Two new vaccines deliver good and bad news for the pandemic

Novavax and J&J data underscore challenge of viral variants

By Jon Cohen

Last week’s efficacy results from two new COVID-19 vaccines bolstered confidence that more of the world will soon be protected from the worst of the pandemic disease, but simultaneously challenged the hopes that this first generation of vaccines will offer a sturdy shield against mild and moderate symptoms.

The COVID-19 vaccines made by Novavax and Johnson & Johnson (J&J) joined six others in showing extremely good protection against severe disease and death caused by SARS-CoV-2. But the multicountry trials conducted by each company found that in some places, the efficacy of their vaccines against mild disease fell far below the 90% to 95% range reported for other vaccines. The lowest efficacy against mild disease—49% and 57%, respectively, for Novavax and J&J—was in South Africa, where almost every case of symptomatic COVID-19 is caused by a mutant of SARS-CoV-2 that can dodge antibodies triggered by natural infection or vaccine-induced immunity.

“The euphoria over the vaccines has certainly been tempered by the recent data on the new variants,” says Soumya Swaminathan, chief scientist for the World Health Organization. But she and others stress that the hope for perfection should not be the enemy of the good. Both of the new vaccines promise to prevent hospitalizations and deaths to the same degree as competitors, even against two of the most concerning viral variants.

In addition to increasing the world’s paltry supply of COVID-19 vaccines, the new options might also speed mass immunization campaigns because of a key logistical advantage: Unlike the two messenger RNA (mRNA) vaccines authorized for use in the United States, which require subzero conditions during transport, they can be stored at 2°C to 8°C—refrigerator temperature. The J&J product offers another major plus: It is the first COVID-19 vaccine shown to work with one dose rather than two.

Company representatives and collaborating researchers revealed the new results within 16 hours of each other, in virtual press conferences and press releases that were often thin on data. First came Novavax, a small biotech firm once considered a dark horse in the COVID-19 vaccine race. In the mRNA vaccines that crossed the finish line first, a snippet of genetic code directs the recipient’s cells to produce the SARS-CoV-2 surface protein, spike. In contrast, the Novavax candidate followed a more established strategy, mixing a labmade version of the viral protein with an immune-boosting adjuvant. A trial in the United Kingdom in more than 15,000 people found the vaccine was 89.3% efficacious against mild disease.

“These are spectacular results,” says Clive Dix, chair of the U.K. Vaccine Taskforce. The vaccine also worked well against a highly transmissible SARS-CoV-2 variant, B.1.1.7, which accounted for more than half of the trial’s COVID-19 cases. But interim results from a trial in South Africa were sobering. Among the 4400 participants, the efficacy of Novavax’s vaccine plummeted to 49.4%—the first clinical evidence that a variant identified in South Africa can indeed sidestep vaccine-induced immunity to an extent, as lab evidence had suggested.

The South African trial also revealed that the variant readily evades natural immunity. Of the people in the placebo group who developed COVID-19, 30% had recovered from an earlier infection—a “really concerning” figure, says Shabir Madhi, dean of the medical school at the University of the Witwatersrand and the study’s lead investigator. “We would have expected a large percentage of the population to have developed immunity from that first exposure.”

Still, the trial results put to rest fears that South Africa’s widespread variant might completely thwart the vaccine. “While there definitely is an impact, it’s perhaps not as bad as we all thought it might be,” says Lynn Morris, a virologist at the University of the Witwatersrand. And no one who was vaccinated died or was hospitalized, although there were only two cases of severe disease in the small trial’s placebo group. Novavax says it is now developing “bivalent” vaccines...
containing both the original spike and spikes altered to mimic variants of concern.

J&J reported similar bottom lines from a far larger study of its vaccine, made by its Janssen Pharmaceuticals division. The candidate, which like several two-dose COVID-19 vaccines uses a harmless adenovirus to deliver the gene for spike, was tested in 44,000 people in the United States, Latin America, and South Africa. The single-dose vaccine had an overall efficacy of 66% against symptomatic disease, rising to 85% against severe symptoms, regardless of a person’s age or underlying medical conditions, the firm said.

The vaccine’s efficacy against mild disease was 72% in the United States and 66% in Latin America, dropping to 57% in South Africa. But no one who received it anywhere required hospitalization for COVID-19 or died. “This represents a dream vaccine for a doctor,” says Glenda Gray, a co-chair of the J&J study and head of the South African Medical Research Council. In South Africa, COVID-19 now is the No. 1 cause of death, eclipsing HIV/AIDS and tuberculosis.

J&J plans to file for emergency use authorization from the U.S. Food and Drug Administration (FDA) this week and projects it can produce 1 billion doses this year at about $10 per dose—one-sixth or less of the price of two doses of the mRNA vaccines. Novavax is discussing with FDA whether to wait for a readout from a larger efficacy trial underway in the United States, but says it can make 150 million doses per month as soon as May. It has not announced a price.

Gray and other researchers say the mRNA vaccines’ spectacular efficacy against any COVID-19 symptoms may have become a misleading benchmark for a successful vaccine given SARS-CoV-2’s evolution. Faced with mutant strains like the one in South Africa, those vaccines might not do much better than Novavax’s and J&J’s products did, they suspect. To many, solidly preventing severe disease, regardless of strain, is a significant win. “Do you want a vaccine that prevents coughs or do you want a vaccine that prevents death?” asks Lawrence Corey of the University of Washington, Seattle, who co-leads a trials network testing the J&J, Novavax, and other vaccines bankrolled by the U.S. government’s Operation Warp Speed.

And as the emerging variants show, delivering COVID-19 vaccines into more arms is urgent, and the more options, the better. “What I take away from this week,” says Nahid Bhadelia, an infectious disease physician at Boston Medical Center, “is that we have two more tools in our toolbox at a very precarious time.”

With reporting by Meredith Wadman.

**COVID-19**

**Danish scientists see tough times ahead as variant rises**

Some say the country should reopen—even if it causes cases to surge—once vulnerable populations are vaccinated

*By Kai Kupferschmidt*

On its face, the curve of COVID-19 infections in Denmark looks reassuring enough. A nationwide lockdown has led numbers to plummet from more than 3000 daily cases in mid-December 2020 to just a few hundred now. But don’t be fooled. “Sure, the numbers look nice,” says Camilla Holten Møller of the Statens Serum Institute, who heads a group of experts modeling the epidemic. “But if we look at our models, this is the calm before the storm.”

That’s because the graph really reflects two epidemics: one, shrinking fast, that’s caused by older variants of SARS-CoV-2, and a smaller, slowly growing outbreak of B.1.1.7, the variant first recognized in England and now driving a big third wave of the pandemic there. If B.1.1.7 keeps spreading at the same pace in Denmark, it will become the dominant variant later this month and cause the overall number of cases to rise again, despite the lockdown, Holten Møller says. “It is a complete game changer.”

The same is likely happening in many countries without being noticed. But a massive virus-sequencing effort has allowed Denmark, a country of 5.8 million, to track the rise of the new COVID-19 variant more closely than any other country. “All eyes are on Denmark right now,” says Kristian Andersen, an infectious diseases researcher at Scripps Research who is advising the Danish government. “When it comes to B.1.1.7, is there a way in which ... we can prevent the kind of calamity that we have seen in the U.K. and Ireland, for example?” he asks.

The data aren’t reassuring. Danish scientists’ best guess is that B.1.1.7 spreads 1.5 times faster than previous variants, Holten Møller says. To keep it from spiraling out of control, the country will have to remain in lockdown—or even add new control measures—until a large part of the population has been vaccinated. That prospect is so unappealing that some epidemiologists say Denmark should consider an alternative: Reopen once the most vulnerable people are vaccinated, even if that means a big new surge in cases.

Denmark reported B.1.1.7 within its borders in December 2020, soon after the United Kingdom put the world on notice, and has since stepped up an already impressive virus-sequencing operation. Mads Albertsen, a bacterial genome researcher at Aalborg University, leads a team that has sequenced virus genomes from more than half of all COVID-19 patients so far this year and hopes to reach 70% soon.

It was clear by early January that B.1.1.7 was roughly doubling in frequency every week, says Lone Simonsen, an epidemiologist at Roskilde University. At that point, Denmark had already closed schools and restaurants; to combat the new threat, the lockdown was tightened by cutting the number of people allowed to gather from 10 to five, for example, and doubling the recommended distance between people from 1 to 2 meters. That helped bring the overall reproductive number (R) to a healthy 0.78, according to the most recent estimate. But B.1.1.7 still has an estimated R of 1.07; in

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**A new virus gathers steam**

Previous SARS-CoV-2 variants are rapidly declining in Denmark (top), but B.1.1.7 is on the rise (bottom).
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