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Covid-19: Remdesivir has little or no impact on survival, WHO trial shows

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The largest trial to date of treatments repurposed for use in the covid-19 pandemic has shown that none of the four drugs studied produced any measurable benefit in mortality or disease course. This includes remdesivir—a drug already recommended by several guidelines and pre-ordered by numerous governments around the world.

Hydroxychloroquine, lopinavir-ritonavir, and interferon beta-1a regimens also seemed to have little or no effect on 28 day mortality. None of the drugs delayed the need for ventilation or shortened the stay of patients admitted to hospital. "For each drug in the study, the effect on mortality was disappointingly unpromising," said the World Health Organization in a statement.

The WHO Solidarity trial followed 11 266 adults at 405 hospitals in 30 countries and, although the results are preliminary, WHO said that the "conclusive" findings "suffice to refute early hopes" in the four drugs studied. The study, which awaits peer review before publication in a medical journal, has been posted on the preprint website medrxiv.org.[1]

None of the drugs showed any real trend towards improved survival, even a non-significant one. The closest approach to statistical significance was a non-significant trend towards lower survival in patients who took hydroxychloroquine or interferon beta-1a.

The largest previous trial of remdesivir in covid-19, the ACTT-1 study sponsored by the US National Institutes of Health, found a significant benefit in time to recovery and what remdesivir's maker, Gilead, called a non-significant trend towards improved survival at 29 days (hazard ratio 0.73 (95% confidence interval 0.52 to 1.03)). That trial, which published its final report last week,[2] led to the drug's authorisation in the UK, the EU, and the US.

Simplicity and clarity

The WHO trial followed five times as many patients taking remdesivir and 10 times as many overall. "The trial is beautiful in its simplicity and clarity of purpose," said Martin Landray, an Oxford University epidemiologist. He said that the poor results seen with hydroxychloroquine and lopinavir-ritonavir were expected, as they had previously failed to show a benefit in the UK Recovery trial, which Landray leads.

"The result for interferon is interesting, and there will doubtless be some debate about whether different doses or routes of administration—for example, by nebuliser—might be more effective," he said. "But the big story is the finding that remdesivir produces no meaningful impact on survival."

He explained that "people will argue about the need for earlier use" of remdesivir but that, even if it brought modest benefits, "the absolute numbers of lives saved would be small."

Landray added, "Remember too that remdesivir is a drug that is given by intravenous infusion for five to 10 days and costs around £2000 [€2205; $2600] per course. Covid affects millions of people. It is not a rare disease. We need scalable, affordable, and equitable treatments. The WHO Solidarity trial has done the world a huge favour by producing clear, independent, and robust results."

Gilead said in a statement that it was "concerned that the data from this open-label global trial have not undergone the rigorous review required to allow for constructive scientific discussion."

WHO said that the Solidarity trial, which continues to recruit about 2000 patients a month, may expand to investigate newer antiviral drugs, immunomodulators, and anti-SARS-CoV-2 monoclonal antibodies.

1 WHO Solidarity Trial Consortium. Repurposed antiviral drugs for covid-19—interim WHO Solidarity trial results. 15 Oct 2020. doi: 10.1101/2020.10.15.20209817.
2 Beigel J, Tomashek K, Dodd LE, et al. Remdesivir for the treatment of covid-19—final report. *N Engl J Med* 2020 Oct 8. doi: 10.1056/NEJMoa2007764. https://www.nejm.org/doi/pdf/10.1056/NEJMoa2007764.