Homing In On a SARS-CoV-2 Correlate of Protection

An analysis of SARS-CoV-2 antibodies from participants in an mRNA-1273 (Moderna) vaccine efficacy trial has brought scientists closer to identifying a correlate of protection against COVID-19. The surrogate immunological markers are needed to accelerate the path to modified or new vaccines and to quickly expand existing vaccines into new groups.

The study, published in Science, included data from 1010 participants in the phase 3 Coronavirus Efficacy, or COVE, trial who received both mRNA-1273 vaccine doses and 137 participants who received placebo. Thirty-four percent were 65 years or older and 40% were at risk of severe COVID-19.

Several binding and neutralizing antibody markers—including 50% inhibitory dilution (ID50) neutralizing antibody titer, a measure of SARS-CoV-2-killing antibody concentration in blood—correlated with vaccine efficacy over 4 months. Participants with ID50 neutralization titers of 10, 100, and 1000 had 78%, 91%, and 96% estimated vaccine efficacy, respectively, against symptomatic laboratory-confirmed COVID-19.

The study is “part of the totality of evidence supporting neutralizing antibody levels as a correlate of protection [and is] one of the most important sources of evidence because of the rigor of a randomized double-blinded placebo-controlled trial,” colead author Peter Gilbert, PhD, of the Fred Hutchinson Cancer Research Center, wrote in an email to JAMA. Replication across other phase 3 trials is needed to further bolster the evidence, he said.

Investigators are planning phase 3 trial analyses directly studying Delta and Omicron variant antibody levels as correlates of protection against Delta and Omicron infections “to validate whether the correlate of protection model transports well across variants,” Gilbert noted.

Studies Suggest COVID-19 Vaccine Boosters Save Lives

The results of 2 large studies comparing severe disease and death among individuals vaccinated against COVID-19 support a benefit of booster doses. Both studies were conducted in Israel, where BNT162b2 (Pfizer-BioNTech) boosters were introduced in July 2021.

One analysis included data from more than 840,000 vaccinated people aged 50 years or older, 90% of whom received a booster dose. The death rate was 0.16 per 100,000 persons per day in the booster group compared with 2.98 per 100,000 persons per day in the nonbooster group. The other study involved almost 4.7 million vaccinated individuals aged 16 years or older. Across age groups, COVID-19 cases and severe illness were substantially lower among those who received a booster, as were deaths among those 60 years old or older who were boosted.

Together, the findings indicated that COVID-19 boosters have a relative effectiveness of 90% to 95% against severe disease or death, according to an editorial that accompanied the studies in the New England Journal of Medicine. “This means that if the absolute effectiveness of two vaccine doses is 90%, the absolute effectiveness of two doses plus a booster is 99 to 100%,” the editorialist, Minal K. Patel, MD, of the US Centers for Disease Control and Prevention’s COVID-19 Response International Task Force, wrote.

The studies, Patel added, “provide much-needed evidence of the effectiveness of the booster dose.” She noted, however, that in 105 countries, less than 40% of the population has received a full primary vaccine series and that increasing primary vaccination uptake throughout the world will make the most difference in preventing severe COVID-19 illness and death.

COVID-19 Vaccine Focused on T-Cell Response Promising in Early Trial

Investigators reported the first clinical trial results for CoVac-1, a COVID-19 vaccine candidate designed to induce T-cell immunity, in Nature. The multipeptide-based vaccine had a favorable safety profile and induced a broad and potent T-cell response.

Developed at the University of Tübingen in Germany, CoVac-1 is an adjuvanted vaccine candidate that includes 6 SARS-CoV-2 peptides recognized by recovering patients’ T cells. The phase 1 open-label trial tested a single subcutaneous CoVac-1 injection among 36 healthy adults in Germany aged 18 to 80 years.

No serious or life-threatening adverse events occurred through day 56. All participants developed an expected injection-site granuloma and about a third reported transient fatigue. Other adverse events included localized redness, swelling, and ulcers, and 22% of participants reported swollen lymph nodes in the groin area. Two individuals experienced reactivations of varicella-zoster virus and herpes simplex virus.

The candidate elicited a range of T-cell responses, including interferon-γ T-cell responses that lasted through 3 months and exceeded those induced by SARS-CoV-2 infection and approved vaccines. In laboratory tests, mutated peptides from SARS-CoV-2 variants of concern including Delta did not affect the T-cell responses.

“This CoVac-1 may well serve as a (complementary) vaccine to induce T-cell immunity, particularly in elderly and immunocompromised individuals with impaired ability to mount sufficient immune responses after SARS-CoV-2 vaccination with currently approved vaccines,” the authors wrote. A trial is now evaluating the investigational vaccine among patients with B-cell deficiencies. – Jennifer Abbasi

Note: Source references are available through embedded hyperlinks in the article text online.