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BRIEF19

A daily review of covid-19 research and policy

BREAKING NEWS RESEARCH BRIEFING

Final remdesivir results published after 139 days of waiting.

The preliminary results of the Adaptive Covid-19 Treatment Trial (ACTT-1) randomized trial were published May 22 in *The New England Journal of Medicine* and covered by *Brief19*. ACTT-1 was a double-blind, randomized, placebo-controlled trial of the antiviral drug remdesivir, given to patients intravenously within 72 hours of laboratory-confirmed diagnosis of SARS-CoV-2, among hospitalized patients.

The primary outcome of the preliminary report was time to recovery from covid-19, which was broadly defined as either being released from the hospital or remaining in the hospital for infection-control purposes only. In the preliminary report, the average time to recovery in the remdesivir group was 11 days versus 15 days in the placebo group. No other results were statistically significant, including mortality or the percent of patients receiving oxygen therapy. Missing from the preliminary report was approximately one-third of patients who were enrolled in the study but had not reached day 29 of follow-up.

139 days later, the final report of the ACTT-1 trial has been published in [*The New England Journal of Medicine*](#) with the remainder of the participants included. Patients receiving remdesivir had a median recovery time of 10 days compared to 15 days in the placebo group. The authors also report that patients receiving remdesivir had non-statistically significant differences in mortality at both day 15 and day 29; by day 15, mortality rates were 6.7 percent (remdesivir) and 11.9 percent (placebo); by day 29, mortality rates were 11.4 percent (remdesivir) vs 15.2 percent (placebo). While these results were *not* statistically significant, the overall confidence intervals of the hazard ratio *suggests* there may be a mortality benefit though the trial itself did not include enough test subjects to detect either a net survival benefit or harm. Any mortality difference would be important, but not “game changing,” in contrast to initial hype. The survival curves suggest that the patients most likely to benefit are those on nasal supplemental oxygen only. Furthermore, it seems that those ages 18 to 40 years and those with an onset of symptoms fewer than 10 days before treatment began are the most likely to benefit from remdesivir.

Similar to the preliminary report, the rate of serious adverse events was actually *less* in the remdesivir group (24.6 percent) compared to those in the placebo group (31.6 percent). One worrying finding emerged when assessing the time it took until recovery, divided into certain subgroups. While it is important to remember that unless subgroups analyses are pre-planned and adequately planned for (statistically), any resulting data should be considered “hypothesis-generating” only. That said, Black, Asian, and Hispanic/Latinx people did not benefit from remdesivir while white patients did. It is uncertain why this is the case and whether this represents ethnic / racial disparities, such as when the medication was given, how severe the cases were, or other potential factors. We hope the authors or other experts will address this issue soon.

Overall, the final report does not change the preliminary conclusions. Based on the research to-date, for critically ill covid-19 patients, remdesivir is unlikely to change survival or the need for mechanical ventilation. The only drug to-date that has shown to improve mortality remains dexamethasone, a generic and inexpensive drug.

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