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BRIEF19

A daily review of covid-19 research and policy

RESEARCH BRIEFING

Monoclonal antibody does not reduce SARS-COV-2 viral load in humans.

Early in the pandemic we published a series of *Briefs* looking at the pathophysiology of SARS-CoV-2 virus. In those briefs, we explained how the SARS-CoV-2 virus binds to receptors on the surface of human cells called angiotensin-converting enzyme 2 (ACE-2) receptors. Binding to ACE-2 allows the virus to connect to the cell and initiate entry. A potential way to prevent covid-19 might be by stopping SARS-CoV-2 entry into human cells via ACE-2.

An antibody that neutralizes the SARS-CoV-2 protein that binds human ACE-2 receptors was developed from the "convalescent" plasma of a patient who recovered from covid-19 and called neutralizing antibody LY-CoV555. Now, the pharmaceutical giant Eli Lilly has published interim results of its Phase 2 randomized clinical trial studying the safety and efficacy of the therapy.

In this study, published yesterday evening in the *New England Journal of Medicine*, patients in the outpatient, non-hospitalized setting who were diagnosed with mild or moderate syndromic covid-19 were randomized to either placebo or a single intravenous infusion of one of three doses of neutralizing antibody (700 mg, 2800 mg, 7000 mg). The primary outcome of the study was the change in nasopharyngeal viral load of SARS-CoV-2 at day 11. Other endpoints assessed included safety, symptoms, and hospitalizations (ER visits and hospitalizations).

The results of the study were interesting but underwhelming. By day 11, most patients had significant decreases in nasopharyngeal viral load, *including the placebo group*, of almost 99.97 percent reduction. Only the 2800 mg infusion of neutralizing antibody LY-CoV555 had a more significant decrease in viral load compared to both 700 mg and, interestingly, the higher dose regimen of 7000 mg as well. The finding many people are excited about is a difference in hospitalization for patients receiving the antibody versus placebo; 1.6 percent and 6.3 percent, respectively. While this sounds good, the sample size is way too small to be confident that this is meaningful. A single patient's outcome could have made a drastic difference here, which is a sign that this finding is on very tenuous ground. A more reliable conclusion is that the antibodies were found to overall be safe when contrasted to the placebo.

The results from the interim analysis of this Phase 2 trial for patients with mild to moderate covid-19 did not appear to significantly reduce viral load of SARS-CoV-2 in non-hospitalized patients. Although the dose of 2800 mg was marginally statistically significant—though of questionable clinical significance—compared to the placebo, it is both irregular and eyebrow raising that the 7000 mg dose was not effective. Regarding the slight decrease in hospitalizations, we take these results as hypothesis generating without knowing more about the patient population and without a sufficient number of events to as to render the data sturdy enough to interpret. *—Joshua Niforatos, MD*

Update on Regeneron: Late yesterday, Regeneron issued a press release (largely for investors) with some data about its monoclonal antibody against SARS-CoV-2. The data are scant. The company says that its antibody, REGN-CoV-2, decreased the viral load in some patients and that subsequent medical visits were lower. But there is no data suggesting a change in rates of hospitalization or death so far. We will follow this closely but remind readers that lowering viral loads is not enough; patients must have better outcomes overall for a therapy to be meaningful. *—Jeremy Samuel Faust, MD MS*