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# Precision medicine Adaptive Network platform Trial in Hypoxaemic acutE respiratory failuRe

**Submission date**
20/03/2025

**Recruitment status**
Recruiting

**Registration date**
02/07/2025

**Overall study status**
Ongoing

**Last Edited**
11/08/2025

**Condition category**
Respiratory

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

**Plain English summary of protocol**
Background and study aims
Acute Respiratory Distress Syndrome (ARDS) is a common severe lung condition in the intensive care unit (ICU) that makes it hard to breathe. Inflammation is a natural process that helps our body fight off harmful substances like infections. However, sometimes it can go into overdrive and damage the lungs. About one out of every four people in the ICU who need a machine to help them breathe (a ventilator) have ARDS. ARDS causes significant death and disability. There are no proven effective medicines to treat it.
We have identified two subgroups of patients with ARDS. We can identify these subgroups by measuring certain substances in the blood. Patients from each subgroup are likely to respond differently to some treatments. We want to be able to identify which patients with ARDS will respond best to a treatment to improve patient care.
We are planning a “platform” clinical trial to test different treatments for ARDS. This type of trial tests several treatments at the same time in a group of people. This means we can find what works and is safe, with the smallest number of patients. We can also test additional treatments during the trial as new information emerges. We hope that this way of testing treatments will help us find effective treatments for ARDS as quickly as possible and save money.

Who can participate?
Critically ill patients in hospital with ARDS or a pandemic-associated syndrome, aged 18 years and over

What does the study involve?
After determining a participant's subphenotype, participants will be randomised to one of the following treatment options:
1. Simvastatin
2. Baricitinib
3. Usual Care
There is evidence that simvastatin and baricitinib may work for ARDS. Patients will be followed up for the duration of their stay in ICU, to hospital discharge. Patients will be contacted for follow-up and to complete quality of life and cognitive function questionnaires at 3 and 6 months from initial randomisation. Vital status will be checked via the medical records at day 90 and 1 year after randomisation.

We will measure how many patients survive and how long it takes survivors to recover. We plan to conduct this research in multiple countries worldwide.

What are the possible benefits and risks of participating?
Benefits:
There may not be any direct benefits of participating in the study, but the results may help future patients and assist doctors in the future in treating people with ARDS more effectively and successfully.

Risks:
ARDS can be life-threatening. Evidence suggests that earlier treatment will benefit the patient. Therefore, to ensure there is no delay to treatment, it is imperative that patients are randomised as soon as they become eligible on ICU. Delays to treatment could affect the scientific validity of the trial, making the results less generalisable to usual practice. Due to their critical illness, most eligible patients for the study will have a reduced level of consciousness and will be unable to give consent at that time. Hence, treatment with the study drugs will need to be started in most cases without prospective consent in place. The specific nature of usual supportive care measures (which includes routinely administered interventions in critical care) are seldom discussed with their families and are presented to patients and their families as a "package deal" when time persists (in contrast to surgical procedures, which are more likely to be discussed in detail).
As this is an emergency situation it is not possible to identify eligible patients in advance of them losing the capacity to provide consent. In addition, relatives are likely to be distressed by the patient´s illness and admission to critical care at the point the patient is eligible for the trial – and are unlikely to have the capacity to make a decision in the short time frame available. The minimisation of further distress has been a priority when deciding on the proposed consent process. The process has been based on qualitative work with family members in similar studies regarding the preferred timing and way of approach for consent. This process has also been used in a number of other similar critical care research studies. After randomisation, the clinical team will identify the next-of-kin (family / relative / friend) recorded in the patients' clinical notes and they will be approached by a member of the clinical research team and asked if they would be happy to provide Personal Legal Consent. The trial will be explained to them, they will be given an information sheet about the trial and they will be asked to give an opinion on the patients' participation in the trial. If a Personal Legal Representative cannot be contacted in an adequate timeframe (approximately 2 hours), a Professional Legal Representative will be approached. This will be a member of the site clinical team, who is directly involved in the patient's care, based in the hospital and is not part of the research team (i.e. not on the research delegation log). They will be informed about the trial and asked to give an opinion on the patients' participation in the trial. Once patients regain capacity in the hospital, they will be approached by a member of the clinical research team, the trial explained to them, including their participation and that the study was discussed with their Personal or Professional Legal Representative while they lacked capacity. They will then be given the patient information sheet and asked to consent to the continuation of the study. All patients in critical care units are monitored closely, and clinical/research staff in this setting are very experienced in assessing mental capacity. Admission of adult patients to ICUs with ARDS will be linked to existing healthcare-related registries and databases in the UK. The following data may be obtained by data linkage with death registries and hospital discharge coding databases in the UK:
1. Hospital readmissions, diagnoses and procedures carried out during readmissions
2. Mortality after discharge from the index hospitalization
We will seek consent from patients to collect this data. If the patient does not have capacity, consent for this data will be sought from a Personal Legal Representative or a Professional Legal Representative if the former is not available. ICNARC will use patient identifiable data (NHS

number, date of birth, post code and sex) which is already collected as part of the CMP national clinical audit to link data with other routinely collected data sets. This allows the research objectives to be achieved in an efficient manner and allows for the best possible follow-up of longer-term survival for patients. This is not possible without patient-identifiable data. The CMP national clinical audit has section 251 approval for the use of patient identifiable data for audit. Confidentiality: Minimal patient identifiable data will be required to enable the trial team to link data to routine data sources. Use of tissues in future research: a total of 30 ml of blood will be collected for future research, and all samples will be stored at the Wellcome-Wolfson Institute for Experimental Medicine for analysis in other ethically approved studies.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
March 2025 to May 2029

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
Ms Janis Best-Lane, panther@imperial.ac.uk

# Contact information

### Type(s)
Principal Investigator

### Contact name
Dr Daniel McAuley

### Contact details
QEQM
St Mary's Hospital
Praed Street
London
United Kingdom
W2 1NY
+44 (0)28 90 976385
d.f.mcauley@qub.ac.uk

### Type(s)
Scientific

### Contact name
Ms Janis Best-Lane

### Contact details
Room 221
Level 2 Medical School Building
Norfolk Place
London

United Kingdom
W2 1PG
-
panther@imperial.ac.uk

# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number
1008743

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
175151, CPMS 58217

# Study information

### Scientific Title
Precision medicine Adaptive Network platform Trial in Hypoxaemic acutE respiratory failuRe

### Acronym
PANTHER

### Study objectives
Primary objective:
To increase the development of new therapies for people with critical illness by creating an international platform trial to test the success of treatments in patients with ARDS and pandemic infection.

Secondary objectives:
1. To develop a framework for identifying, developing and testing additional subgroups and therapies in the ongoing platform trial.
2. To play a leading role in international collaboration in research.
3. To provide opportunities for early career investigators to build clinical trial experience.
4. To help collaborate with commercial partners to test promising new treatments for ARDS
5. To be more sustainable through academic and commercial funding opportunities.
6. To collect samples and data on other precision medicine factors
7. To be able to quickly change focus in the event of a new pandemic related to respiratory failure, providing tools to be prepared for a pandemic if needed.

### Ethics approval required
Ethics approval required

### Ethics approval(s)
Not yet submitted, ref: 25/NW/0103

## Study design
Open randomized controlled parallel-group adaptive platform trial

## Primary study design
Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
Hospital

## Study type(s)
Efficacy

## Participant information sheet

## Health condition(s) or problem(s) studied
Critical illnesses including acute respiratory disease syndrome and pandemic infection

## Interventions
Simvastatin:
Simvastatin may help repair the lungs by reducing inflammation and repairing the blood vessels in the lungs. Simvastatin will be administered at a dose of 80 mg once daily via the enteral route until study day 28 or ICU discharge, whichever comes first.

Baricitinib:
Baricitinib may help repair the lungs by reducing inflammation. Baricitinib will be administered at a dose of 4mg via the enteral route for 10 days or until hospital discharge, whichever occurs first

Usual care:
Local hospitals' usual care for ARDS as directed by international treatment guidelines, such as the European Society of Intensive Care Medicine ARDS guidelines. Usual care will act as a control for each subphenotype.

## Intervention Type
Drug

## Pharmaceutical study type(s)
Therapy

## Phase
Phase II

## Drug/device/biological/vaccine name(s)
Simvastatin, baricitnib

## Primary outcome measure
28-day organ support-free days, incorporating mortality as a composite on an ordinal scale. Organ support is defined as needing either respiratory or cardiovascular support

### Secondary outcome measures
1. Progression to invasive mechanical ventilation, extracorporeal membrane oxygenation or death among those not receiving that support at baseline
2. 28-day vasopressor-free days
3. 28-day respiratory support–free days
4. Receiving new renal replacement therapy
5. ICU length of stay
6. Hospital length of stay
7. All-cause mortality at 28 and 90 days
8. Safety outcomes:
8.1. Elevated Creatine Kinase more than 10 times the upper limit of normal
8.2. Alanine Transaminase or Aspartate Transaminase or both more than 8 times the upper limit of normal
8.3. Serious infection, defined as positive blood cultures requiring treatment and positive pulmonary aspergillosis requiring treatment
8.4. Venous thromboembolism
8.5.Stroke
8.6. Myocardial infarction
8.7. Ischaemic bowel
8.8. Gastrointestinal perforation
8.9. Clinically important gastrointestinal (GI) bleeding confirmed on upper endoscopy
9. Serious adverse events
10. Physical function measured using Short Physical Performance Battery (SPPB) at hospital discharge (up to 1 week prior to discharge)
11. Cognitive impairment measured using the Montreal Cognitive Assessment (MoCA) at hospital discharge (up to 1 week prior to discharge)

Tertiary outcome measures:
1. 14-day delirium and coma-free days*
2. Incidence of ICU-acquired weakness (MMST and hand grip strength dynamometry and maximal inspiratory) at day 7 and ICU discharge*
3. Health-related quality of life (EQ-5D-5L), Hospital Anxiety and Depression Scale (HADS), Social and Wellbeing (SF-36), Impact of Events Scale (6 item), care and wellbeing needs and cognitive impairment (MoCA) at 90 days and 180 days*

*Not all sites are expected to collect these endpoints

90 days from randomisation is the final endpoint

### Overall study start date
18/03/2025

### Completion date
31/05/2029

## Eligibility

### Key inclusion criteria
1. Critically ill patients in hospital and at least one of the following:
1.1. ARDS

1.2. A pandemic-associated syndrome*
*This will be triggered if a pandemic is declared

ARDS as defined by:
1. A known acute clinical insult or new or worsening respiratory dysfunction, and
2. Receiving respiratory support via invasive mechanical ventilation or non-invasive ventilation including continuous positive airway pressure, or high-flow nasal oxygen ≥30L/min and
3. Within the same 24-hour time period:
3.1. Bilateral opacities on chest imaging not fully explained by effusions, lobar/lung collapse /atelectasis, or nodules, and
3.2. Respiratory failure not fully explained by cardiac failure, fluid overload, pulmonary embolism, acute airways disease, or interstitial lung disease and,
3.3. PaO2/FiO2 ratio <40 kPa from arterial blood gases, or SpO2/FiO2 <315 from pulse oximetry where SpO2 <97.

The time of onset of ARDS is when the last criterion in 3 is met.

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
1563

### Key exclusion criteria
1. >48 hours from diagnosis of ARDS
2. Planned withdrawal of life-sustaining treatment within the next 24 hours
3. Previous enrolment in the PANTHER trial in the last 12 months
4. Declined consent
5. Aged <18 years

### Date of first enrolment
31/05/2025

### Date of final enrolment
31/05/2029

## Locations

### Countries of recruitment
England

United Kingdom

**Study participating centre**
**Not provided at time of registration**
United Kingdom
-

# Sponsor information

**Organisation**
Imperial College London

**Sponsor details**
QEQM Building
St Mary’s Hospital
Praed Street
London
England
United Kingdom
W2 1NY
-
rgit.ctimp.team@imperial.ac.uk

**Sponsor type**
University/education

**Website**
https://www.imperial.ac.uk

**ROR**
https://ror.org/041kmwe10

# Funder(s)

**Funder type**
Government

**Funder Name**
National Institute for Health and Care Research

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

### Funding Body Type
Government organisation

### Funding Body Subtype
National government

### Location
United Kingdom

## Results and Publications

### Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Other publication
5. The results of the trial will be made publicly available via institutional websites and also through charity/patient groups (e.g. ICU Steps, Intensive Care Foundation)
5. Participants will not routinely be given results as this is a trial that is unlikely to offer individual patients or their doctors any information that will be of relevance to their ongoing or future clinical care

### Intention to publish date
31/05/2030

### 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