RECOVERY trial investigators

8 January 2021

Dear Colleagues

Tocilizumab and Convalescent Plasma in the RECOVERY trial

Thank you very much indeed for your huge contribution to the RECOVERY trial. With your support, RECOVERY remains the largest trial of treatments in COVID-19, with over 25,000 participants to date. With the help of all of you and of those patients, we have already answered 4 important questions, most notably the benefit of dexamethasone for patients requiring oxygen or ventilation.

The independent RECOVERY Data Monitoring Committee (DMC) held a routine meeting yesterday (7th January). We have appended a copy of their letter. The DMC will review the situation at their next meeting on 14th January.

Convalescent plasma

Recruitment of patients requiring invasive mechanical ventilation or extra-corporal membranous oxygenation (ECMO) to the convalescent plasma arm should be paused immediately. The study randomisation system now enforces this exclusion.

The Data Monitoring Committee strongly encouraged continued recruitment of all other eligible patients to the convalescent plasma comparison. Thus recruitment of patients requiring non-invasive ventilation (e.g. CPAP, high flow oxygen, other forms of non-invasive ventilation), oxygen, or no respiratory support remains open.

Tocilizumab

Recruitment of patients to tocilizumab continues. The independent Data Monitoring Committee, has reviewed the available information from the previous trials, including REMAP-CAP (see next page for details) and the unblinded data from RECOVERY. The DMC recommended continuing recruitment of all eligible patients to the tocilizumab arm of the trial.

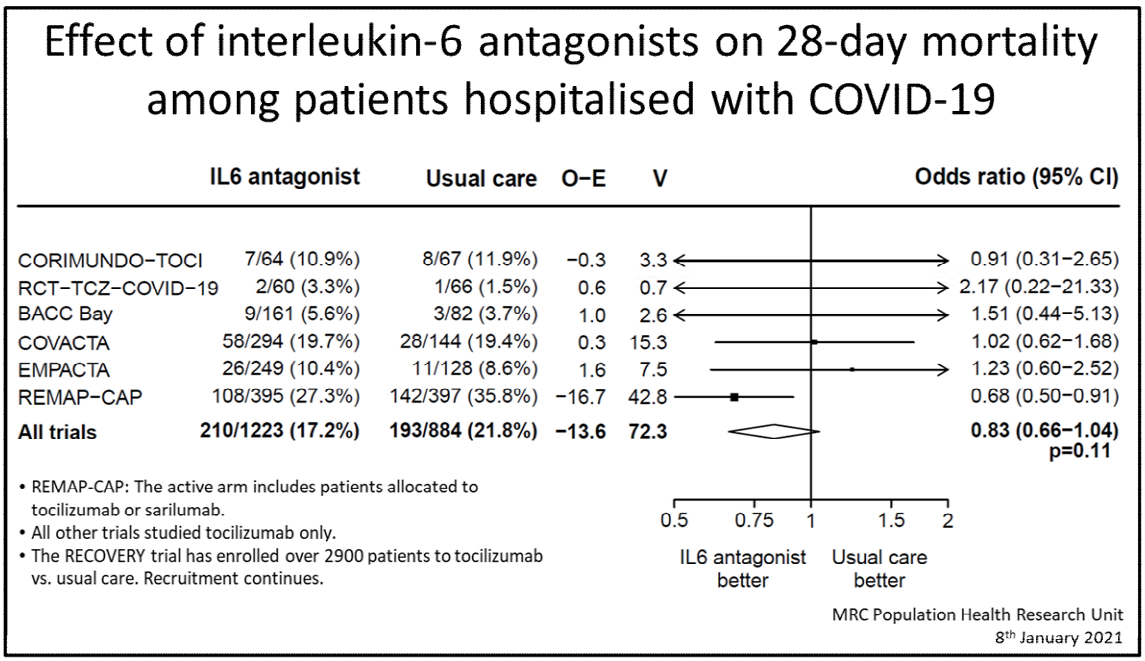
Aspirin, Colchicine, REGN-COV2 monoclonal antibody cocktail

Recruitment of all eligible patients to these treatment comparisons continues as planned.

Additional information on the evidence for tocilizumab as a treatment for COVID-19

Yesterday, the results were announced for the tocilizumab and sarilumab arms of the the REMAP-CAP trial in critically ill patients.[1] The primary outcome of number of organ support-free days was greater among those in the tocilizumab and sarilumab groups compared with the controls (median 10 days [IQR -1 to 16], 11 days [IQR 0 to 16] and 0 days [IQR -1 to 15] for tocilizumab, sarilumab and control respectively). There was also a significant reduction in death: 98/350 (28.0%) of participants allocated tocilizumab died, compared to 142/397 (35.8%) of participants allocated control.

REMAP-CAP is the sixth randomised trial of tocilizumab (or sarilumab) for patients with COVID reported to date. Overall, there is a statistically non-significant reduction in the risk of death (odds ratio 0.83; 95% CI 0.66-1.04; p=0.11).



In RECOVERY, over 2900 participants have been randomly allocated to tocilizumab vs. usual care alone (of whom over 750 are known to have died). Thus the RECOVERY trial contains around twice as much information on the effects of tocilizumab as all the other trials combined. After reviewing all this evidence, the Data Monitoring Committee recommended continuing recruitment.

[1] https://www.medrxiv.org/content/10.1101/2021.01.07.21249390v1

NHS England and NHS Improvement will release guidance for trusts in the coming days. This will reiterate that **"Our [NHSE & NHSI] position remains that participating provider organisations should continue to prioritise recruitment to the RECOVERY trial where applicable."** They will provide guidance for trusts where this is not possible.

We are very grateful for all your support in helping to provide such important data for the benefit of future patients.

Yours sincerely

Peter Horby PhD FRCP Martin Landray PhD FRCP

Chief Investigators for the RECOVERY trial

Appendix (next page): RECOVERY DMC letter 7th January 2021

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Edinburgh Neuroscience

CCBS
Centre for Clinical Brain Sciences

Professor Peter Horby, Professor Martin Landray
RECOVERY trial Co-chairs
Nuffield Department of Population Health
Oxford

7th January 2021

Dear Peter and Martin

RECOVERY trial DMC report

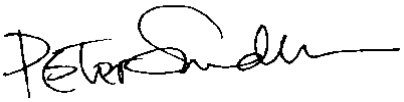
The RECOVERY trial DMC reviewed the safety and efficacy data that were available today for the 23,935 patients randomised. For the interventions still in active recruitment, the numbers included in the comparison of each agent with its control were respectively: convalescent plasma (8,607), tocilizumab (2,718), REGN-COV2 (2,610), aspirin (4,578) and colchicine (2,363).

For patients being considered for treatment with convalescent plasma, we recommend that recruitment of patients who require invasive mechanical ventilation or ECMO at the time of randomisation should be paused. Follow-up of these patients should continue. However, we strongly encourage continuing recruitment of all those patients who, at randomisation, do not require invasive mechanical ventilation or ECMO.

For all the other treatments under study in RECOVERY, in the light of the available trial data and all relevant external information (including the recent announcement of the REMAP-CAP results for Tocilizumab and Sarilumab), we see no cogent reason to modify the protocol or intake to the study. For all these treatments, we therefore recommend continuing recruitment.

The DMC will next review the safety and efficacy data for all treatments on 14th January 2021.

Yours sincerely



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