28
10. Quality of life measured using EQ-5D-5L (home setting only) on Day 1, Day 7, Day 15 and Day 28
11. Changes in daily breathlessness, cough and sputum scale (BCSS) score during the study period (including disaggregated scores). Time Frame: Daily up until Day 15 and on Day 28
12. Virus clearance/load (if samples are available, hospital setting only) on Day 1 to Day 15 optional depending on whether the site has the correct experience/facilities:
12.1. Time to viral clearance measured using a nose or throat swab Day 1 to Day 15
12.2. Viral load measured using a nose or throat swab Day 1 to Day 15
13. Safety and tolerability – vital signs, adverse events and concomitant medications. Time Frame: daily up to Day 15
14. Blood and sputum biomarkers (if samples are available); Time Frame: (blood - hospital setting

only) safety bloods (blood test by venepuncture for full blood count, urea and electrolytes, liver function tests, troponin, C-reactive protein). Day 1 and Day 15 (Day 15 not applicable if discharged). Sputum biomarkers (spontaneous sample) optional daily to Day 15 depending on whether the patient can produce sputum and site has the correct experience/facilities and time. Biomarkers (blood test by venepuncture) optional daily to Day 15 depending whether the site has the correct experience/facilities
15. Contact with health services (home setting only) assessed verbally by daily contact with study team. Time Frame: Occurring at any point from Day 1 to Day 28
16. Consumption of antibiotics (home setting only) assessed verbally by daily contact with study team. Time Frame: Occurring at any point from Day 1 to Day 15

Completion date
31/05/2021

Eligibility

Key inclusion criteria
1.1. Hospital setting: positive virus test for SARS-CoV-2 using RT-PCR, or positive point-of-care viral infection test in the presence of strong clinical suspicion of SARS-CoV-2 infection
1.2. Home setting: positive virus test for SARS-CoV-2 using a molecular assay e.g. RT-PCR in the presence of strong clinical suspicion of SARS-CoV-2 infection
2. Male or female, ≥18 years of age (hospital setting) or ≥50 years of age (home setting) at the time of consent
3.1. Hospital setting: patients admitted to hospital due to the severity of their COVID-19 disease OR
3.2. Home setting: non-hospitalised patients from high-risk groups, defined as ≥65-years of age, or ≥50 years of age and with any of the following risk factors:
3.2.1. Arterial hypertension
3.2.2. Cardiovascular disease
3.2.3. Diabetes mellitus
3.2.4. Chronic lung disease
3.2.5. Chronic kidney disease (eGFR <60 mL/min/1.73m2)
3.2.6. Chronic liver disease
3.2.7. Immunodeficiency due to a serious illness or medication
3.2.8. Cerebrovascular disease
3.2.9. Malignancy (except basal cell carcinoma) diagnosed in the last 5 years
3.2.10. Body Mass Index ≥30
who present with clinical symptoms consistent with COVID-19:
3.2.11. High temperature and/or
3.2.12. New, continuous cough
3.2.13. Loss or change to sense of smell and/or taste
4. Provide informed consent
5.1. Hospital setting: hospitalised female patients must be ≥1 year post-menopausal, surgically sterile, or using an acceptable method of contraception
5.2. Home setting: non-hospitalised female patients must be ≥1 year post-menopausal or surgically sterile

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. > 24 hours after confirmation of SARS-CoV-2 infection by a molecular assay e.g. RT-PCR test (hospital and home settings) or >24 hours after a positive point-of-care viral infection test (hospital setting only). This criterion does not apply to patients in the hospital setting who had their positive RT-PCR test for SARS-CoV-2 performed prior to hospitalisation
2. >96 hours from onset of COVID-19 symptoms (cough and/or fever and/or loss or change to sense of smell and/or taste; home setting only)
3. Any condition, including findings in the patients' medical history or in the pre-randomisation study assessments that in the opinion of the Investigator, constitute a risk or a contraindication for the participation of the patient into the study or that could interfere with the study objectives, conduct or evaluation
4. Current or previous participation in another clinical trial where the patient has received a dose of an Investigational Medicinal Product (IMP) containing small molecules within 30 days or 5 half-lives (whichever is longer) prior to entry into this study or containing biologicals within 3 months prior to entry into this study
5. Ventilated or in intensive care
6. Inability to use a nebuliser with a mouthpiece
7. History of hypersensitivity to natural or recombinant IFN-β or to any of the excipients in the drug preparation
8. Females who are breast-feeding, lactating, pregnant or intending to become pregnant

Date of first enrolment
30/03/2020

Date of final enrolment
30/04/2021

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Study participating centre

Southampton General Hospital
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Study participating centre
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Study participating centre
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Study participating centre

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Sponsor information

Organisation
Synairgen Research Ltd

Funder(s)

Funder type
Industry

Funder Name
Synairgen Research Ltd

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study 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	pilot results in hospitalised patients	12/11/2020	26/11/2020	Yes	No
Results article	at home setting results	19/12/2023	30/01/2024	Yes	No
HRA research summary			26/07/2023	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