<u>BRIEF19</u>

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Remdesivir finds no benefit for patients with moderate covid-19 illness.

In May, preliminary results of the ACTT-1 clinical trial found that remdesivir may have potential benefit in the treatment of covid-19. That trial, published in the *New England Journal of Medicine,* showed that patients admitted to the hospital with *severe* covid-19 pneumonia who received remdesivir had a shorter hospital length of stay (11 versus 15 days). Since those results were published, the medical community has eagerly awaited more complete results. In particular, the 28-day mortality data from that trial, funded by the National Institute of Allergy and Infectious Diseases (NIAID), has yet to be published, three months on.

Today, more results, this time in a study funded by Gilead, were published in the *Journal of the American Medical Association*. This time, patients admitted to the hospital with *moderate* covid-19 pneumonia (thee ACTT-1 trial focused on *severe* covid-19 illness)—defined as infiltration of the lungs by SARS-CoV-2 and oxygen saturation >94 percent—were randomized to one of three treatment arms: a 10-day course of remdesivir, a five-day course, or standard-of-care. The primary outcome of this trial was the clinical outcomes in these three treatment arms measured on day 11, using a seven point scale ranging from death to discharge.

This study included over 500 patients across 105 hospitals and three continents (North America, Europe and Asia). By day 11, patients in the five-day remdesivir arm had higher odds of improving compared to those who received 10 days of the drug or standard-of-care (odds ratio, 1.65; with 95 percent chance that the odds are between 1.09 and 2.48). (Of note, patients randomized to receive 10 days of the trial drug on average only received the drug for 6 days). The score among patients in the 10-day arm was not statistically different from patients who received standard of care only. However, by day 14, there were similar improvements in clinical status distribution for both 10-day and five-day remdesivir treatments compared to standard-of-care. Interestingly, by day 28 *only* those in the 10-day remdesivir group showed improvement in clinical status distribution compared to standard-of-care. There was no improvement for the five-day group. Additionally, there was no statistical difference between the three groups with respect to 28-day mortality. Regarding side effects, nausea, low potassium levels, and headaches were more common in the patients who received remdesivir.

Ultimately, as was seen with ACTT-1, there remains a lack of impressive evidence to state that remdesivir improves mortality in patients with covid-19 pneumonia. ACTT-1 *was* able to show that those receiving remdesivir are discharged from the hospital slightly earlier. This new trial similarly confirms that by day 11 and 14, patients receiving remdesivir are likely to have improvement in clinical status or be discharged from the hospital. But for patients who are not improving by day 14, the data seems to suggest that remdesivir is unable to change the covid-19 disease trajectory in those destined for lengthy hospital admissions. It is unclear why there was any difference between the 5-day and 10-day treatment arms given that the average patient in the 10-day arm only took remdesivir for six days. Nevertheless, Gilead's study adds to the growing body of literature that remdesivir seems to be relatively safe.

Hope still remains that the 28-day ACTT-1 trial will show some mortality benefit. Regardless, the mortality rate of those with moderate covid-19 pneumonia who are admitted to the hospital remains around one percent. *21 August 2020.*

—Joshua Niforatos, MD, Research Section Editor

Covid-19, race, and hospital mortality. A large study provides insight.

There is a disproportionate incidence of covid-19 cases in minority populations. Covid-19 mortality has also been revealed to be higher in these populations. However, available national-level data for covid-19 cases are missing a large proportion of race/ethnicity data. Out of the 65 percent of states that have reported race and ethnicity data, Black patients accounted for a greater proportion of covid-19 cases compared to the Black population in those states. For example, Louisiana reported 59 percent of their confirmed covid-19 cases in Black patients, with Mississippi reporting 66 percent, and the District of Columbia reporting 75 percent.

A brand new study in *JAMA Network Open* entitled "Association of Race With Mortality Among Patients Hospitalized With Coronavirus Disease 2019 (COVID-19) at 92 US Hospitals" aims to understand the impact of race on covid-19 hospital mortality. This study evaluated patients 18 years and older presenting to Ascension hospitals from February 19, 2020 to May 31, 2020. Patients who were admitted during this time period were tracked until June 25, 2020. Individuals who were in the hospital beyond this date were not included in the time-to-event analyses. The Ascension hospitals that were included in this study spanned across 12 states, included 92 hospitals, and 11,210 patients. Approximately, 37.3 percent of the participants in this study were Black.

Compared to White patients, Black patients were younger with the median age being 66 and were more likely to have Medicaid insurance. Further they had a greater neighborhood deprivation index (NDI) score which is a composite of material and social deprivation derived from American Community Survey (ACS) variables that focuses on poverty, employment, education, and housing. The higher the number, the higher the associated deprivation score. This study also revealed a higher Elixhauser Comorbidity Index (ECI) for Black patients which is a calculated comorbidity assessment.

This study also revealed that Black and White patients were admitted to intensive care units and required invasive mechanical ventilation at similar rates. Among all hospitalized patients, mortality for White patients was 23.1 percent and 19.2 percent for Black patients. For patients sick enough to need the ICU, mortality for White patients was 36.4 percent and 35.2 percent for Black patients.

In this study older age was the strongest risk factor for mortality among hospitalized patients. Male sex, chronic kidney disease, coronary artery disease were also associated with an increased risk of dying. It was also noted that patients with Medicare and unknown insurance statuses had a higher risk of mortality. Overall, race was not associated with an increased risk of mortality for those who were able to access hospital care and were admitted. However this study does have its limitations, since authors did not follow up with patients during the discharge period. There was also variable race data available, and the researchers studied only patients admitted to the hospital. This implies that a combination of pre-existing conditions and other societal factors (such as disparities in long term healthcare access and structural racism), and not hospital care itself, most likely explains the fact that higher percentages of Black people have required hospitalization for covid-19 than census data would predict. *18 August 2020.*   —*Onyeka Otugo MD, MPH*