Development Safety Update Report (DSUR)

Report Number 1

Investigational drug(s)	Hydroxychloroquine Dexamethasone Lopinavir-ritonavir Azithromycin Tocilizumab REGN-COV2 Aspirin Colchicine Baricitinib Dimethyl fumarate Methylprednisolone Intravenous immunoglobulin Anakinra Infliximab
Refers to CTIMP	Randomised Evaluation of COVID-19 Therapy (RECOVERY
DIBD	17-Mar-2020
Reporting period	17-Mar-2020 to 31-Mar-2021
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Sponsor	University of Oxford
Address of Sponsor	Joint Research Office 1st Floor, Boundary Brook House Churchill Drive Headington Oxford OX3 7GB

This report was prepared by the Clinical Trial Service Unit (a Registered Clinical Trials Unit) on behalf of the Sponsor, and contains confidential information.

Name of Chief Investigator: Professor Peter Horby

Signature of Chief Investigator:

EXECUTIVE SUMMARY

The Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial was established rapidly at the start of the COVID-19 pandemic in the UK. It is funded by the UK government (via UKRI and NIHR) and the regulatory sponsor in the University of Oxford. RECOVERY is being conducted at 177 NHS organisations in all four nations of the UK, as well as at international sites in Nepal and Indonesia.

RECOVERY is a platform trial, allowing multiple different IMPs to be assessed among patients hospitalised with COVID-19. Patients of any age who have been admitted to hospital with proven or suspected COVID-19 are eligible, as long as there is no medical history that might, in the opinion of the attending clinician, put the patient at significant risk if he/she were to participate in the trial. Pregnant women were included in the trial, but excluded from the assessment of certain IMPs for which the risks to the unborn child were considered too great.

The primary outcome is all-cause mortality within 28 days of randomisation. Secondary outcomes include the duration of admission and (among participants not on invasive mechanical ventilation at baseline) the composite of invasive mechanical ventilation or death.

IMPs

The RECOVERY Trial has assessed a number of IMPs (see Table).

IMP	Number in comparison	Number on active IMP	Note
Hydroxychloroquine	4716	1561	Recruitment completed 5-Jun-2020
Dexamethasone	6425	2104	Recruitment completed 8-Jun-2020
Lopinavir-ritonavir	5040	1616	Recruitment completed 29-Jun-2020
Azithromycin	7763	2582	Recruitment completed 27-Nov-2020
Colchicine	11,340	5610	Recruitment completed 4-Mar-2021
Tocilizumab	4116	2022	Recruitment completed 24-Jan-2021
Convalescent plasma*	11,558	5795	Recruitment completed 15-Jan-2021
REGN-COV2	9601	4759	Recruitment ongoing
Aspirin	14,892	7351	Recruitment completed 21-Mar-2021
Baricitinib	3008	1505	Recruitment ongoing
Dimethyl fumarate	45	22	Recruitment ongoing
Corticosteroids (children)	120	54	Recruitment ongoing
Intravenous immunoglobulin	116	64	Recruitment ongoing
Anakinra	9	6	Recruitment ongoing
High-dose corticosteroids	-	-	Recruitment yet to start
Infliximab	-	-	Recruitment yet to start

* not an IMP but included for information

Safety assessment

The completed comparisons have demonstrated that dexamethasone reduces the risk of death in patients receiving oxygen and is now the standard of care worldwide for such patients with COVID-19. RECOVERY has also demonstrated that tocilizumab reduces this risk further, such that the combination may reduce the risk of death by between one-third and one-half. Six other comparisons have completed; five of these demonstrated no material benefit of the IMP (nor any conclusive hazard) and follow-up

and analysis continues for the sixth. There are six ongoing comparisons and a further two yet to start. The unblinded interim data for these comparisons is reviewed regularly by the independent Data Monitoring Committee and no safety concerns have been identified.

Conclusion

The RECOVERY trial has demonstrated that it is possible to embed a robust randomised controlled platform trial into routine clinical care during a pandemic, which can then provide reliable information on the safety and efficacy of many treatments recommended for COVID-19.

Unblinded data from the ongoing comparisons within RECOVERY are being regularly reviewed by the independent Data Monitoring Committee who have not raised any safety concerns with these IMPs. Recruitment will continue until sufficient numbers of participants have been recruited to reliably assess the effects of the IMPs, unless the DMC recommend otherwise first.