



Novavax's protein-based vaccine relies on tried-and-tested technology.

NOVAVAX COVID VACCINE PROTECTS PEOPLE AGAINST VARIANTS

But the experimental shot saw a worrying drop in efficacy against a lineage detected in South Africa.

By Ewen Callaway & Smriti Mallapaty

The biotech firm Novavax has unveiled that its experimental vaccine is effective against rapidly spreading variants of the coronavirus. But its data bring mixed news: although the vaccine was more than 85% effective against a COVID-19 variant identified in the United Kingdom, it was less than 50% effective against a worrying lineage called 501Y.V2, which was detected in South Africa and is spreading around the world.

The findings, announced on 28 January, come from a pair of efficacy trials of Novavax's protein-based vaccine. The South African trial has enrolled more than 4,400 participants, the UK trial around 15,000.

The South African study is the first in people to show, reassuringly, that the 501Y.V2 variant can be quelled using vaccines. Recent data from laboratory experiments had suggested that this variant was partly resistant to antibodies generated by people who had recovered from COVID-19, as well as to those triggered by other vaccines.

"We're still seeing vaccine efficacy, and that's incredibly important," said Glenda Gray, head of the South African Medical Research Council, at a press briefing announcing the

findings. "This will have both an individual and a public health benefit."

But the results raise the worrying possibility that 501Y.V2 and similar variants will cause a significant drop in the effectiveness of other vaccines, says David Ho, a virologist at Columbia University in New York City. His team was one of several that linked 501Y.V2 to a drop in the potency of antibodies elicited by the RNA-based Pfizer and Moderna vaccines.

Trial timing

It was only by chance that the South African trial of the Novavax vaccine was able to measure the effects of 501Y.V2. In late 2020, the variant was identified and linked to a fast-growing epidemic that started in the country's Eastern Cape province and has since spread across the country and beyond. The variant now accounts for more than 90% of COVID-19 cases in South Africa, and it carries mutations in the SARS-CoV-2 spike protein – the immune system's main target against coronaviruses and the basis for most vaccines, including Novavax's.

"None of the vaccines were necessarily designed against this variant," said trial leader Shabir Madhi at the briefing. "It's a very different virus that's infecting people in South Africa right now," added Madhi, a vaccinologist at the

University of Witwatersrand in Johannesburg.

The 501Y.V2 lineage spread so rapidly that it caused nearly all of the COVID-19 cases that the trial recorded. In the group of people who received two vaccine doses, 15 developed COVID-19, compared with 29 of the participants who received a placebo injection. This equates to an efficacy of 49.4%. The study enrolled 240 people who are HIV-positive, and when Madhi's team excluded this group from the analysis, the vaccine was 60% effective.

Madhi says that he'd expected the vaccine to perform much worse against 501Y.V2 than against other variants. That's because emerging data had shown that the variant was impervious to many of the potent 'neutralizing', or virus-blocking, antibodies generated by people who had received other vaccines or had recovered from infection. "A vaccine efficacy of 60% is something which I certainly didn't dream of when I started to see all of the other data that was coming out."

The South African trial was not large enough to determine whether the vaccine is better at preventing severe cases of COVID-19 than it is at preventing milder infections. But evidence that other COVID-19 vaccines work in this way suggests that the Novavax jab will do, too, says Madhi. "I believe this vaccine will impact on hospitalization and severe disease, probably north of 60%."

Trial data also suggested that people who had previously been infected with the original lineage were not protected against re-infection by 501Y.V2. Participants who received the placebo were just as likely to get COVID-19, whether they had antibodies against the virus or not. The data need further scrutiny, but they are "very worrisome", says Marm Kilpatrick, an infectious-disease researcher at the University of California, Santa Cruz.

The results from the UK trial are easier to compare with those for other vaccines. In this trial, investigators detected just 6 infections in the vaccine group, compared with 56 in the placebo arm, equating to an efficacy of 89.3%. The UK trial, too, occurred as a fast-spreading variant, called B.1.1.7, was taking hold. Lab studies have raised fewer concerns about this variant's ability to evade immune responses, and the trial results confirm this. Researchers estimated that the Novavax shot was more than 95.6% effective against the original virus, compared with 85.6% against B.1.1.7.

"This means there will be likely another vaccine that is licensed," says Florian Krammer, a virologist at Icahn School of Medicine at Mount Sinai in New York City. The data from South Africa are concerning, but Krammer would like to see more details before passing judgement. "If it turns out that the vaccine protects 50% against symptomatic disease caused by the variant, and to a much higher degree against moderate-severe disease, we are still in good shape," he says.