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Preventative treatment for patients at risk of COVID-19 infection (PROTECT)

Submission date	Recruitment status	[X] Prospectively registered
24/04/2020	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
14/05/2020	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
11/04/2024	Infections and Infestations	[_] Record updated in last year

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 March 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.

Currently, there are no drugs proven to treat or delay the progression of COVID-19 and no vaccine is yet available. Efforts are underway to repurpose established drugs with well-understood drug interactions and safety profiles. A number of clinical trials have been established at great speed following the onset of the pandemic, but none of these is enrolling participants with significantly reduced kidney function and/or receiving certain kinds of immunosuppressive medicines such as solid organ transplant recipients. Patients receiving in-centre dialysis are at extremely high risk from COVID-19, particularly as they are unable to self-isolate.

The PROTECT trial aims to enrol patients at particularly high risk of COVID-19 and its complications (such as kidney dialysis patients, vasculitis, and transplant patients), seeking to test treatments that either might prevent the disease from occurring or may reduce the number of cases where the disease becomes serious or life-threatening.

Dialysis is a procedure to remove waste products and excess fluid from the blood when the kidneys stop working properly. It often involves diverting blood to a machine to be cleaned.

Vasculitis is inflammation of blood vessels. It causes changes in the blood vessel walls, including thickening, weakening, narrowing or scarring. These changes can restrict blood flow, resulting in organ and tissue damage.

Organ transplantation is a medical procedure in which an organ is removed from one body and placed in the body of a recipient, to replace a damaged or missing organ. Transplant recipients must take medication to suppress the immune system which puts them at risk of infection.

Who can participate?
Adults over 18 years, in a vulnerable population (dialysis, vasculitis, or transplant) patients with no symptoms of or confirmed COVID-19 diagnosis.

What does the study involve?
Patients will be randomised to receive either oral hydroxychloroquine (HCQ) or standard care. HCQ is a widely used anti-malarial drug which has an effect on the immune system and may as an anti-viral agent in this setting.
The PROTECT study has been designed to place the minimum burden on patients, and on the healthcare workers looking after them at this time. They will not have to attend the hospital for any extra study visits but will be asked to complete follow-up questionnaires. There is also a small chance that they may experience one of the side effects of HQC listed in the patient information sheet.

What are the possible benefits and risks of participating?
There is no guarantee that patients will benefit from taking part in this trial. They may be protected from COVID-19 by HCQ, Niclosamide, but it is also possible that HCQ may not protect them from COVID-19. The researchers do not yet know if hydroxychloroquine will be an effective medication for these patients. However, information collected as part of their participation in this trial will help other people in the future. If successful, this trial will reduce the burden of infection amongst high-risk patient groups, in a time-efficient and cost-effective manner, and help to ease the pressures on an already strained healthcare system.

Where is the study run from?
Addenbrookes Hospital (UK)

When is the study starting and how long is it expected to run for?
May 2020 to May 2025

Who is funding the study?
April Trust (UK)

Who is the main contact?
Dr. Rona Smith, add-tr.protect@nhs.net
Mr. Francis Dowling, add-tr.protect@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Thomas Hiemstra

ORCID ID
https://orcid.org/0000-0002-2115-8689

Contact details
Cambridge Clinical Trials Unit
Box 401 Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ
+44 (0)1223 336817
add-tr.protect@nhs.net

Type(s)
Public

Contact name
Dr Kerry Brusby

Contact details
Cambridge Clinical Trials Unit
Box 401 Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ
+44 (0)1223 25 4472
add-tr.protect@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
2020-004144-28

Integrated Research Application System (IRAS)
288652

ClinicalTrials.gov (NCT)
NCT04870333

Protocol serial number
Current Study CCTU0307, IRAS 288652; Previous Study CCTU0307, IRAS 282317

Study information

Scientific Title

PROphylaxis for paTiEnts at risk of COVID-19 infecTion (PROTECT)

Acronym
PROTECT V

Study objectives
Current study hypothesis as of 05/09/2023 (updated 12/03/2024):

The use of intravenous Sotrovimab prophylaxis in at risk patients population (i.e. dialysis, vasculitis, glomerulonephritis, and kidney and organ transplant patients, primary immunodeficiency, oncology, automimmune/inflammatory disease patients, and those currently receiving immunosuppression) and a confirmed COVID-19 infection in this at-risk population compared to standard care.

Previous study hypothesis as of 24/11/2020 (updated 12/03/2024):

The use of intranasal Niclosamide prophylaxix against SARS-CoV2 infection in at risk patients (i.e. Dialysis, Vasculitis, glomerulonephritis and kidney transplant patients) populations at particularly high risk of COVID-19 and a confirmed COVID-19 infection in this at-risk population compared to standard care.

Previous study hypothesis:
The use of hydroxychloroquine (HCQ) prophylaxis in at risk patients (i.e. haemodialysis, vasculitis, and transplant patients) will increase the time to confirmed COVID-19 infection in this at-risk population compared to standard care.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 24/11/2020, South Central Berkshire Research Ethics Committee (Bristol Research Ethics Committee Centre, Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 020 7104 8057; berkshire.rec@hra.nhs.uk), ref: 20/SC/0403

2. approved 02/06/2020, East of England - Cambridge East Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8102; CambridgeEast.REC@hra.nhs.uk), ref: 20/EE/0146

3. approved 23/10/2020, South Central - South Central Berkshire Research Ethics Committee (Bristol REC Centre, Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 (0)207 104 8057; Berkshire.REC@hra.nhs.uk), ref: 20/SC/0403

Study design
Open-label multi-centre randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection) in dialysis, vasculitis, and kidney transplant patients

Interventions
Current Intervention (04/01/2022) (updated 12/03/2024):

Patients will be randomised on 1:1 to receive either a single Intravenous Sotrovimab or standard care (placebo). Randomisation will be carried out using a validated bespoke automated randomisation system. Randomisation will be stratified by PROTECT V sub-group, age and site. Dosing: A 2g single infusion.

Niclosamide (17/12/2020) (updated 12/03/2024):

Patients will be randomised on 1:1 to receive either Nasal Niclosamide or standard care (placebo). Randomisation will be carried out using a validated bespoke automated randomisation system. Randomisation will be stratified by PROTECT V sub-group, age and site. Dosing: 1.4mg per nostril twice daily approximately 12 hours apart. Total daily dose of 5.6mg niclosamide ethanolamine salt

Previous Intervention:

Patients will be randomised to receive either 1:1 oral hydroxychloroquine (HCQ) or standard care (no HCQ). Randomisation will be carried out using a validated bespoke automated randomisation system. Randomisation will be stratified by PROTECT sub-group, age and centre.

Haemodialysis subgroup
Dosing: 600 mg per week given as 200 mg three times per week after each haemodialysis session for 6 months

Vasculitis and transplant subgroups
Dosing: 800 mg for first 2 days followed by 400 mg once a week for 6 months

Duration of follow up (all subgroups):
Until the end of the trial, on average 6 months

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Niclosamide, sotrovimab (current study), hydroxychloroquine sulfate (previous study)

Primary outcome(s)
Time to confirmed COVID-19 diagnosis via online questionnaires at 6 weekly intervals

Key secondary outcome(s))
Duration and severity of illness (including mortality) collected through linkage to medical databases and through review of medical records.

Completion date
03/05/2025

Eligibility

Key inclusion criteria
1.1. Dialysis patients receiving in-centre haemodialysis, or
1.2. Diagnosis of vasculitis (according to Chapel Hill Consensus Conference 2012 definitions) and have received immunosuppression (including prednisolone ≥5 mg daily and/or an immunosuppressive agent (cyclophosphamide (oral or IV), rituximab, azathioprine, MMF, methotrexate, tociluzumab, alemtuzumab, abatacept, leflunomide) in the last 3 years, or
1.3. Transplant patients that have a functional kidney transplant (updated 15/05/2020, previously: Transplant patients)
2. Aged at least 18 years
3. No previous confirmed COVID-19 diagnosis
4. No symptoms highly suggestive of COVID-19 infection at screening or since 1st March 2020

Additional Inclusion Criteria (added 05/09/2023) (updated 12/03/2024):

5. Be a member of an immunocompromised population, which includes but is not limited to those groups listed in the core protocol as well as the following:
5.1. Primary immunodeficiency
5.2. Any Oncology, Haematology-Oncology or Haematology patient who is currently receiving or has received chemotherapy or who is immunocompromised as a result of their disease or treatment
5.3. Have a diagnosis of an autoimmune/inflammatory disease currently receiving immunosuppression including those individuals currently on Prednisolone ≥20mg daily for at least 4 weeks. Those who have received Rituximab or Alemtuzumab within the last 12 months would also be eligible.
5.4. Solid organ and haematopoietic stem cell transplant recipients

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Inability to provide informed consent
2. Hypersensitivity reaction to hydroxychloroquine, chloroquine or 4-aminoquinolines
3. Contraindication to taking hydroxychloroquine as prophylaxis e.g known epilepsy

4. Already taking chloroquine, hydroxychloroquine or 4-aminoquinolines
5. History of any retinopathy including diabetic retinopathy requiring laser therapy
6. Taking medications which are contra-indicated alongside HCQ - digoxin, halofantrine, amiodarone, moxifloxacin, cyclosporin, mefloquine, praziquantel
7. Known history of prolonged QTc
8. eGFR <15 ml/min
9. Multi-organ transplant recipient (added 15/05/2020)

Additional Exclusion Criteria (added 05/09/2023) (updated 12/03/2024):
In addition to the core exclusion criteria in the master protocol, the presence of any of the following will preclude participant inclusion:

10. If in the opinion of the PI it is not in the best interests of the participant to take part in the study - for example due to limited life expectancy (≤12 months) due to pre-existing co-morbidities
11. History of hypersensitivity reaction to sotrovimab, one of its excipients or any other monoclonal antibody targeting SARS CoV-2
12. History of receiving any monoclonal antibody targeting SARS CoV-2 within the last 6 months
13. Admission to hospital for acute, unplanned care at the time of randomisation or in the two weeks prior to screening
14. History of receiving chimeric antigen receptor T-cell (CAR-T) therapy less than 4 weeks prior to consenting to take part in the study

Date of first enrolment
01/10/2020

Date of final enrolment
01/12/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Addenbrookes Hospital
Cambridge University Hospitals NHS Foundation Trust
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre

Gloucestershire Hospitals Nhs Foundation Trust
Trust HQ
Alexandra House
Cheltenham
United Kingdom
GL53 7AN

Study participating centre
Shrewsbury And Telford Hospital Nhs Trust
Mytton Oak Road
Shrewsbury
United Kingdom
SY3 8XQ

Study participating centre
Basildon and Thurrock University Hospital
Nethermayne
Basildon
United Kingdom
SS16 5NL

Study participating centre
Kent & Canterbury Hospital
East Kent Hospitals University Nhs Foundation Trust
Ethelbert Road
Canterbury
United Kingdom
CT1 3NG

Study participating centre
Nottingham University Hospitals NHS Trust
Trust Headquarters
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Royal Stoke University Hospital
Newcastle Road

Stoke-on-Trent
United Kingdom
ST4 6QG

Study participating centre
Bradford Royal Infirmary
Bradford Teaching Hospitals NHS Foundation Trust
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
Northern General Hospital
Sheffield Teaching Hospitals NHS Foundation Trust
Herries Road
Sheffield
South Yorkshire
Sheffield
United Kingdom
S5 7AU

Study participating centre
The Royal London Hospital
Whitechapel Road
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Imperial College Healthcare Nhs Trust
The Bays
St. Marys Hospital
South Wharf Road
London
United Kingdom
W2 1BL

Study participating centre

St George's Hospital
St George's University Hospitals Nhs Foundation Trust
Blackshaw Road
Tooting
London
United Kingdom
SW17 0QT

Study participating centre
Royal Liverpool University Hospital
Liverpool University Hospitals Nhs Foundation Trust
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
East Surrey Hospital
Surrey And Sussex Healthcare Nhs Trust
Canada Avenue
Redhill
United Kingdom
RH1 5RH

Study participating centre
Salford Royal
Salford Royal Nhs Foundation Trust
Stott Lane
Salford
United Kingdom
M6 8HD

Study participating centre
Sunderland Royal Hospital
South Tyneside And Sunderland Nhs Foundation Trust
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre

Royal Derby Hospital
University Hospitals Of Derby And Burton Nhs Foundation Trust
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
St Helier Hospital
Epsom And St Helier University Hospitals Nhs Trust
Wrythe Lane
Carshalton
United Kingdom
SM5 1AA

Study participating centre
NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
King's College Hospital Nhs Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
NHS Tayside
Kings Croos
Clepington Road
Dundee
United Kingdom
DD3 8EA

Study participating centre

Queen Alexandra Hospital
Portsmouth Hospitals Nhs Trust
Southwick Hill Road
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
Leicester Royal Infirmary
University Hospitals of Leicester Nhs Trust
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Freeman Hospital
The Newcastle Upon Tyne Hospitals Nhs Foundation Trust
Freeman Road
High Heaton
Newcastle-upon-tyne
United Kingdom
NE7 7DN

Study participating centre
Doncaster Royal Infirmary
Doncaster and Bassetlaw Teaching Hospitals Nhs Foundation Trust
Armthorpe Road
Doncaster
United Kingdom
DN2 5LT

Study participating centre
Royal Devon & Exeter Hospital
Royal Devon and Exeter Nhs Foundation Trust
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre

NHS Lanarkshire
14 Beckford Street
Hamilton
United Kingdom
ML3 0TA

Study participating centre
Arrowe Park Hospital
Wirral University Teaching Hospital Nhs Foundation Trust
Arrowe Park Road
Upton
Wirral
United Kingdom
CH49 5PE

Study participating centre
Southmead Hospital
North Bristol Nhs Trust
Southmead Road
Westbury-on-trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
Royal Preston Hospital
Lancashire Teaching Hospitals Nhs Foundation Trust
Sharoe Green Lane
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
Royal Berkshire Hospital
Royal Berkshire Nhs Foundation Trust
London Road
Reading
United Kingdom
RG1 5AN

Study participating centre
New Cross Hospital
The Royal Wolverhampton Nhs Trust
Wolverhampton Road
Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Torbay Hospital
Torbay and South Devon Nhs Foundation Trust
Newton Road
Torquay
United Kingdom
TQ2 7AA

Study participating centre
Norfolk And Norwich University Hospitals Nhs Foundation Trust
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre
Royal Free Hospital
Royal Free London Nhs Foundation Trust
Pond Street
London
United Kingdom
NW3 2QG

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Organisation
University of Cambridge

ROR
https://ror.org/013meh722

Funder(s)

Funder type
Charity

Funder Name
April Trust

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available on reasonable request from add-tr.protect@nhs.net

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	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