

RECOVERY Central Coordinating Office
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To all RECOVERY Principal Investigators

Recruitment to the RECOVERY trial (including the Hydroxychloroquine arm) REMAINS OPEN

On Friday 22nd May we received a letter from the MHRA in which they notified us of their concerns relating to the use of hydroxychloroquine as a treatment for patients with COVID-19 in the light of the recent publication by Mehra et al in The Lancet on 22 May 2020.

We have held two videoconferences with the MHRA and provided a detailed response which is summarised below.

This morning **we have received written confirmation from the MHRA that, "it is acceptable to allow continued randomisation into the hydroxychloroquine arm of the trial."**

Further details are provided below:

- There have been two recent observational analyses of the use of hydroxychloroquine (HCQ) for treatment of COVID-19. One reported no significant effect on the outcome of intubation or death (Geleris et al, New Engl J Med 7 May 2020), while the other reported a hazard ratio of 1.33 for all-cause mortality (Mehra et al, Lancet 22 May 2020). The authors of both papers conclude that their findings should be interpreted with caution, are not definitive, and that randomised controlled trials are required to reach any conclusion about the benefit or harm of HCQ for COVID-19.
- The RECOVERY trial is currently the largest randomised controlled trial of HCQ for COVID-19 but is not yet sufficiently large to detect (or rule out) moderate yet important treatment effects.
- In response to the letter provided by MHRA, the Chair of the independent DMC conducted an urgent review of unblinded data for the HCQ vs. Standard of Care comparison within RECOVERY. Following an initial review by the DMC Chair and further discussions between the RECOVERY Chief Investigators and the MHRA, the independent Data Monitoring Committee then held a full meeting by videoconference and issued a letter indicating that, "***the Data Monitoring Committee saw no cogent reason to suspend recruitment for safety reasons and recommended the trial continue recruitment without interruption.***"

- Given the additional review of unblinded data conducted by the full independent Data Monitoring Committee yesterday and their recommendation to continue without interruption, it is the view of the Chief Investigators that any pause in recruitment would be unjustified and would not be in the interests of trial participants or public health.
- The RECOVERY trial provides the best and most rapid opportunity to produce robust information on the overall effects of HCQ on the risk of death from COVID-19. These results will be of huge importance to the millions of patients who are (or will be) treated with HCQ and could have a major impact on a disease that has already caused hundreds of thousands of deaths.

In the light of the information provided in this response, and the ongoing monitoring of the safety of hydroxychloroquine by the independent Data Monitoring Committee, the **MHRA has confirmed in writing that "it is acceptable to allow continued randomisation into the hydroxychloroquine arm of the trial."**

The RECOVERY trial therefore continues as planned, with no alteration to the protocol, and all treatment arms remain open to enrolment.

Yours sincerely



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Martin Landray PhD FRCP
Professor of Medicine & Epidemiology

Chief Investigators for the RECOVERY trial

cc. Richard Haynes, Professor of Clinical Trials & Nephrology, Clinical Coordinator for RECOVERY
Heather House, Clinical Trials & Research Governance, University of Oxford