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BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Message in a bottle. Moderna's mRNA vaccine candidate makes a splash. In the past few years, the prospect of a producing vaccines that use messenger RNA instead of proteins derived from infectious pathogens including viruses and bacteria has captivated the biotechnology industry. While potential vaccines for many diseases have been synthesized, none have been approved for use anywhere in the world. Yesterday, Moderna, a company in Massachusetts, announced favorable results from a phase 1 trial testing their first vaccine candidate against SARS-CoV-2. Phase 1 trials are designed to establish doses and safety profiles for drugs and vaccines in development. Generally, phase 1 trials are small and enroll 20 or more test subjects. In addition to reporting on the safety of the vaccine—which so far appears to have caused only minimal side effects—the company announced that the vaccine, known as mRNA-1273, elicited an immune responses in the first eight volunteers who received the vaccine for whom data is currently available. This candidate vaccine is composed of genetic material (mRNA) that codes for a spike protein which extrudes from the surface of SARS-CoV-2 particles. While the theory is well-grounded, reality is what matters. It is therefore encouraging that blood later drawn from test subjects in this phase 1 study exhibited antibody levels that were similar or higher than the levels that have been detected in patients known to have recovered from SARS-CoV-2 infection. The company reports that all participants in the study "seroconverted" with respect to neutralizing antibodies, regardless of the dose given. This suggests that the subjects' immune systems recognized the vaccine appropriately ("immunogenicity") though it does not necessarily mean that these responses rendered the patients immune. But there appears to be good news on that front as well. The first eight patients were also found to have mounted "neutralizing" antibody responses 43 days after the vaccines were given. The blood from these patients were taken to labs and placed on plaques of viral particles. The plaques were observed to have been reduced in size, suggesting that the viral particles were being effectively killed. The levels of neutralizing antibodies were either similar or greater than those observed in blood from recovered covid-19 patients ("convalescent sera"). Based upon these findings, the FDA has permitted a phase 2 trial to begin on an expedited basis, which will further assess the safety of the vaccine using the dose that appears to be most promising. Hundreds of patients are to be enrolled. Generally, potential drugs and vaccines that carry serious but rare side effects are unlikely to be detected in phase 1 trials. The results of phase 2 data (as well as a phase 3 trial which would include thousands of patients and is already being planned for rollout as soon as July) will be watched closely for this reason. If the vaccine works but causes unacceptable rates of serious side effects during phase 2 or phase 3 trials, it would be back to square one. Nevertheless, the stock market rewarded this news in trading yesterday.

–Jeremy Samuel Faust MD MS

POLICY BRIEFING

President Trump says he takes hydroxychloroquine. During an event yesterday, President Trump said that for several weeks he has been taking the anti-malarial drug hydroxychloroquine. The drug helps patients with lupus and rheumatoid arthritis but has not been shown to prevent or treat covid-19, as covered extensively in *Brief19.* A letter published yesterday by Dr. Sean

Conley, the president's physician, stated that he and Mr. Trump had discussed the drug on several occasions and decided that taking the drug was warranted. Current guidelines from the National Institutes of Health and the FDA do not recommend taking hydroxychloroquine for any coronavirus-related reason outside of a clinical trial. Previously, Trump announced his support for the unproven treatment, saying, "what do you have to lose?" Hydroxychloroquine is known to have cardiac side effects, and can lead to life-threatening abnormal heart rhythms, especially if combined with other medications with similar side effects. In the past, the president was reported as having been using antibiotic creams for rosacea, a mild skin condition. Many of these creams have active ingredients that possess similar cardiac side effects as hydroxychloroquine. If the president is still taking one of these medications, the cardiac risk from the two drugs could be additive. So far, the president reports no problems have occured. *–Jeremy Samuel Faust MD MS.*

Pandemic exacerbates partisan divide. Instead of pulling the country together, the coronavirus pandemic is pulling it apart along familiar partisan lines, an article in the *Wall Street Journal* points out. One reason: Six of the seven hardest-hit states are led by Democratic governors. Those six states, home to densely packed metropolises and accounting for a third of our country's population, are only represented by 12% of senators. For most senators, therefore, the pandemic is not causing a significant human toll back home, even while it is causing economic devastation. For that majority of senators, the pressure to relieve the economic pain is more intense than the pressure to minimize deaths from the virus. It is not surprising, then, that the Senate is reluctant to pass legislation that would prolong the shutdown and is instead looking to re-open communities as soon as possible. *Wall Street Journal*. *–Kimi Chernoby, MD, JD.*

Tensions over pandemic response surfacing. Yesterday, White House Trade Advisor Peter Navarro accused the Centers for Disease Control and Prevention of letting the country down by fumbling the initial roll out of coronavirus testing. This accusation comes in response to reports of lab error at the CDC that delayed the initial start of coronavirus testing. Just days prior, President Trump called Dr. Anthony Fauci's Senate testimony last week "unacceptable". In his testimony, Dr. Fauci warned against opening the country up too early. The administration on the other hand is under pressure to re-open in the face of a severely depressed economy. These public remarks hint at ongoing in-fighting between the political and scientific arms of the federal government. Last month, Dr. Rick Bright was dismissed from his position overseeing federal vaccine development after not supporting hydroxychloroquine. His dismissal has since resulted in a whistleblower complaint. *CNBC.* *–Kimi Chernoby, MD, JD.*

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