Phase 3 clinical trial of investigational vaccine for COVID-19 begins

July 27 2020

Credit: CC0 Public Domain

A Phase 3 clinical trial designed to evaluate if an investigational vaccine can prevent symptomatic coronavirus disease 2019 (COVID-19) in adults has begun. The vaccine, known as mRNA-1273, was co-developed by the Cambridge, Massachusetts-based biotechnology company Moderna, Inc., and the National Institute of Allergy and

Infectious Diseases (NIAID), part of the National Institutes of Health. The trial, which will be conducted at U.S. clinical research sites, is expected to enroll approximately 30,000 adult volunteers who do not have COVID-19.

"Although face coverings, physical distancing and proper isolation and quarantine of infected individuals and contacts can help us mitigate SARS-CoV-2 spread, we urgently need a safe and effective preventive vaccine to ultimately control this pandemic," said NIAID Director Anthony S. Fauci, M.D. "Results from early-stage clinical testing indicate the investigational mRNA-1273 vaccine is safe and immunogenic, supporting the initiation of a Phase 3 clinical trial. This scientifically rigorous, randomized, placebo-controlled trial is designed to determine if the vaccine can prevent COVID-19 and for how long such protection may last."

Moderna is leading the trial as the regulatory sponsor and is providing the investigational vaccine for the trial. The Biomedical Advanced Research and Development Authority (BARDA), of the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response and NIAID are providing funding support for the trial. The vaccine efficacy trial is the first to be implemented under Operation Warp Speed, a multi-agency collaboration led by HHS that aims to accelerate the development, manufacturing and distribution of medical countermeasures for COVID-19.

"Having a safe and effective vaccine distributed by the end of 2020 is a stretch goal, but it's the right goal for the American people," said NIH Director Francis S. Collins, M.D., Ph.D. "The launch of this Phase 3 trial in record time while maintaining the most stringent safety measures demonstrates American ingenuity at its best and what can be done when stakeholders come together with unassailable objectivity toward a common goal."

The NIH Coronavirus Prevention Network (CoVPN) will participate in conducting the trial. The network brings together expertise from existing NIAID-supported clinical research networks. The mRNA-1273 vaccine candidate will be tested at approximately 89 clinical research sites in the United States, 24 of which are part of the CoVPN. Investigators will use public health data and incidence trajectory modeling to identify sustained high-incidence areas and emerging hot zones, so sites near these locations can be prioritized for enrollment.

"Thanks to President Trump's leadership and the hard work of American scientists, the investigational vaccine developed by NIH and Moderna has reached this Phase 3 trial at record pace," said HHS Secretary Alex Azar. "Operation Warp Speed is supporting a portfolio of vaccines like the NIH/Moderna candidate so that, if the results of clinical trials meet FDA's gold standard, these products can reach Americans without a day's delay."

NIAID scientists developed the stabilized SARS-CoV-2 spike immunogen (S-2P). SARS-CoV-2 is the virus that causes COVID-19; the spike protein on its surface facilitates entry into a cell. Moderna's mRNA-1273 uses the mRNA (messenger RNA) delivery platform to encode for an S-2P immunogen. The investigational vaccine directs the body's cells to express the spike protein to elicit a broad immune response. A Phase 1 clinical trial found the candidate vaccine to be safe, generally well-tolerated and able to induce antibodies with high levels of virus-neutralizing activity. Moderna initiated Phase 2 testing of the vaccine in May 2020.

Hana M. El Sahly, M.D., principal investigator of the NIAID-funded Infectious Diseases Clinical Research Consortium site at Baylor College of Medicine in Houston; Lindsey R. Baden, M.D., principal investigator of the NIAID-funded Harvard HIV Vaccine Clinical Trials Unit at Brigham and Women's Hospital in Boston; and Brandon Essink, M.D.,

principal investigator and medical director of Meridian Clinical Research, will serve as co-principal investigators for the Phase 3 trial of mRNA-1273.

As part of the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership, NIH and other HHS agencies and government partners, in collaboration with representatives from academia, philanthropic organizations, and numerous biopharmaceutical companies, advised on the trial protocol design and endpoints to ensure a harmonized approach across multiple vaccine efficacy trials.

The trial is designed to evaluate the safety of mRNA-1273 and to determine if the vaccine can prevent symptomatic COVID-19 after two doses. As secondary goals, the trial also aims to study whether the vaccine can prevent severe COVID-19 or laboratory-confirmed SARS-CoV-2 infection with or without disease symptoms. The trial also seeks to answer if the vaccine can prevent death caused by COVID-19 and whether just one dose can prevent symptomatic COVID-19, among other objectives.

Trial volunteers will receive two intramuscular injections approximately 28 days apart. Participants will be randomly assigned 1:1 to receive either two 100 microgram (mcg) injections of mRNA-1273 or two shots of a saline placebo. The trial is blinded, so the investigators and the participants will not know who is assigned to which group.

Volunteers must provide informed consent to participate in the trial. They will be asked to provide a nasopharyngeal swab and a blood sample at an initial screening visit and additional blood samples at specified time points after each vaccination and over the two years following the second vaccination. Scientists will examine blood samples in the laboratory to detect and quantify immune responses to SARS-CoV-2.

Investigators will closely monitor participant safety. They will call participants after each vaccination to discuss any symptoms and will provide participants with a diary to record symptoms and a thermometer for temperature readings.

If a participant is suspected to have COVID-19, the participant will be asked to provide a nasal swab for testing within 72 hours. If the test is positive for SARS-CoV-2 infection, the participant will be followed closely and referred for medical care if symptoms worsen. Participants will be asked to provide a daily assessment of symptoms through resolution and have saliva sampled periodically, so investigators can test for SARS-CoV-2 infection.

Study investigators will regularly review trial safety data. An independent data and safety monitoring board (DSMB) will review blinded and unblinded data—including safety data and cases of COVID-19 in both groups—at scheduled data review meetings.

Provided by NIH/National Institute of Allergy and Infectious Diseases