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Covid-19: Remdesivir has “small effect” against death or progression to ventilation, WHO trial finds

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Remdesivir has no significant effect on patients with covid-19 who are already being ventilated but has a small effect against death or progression to ventilation among other patients admitted to hospital, the World Health Organization’s Solidarity trial has found.¹

This appears to be a change from findings reported in February 2021, when preliminary trial data suggested that remdesivir “had little or no effect on patients admitted to hospital with covid-19.”²

The Solidarity trial recruited over 14 000 patients from 454 hospitals across 35 countries between March 2020 and January 2021, of which over 8000 were allocated 1:1 to remdesivir (10 daily infusions) or control (no drug).

The updated results, published in the *Lancet*, reported that overall 14.5% (602 of 4146) of patients assigned to remdesivir died compared with 15.6% (643 of 4129) assigned to the control group (mortality rate ratio 0.91, 95% confidence interval 0.82 to 1.02, P=0.12).

Looking at patients who were already ventilated, 42.1% (151 of 359) assigned to remdesivir died compared with 38.6% (134 of 347) assigned to control (RR 1.13, 95% CI 0.89 to 1.42, P=0.32). For those who were not already ventilated, however, 11.9% in the remdesivir group, compared with 13.5% in the control group, died (RR 0.86, 95% CI 0.76 to 0.98, P=0.02), while 14.1% v 15.7% progressed to ventilation (RR 0.88, 95% CI 0.77 to 1.00, P=0.04).

Additionally, when looking at death or progression to ventilation together, the researchers found that the remdesivir group performed better than the control (19.6% v 22.5%, RR 0.84, 95% CI 0.75 to 0.93, P=0.001).

The authors highlighted limitations to their study, including that as high flow and low flow oxygen were not recorded separately at enrolment in the trial, it’s not known whether any protective effect in non-ventilated patients extends to those on high flow oxygen.

Delayed publication

The release of these results has prompted questions about why it has taken so long to publish these data, especially considering WHO’s recommendation against the use of remdesivir in patients with covid-19.³

Todd Lee, associate professor of medicine, McGill University, and co-investigator on the Canadian arm of Solidarity, told *The BMJ*, “WHO Solidarity was an important movement towards establishing a global trial during the pandemic. Unfortunately, delays in

bringing remdesivir results to co-investigators and the public have likely contributed to under-utilisation of this drug in many jurisdictions. There should be an examination of the reasons for delay and these should inform us that future international endeavours will need to be more agile and transparent.”

Lee and his colleagues published the results from the Canadian arm of the trial in February. They concluded that compared with standard care remdesivir has a “modest but significant effect on outcomes important to patients and health systems, such as the need for mechanical ventilation.”⁴

Tom Yates, clinical lecturer at the University College London, has also questioned why the WHO trials team has “sat on these data for more than a year.”

“The updated Solidarity results suggest that the drug may offer a meaningful mortality benefit in hospital patients not yet needing mechanical ventilation. WHO should explain why it has taken so long to release these results,” Yates said. “I am surprised that the results were not released as a preprint. Where data may impact practice, as is the case here, it is usual to make the manuscript available while awaiting peer review.”

The BMJ contacted study author and head of the WHO research and development unit Ana-Maria Henao-Restrepo regarding the delay but had not received a response at time of publication.

- 1 WHO Solidarity Trial Consortium. Remdesivir and three other drugs for hospitalised patients with covid-19: final results of the WHO Solidarity randomised trial and updated meta-analyses. *Lancet* 2022. [www.thelancet.com/action/showPdf?pii=S0140-6736\(22\)2900519-0](http://www.thelancet.com/action/showPdf?pii=S0140-6736(22)2900519-0).
- 2 Pan H, Peto R, Henao-Restrepo AM, et al. WHO Solidarity Trial Consortium. Repurposed antiviral drugs for covid-19: interim WHO solidarity trial results. *N Engl J Med* 2021;384:497-511. doi: 10.1056/NEJMoa2023184 pmid: 33264556
- 3 WHO recommends against the use of remdesivir in covid-19 patients. www.who.int/news-room/feature-stories/detail/who-recommends-against-the-use-of-remdesivir-in-covid-19-patients.
- 4 Ali K, Azher T, Baqi M, et al. Canadian Treatments for COVID-19 (CATCO) Association of Medical Microbiology and Infectious Disease Canada (AMMI) Clinical Research Network and the Canadian Critical Care Trials Group. Remdesivir for the treatment of patients in hospital with COVID-19 in Canada: a randomized controlled trial. *CMAJ* 2022;194:E242-51. doi: 10.1503/cmaj.211698 pmid: 35045989

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