

# Adaptive COVID-19 treatment trial in the EU & UK

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

[mrcctu.insightcovid@ucl.ac.uk](mailto:mrcctu.insightcovid@ucl.ac.uk)

## Contact information

**Type(s)**

Scientific

**Contact name**

Prof Sarah Pett

**ORCID ID**

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

**Contact details**

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## **Additional identifiers**

**ClinicalTrials.gov (NCT)**  
NCT04280705

**Clinical Trials Information System (CTIS)**  
2020-001052-18

**Integrated Research Application System (IRAS)**  
281800

**Central Portfolio Management System (CPMS)**  
45521

**Protocol serial number**  
DMID Protocol Number: 20-0006, INSIGHT Protocol Number: 010, UPHR -

## **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 objectives**  
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

## **Study type(s)**

Treatment

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

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(s)**

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

### **Key secondary outcome(s)**

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

### **Completion date**

30/08/2020

## **Eligibility**

### **Key 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  $\geq 18$  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  $\geq 72$  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<sub>2</sub>  $\leq 94\%$  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

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

**Total final enrolment**

1063

**Key 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

**Date of first enrolment**

31/03/2020

**Date of final enrolment**

30/06/2020

**Locations**

**Countries of recruitment**

United Kingdom

England

Denmark

Greece

**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  
United Kingdom  
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  
Leeds  
United Kingdom  
LS9 7TK

**Study participating centre**  
**John Radcliffe Hospital**  
Headington  
Oxford  
United Kingdom  
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  
Athens  
Greece  
GR-10675

## **Sponsor information**

**Organisation**  
University of Minnesota

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, DMID, NIAID

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

### Location

United States of America

## Results and Publications

### 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?
<a href="#">Results article</a>		05/11/2020	14/04/2021	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Protocol file</a>	version 3.0	26/05/2020	06/10/2022	No	No