Remdesivir Is Not the Magic Bullet for COVID-19

BY RORY SPIEGEL, MD

The global suffering wrought by the SARS-CoV-2 pandemic is undeniable, but so is the ferocity with which the world has pursued a cure. Some potential remedies seemed more promising than others, but the enthusiasm supporting these novel treatments often outpaced their evidentiary support. In fact, none has demonstrated efficacy backed by high-quality randomized controlled trial data.


The ACTT-1 study did not find a significant difference in mortality in those receiving remdesivir

Beigel, et al., enrolled adult patients with a PCR-confirmed SARS-CoV-2 infection with at least one of the following: radiographic infiltrates by imaging study, a peripheral oxygen saturation of ≤94% on room air, or requiring supplemental oxygen to maintain an adequate oxygen saturation, mechanical ventilation, or extracorporeal membrane oxygenation.

Eligible patients were randomized to receive either 200 mg of IV remdesivir or placebo on day one, followed by 100 mg daily for 10 days. The authors randomized 1063 patients, 541 in the remdesivir group and 522 in the placebo group. Some sites were required to use normal saline due to a shortage of the matching placebo, but the authors attempted to maintain blinding by putting opaque bags over the medication and IV tubing.

The authors reported a statistically significant benefit in patients receiving remdesivir in their primary outcome, time to recovery, as defined by improvements on an eight-category ordinal scale attempting to quantify the severity of respiratory illness. Median time to recovery was 11 v. 15 days in the remdesivir and placebo groups, respectively.

In patients with the most severe disease, those requiring noninvasive or invasive mechanical ventilation, remdesivir appeared to be less efficacious, though given the limitation of power in this subgroup, it is difficult to take much from this finding. Despite a numerically lower value, the authors did not find a statistically significant difference in mortality in patients who received remdesivir (7.6% and 13.4% at 15 days, hazard ratio for death, 0.70; 95% CI, 0.47 to 1.04).

Incomplete Data
The ordinal scale used by these authors to demonstrate benefit is compelling, especially when one examines the bar plots in Fig. S1 in the supplementary appendix, but does a 15-day metric truly encapsulate the breadth and length of this disease’s clinical course? At 15 days, 49.5 percent of patients in the placebo group v. 59.2 percent of patients in the remdesivir group were discharged home.

The authors found that 17.5 percent v. 21 percent of the placebo and remdesivir groups required high-flow nasal cannula and noninvasive or invasive mechanical ventilation, respectively. Most notably, 301 patients did not have complete 29-day data available at the time of collection for this preliminary report.

This is known as censoring, which occurs when data regarding an event of interest are incomplete. In this case, what has occurred is known as right censoring, when the event of interest are incomplete. In this case, what has occurred is known as right censoring, when the final analysis of this data set is published, especially if the results are less favorable than this initial report.

I don’t think remdesivir or any of its lauded predecessors will be the saviors that will ultimately turn the tide of this pandemic. Rather, our eventual triumph will be due to the implementation of vital public health measures and front-line clinicians caring for patients at the bedside. EMN

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