

30 April 2020

## **BRIEF19**

*A daily review of covid-19 research and policy.*

### **RESEARCH BRIEFING**

**The remdesivir saga continues.** Results from three clinical trials were announced regarding the efficacy of the anti-viral medication remdesivir on clinical outcomes in covid-19 patients. Importantly, two of the trials were press releases which did not contain enough details for experts to meaningfully analyze the results. The third was a clinical trial published in *The Lancet*, that we covered yesterday as a breaking news [Brief](#). In that trial no benefit was found for patients who received remdesivir. However, the study was stopped early as there were no more patients to enroll who had SARS-Cov-2 as China had effectively stopped the spread of the virus. This means that the study was not sufficiently powered to detect a clinically meaningful difference between the two groups. However, at the time the trial was stopped, there was no sign of an impending favorable result with respect to mortality.

The two press releases grabbed headlines quickly. One study, announced by the pharmaceutical company Gilead, did not have a control group. In the [study](#), one group of patients received a five day treatment of remdesivir while the other group received a ten day treatment. Over 50 percent of all patients were discharged from the hospital within 14 days. Patients who received the shorter treatment were more frequently discharged than those who received the longer treatment. **Analysis:** We haven't seen the actual data and thus the results are uninterpretable. However, we already know that there was no control arm. This means we will have no way of knowing if the drug helped patients in either the five or ten-day treatment group compared to patients who did not receive the drug. Moreover, we are left to wonder whether the patients who received the shorter five-day course were simply less sick than those who received the 10-day course. This seems likely. Finally, this study was designed in a way that makes it impossible for it to appear that the drug failed. If the 5-day course patients do better, the researchers' conclusions would likely be that early treatment is important. If the 10-day course patients do better, the researchers would conclude that longer treatments are needed before the effect is observable. And if both groups do equally well, the researchers are likely to say that the drug helps everyone.

The other trial was [announced](#) by Dr. Fauci from the *National Institute of Allergy and Infectious Diseases* (NIAID). The protocol for the trial can be found on [ClinicalTrials.gov](#). Again, this is a press release and data are not available for us to scrutinize. The study design -- an adaptive, randomized, double-blind, placebo-controlled trial -- is far more robust than the previously discussed study, designed by Gilead. The NIAID trial aimed to evaluate the safety and efficacy of remdesivir in hospitalized adults diagnosed with covid-19. Patients who received remdesivir recovered 31% faster than those who received the placebo (median time to hospital discharge of 11 days and 15 days, respectively). Furthermore, Dr. Fauci reported that the mortality rate was 8 percent for those receiving remdesivir and 11.6 percent for those receiving placebo, respectively. Although this result was not 'statistically significant', the absolute risk reduction of 3% in a disease that this deadly could have an impact. However, if these data turn out to be statistically

significant (when more patient data is added to the study), 28 patients with covid-19 would need to be treated with remdesivir to save just one life. Additionally, the primary outcome that researchers were assessing was changed less than two weeks ago. Initially the trial was designed to assess mortality and mechanical ventilator use. That was abandoned in favor of a much less impactful primary goal of time to hospital discharge. Additionally, patients were initially meant to be tracked for 14 days. That was changed to 28 days. These changes requires justification from the authors. What we can conclude is that, thus far, no statistically significant survival benefit, has been shown. However, patients leaving the hospital sooner does have benefits. It may help reduce the amount of PPE providers use and free up hospital resources for other patients.

–Joshua Niforatos, MD, Research Section Editor

### **POLICY BRIEFING**

**Covid-19 research faces challenges.** As the push to find drugs and vaccines for covid-19 accelerates, scientists are reporting [difficulties](#) in completing their research due to various factors: Social lockdowns have made it hard to find subjects. Researchers doing vaccine studies are concerned that there may not be enough community exposure to the virus to achieve statistically significant results. In this context, some researchers are deciding to forego standards such as research controls in order to speed up their trials, which could make their findings harder to interpret. *WSJ*.

–Jordan M. Warchol, MD, MPH

**Restarting the economy likely to worsen inequality.** Covid-19 has already deepened [racial inequality](#), with Black and Hispanic Americans both dying and losing their jobs and income at higher rates than whites. As the country slowly reopens, racial and ethnic divides will likely become wider, with wealthier, mostly white Americans able to continue working from home and poorer Americans, many of them Black and Hispanic, forced to choose between financial ruin and returning to workplaces that may not be safe. *New York Times*.

–[Annie Gensel](#), MS

**Remdesivir poised to obtain emergency use authorization despite mixed data.** Yesterday President Trump and Dr. Anthony Fauci both celebrated preliminary data from an NIH trial suggesting that remdesivir can shorten recovery time for some covid-19 patients, even as *The Lancet* published a trial that found no statistically significant clinical benefit for patients with severe covid-19 receiving the drug. Now the FDA is [likely to issue](#) an Emergency Use Authorization for remdesivir, an administration official told the *New York Times*. An EUA is a temporary approval the FDA can grant a drug or device that has not otherwise met the criteria for FDA approval, including rigorous, peer-reviewed clinical trials. Just a few weeks ago the FDA issued an EUA for hydroxychloroquine, another drug President Trump has touted as a game-changer, as a covid-19 therapeutic. There are now allegations that the FDA was responding to political pressure, prompting a Congressional investigation. *New York Times*.

–Kimi Chernoby, MD, JD, Policy Section Editor

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*Brief19* is a daily executive summary of covid-19-related medical research, news, and public policy. It was founded and created by frontline emergency medicine physicians with expertise in medical research critique, health policy, and public policy.