

# A therapeutic study in pre-ICU patients admitted with coronavirus using repurposed drugs

<b>Submission date</b>	<b>Recruitment status</b>	<input type="checkbox"/> Prospectively registered
15/05/2020	No longer recruiting	<input checked="" type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input type="checkbox"/> Statistical analysis plan
15/05/2020	Completed	<input checked="" type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
05/03/2024	Infections and Infestations	

## 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.

Current knowledge about severe COVID-19 related disease suggests that patients develop an over activation of their immune system in response to the infection, which may lead to organ. Several medications licensed for patients with autoimmune disease can be used to prevent such over activation of the immune response.

This trial plans to recruit patients at an early stage in the disease course, around early infection and when the patient is starting to show mild lung complications. The purpose is to prevent organ damage and reduce the need to transfer patients to ICU and for ventilated breathing support.

## Who can participate?

Adults over 18 years, strongly suspected to have a COVID-19 related disease (with or without a positive COVID-19 test), who are suitable candidates for the intervention.

## What does the study involve?

Participants will be randomly allocated to receive Baricitinib in addition to standard of care, or Ravulizumab in addition to standard of care, or standard of care only. Participants will be monitored for up to 14 days with follow up visits at day 28 and day 90 after the first dosing visit.

## What are the possible benefits and risks of participating?

There are no known benefits of participating in this trial.

The effect of the drugs will be analysed during the trial to make efficient decisions about efficacy and futility (e.g. lack of efficacy and risk of harm) of the trial treatments. This enables us to stop recruiting if any serious risks arise.

## 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 October 2021

## Who is funding the study?

1. Eli Lilly and Company UK Ltd.
2. Alexion Pharmaceuticals UK

## Who is the main contact?

Unfortunately, this study is not recruiting public volunteers at this time. This is because the research isn't ready for volunteers yet or the researchers are directly identifying volunteers in certain areas or hospitals. Please do not contact the research team as they will not be able to respond. For more information about COVID-19 research, visit the Be Part of Research homepage (<https://bepartofresearch.nihr.ac.uk/>).

# Contact information

## Type(s)

Scientific

## Contact name

Dr Joseph Cherian

## ORCID ID

<https://orcid.org/0000-0001-6921-1592>

## Contact details

Cambridge University Hospitals NHS Trust/Univ of Cambridge  
Box 110, Level 3

ACCI Building  
Cambridge University Hospitals NHS FT  
Hills Rd  
Cambridge  
United Kingdom

CB2 0QQ  
+44 (0)1223 336517  
eh560@medschl.cam.ac.uk

**Type(s)**  
Public

**Contact name**  
Miss Elena Hernan Sancho

**Contact details**  
Cambridge Clinical Trials Unit  
Cambridge University Hospitals NHS Foundation Trust, Addenbrooke's Hospital  
Cambridge  
United Kingdom  
CB2 0QQ  
+44 (0)1223 349132  
cuh.cctu@nhs.net

## Additional identifiers

**Clinical Trials Information System (CTIS)**  
2020-001354-22

**Integrated Research Application System (IRAS)**  
282213

**ClinicalTrials.gov (NCT)**  
NCT04390464

**Protocol serial number**  
CCTU0303; IRAS 282213

## Study information

**Scientific Title**  
multi-Arm Therapeutic study in pre-ICU patients admitted with Covid-19 – Repurposed Drugs (TACTIC-R)

**Acronym**  
TACTIC-R

### Study objectives

1. Immune modulatory therapy is superior to standard of care alone
2. Reduction of exaggerated host immune response to COVID-19 in patients at late stage 1/early stage 2 disease, reduces the composite of progression of these patients to organ failure or death and also reduces late sequelae of infection
3. Clinical and biochemical markers can be used to stratify each patient to an effective therapeutic agent and can report early on efficacy of the therapeutic approach

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Approved 04/05/2020, East of England - Cambridge Central Research Ethics Committee (Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8388; cambridgecentral.rec@hra.nhs.uk), ref: 20/EE/0135

## **Study design**

Randomized parallel arm open-label multicentre Phase IV platform trial

## **Primary study design**

Interventional

## **Study type(s)**

Treatment

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

Late stage 1/stage 2 COVID-19-related disease, COVID-19 (SARS-CoV-2 infection)

## **Interventions**

Eligible patients will be randomised to receive 1:1:1 to one of the following treatment arms (each in addition to standard of care (SoC))

Arm 1: Baricitinib oral tablets (4mg OD) in addition to standard of care

Arm 2: Ravulizumab intravenous infusion (single dose, weight-based dosing) in addition to standard of care

Arm 3: Standard of care

Randomisation will be carried out using a validated central automated web-based randomisation system.

Arm 1 Participants will be given 4mg of Baricitinib PO (2 x 2mg tablets, once daily) on days 1-14 PO.

Dose adjustments for age and renal function.

Arm 2 Participants will receive Ravulizumab as a single intravenous infusion, Ravulizumab weight-based dosing regimen:

Body weight range (kg) Dose (mg)

≥ 40 to < 60 2,400

≥ 60 to < 100 2,700

≥ 100 3,000

Duration of follow up:

There will be two follow up visits at day 28 and day 90 after the first dosing visit.

Assessments will include the following:

- Discharge status
- Vaccination status (for ravulizumab arm only)
- Return to normal function status (numeric rating scale 0-10)
- Mortality status

- Adverse event reporting
- ECOG and MRC scores

## Intervention Type

Drug

## Phase

Phase IV

## Drug/device/biological/vaccine name(s)

Baricitinib, ravulizumab

## Primary outcome(s)

Time to incidence (up to Day 14) of the composite endpoint of:

1. Death
2. Mechanical ventilation
3. Extracorporeal membrane oxygenation
4. Cardiovascular organ support (balloon pump or inotropes)
5. Renal failure (estimated creatinine clearance (by Cockcroft-Gault formula)  $<15 \text{ ml/min/1.73 m}^2$ ), haemofiltration or dialysis

All measured using patient records

## Key secondary outcome(s)

Measured using patient records:

1. Change in clinical status as assessed on 7-point ordinal scale compared to baseline
2. Time to each of the individual endpoints of the composite primary outcome measure
3. Proportion of patients with adverse events of special interest in each treatment arm
4. Time to  $\text{SpO}_2 >94\%$  on room air (excluding chronically hypoxic individuals)
5. Time to first negative SARS-CoV2 PCR
6. Duration of oxygen therapy (days)
7. Duration of hospitalisation (days)
8. All cause mortality at day 28
9. Time to clinical improvement (defined as  $>2$  point improvement from day 1 on 7-point ordinal scale)

Pulmonary 7-point scale:

- 1 Death
- 2 Mechanical Ventilation or ECMO
- 3 Non-invasive ventilation or high flow oxygen
- 4 Low flow oxygen
- 5 Hospitalised – no oxygen
- 6 Discharged; normal activities not resumed
- 7 Discharged; normal activities resumed

## Completion date

01/10/2021

## Eligibility

### Key inclusion criteria

1. Be aged 18 years and over
2. Have clinical picture strongly suggestive of COVID-19-related disease (with/without positive COVID-19 test) AND
  - 2.1. Risk count (as defined above) >3 OR
  - 2.3. Risk count 3 if risk count includes "Radiographic severity score >3"
3. Be considered an appropriate subject for intervention with immunomodulatory in the opinion of the investigator
4. Be able to be maintained on venous thromboembolism prophylaxis or current maintenance therapy during inpatient dosing period, according to local guidelines

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Total final enrolment**

417

**Key exclusion criteria**

1. Inability to supply direct informed consent from patient or from Next of Kin or Independent Healthcare Provider on behalf of patient
2. Mechanical ventilation at time of prior to dosing
3. Contraindications to study drugs, including hypersensitivity to the active substances or any of the excipients
4. Currently on any of the study investigational medicinal products
5. Known unresolved *Neisseria meningitidis* infection
6. Unwilling to be vaccinated against *Neisseria meningitidis* or receive prophylactic antibiotic cover until 2 weeks after vaccination
7. Known active tuberculosis (no blood screening required)
8. Known active Hepatitis B or C (no blood screening required); active varicella zoster.
9. Concurrent participation in any interventional clinical trial including COVID-19-related disease trials (observational studies allowed)
10. Patient moribund at presentation or screening
11. Pregnancy at screening (or unwillingness to adhere to pregnancy advice in protocol)
12. Unwillingness to adhere to breastfeeding advice in protocol.
13. Either alanine transaminase or aspartate transaminase (ALT or AST) > 5 times the upper limit of normal
14. Stage 4 severe chronic kidney disease or requiring dialysis (i.e. Cockcroft Gault estimated creatinine clearance < 30 ml /min/1.73 m<sup>2</sup>)
15. Currently receiving probenecid or chronic IVIG treatment

16. Any medical history or clinically relevant abnormality that is deemed by the principal investigator and/or medical monitor to make the patient ineligible for inclusion because of a safety concern

**Date of first enrolment**

07/05/2020

**Date of final enrolment**

22/06/2021

## Locations

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Addenbrookes Hospital**

Cambridge University Hospitals NHS Foundation Trust

Hills Road

Cambridge

United Kingdom

CB2 0QQ

**Study participating centre**

**King's College Hospital**

Kings' College Hospital NHS Foundation Trust

Denmark Hill

London

United Kingdom

SE5 9RS

**Study participating centre**

**Guy's and St Thomas's Hospital**

Guy's and St Thomas's NHS Foundation Trust

Great Maze Pond

London

United Kingdom

SE1 9RT

## Sponsor information

**Organisation**

Cambridge University Hospitals NHS Foundation Trust

**ROR**

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

**Funder(s)****Funder type**

Industry

**Funder Name**

Eli Lilly and Company

**Alternative Name(s)**

Lilly, Eli Lilly & Company, Eli Lilly & Co., Eli Lilly And Co, Eli Lilly & Co

**Funding Body Type**

Government organisation

**Funding Body Subtype**

For-profit companies (industry)

**Location**

United States of America

**Funder Name**

Alexion Pharmaceuticals

**Alternative Name(s)**

Alexion

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

For-profit companies (industry)

**Location**

United States of America

**Results and Publications**

## Individual participant data (IPD) sharing plan

Full individual participant data (deidentified) will be available to researchers who provide a methodologically sound proposal, available for 24 months after publication of the trial.

Proposals should be directed to Dr Frances C Hall (fch22@medsch.cam.ac.uk). Data requestors will need to sign a data access agreement. Data will be shared via a secure data access system.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		14/11/2023	05/03/2024	Yes	No
<a href="#">Protocol article</a>	protocol	08/07/2020	10/07/2020	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes