

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

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| <b>Submission date</b><br>24/04/2020   | <b>Recruitment status</b><br>No longer recruiting        | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol            |
| <b>Registration date</b><br>14/05/2020 | <b>Overall study status</b><br>Completed                 | <input type="checkbox"/> Statistical analysis plan<br><input type="checkbox"/> Results                       |
| <b>Last Edited</b><br>11/04/2024       | <b>Condition category</b><br>Infections and Infestations | <input type="checkbox"/> Individual participant data<br><input type="checkbox"/> 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](mailto:add-tr.protect@nhs.net)

Mr. Francis Dowling, [add-tr.protect@nhs.net](mailto:add-tr.protect@nhs.net)

**Study website**

[https://www.camcovidtrials.net/trials/view,protect\\_50.htm](https://www.camcovidtrials.net/trials/view,protect_50.htm)

## Contact information

**Type(s)**

Scientific

**Contact name**

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**Contact details**

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CB2 0QQ  
+44 (0)1223 336817  
[add-tr.protect@nhs.net](mailto:add-tr.protect@nhs.net)

**Type(s)**

Public

**Contact name**

Dr Kerry Brusby

**Contact details**

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CB2 0QQ  
+44 (0)1223 25 4472  
[add-tr.protect@nhs.net](mailto:add-tr.protect@nhs.net)

**Additional identifiers****EudraCT/CTIS number**

2020-004144-28

**IRAS number**

288652

**ClinicalTrials.gov number**

NCT04870333

**Secondary identifying numbers**

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 prophylaxis 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

## **Secondary study design**

Randomised controlled trial

## **Study setting(s)**

Hospital

## **Study type(s)**

Prevention

## **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) 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 measure**

Time to confirmed COVID-19 diagnosis via online questionnaires at 6 weekly intervals

## **Secondary outcome measures**

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

## **Overall study start date**

03/04/2020

## **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  $\geq 5$  mg daily and/or an immunosuppressive agent (cyclophosphamide (oral or IV), rituximab, azathioprine, MMF, methotrexate, tocilizumab, 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  $\geq 20$ mg 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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

5000

**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 ( $\leq 12$  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**

England

Scotland

United Kingdom

**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  
Cleington 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

### Sponsor details

Hills Road  
Cambridge  
England  
United Kingdom  
CB2 0QQ  
+44 (0)1223 254472  
cctu@addenbrookes.nhs.uk

### Sponsor type

Hospital/treatment centre

### Website

<http://www.cuh.org.uk/>

### ROR

<https://ror.org/04v54gj93>

### Organisation

University of Cambridge

### Sponsor details

Trinity Lane  
Cambridge  
England  
United Kingdom  
CB2 1TN  
+44 (0)1223 337733  
researchgovernance@medschl.cam.ac.uk

### Sponsor type

University/education

### Website

<http://www.cam.ac.uk/>

ROR

<https://ror.org/013meh722>

## Funder(s)

### Funder type

Charity

### Funder Name

April Trust

## Results and Publications

### Publication and dissemination plan

All publications will be approved by the PROTECT steering group. Reporting of results will be through publication of manuscripts in peer-reviewed journals and oral or poster presentations at relevant National or International meetings. As COVID-19 represents an emerging challenge, interim analyses may be made available via pre-print repositories ahead of publication in peer-reviewed journals or meetings. Audit datasets will be disseminated to relevant organisations with the agreement of the PROTECT steering group.

Important findings may be communicated through local or National media as approved by the PROTECT steering group and Sponsor Communications teams.

All publications will be approved by the PROTECT SG. Reporting of results will be through publication of manuscripts in peer-reviewed journals and oral or poster presentations at relevant National or International meetings.

As COVID-19 represents an emerging challenge, interim analyses may be made available via pre-print repositories ahead of publication in peer-reviewed journals or meetings.

Important findings may be communicated through local or National media as approved by the PROTECT steering group and Sponsor Communications teams.

### Intention to publish date

01/12/2025

### 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](mailto: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? |
|--------------------------------------|---------|--------------|------------|----------------|-----------------|
| <a href="#">HRA research summary</a> |         |              | 28/06/2023 | No             | No              |