



Centre for Tropical Medicine and Global Health

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Cambridge East REC
E-submission

30 May 2022

Dear Dr Lamont

Trial: Randomised evaluation of Covid-19 therapy (RECOVERY)
EudraCT: 2020-001113-21
IRAS: 281712
REC ref: 20/EE/0101

Thank you very much for your committee's recent review of our urgent safety measure related protocol amendment. After your approval, we recognized that there was an issue we had not covered in that amendment.

Paxlovid is known to increase exposure to dexamethasone due to its effects on drug metabolism, and consequently participants receiving both drugs are exposed to the equivalent of higher doses of dexamethasone. For participants not on oxygen or only receiving simple oxygen therapy this combination is therefore not ideal.

Other glucocorticoids (prednisolone, hydrocortisone, methylprednisolone) do not interact with Paxlovid in this way, but a WHO-led meta-analysis has shown that they have similar benefits to dexamethasone in COVID-19. Therefore we think it is safest to recommend to investigators that participants allocated Paxlovid are not prescribed dexamethasone, but instead an alternative glucocorticoid is prescribed instead. (Not all participants receiving Paxlovid will require a glucocorticoid as they are only indicated for participants needing oxygen.)

We will instruct our investigators to change any current prescriptions once this amendment is approved (and explain sensitively to participants why this is being done). We apologise that this was not included in the previous amendment.

I believe all the necessary documentation required for this submission is attached and look forward to hearing the outcome.

Please let us know if you require any further information.

Yours faithfully



Professor Sir Peter W. Horby

BSc MSc MBBS FRCP FFPH PhD

Chief Investigator, RECOVERY Trial

Professor of Emerging Infectious Diseases and Global Health

Enc:

1. RECOVERY protocol V25.0 (tracked and clean)
2. Amendment Tool
3. Sponsor approval