

UNDER EMBARGO UNTIL 15:00 GMT THURSDAY 3 MARCH 2022

New RECOVERY trial result: Baricitinib reduces deaths in patients hospitalised with COVID-19

The Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial has demonstrated that baricitinib, an anti-inflammatory treatment normally used to treat rheumatoid arthritis, reduces the risk of death when given to hospitalised patients with severe COVID-19. The benefit was in addition to those of dexamethasone and tocilizumab, two other anti-inflammatory treatments which have previously been shown to reduce the risk of death in these patients.

The University of Oxford-led RECOVERY trial has been testing a range of potential treatments for patients admitted to hospital for COVID-19 since March 2020. Between February and December 2021, 4008 patients randomly allocated to usual care alone were compared with 4148 patients who were randomly allocated to usual care plus baricitinib. The dose of baricitinib was a 4mg tablet once daily for 10 days (or until discharge from hospital if sooner). At randomisation, 95% of patients were receiving a corticosteroid such as dexamethasone, 23% were receiving tocilizumab, and 20% were receiving the anti-viral drug remdesivir. Two-thirds (68%) of patients were receiving oxygen and one quarter (27%) were receiving additional respiratory support.

Treatment with baricitinib significantly reduced deaths: 513 (12%) of the patients in the baricitinib group died within 28 days compared with 546 (14%) patients in the usual care group, **a reduction of 13%** (age-adjusted rate ratio 0.87, 95% confidence interval [CI] 0.77 to 0.98; $p=0.026$). The benefit of baricitinib was consistent regardless of which other COVID-19 treatments the patients were also receiving, including corticosteroids, tocilizumab, or remdesivir.

Patients receiving baricitinib were also more likely to be discharged alive within 28 days (80% vs. 78%, age-adjusted rate ratio 1.10, 95% CI 1.04-1.15; $p<0.001$). Among patients not on invasive mechanical ventilation when entered into the trial, baricitinib reduced the chance of progressing to invasive mechanical ventilation or death from 17% to 16% (risk ratio 0.90, [95% CI 0.81 to 0.99], $p=0.026$). There was no evidence that the short course of baricitinib used in RECOVERY increased the risk of other infections or of thrombosis (complications of blood clotting).

RECOVERY considerably strengthens the evidence from earlier trials that baricitinib is beneficial in severe COVID-19, and provides new evidence of the additional benefit of baricitinib on top of other immunomodulatory treatments. RECOVERY is twice as large as the eight previous trials of baricitinib and similar drugs (known as JAK inhibitors) for the treatment of COVID-19 combined. **Overall the nine trials, which involve about 12,000 patients, found that the use of baricitinib (or another JAK inhibitor) reduced deaths in patients hospitalised for COVID-19 by about one-fifth** (rate ratio 0.80, 95% CI 0.71 to 0.89; $p<0.001$).

Sir Martin Landray, Professor of Medicine and Epidemiology at Oxford Population Health, and Joint Chief Investigator for RECOVERY, said 'It is now well-established that in people admitted to hospital because of severe COVID-19, an over-active immune response is a key driver of lung damage. Today's results not only show that treatment with baricitinib improves the chances of survival for patients with severe COVID-19, but that this benefit is additional to that from other treatments that dampen down the over-active immune response, such as dexamethasone and tocilizumab. This opens up the possibility of using combinations of anti-inflammatory drugs to further drive down the risk of death for some of the sickest patients.'

Sir Peter Horby, Professor of Emerging Infectious Diseases in the Nuffield Department of Medicine, University of Oxford, and Joint Chief Investigator for RECOVERY, said 'This result confirms and extends earlier findings, providing greater certainty that baricitinib is beneficial and new data to guide the treatment of COVID-19 patients with a combination of drugs to dampen the immune response. As always, the next challenge is ensuring this and other COVID-19 treatments are available and affordable for everyone who can benefit, regardless of where they live.'

Mark Rivvers (51), deputy head porter at Fitzwilliam College, University of Cambridge, took part in the baricitinib study in the RECOVERY trial when he was admitted to Addenbrooke's Hospital with severe COVID-19 in September 2021. He said: 'I was in hospital for almost a month, mostly in an intensive care unit. Everything in my body seemed to be fighting against everything else: I was on almost constant respiratory support, I developed sepsis, and I had pneumonia all across my lungs. But I saw it as my duty to take part in the RECOVERY trial, because I knew that no matter what happened to me, I was doing something positive to help others. I'm really pleased about the result with baricitinib, and hope that it can now be used to benefit many others. I'd like to thank the RECOVERY trial leaders, and also all the staff at Addenbrooke's Hospital, who were phenomenal.'

Health and Social Care Secretary Sajid Javid said: 'As we learn to live with COVID, having access to a growing number of safe and effective treatments for the virus, like our game-changing dexamethasone, will be absolutely vital.'

'This is promising news from the government-funded RECOVERY trial and shows, once again, how the UK is leading the world in identifying life-saving treatments for NHS patients.'

'A big thank you to all of the researchers, doctors and volunteers involved in this work. Our medical and scientific experts will now consider the results before any decisions are made on next steps.'

Baricitinib is the fourth treatment that the RECOVERY trial has shown to save lives, following [the steroid dexamethasone](#) (June 2020), [the arthritis treatment tocilizumab](#) (February 2021), and a combination of monoclonal antibodies (casirivimab plus imdevimab) targeting the viral spike protein, known as [Ronapreve](#) (June 2021). These discoveries have changed clinical practice worldwide and been credited with saving hundreds of thousands, if not millions, of lives.

Professor Nick Lemoine, National Institute for Health Research said: 'The incredible contribution of all those involved in the NIHR-supported RECOVERY trial has led to the discovery of a further life-saving treatment against COVID-19. We're particularly grateful to the 47,000 participants who have taken part in the study so far - without whom these game-changing discoveries would not be possible.'

Professor Patrick Chinnery, clinical director at the Medical Research Council said: 'These new results from RECOVERY show that even more patient lives can be saved by targeting the immune system in a specific way, adding to the benefits already shown with dexamethasone.'

A manuscript providing further details on these results has been submitted to medRxiv and will be submitted to a peer-reviewed medical journal shortly.

Editor's notes

For further information or interview requests with the chief investigators, please contact Dr Caroline Wood, Communications Officer, Oxford Population Health, caroline.wood@ndph.ox.ac.uk or Anne Whitehouse, Director of Communications and Public Engagement, Oxford Population Health, anne.whitehouse@ndph.ox.ac.uk.

Full details of the study protocol and related materials are available at www.recoverytrial.net.

The **RECOVERY trial** is conducted by the registered clinical trials units with the Nuffield Department of Population Health in partnership with the Nuffield Department of Medicine. The trial is supported by a grant to the University of Oxford from UK Research and Innovation/ the National Institute for Health Research (NIHR), and by core funding provided by the Bill and Melinda Gates Foundation, the Foreign, Commonwealth & Development Office, Health Data Research UK, the Medical Research Council Population Health Research Unit, the NIHR Oxford Biomedical Research Centre, NIHR Clinical Trials Unit Support Funding, and Wellcome. Funding for RECOVERY outside the UK is provided by Wellcome through the COVID-19 Therapeutics Accelerator. Supplies of baricitinib for the RECOVERY trial were provided from NHS stock.

The RECOVERY trial currently involves many thousands of doctors, nurses, pharmacists, and research administrators at 178 hospitals across the whole of the UK. In the UK, the trial is supported by staff at the NIHR Clinical Research Network, NHS DigiTrials, Public Health England, Department of Health & Social Care, the Intensive Care National Audit & Research Centre, Public Health Scotland, the Secure Anonymised Information Linkage at the University of Swansea, and the NHS in England, Scotland, Wales and Northern Ireland.