ISRCTN13035264 https://doi.org/10.1186/ISRCTN13035264

Adaptive COVID-19 treatment trial in the EU & UK

Submission date
11/07/2020

Recruitment status
No longer recruiting

Registration date
24/07/2020

Overall study status
Completed

Last Edited
06/10/2022

Condition category
Infections and Infestations

[_] Prospectively registered
[X] 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 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

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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

Primary study design
Interventional

Study design
Multicenter adaptive randomized double-blind placebo-controlled trial

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 ≥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 SpO2 ≤ 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?
Results article		05/11/2020	14/04/2021	Yes	No
HRA research summary			28/06/2023	No	No
Protocol file	version 3.0	26/05/2020	06/10/2022	No	No