NIH Begins Clinical Trial Evaluating Second COVID-19 Booster Shots in Adults

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A Phase 2 clinical trial evaluating various additional COVID-19 booster shots has begun enrolling adult participants in the United States. The trial aims to understand if different vaccine regimens—prototype and variant vaccines alone and in combinations—can broaden immune responses in adults who already have received a primary vaccination series and a first booster shot. The study, known as the COVID-19 Variant Immunologic Landscape (COVAIL) trial, is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

“We are looking beyond the Omicron variant to determine the best strategy to protect against future variants,” said NIAID Director Anthony S. Fauci, MD. “This trial will help us understand if we can use prototype and variant vaccines alone or together to shift immune responses to cover existing and emerging COVID-19 variants.”

Despite waning protection against infection and mild illness during the Omicron wave, COVID-19 vaccines available in the United States so far have maintained durable protection against severe COVID-19. However, NIAID is preparing for the possibility of future variants evading protection against currently available COVID-19 vaccines.

COVID-19 vaccine manufacturers can adjust prototype vaccines to target specific variants, a process similar to how manufacturers update seasonal influenza vaccines every year to target circulating strains. However, predicting if, when and where new COVID-19 variants will emerge and how they will affect the population, remains challenging. Studies indicate that Omicron has a combination of mutations that make it substantially different from prior SARS-CoV-2 variants. Should a new variant emerge that more closely resembles ancestral SARS-CoV-2 or, for example, the Delta variant, an Omicron-specific vaccine may not offer substantial protection. An individual’s response to booster shots may also be impacted by their history of prior infection and vaccination, or both, and what type of COVID-19 vaccines they received.

Vaccine manufacturers have previously studied some variant vaccine candidates and are currently conducting clinical trials of Omicron-specific vaccines. The COVAIL trial will gather data on the immune responses induced by prototype vaccines and variant vaccine candidates—including

bivalent vaccines, which target two SARS-CoV-2 variants—to inform booster shot recommendations.

Nadine Rouphael, MD, director of the Hope Clinic at the Emory Vaccine Center in Atlanta, and Angela Branche, MD, associate professor of medicine at the University of Rochester Medical Center in New York, are leading the trial. Site investigators at 24 clinics are enrolling 600 participants 18 years and older who already have received a primary COVID-19 vaccination series and booster shot. Participants are randomly assigned to one of six vaccine regimens:

1. One 50-microgram (mcg) injection of the mRNA-1273 (Spikevax) prototype vaccine, which is the same vaccine currently authorized in the United States as a booster shot for adults
2. One 50-mcg injection consisting of mRNA-1273.351 (an investigational vaccine targeting the Beta variant) and mRNA-1273.529 (an investigational vaccine targeting the Omicron variant)
3. Two vaccinations administered two months apart: each vaccination is one 50-mcg injection containing both mRNA-1273.351 and mRNA-1273.529
4. One 50-mcg injection consisting of mRNA-1273.617.2 (an investigational vaccine targeting the Delta variant) and mRNA-1273.529
5. One 50-mcg injection of mRNA-1273.529
6. One 50-mcg injection consisting of mRNA-1273 (Spikevax) and mRNA-1273.529

The first stage of this trial is being conducted in collaboration with Moderna, Inc., based in Cambridge, Massachusetts, and Moderna is manufacturing the study vaccines that will be administered. The trial will be adapted to enroll more participants to evaluate additional vaccine platforms and variant vaccines from other manufacturers as needed to further inform public health decisions.

Participants will be monitored for symptoms and adverse events following vaccination and will be asked to return to the clinic during set times over the course of 12-14 months to provide blood samples. Investigators will evaluate the samples in the laboratory to measure and characterize immune responses to SARS-CoV-2 strains. Investigators aim to have initial findings available by August 2022.

The study is being conducted in collaboration with academic medical centers across the U.S., NIAID's Infectious Diseases Clinical Research Consortium (IDCRC) and the NIAID SARS-CoV-2 Assessment of Viral Evolution (SAVE) Program.

For more information about the trial, including specific site locations, and for details on how to participate, please visit clinicaltrials.gov and search identifier NCT05289037. The trial is funded through a contract to Frederick National Laboratory for Cancer Research, operated by Leidos Biomedical Research (75N91019D00024) in Frederick, Maryland. The IDCRC's protocol development work is supported by cooperative agreement UM1AI148684.

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