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Adalimumab for coronavirus in community care

Submission date
19/08/2020

Recruitment status
Stopped

Registration date
20/08/2020

Overall study status
Stopped

Last Edited
20/10/2021

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Coronavirus-induced disease (COVID-19) is a global health emergency. In a few months millions of people around the world have been infected by the virus and nearly 50,000 patients have died in the UK alone (July 2020). The virus enters the body through the lungs and causes mild shortness of breath, cough and fever in the majority of cases. However, for reasons that remain unclear, in certain patients the disease can progress to severe respiratory failure, which may be fatal. This does not occur immediately but seems to progress over 7-10 days from first developing symptoms of COVID-19.
Recently, a commonly available drug, dexamethasone has been shown to reduce mortality in patients with the most severe disease, but there remains unmet need for a treatment that prevents progression to severe disease.
The outcomes of residents of care homes have been particularly poor during this pandemic; infection rates have been high and many have died. Many of these residents enjoy a good quality of life but are frail and may not be suitable for intensive care therapy. There is a pressing need for an effective treatment to prevent respiratory failure or death in these patients.
Across the UK, several NHS Trusts have set up 'Hospital at Home' teams. These teams are there to provide healthcare to individuals at home (whether that is a private home or a residential care home) as an alternative to hospital admission. These teams work like a hospital ward team and have regular multi-disciplinary meetings where they discuss the patients they are looking after. The service is designed to give patients extra support so that they are not admitted to hospital. Hospital at home teams can include doctors, nurses, paramedics and health care assistants. When the team arrive to see an individual they can bring with them equipment that helps with the diagnosis of conditions such as blood testing machines and they also carry some of the drugs routinely given at a hospital.

The hospital at home care pathway therefore provides an unique means to reach patients in the community that are suspected of having COVID-19 and starting to treat them early thus hopefully avoiding admission to hospital due to getting worse.

Who can participate?
Adults, 18 years of age or older, assessed in by Hospital at Home or similar system in the UK who have confirmed COVID-19.

What does the study involve?
The AVID-CC Trial will investigate whether giving a drug called adalimumab (which is an anti-inflammatory drug that blocks a chemical called Tumour Necrosis Factor (TNF)) to patients outside hospital with COVID-19 who are at increased risk of worsening can prevent progression to respiratory failure or death.
Anti-TNF antibody drugs have proven effective in a wide range of inflammatory conditions, and they seem to play an important role in preventing the triggering of severe inflammation, as is seen in conditions such as COVID-19.
In addition blood will be collected with the aim of identifying markers that predict those that may be at increased risk and those that respond to treatment. This may inform the design of future clinical studies which may involve combinations of treatments.
Those participating will either receive adalimumab in addition to standard care for COVID-19 in the community or standard care alone. Participants will be asked to complete questionnaires and give blood samples from randomisation to 120 days at set time points.

What are the possible benefits and risks of participating?
The information from this study we hope will answer the question of whether Adalimumab is a drug that should be given to or not given to patients who are not in hospital who have tested positive for COVID-19. We cannot promise the be shown to be positive, but the information we get has the potential to be of benefit to those who start to show COVID-19 symptoms.
Although Adalimumab has been widely used in people who are pregnant without evidence of harm to mother or baby, in this study women who are pregnant will not be able to participate in the study. Please note, women of child bearing potential, need to use effective contraception during the study and for 5 months afterwards.

People sometimes feel uncomfortable answering certain questions about their health, or may be unable to answer. If you people feel uncomfortable at any point, then they do not have to answer the questions.

Where is the study run from?
The Oxford Clinical Trials Research Unit (OCTRU) based at the University of Oxford (UK)

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

Who is funding the study?
The Wellcome Trust (UK)

Who is the main contact?
The AVID-CC trial manager, avid-cc@ndorms.ox.ac.uk

Study website
https://avid-cc.octru.ox.ac.uk/

Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number
2020-003628-18

IRAS number
287434

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 287434

Study information

Scientific Title
Adalimumab in COVID-19 to prevent respiratory failure in community care (AVID-CC): A randomised controlled trial

Acronym
AVID-CC

Study objectives
Use of adalimumab up to 2 times in the first 14 days from randomisation is effective in preventing and/or reducing the severity of COVID-19 disease at 28 days post randomisation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/09/2020, South Central - Berkshire Research Ethics Committee (Bristol REC Centre, Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT; +44 (0)207 104 8224; berkshire.rec@hra.nhs.uk), ref: 20/SC/0352

Study design
Multi-centre interventional open label randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

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

Interventions
Intervention: Adalimumab

Regimen 1. A loading dose of 80 mg adalimumab given as two injections of 40 mg at separate sites in the thigh or abdomen. Subjects with persistent symptoms and signs may receive a second dose of adalimumab 40 mg after 14 days.

Regimen 2. A loading dose of 160 mg adalimumab given as four injections of 40 mg at separate sites in the thigh or abdomen. Subjects with persistent symptoms and signs may receive a second dose of adalimumab 80 mg after 14 days.

This is in addition to standard care as per local Hospital at Home network treatment pathways.

Note: The second regimen will start recruitment following a preliminary assessment of safety of the first regimen (25 subjects randomised to regimen 1).

Comparator: Standard care as per local treatment pathways for those with confirmed COVID-19 being managed in the community.

Participants will be followed up for up to 120 days.

Eligible patients will be randomised using the centralised validated computer randomisation program through a secure (encrypted) web-based service, RRAMP (https://rramp.octru.ox.ac.uk), provided by the Oxford Clinical Trials Research Unit (OCTRU), accessed via the study's RedCap instance, with a minimisation algorithm to ensure balanced allocation across treatment groups, (incorporating a non-deterministic random element) to include age, gender and presence of metabolic or cardiovascular co-morbidities in a 1:1 ratio to either adalimumab (2 regimens) with standard usual care or standard usual care. Within the adalimumab arm, following the review of the initial 25 patients who will receive regimen one, patients within adalimumab will be randomly allocated 1:1 to the first or the second dosing regimen

Intervention Type

Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Adalimumab administered as Hyrimoz

Primary outcome measure
Rate of progression to severe disease as defined by severe illness, or critical illness, or death from any cause in community care patients with COVID-19 at 28 days from randomisation measured using patient records

Secondary outcome measures
Recorded out to 120 days post randomisation using patient records:
1. Serious Adverse Events
2. Adverse events (frequency and severity)
3. Clinical status (9 point ordinal scale)
4. COVID symptom score measured using COVID-19 Core Outcome Set scales
5. Admission to secondary care hospital, ICU or HDU
6. Discharge from secondary care hospital
7. Secondary care hospital assessment without admission
8. Degree of dependency measured by the Barthel scale
9. Frailty measured using Clinical Frailty Scale
10. Incidence and duration of delirium (4AT score)
11. Incidence of venous thromboembolism and acute kidney injury
12. Frequency of prescription of antibiotics

Overall study start date
01/07/2020

Completion date
31/12/2021

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Aged ≥18 years
2. Confirmed SARS-CoV-2 infection based on a validated test
3. CRP >50 mg/l or lymphopaenia (<1.5 x 10(9)/l) or neutrophilia (>7.5 x 10(9)/l)
4. Oxygen saturation >93% on air (pulse oximeter)
Note: Point of care testing and the associated results are acceptable for assessment of eligibility

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
750

Total final enrolment
0

Key exclusion criteria
1. Subject is considered to be in their last few weeks of life prior to this acute illness
2. Clinical frailty score of 8 or 9 prior to this acute illness
3. History of haematopoietic stem cell transplant or solid organ transplant
4. Chronic obstructive pulmonary disease (COPD) on long term oxygen therapy (Subjects with FEV1 known to be <50% will also be excluded)
5. Concomitant use of DMARDs (including csDMARDs, tsDMARDs and bDMARDs) or other immuno-suppressants
6. Previous malignancy and lymphoproliferative disorders (within the last 5 years) with the exception of stable prostate cancer and basal cell carcinoma
7. Current participation in another therapeutic interventional clinical study for COVID-19
8. De-myelinating disease
9. Known to be co-infected with Hepatitis B Virus, HIV
10. Severe hepatic impairment
11. Acute Kidney Injury Stage 3 (NHS England Acute Kidney Injury algorithm)
12. Patients with tuberculosis or other severe infections such as (non-COVID-19) sepsis, abscesses, fungal superinfection and opportunistic infections requiring treatment.
13. Moderate or severe heart failure (NYHA class III/IV)
14. Treatment with anti-TNF drug in past 180 days (9 half lives of the drug)
15. Pregnancy
16. Lactating females
17. Women of childbearing potential who are unwilling to use effective contraception (i.e. barrier, oral contraceptive pill, implanted contraception, or previous hysterectomy, bilateral oophorectomy) for the study and 5 months afterwards

Date of first enrolment
20/10/2020

Date of final enrolment
30/09/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Headley Way
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation
University of Oxford

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Joint Research Office, 1st Floor
Boundary Brook House
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OX3 7LQ
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Sponsor type
University/education

Website
https://researchsupport.admin.ox.ac.uk/ctrg

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name

Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Publications will acknowledge the funders with the following text: The research was funded by the Wellcome Trust (221575/Z/20/Z) and Sandoz. The study drug is initially being provided free-of-charge by Sandoz, who had no part in the study design, conduct or analysis.

The publication policy will be implemented taking into account the principles of research transparency. The Trial Management Group will be responsible for drafting the main reports from the study and for review of any other reports. In general, papers initiated by the Group (including the primary manuscript) will be written in the name of the AVID-CC protocol, with individual investigators named personally at the end of the report (or, to comply with journal requirements, in web-based material posted with the report).

This trial is a response to the public health emergency of COVID-19. Consistent with the statement by Wellcome Trust and other leading research institutions we will:
• Seek to publish the clinical findings of the study in a peer reviewed journal as soon as possible after they are available
• Make peer-reviewed research publications resulting from this work available through open access
• Share the research findings with the WHO upon journal submission
• Make research findings available via preprint servers before journal publication
• Data generated by this project will be deposited, where possible and appropriate, in sustainable, community databases (e.g. Transmart, Zenodo, FlowRepository) along with appropriate metadata to promote their findability, accessibility, interoperability and reusability. We will actively encourage access to the clinical data. Access will not be unreasonably withheld but we will require that proposers provide a robust analysis and dissemination plan prior to accessing the data.

In addition, results will be uploaded to the European Clinical Trial (EudraCT) Database within 6 months of the end of trial declaration by the CI or their delegate.

Intention to publish date
01/06/2022

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a publically available repository.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No