*Week in Review: 16 – 20 November 2020*

# ***BRIEF19***

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

## ***RESEARCH BRIEFING***

**Moderna announces interim covid-19 vaccine data; reports 94.5% effectiveness.**

As we mentioned last week with our briefing on Pfizer's mRNA covid-19 vaccine, the short-term future of the country may be riding on an effective vaccine. A glimmer of hope was revealed last week as Pfizer and BioNTech released interim data from their phase 3 randomized clinical trial of an mRNA vaccine candidate that was reported to be "90% effective". Enter the 94.5% effective Moderna vaccine.

In breaking news today, the Cambridge, Massachusetts-based biotechnology company Moderna, Inc. (Nasdaq: MRNA) announced interim results of its phase 3 randomized clinical trial (RCT) of an mRNA vaccine candidate. In this trial, 30,000 individuals aged 18 years of age and older were enrolled and randomized to receive either the mRNA vaccine or a placebo injection on day 1 *and* day 29.

The primary outcome of the study was the number of participants with a first occurence of *syndromic* covid-19 occurring 14 days after the day 29 second dose of the mRNA vaccine, as well as incidence of side effects.

The data provided by Moderna today were limited. So far, we know that 95 cases of symptomatic covid-19 were detected, 90 of which were in the placebo group (i.e. those who did not receive the mRNA vaccine). There were a total of 11 severe cases, *all* of which occurred in the placebo group and *zero* in the mRNA vaccine group. The side effect profile was considered tolerable with only common vaccine side effects, such as pain at the injection site, fatigue and aching muscles and joints noted.

How does this compare to last week's news that Pfizer/BioNTech covid-19 vaccine was "90% effective"? To summarize, in the Pfizer/BioNTech's vaccine results made public last week, 90% of participants who received the candidate vaccine did not develop *symptomatic covid-19*--though it remains possible that people who received the vaccine could still contracted the SARS-CoV-2 virus but were asymptomatic carriers and vectors (i.e. could still spread) of the disease. *We still don't know.*

Key differences between the Moderna and Pfizer/BioNTech vaccine are described in the infographic accompanying this article. One advantage of the Moderna vaccine is that it can be stored in warmer conditions, including normal refrigeration up to 30 days. Another advantage includes increased effectiveness in preventing covid-19 symptoms (94.5% vs 90%). But both vaccine trials had similarities that are important to highlight, including large and diverse patient populations and the fact that overall no major safety concerns emerged. What we still do not know regarding the Pfizer vaccine is the exact breakdown of how many covid-19 cases occurred in the placebo versus the vaccine group, and how many cases of severe covid-19 occurred in the vaccine group. This is in contrast to information provided by Moderna that shared slightly more granular data.

What does this news mean? In one respect, little has changed. We still do not know whether these vaccines prevent infection and spread, and for how long protection lasts. (The vaccine uses mRNA vaccine technology that has only recently become feasible and has never been approved for similar purposes). Does the vaccine protect the elderly? Does it protect those with immune system dysfunction? Time will tell. On the other hand, we now have a second vaccine that targets the surface proteins of SARS-CoV-2 that shows signs of effectiveness. This ratifies the scientific community's general approach to developing a vaccine faster than at any time in human history. *17 November 2020.*

*—Joshua Niforatos, MD, MTS*

**Remdesivir loses support from the WHO**

Thursday evening, a new review from the World Health Organization was published by the *British Medical Journal*, entitled "A living WHO guideline on drugs for covid-19." This comprehensive document addresses drug interventions in treating covid-19 and this latest version focuses on the use of the anti-viral medication remdesivir. Sure to bring controversary to an already contentious topic is the new stance taken by the WHO which provided a "weak or conditional" recommendation on the use of remdesivir in hospitalized patients. Behind the new WHO stance (in direct opposition to the US FDA) are the results of the WHO Solidarity trial, released as a preprint in October. This over 11,000 patient multi-site multi-national study investigating not only remdesivir but hydroxychloroquine, lopinavir and interferon showed the drug had little or no effect on mortality, decreasing need for mechanical ventilation, or significantly changing hospital duration. Despite previous studies published in the *New England Journal of Medicine* the panel still felt that the extant available evidence is either low quality or low certainty and there is no current proof that remdesivir improves patient-important outcomes. An important clarification the authors made was this does that imply ineffectiveness. Rather, the sum of all current research shows a small and uncertain benefit that must be weighed against the harms. Consideration must be made of socio-economic factors such as equity, feasibility and resources across all healthcare systems worldwide. An accompanying editorial asks if remdesivir simply "Tamiflu redux"? Tamiflu (Oseltamivir) is an expensive influenza medication with limited benefit. Despite its widespread use, it has no real record of saving of lives.

However, The WHO Solidarity trial has been called into question by the drug manufacturer Gilead because it was "open label" (not blinded) and did not have a placebo. That may sound compelling but generally unblinded trials *favor* the intervention, as researchers and healthcare providers on some level "want" new treatements to work.

Will the WHO study tip the scales against the drug? It might. Its enrollment numbers far exceeded previous studies used to justify the use of remdesivir in covid-19 patients. That does not mean that the US FDA will change course though, though the agency has come under fire for its subpar appraisal of literature during the pandemic. One thing is certain; remdesivir does not appear to be the savior many hoped it would be. *20 November 2020*. *—Christopher Sampson, MD, FACEP*

**First coronavirus home test granted emergency use authorization.**

On Tuesday the US FDA announced an Emergency Use Authorization (EUA) for the first rapid coronavirus home test. The Lucira COVID-19 All-In-One Test Kit test uses a nasopharyngeal swab sample that is run on the included device, with results available in 30 minutes. The test is available by prescription for ages 14 and up, with providers required to report all home test results to health department officials in accordance with applicable laws. In addition to the home standards, the EUA also allows the device's use in point-of-care settings, but a healthcare provider must collect the sample for patients under 14. This new at-home test adds to the growing list of easier, faster tests with EUAs aimed at closing the surveillance gap that has plagued accurate tracking during the pandemic. *The FDA. 20 November 2020*. *—Joshua Lesko, MD*

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