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BRIEF19

A daily review of covid-19 research and policy

RESEARCH BRIEFING

Johnson & Johnson publishes early data for its covid-19 vaccine candidate. The vaccine is a few months behind the mRNA options but may eventually offer advantages.

The past month has been a busy one on the coronavirus vaccine front. With the US FDA granting emergency authorization of the Pfizer and Moderna covid-19 shots, rollouts have begun among healthcare workers and other high-risk persons. We've been able to examine data from both of these mRNA vaccines as well as a third option, the Oxford-AstraZeneca candidate (the current DNA-based vaccine frontrunner).

Today, new data published in *The New England Journal of Medicine* on the Ad26.COV2.S coronavirus vaccine, being developed and tested by Johnson & Johnson. This vaccine is a "recombinant adenoviral vector" vaccine, and it uses a mechanism similar to the Oxford-AstraZeneca approach. Scientists spliced a small piece of the SARS-CoV-2 genetic material in a harmless version of an adenovirus (naturally occuring adenoviruses can and do cause flu-like illnesses; the strains used for vaccines do not). One administered, the vaccine generates an immune response from the body.

Today's results are from the Phase 1-2a trial of 805 participants which took place at multiple sites across the United States and Belgium. Three main cohorts were established and studied. Data from two of those cohorts were reported today: subjects between 18 and 55 years of age and those greater than 65 years of age. (Data from another cohort which will allow long term comparisons between one and two dose regimens were not reported in this new paper). The two cohorts in this study received either a low or high dose intramuscular shot in either a single dose or in a two-dose regimen scheduled 56 days apart. Participants were randomized to one of five groups: low dose followed by low dose, low dose followed by placebo, high dose followed by high dose, high dose followed by placebo and placebo followed by placebo. The main goal of the study was safety and reactogenicity (Phase 1 and Phase 2 trials are not adequately large enough to study efficacy). This differs from the recent vaccine studies which focused on efficacy and made global headlines when they were found to be around 95 percent effective in preventing covid-19 disease.

At day 29 after the first dose, neutralizing antibody levels (titers) were detected in 90 percent or more of all participants. That number increased to 100 percent by day 57. These titers remained stable until day 71. Of note, the second booster dose was associated with antibody levels that were 2.6-2.9 times above levels after the first dose. This implies that a booster shot might provide a great deal of protection, but this study was not designed to study outcomes. Therefore, we do not know whether these higher titers mean greater and longer durability of protection, though it certainly implies that advantage.

Meanwhile, side effects were similar to the mRNA vaccines, with most common complaints being fatigue, headache, myalgia and injection site pain. These effects were reported more often in the high-dose groups.

Similar to the mRNA vaccines, adenovirus-based vaccines cause our cells to produce just the spike protein of SARS-CoV-2 (which our body then generates antibodies to), but not the rest of the virus. In addition, adenovirus itself is "replication incompetent," meaning it has been engineered so that it can't replicate and spread in our bodies. Unlike mRNA vaccines, adenoviruses have been used in the past. A current example of an adenoviral vaccine is the rabies vaccine.

One criticism of adenoviral vaccines is that booster shots may be required, given a waning response over time. Another is that since in general, adenoviruses are common, some individuals may already have immunity prior to vaccine administration. In other words, if someone is immune to the adenovirus itself, the vaccine might fail to work because our body would neutralize it before it gains entry into our cells, a necessary step in order for the coronavirus spike protein to be manufactured and to then trigger an immune response.

However, adenovirus vaccines have a major advantage: storage. Unlike the mRNA vaccines, the Johnson and Johnson vaccine is expected to be stable at normal freezer temperatures for two years or longer. Even at refrigerator temperatures, the vaccine is thought to have a three-month shelf life. The mRNA vaccines require freezers that are so cold that even most pharmacies don't have them, and transportation requires dry ice or unusually cold (and hard-to-come-by) freezers. So if this vaccine works as well as the mRNA options do, it will have substantial appeal.

It must be cautioned that these data reflect early research of Phase 1-2a trials. The report provides information that supports further development of this method as a future vaccine candidate. Phase 3 trials will assess whether this vaccine is as protective as the current available options. While these initial results are promising, nothing can replace Phase 3 data, which we await with anticipation.

—Christopher Sampson, MD, FACEP

POLICY BRIEFING

Supreme court limits abortion pill access during covid-19 pandemic.

On Tuesday, the Supreme Court of the United States granted the Trump Administration's request to reinstate restrictions on those seeking abortions during the covid-19 pandemic. The case, *Food and Drug Administration (FDA) et al v. American College of Obstetricians and Gynecologists (ACOG)*, was fought in light of barriers surrounding in-person medical care that have bene present throughout the pandemic. While the FDA and HHS have waived in-person requirements to obtain several drugs during the national emergency, they did not make the same allowances for an abortion pill, mifepristone, which can end a pregnancy that is under 10 weeks.

Three lower courts previously blocked the FDA's in-person pick-up requirement for mifepristone, citing the risk of contracting covid-19 at a doctor's office or hospital, and the fact that the government had waived several in-person requirements for dispensing other drugs, including opioids. The Supreme Court, however, contradicted that ruling with this one.

Citing technicalities, Chief Justice John Roberts' majority opinion asserted that it was not any court's duty to overrule the FDA's guidance, rather than speaking to whether the case restricted abortion access. Nevertheless, Justice Sotomayor's dissent, arguing that requiring in-person appointments during the deadly pandemic constituted an undue burden on a woman's right to an abortion, and placed a disproportionate strain on marginalized communities, not to mention pregnant women, who already may face greater health risks from covid-19. Moreover, Sotomayor cited statistics that women of color receive more than half of abortions in the US, face a threefold risk of death related to maternal complications, and pointed out that the vast majority of women obtaining abortions, "rely on public transportation to get a clinic to pick up their medication, [and] such patients must bear further risk of exposure when they travel."

Groups representing physicians, including ACOG, emphasized the risk posed to patients, workers and doctors by requiring in-person care, and reiterated that any related counseling can be done via telemedicine visits, after which the drug may be safely taken at home. Justice

Sotomayor thus took issue with the targeting of mifepristone for in-person treatment during the pandemic, writing, "this country's laws have long singled out abortions for more onerous treatment than other medical procedures." Many eyes will be focused on Biden's incoming FDA to reverse course on this and other executive branch policies.

—Miranda Yaver, PhD

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