EMBARGOED UNTIL 13:00 GMT, Monday 14 December 2020

RECOVERY
Randomised Evaluation of COVID-19 Therapy

UNIVERSITY OF OXFORD

Statement from the Chief Investigators of the Randomised Evaluation of COVid-19 thERapY (RECOVERY) Trial on azithromycin, 14 December 2020

RECOVERY trial finds no benefit from azithromycin in patients hospitalised with COVID-19

In March 2020, the RECOVERY trial was established as a randomised clinical trial to test a range of potential treatments for COVID-19, including azithromycin. Azithromycin is a widely used antibiotic that also reduces inflammation, a key feature of severe COVID-19, and also has some activity against the virus responsible for COVID-19. To date there has been no convincing evidence of its effect on clinical outcomes in COVID-19.

Over 20,000 patients have been enrolled in the RECOVERY trial so far from 176 NHS hospitals in the UK. The azithromycin arm of the trial was closed on 27 November since, in the view of the Trial Steering Committee, sufficient patients had been enrolled to establish clearly whether or not the drug had a meaningful benefit among patients hospitalised with COVID-19.

A total of 2582 patients were randomised to azithromycin and compared with 5182 patients randomised to usual care alone. Patients entered the study an average of 8 days after the onset of symptoms. Follow-up is complete for 73% of the participants and will be fully complete by the end of December. A preliminary analysis shows no significant difference in the primary endpoint of 28-day mortality (19% azithromycin vs. 19% usual care; relative risk 1.00 [95% confidence interval 0.90-1.12]; p=0.99). There was also no evidence of beneficial effects on the risk of progression to mechanical ventilation or length of hospital stay. The results were consistent in different subgroups of patients.

These data convincingly rule out any meaningful clinical benefit of azithromycin in the hospitalised COVID-19 patients we studied. The preliminary results will be available as a pre-print on medRxiv shortly after 13:00 GMT on Monday 14 December. Full results will be made available as a peer-reviewed publication once follow-up has been completed for all participants. We did not study patients in the community and are not able to make conclusions about the effectiveness of azithromycin outside the hospital setting.

Peter Horby, Professor of Emerging Infectious Diseases and Global Health in the Nuffield Department of Medicine, University of Oxford, and Chief Investigator for the trial, said: 'Azithromycin has been widely used to treat COVID patients because of its theoretical potential to reduce lung inflammation. Our results show very clearly that for patients hospitalised with COVID-19 azithromycin is not an effective treatment. While that is disappointing, it is nonetheless an important result that will guide clinical care around the world. Looking ahead, RECOVERY continues to study several promising treatments, including convalescent plasma and Regeneron's antibody cocktail targeted at the virus. Further results are likely over the next couple of months.'

Martin Landray, Professor of Medicine and Epidemiology at the Nuffield Department of Population Health, University of Oxford, and Deputy Chief Investigator, said 'We have seen time and again during this epidemic the importance of large randomised clinical trials in determining which of the many promising treatments deliver real benefits for patients.

'Once again, we thank the thousands of NHS doctors, nurses, pharmacists, and research staff who have contributed to the RECOVERY trial and the quest for knowledge about how best to reduce the terrible burden of this disease. Above all we must thank the 20,000 patients who have taken part in this extraordinary and truly world-leading effort. The improved care of COVID patients today is thanks to the selfless contribution of RECOVERY participants in the past – and in turn, the care of patients tomorrow will be better as a consequence of those volunteering today. Thank you.'

Professor Fiona Watt, Executive Chair of the Medical Research Council, which helped fund the trial, said 'Although it is disappointing that azithromycin isn't an effective treatment for hospitalised COVID-19 patients, negative results are important so that clinicians can focus patient care on drugs that have been shown to work. This is particularly vital for antibiotics like azithromycin, because inappropriate use of antibiotics contributes to bacteria in the body becoming resistant.

'The UK's RECOVERY trial, as the world's largest randomised trial of potential COVID-19 treatments, plays a key role in providing evidence of which drugs for COVID-19 can help to save lives.'

Notes

For further information or interviews with the chief investigators, please contact Dr Caroline Wood, caroline.wood@ndph.ox.ac.uk.

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

The RECOVERY trial is a large, randomised controlled trial of possible treatments for patients admitted to hospital with COVID-19. Over 20,200 patients have taken part. The trial continues to study the following treatments, each compared with usual standard of care alone:

- Tocilizumab (an anti-inflammatory treatment given by injection)
- Convalescent plasma (collected from donors who have recovered from COVID-19 and contains antibodies against the SARS-CoV-2 virus)
- Regeneron's antibody cocktail (a combination of monoclonal antibodies directed against coronavirus)
- Aspirin (commonly used to thin the blood)
- Colchicine (a commonly used anti-inflammatory drug).

The azithromycin arm reported today is now the fourth result to come out of the RECOVERY trial. The trial previously showed that neither hydroxychloroquine nor lopinavir (a treatment for HIV) are effective in this population. By contrast, it showed very clearly that dexamethasone reduces the risk of death by about one-third among patients receiving ventilation and by one-fifth in those requiring oxygen alone (but with no benefit among those not requiring respiratory support).

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/National Institute for Health Research (NIHR) and by core funding provided by NIHR Oxford Biomedical Research Centre, Wellcome, the Bill and Melinda Gates Foundation, the Foreign, Commonwealth & Development Office, Health Data Research UK, the Medical Research Council Population Health Research Unit, and NIHR Clinical Trials Unit Support Funding.

The RECOVERY trial involves many thousands of doctors, nurses, pharmacists, and research administrators at 176 hospitals across the whole of the UK, 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 Asnonymised Information Linkage at University of Swansea, and the NHS in England, Scotland, Wales and Northern Ireland.