

# National trial launched to find Covid-19 treatment

16 May 2020

TACTIC, as the trial is known, will test whether re-purposing existing drugs, which target the body's own immune response, can prevent people suffering severe organ failure or death. The trial is part of the coordinated national approach by the UK Government to support the early phase development of potential new treatments for COVID-19.

For the majority of people with Covid-19, the infection causes only mild symptoms, including a fever and cough. However, around 15% of patients develop severe disease, including serious damage to the lungs and multiple organ failure, and about two percent die.

The serious symptoms appear to be mostly caused by the body's own immune system responding to the presence of infected cells and 'over-reacting', destroying healthy cells as well as virus-infected ones.

Two drugs will initially be tested through TACTIC on patients at a network of hospitals across the UK, including Cambridge University Hospitals NHS Foundation Trust (CUH), Guy's and St Thomas' NHS Foundation Trust, and King's College Hospital.

The first patient was recruited onto the study at Addenbrooke's hospital in Cambridge on Friday 08 May



The two drugs, Ravulizumab and Baricitinib,

have been carefully selected by a consortium of doctors and scientists with expertise in

treating immune-response diseases. They are both thought to have a high chance of reducing the sometimes fatal over-reaction of the immune system seen in very sick patients with Covid-19.

This study is one of a number of COVID-19 studies that have been given urgent public health research status by the Department of Health and Social Care. It is supported by the National Institute for Health Research (NIHR) Biomedical Research Centres at Cambridge and Guy's and St Thomas' and UK Research and Innovation; the drug manufacturers, Lilly and Alexion, have each supplied the drug for up to 469 subjects as well as contributing up to £200,000 in running costs for the project.

If the trial demonstrates that a drug is effective, it will be quickly moved into NHS care pathways, to treat the patients with severe Covid-19 related disease. Similarly, if the trial reveals that a drug is not effective, it can be quickly removed so that other options can be tested.

UK Research and Innovation Chief Executive, Professor Sir Mark Walport, said: "By supporting the rapid progress of these re-purposed drugs into early clinical trials we will test whether they can prevent the development of severe COVID-19 symptoms. Trialling drugs that have the potential to suppress the severe inflammation caused by an over-reaction of the immune system is an important part of tackling the COVID pandemic."

Dr Frances Hall, Consultant Rheumatologist, CUH, and TACTIC Chief Investigator, said: "It is striking that the severe Covid-19-related disease is associated with the person's own immune system causing most of the damage. It seems that, while most people's immune system attacks the virus appropriately, in those who become really sick, the immune response appears to overreact.

"We have selected the first two drugs for the TACTIC study based on their ability to 'dial-down', or block, two distinct types of response, each of which appear important in the immune response which causes damage to lungs and other organs in Covid-19-related disease. Baricitinib acts through the network of cytokines (soluble immune system signals running between cells); it reduces the upscaling of the cytokine response which leads to the "cytokine storm" evident in severe Covid-19-related disease. On the other hand Ravulizumab inhibits the activation of a trigger in a "tag-team" of molecules, called the complement cascade, which serves to rapidly ramp up inflammation and cell killing.

"Both of these drug are used routinely – Baricitinib in severe rheumatoid arthritis and Ravulizumab in blood diseases where complement activation destroys red blood cells. There is good reason to believe that either or both of these strategies could help prevent severe organ failure and even death in patients with Covid-19. I want to thank all the patients who agree to take part in this important trial – you are part of the solution to Covid-19."

Professor Ian Wilkinson, Director of the Cambridge Clinical Trials Unit, and Professor of

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Therapeutics at the University of Cambridge, said: "This is a time of huge national effort in the fight against Covid-19 and I am delighted that Cambridge is playing a key role in this. TACTIC will test the effectiveness of a number of existing and new drugs in patients admitted to hospital, in a similar way to the RECOVERY trial, but with a strong focus on modulating the immune response and collecting high quality data that can be used by our partner pharmaceutical companies to seek the necessary approvals for widespread international use."

Professor Andrew Cope is a consultant rheumatologist at Guy's and St Thomas' and Head of the Centre for Rheumatic Diseases at King's College London. He said: "Research is going to be vital in tackling this pandemic. Guy's and St Thomas' is one of the top Trusts in the country for translational research, and partnered with King's College, we are bringing together the best possible clinical and research expertise.

Dr James Galloway, Senior Lecturer in Rheumatology at King's College London, and a Co-Investigator on the TACTIC trial, said: "By testing existing drugs that we think have the best chance of working against Covid-19, we hope that we can find proven ways to treat the disease. Identifying the high risk patients taking part in this research will be key, and we're incredibly grateful to the patients who have been so willing to take part, and their families."

Additional information on drugs being tested:

## **Ravulizumab**

The immune system has several ways to attack viruses and other infections, and TACTIC will initially test 2 drugs that target different aspects of the immune response and are already in use to treat other conditions caused by overactive immune responses.

One of the first systems triggered when the immune system spots a pathogen (a bacterium or virus) is known as the 'complement system'. Parts of the complement system are constantly waiting in the blood, ready to spot infections. When activated, it acts as a 'first responder' setting off a rapid chain of events that both alerts the rest of the immune system and also directly destroys cells. Excessive activity by the complement system is thought to be responsible for at least some of the severe organ damage seen in COVID-19. This trial will test a drug called Ravulizumab that is used to treat a condition where the complement system destroys red blood cells. It blocks an important "on-switch" in the complement cascade, thereby reducing alerting of the immune system and blocking direct cell killing by complement.

## **Baricitinib**

The cells in the body that fight infection 'talk' to each other using tiny chemical messages known as cytokines. Different cytokines give different instructions to other immune cells, telling them to make more cytokines, multiply themselves to make more immune cells or to

destroy other cells showing signs of infection. The right amount of the right cytokines gives the best immune response – but too much of the wrong cytokines causes inflammation that can damage healthy cells and tissues. This is known as a ‘cytokine storm’ and is thought to be another contributor to severe COVID-19 responses. The TACTIC trial aims to test whether Baricitinib, a drug that is regularly used to ‘dial down’ excessive cytokines in people with rheumatoid arthritis, can effectively reduce the cytokine storm experienced by patients with severe COVID-19 symptoms.

For further information on the trial please visit [www.tactictrial.net](http://www.tactictrial.net)

### **For more information or to request interviews please contact:**

Sarah Vincent, Head of External Affairs, CUH on [sarah.vincent@addenbrookes.nhs.uk](mailto:sarah.vincent@addenbrookes.nhs.uk) or mb +44 7542 229210

CUH Press Office Tel: + 44 1223 274433

Email: [press@addenbrookes.nhs.uk](mailto:press@addenbrookes.nhs.uk)

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### **More about Cambridge University Hospitals (CUH) visit:**

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

### **About NIHR**

The National Institute for Health Research (NIHR) is the nation's largest funder of health and care research. The NIHR:

Funds, supports and delivers high quality research that benefits the NHS, public health and social care

Engages and involves patients, carers and the public in order to improve the reach, quality and impact of research

Attracts, trains and supports the best researchers to tackle the complex health and care challenges of the future

Invests in world-class infrastructure and a skilled delivery workforce to translate discoveries

into improved treatments and services

Partners with other public funders, charities and industry to maximise the value of research to patients and the economy

The NIHR was established in 2006 to improve the health and wealth of the nation through research, and is funded by the Department of Health and Social Care. In addition to its national role, the NIHR commissions applied health research to benefit the poorest people in low- and middle-income countries, using Official Development Assistance funding.

This work uses data provided by patients and collected by the NHS as part of their care and support and would not have been possible without access to this data. The NIHR recognises and values the role of patient data, securely accessed and stored, both in underpinning and leading to improvements in research and care. [www.nihr.ac.uk/patientdata](http://www.nihr.ac.uk/patientdata)

## **About NIHR Cambridge Biomedical Research Centre**

Based within the most outstanding NHS and University partnerships in the country, the Biomedical Research Centres are leaders in scientific translation. Located on the Cambridge Biomedical Campus, they receive substantial levels of funding from the National Institute for Health Research (NIHR) to translate fundamental biomedical research into clinical research that benefits patients and they are early adopters of new treatments.

## **About the NIHR Biomedical Research Centre at Guy's and St Thomas'**

The NIHR Biomedical Research Centre (BRC) at Guy's and St Thomas' NHS Foundation Trust and King's College London works to develop and deliver new medicines and diagnostics to patients, drive research and innovation into the NHS, and provide national systems leadership for maximum impact to patients.

With our research activity organised into nine themes, each holding an individual Athena Swan Silver award highlighting our commitment to equality and diversity, and supported by our interdisciplinary, world leading infrastructure, we are poised to deliver the next step change for the health and wealth of our nation. <http://www.guysandstthomasbrc.nihr.ac.uk/>

## **Cambridge University Hospitals**

Cambridge University Hospitals NHS Foundation Trust (CUH) is one of the largest and best known trusts in the country, delivering high-quality patient care through Addenbrooke's and the Rosie Hospitals. CUH is a leading national centre for specialist treatment for rare or complex conditions and a university teaching hospital with a worldwide reputation.

CUH is a key partner in Cambridge University Health Partners (CUHP), one of only six academic health science centres in the UK, and is at the heart of the development of the

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Cambridge Biomedical Campus (CBC), which brings together on one site world-class biomedical research, patient care and education. The Campus is one of the government's National Institute for Health Research (NIHR) comprehensive biomedical research centres.

## **King's College London**

King's College London is one of the top 10 UK universities in the world (QS World University Rankings, 2018/19) and among the oldest in England. King's has more than 31,000 students (including more than 12,800 postgraduates) from some 150 countries worldwide, and some 8,500 staff.

King's has an outstanding reputation for world-class teaching and cutting-edge research. In the 2014 Research Excellence Framework (REF), eighty-four per cent of research at King's was deemed 'world-leading' or 'internationally excellent' (3\* and 4\*).

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