

Adaptive COVID-19 treatment trial in the EU & UK

Submission date 11/07/2020	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 24/07/2020	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 06/10/2022	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data

Plain English Summary

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 April 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.

The aim of this study is to assess the safety and effectiveness of new treatments in hospitalized adults diagnosed with COVID-19. This study will test a drug in adult patients who are hospitalized with COVID-19. The drug has been tested before in humans with other diseases. In this study, the researchers would like to make sure that it is safe for use in humans with COVID-19 and see if it can improve patients' health when they are sick with COVID-19. They are studying a drug called remdesivir, which is given as an infusion, which means that it is given through a plastic tube attached to a needle that is put into a vein in the arm.

Who can participate?

Men or non-pregnant women aged 18 and over who are hospitalised with COVID-19 with evidence of COVID-19-related respiratory (lung) disease

What does the study involve?

To find out if remdesivir (the study drug) works, the researchers need to compare it to getting something that does not have the drug in it, something called a placebo. The placebo is an inactive salt solution that looks like the study drug but does not have the drug in it. Using a

placebo is common in research studies. The placebo is also given as an infusion. Some people in the study will get the placebo. All participants will undergo a series of assessments. Safety laboratory tests and blood samples and oropharyngeal (throat) swabs will be obtained on Days 1 (before the infusion) and Days 3, 5, 8, and 11 (while hospitalized). Swabs and blood (serum only) plus safety laboratory tests will be collected on Day 15 and 29 (if the participant attends an in-person visit or is still hospitalized). Participants will be assessed daily while hospitalized. If they are discharged from the hospital, they will have a study visit at Days 15, 22, and 29 as an outpatient. For discharged subjects, it is preferred that the Day 15 and 29 visits are in-person to obtain safety laboratory tests and swab and blood (serum only) samples for secondary research as well as clinical outcome data. However, infection control or other restrictions may limit the ability of the participant to return to the clinic. In this case, Day 15 and 29 visits may be conducted by phone, and only clinical data will be obtained. The Day 22 visit does not have laboratory tests or collection of samples and may also be conducted by phone.

What are the possible benefits and risks of participating?

Remdesivir may or may not improve the clinical outcome of the participants. However, there is a potential benefit to society from their participation in this study resulting from insights gained about the treatment under study as well as the natural history of the disease. While there may not be benefits for an individual participant, there may be benefits to society if a safe, effective treatment can be identified during this global COVID-19 outbreak. Potential risks of participating are those associated with having blood drawn, the IV cannulation, possible reactions to remdesivir, and breach of confidentiality.

Where is the study run from?

Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases (USA)

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

March 2020 to August 2020

Who is funding the study?

Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases (USA)

Who is the main contact?

Prof. Sarah Pett

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Contact information

Type(s)

Scientific

Contact name

Prof Sarah Pett

ORCID ID

<http://orcid.org/0000-0002-4851-4727>

Contact details

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Additional identifiers

EudraCT/CTIS number
2020-001052-18

IRAS number
281800

ClinicalTrials.gov number
NCT04280705

Secondary identifying numbers

DMID Protocol Number: 20-0006, INSIGHT Protocol Number: 010, UPHR - CPMS 45521, IRAS 281800

Study information

Scientific Title

A multicentre, adaptive, randomized blinded controlled trial of the safety and efficacy of investigational therapeutics for the treatment of COVID-19 in hospitalized adults – version for European Union/United Kingdom sites

Acronym

ACTT-EU/UK

Study hypothesis

COVID-19 is a respiratory disease caused by a novel coronavirus (SARS-CoV-2) and causes substantial morbidity and mortality. There is currently no vaccine to prevent infection with SARS-CoV-2 or therapeutic agent to treat COVID-19. This clinical trial is designed to evaluate investigational therapeutics for the treatment of adults hospitalized with COVID-19.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 26/03/2020, South Central - Hampshire B Research Ethics Committee (Previously Southampton B IRB00005934) (Level 3 Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207 104 8045, +44 (0)207 104 8057, +44 (0)207 104 8054; hampshireb.rec@hra.nhs.uk), REC ref: 20/SC/0154

Study design

Multicenter adaptive randomized double-blind placebo-controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet: mrcctu.insightcovid@ucl.ac.uk

Condition

COVID-19 (SARS-CoV-2 infection)

Interventions

Initially, the trial will have two arms and subjects will be randomized to receive either active product or placebo as follows:

1. Remdesivir will be administered as a 200 mg intravenous (IV) loading dose on Day 1, followed by a 100 mg once-daily IV maintenance dose for the duration of the hospitalization up to a 10-day total course.
2. A placebo of normal saline will be given at an equal volume at the same schedule. IV bags of study treatment will be covered to mask the slight color difference between the remdesivir solution and placebo to maintain the study blind.

The study will randomize subjects 1:1 to placebo or investigational product. Randomization will be stratified by site and severity (severe versus mild-moderate). If additional arms are added to or dropped from the trial, randomization will proceed with an equal probability of assignment to each of the remaining arms. As new interventions are added, the protocol will be amended and reviewed by IRB/IEC and applicable regulatory agencies before implementation. Duration of follow-up is 29 days.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Remdesivir

Primary outcome measure

Time to recovery: day of recovery is defined as the first day on which the subject satisfies one of the following three categories from the ordinal scale:

1. Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care
 2. Not hospitalized, limitation on activities and/or requiring home oxygen
 3. Not hospitalized, no limitations on activities
- Measured from Day 1 to Day 29

Secondary outcome measures

1. Clinical status measured using an eight-category ordinal scale from Day 3 to Day 29
2. Cumulative incidence of Grade 3 and 4 clinical and/or laboratory adverse events (AEs) measured using patients' medical records from Day 1 to Day 29
3. Cumulative incidence of serious adverse events (SAEs) measured using patients' medical records from Day 1 to Day 29
4. Duration of hospitalization measured using patients' medical records from Day 1 to Day 29
5. 14-day mortality measured using patients' medical records from Day 1 to Day 15
6. 29-day mortality measured using patients' medical records from Day 1 to Day 29

Overall study start date

17/03/2020

Overall study end date

30/08/2020

Eligibility

Participant inclusion criteria

1. Admitted to a hospital with symptoms suggestive of COVID-19 infection
2. Subject (or legally authorized representative) provides written informed consent prior to initiation of any study procedures
3. Subject (or legally authorized representative) understands and agrees to comply with planned study procedures
4. Male or non-pregnant female adult ≥ 18 years of age at time of enrollment
5. Has laboratory-confirmed SARS-CoV-2 infection as determined by PCR or other commercial or public health assay in any specimen collected < 72 hours prior to randomization. Note – 72 hours is not necessarily time from initial diagnosis. If ≥ 72 hours since positive PCR, the PCR may be repeated to assess eligibility
6. Illness of any duration, and at least one of the following:
 - 6.1. Radiographic infiltrates by imaging (chest x-ray, CT scan, etc.), OR
 - 6.2. Clinical assessment (evidence of rales/crackles on exam) AND $SpO_2 \leq 94\%$ on room air, OR
 - 6.3. Requiring supplemental oxygen, OR
 - 6.4. Requiring mechanical ventilation
7. Women of childbearing potential must agree to either abstinence or use at least one primary form of contraception not including hormonal contraception from the time of screening through Day 29.
8. Agrees to not participate in another clinical trial for the treatment of COVID-19 or SARS-CoV-2 through Day 29

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Initial 400

Total final enrolment

1063

Participant exclusion criteria

1. ALT/AST > 5 times the upper limit of normal
2. Estimated glomerular filtration rate (eGFR) < 50 or requiring dialysis
3. Pregnancy or breastfeeding
4. Anticipated transfer to another hospital which is not a study site within 72 hours
5. Allergy to any study medication

Recruitment start date

31/03/2020

Recruitment end date

30/06/2020

Locations**Countries of recruitment**

Denmark

England

Greece

United Kingdom

Study participating centre**Royal Victoria Infirmary**

Queen Victoria Road

Newcastle upon Tyne

United Kingdom

NE1 4LP

Study participating centre**Royal Sussex County Hospital**

Department of Intensive Care Medicine

Brighton

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BN2 5BE

Study participating centre

St Thomas' Hospital

Directorate of Infection
London
United Kingdom
SE1 7EH

Study participating centre

St. James's University Hospital

Infectious Diseases
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LS9 7TK

Study participating centre

John Radcliffe Hospital

Headington
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OX3 9DU

Study participating centre

AHEPA University Hospital

1st Department of Internal Medicine
Thessaloniki
Greece
54636

Study participating centre

Medical School of Athens University

Evangelismos Hospital
Department of Critical Care and Pulmonary Services
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Sponsor information

Organisation

University of Minnesota

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Sponsor type

University/education

Website

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ROR

<https://ror.org/017zqws13>

Funder(s)

Funder type

Government

Funder Name

Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases

Alternative Name(s)

Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, DMID, NIAID, DMID

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United States of America

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal by September 2020.

Intention to publish date

01/09/2020

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	version 3.0	05/11/2020	14/04/2021	Yes	No
Protocol file		26/05/2020	06/10/2022	No	No
HRA research summary			28/06/2023	No	No