Novel COVID-19 vaccine may provide protection for cancer patients with B-cell deficiencies

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CoVac-1, a new vaccine against SARS-CoV-2, induced T-cell immune responses in 93 percent of patients with B-cell deficiencies, including many patients with leukemia and lymphoma, according to results

presented at the AACR Annual Meeting 2022, held April 8-13.

"To our knowledge, CoVac-1 is currently the only peptide-based vaccine candidate specifically developed and evaluated for immunocompromised patients," said Juliane Walz, MD, senior author of the study and a professor of peptide-based immunotherapy at the University Hospital Tübingen in Germany.

While vaccination induces a robust immune response against the SARS-CoV-2 virus in the majority of individuals, approved vaccines have shown decreased efficacy in many immunocompromised people. Patients undergoing treatment for blood cancers represent one such population, as their treatment regimens often damage healthy immune cells, particularly B cells, in addition to malignant ones.

"In the clinic, we see many cancer patients who do not mount sufficient humoral immune responses after vaccination with available SARS-CoV-2 vaccines," Walz said. "These patients are thus at a high risk for a severe course of COVID-19."

Many chemotherapies and some immunotherapies destroy B cells, the immune cells responsible for humoral (antibody-mediated) responses. Currently approved SARS-CoV-2 vaccines rely heavily on humoral responses, which may be impaired in patients with a B-cell deficiency. One way to compensate for this is to enhance the response from T cells, another type of immune cell.

"T-cell immune responses against SARS-CoV-2 are of particular importance for patients with B-cell deficiencies, who develop very limited antibody responses after infection or vaccination," said Claudia Tandler, MSc, a graduate student at the University of Tübingen, who presented the study. "T cell-mediated immunity is indispensable for developing protective antiviral responses, and previous evidence has

shown that T cells can combat COVID-19 even in the absence of neutralizing antibodies."

Designing a vaccine to stimulate T cells, Tandler explained, requires the careful selection of SARS-CoV-2 antigens—small pieces of viral proteins that can stimulate immune cells. While the current mRNA-based vaccines produce a larger piece of a single protein—the spike protein—which our cells can break down into antigens, Tandler and colleagues chose six specific antigens from different parts of the virus (not limited to spike) to make up their vaccine. CoVac-1 is a peptide vaccine, meaning that the protein pieces are injected directly, rather than being encoded via mRNA.

"CoVac-1-induced T-cell immunity is far more intense and broader, as it is directed to different viral components than mRNA-based or adenoviral vector-based vaccines that are limited to the spike protein and are thus prone to loss of activity due to viral mutations," Tandler said.

The researchers previously tested the safety and preliminary efficacy of CoVac-1 in individuals without immune deficiency and found that all those who received the vaccine maintained robust T-cell responses three months after vaccination, including responses against omicron and other SARS-CoV-2 variants of concern, with minimal systemic side effects. These results provided the foundation for a phase I/II clinical trial testing the vaccine's efficacy in immunocompromised patients.

In the phase I part of this trial, the researchers recruited 14 patients with a B-cell deficiency, including 12 patients with leukemia or lymphoma. The patients were given a single dose of CoVac-1 and monitored for up to six months for safety and immunogenicity. Notably, 64 percent of the patients in this study had been previously vaccinated with an approved SARS-CoV-2 vaccine that failed to elicit a humoral immune response.

Fourteen days after vaccination, T-cell immune responses were observed in 71 percent of patients, which rose to 93 percent of patients 28 days after vaccination. The researchers measured the potency of CoVac-1-induced T-cell responses and found them to exceed spike-specific T-cell responses observed in B cell-deficient patients after vaccination with mRNA vaccines. T-cell responses from CoVac-1 also exceeded those mounted by individuals who are not immunocompromised following a SARS-CoV-2 infection.

The researchers are currently preparing a phase III clinical trial to evaluate CoVac-1 in a larger population of immunocompromised individuals, and Walz is hopeful that the results will allow this new vaccine to protect cancer patients with B-cell deficiencies from severe cases of COVID-19.

"CoVac-1 is designed to induce broad and long-lasting SARS-CoV-2 T-cell immunity, even in individuals who have impaired ability to mount sufficient immunity from a currently approved vaccine, and thus protect these high-risk patients from a severe course of COVID-19," Walz said.

Limitations of this study include a relatively small sample size with low racial and ethnic diversity.

More information: Conference: www.aacr.org/meeting/aacr-annual-meeting-2022/

Jonas S. Heitmann et al, A COVID-19 peptide vaccine for the induction of SARS-CoV-2 T cell immunity, *Nature* (2021). DOI: 10.1038/s41586-021-04232-5

Clinical trial: clinicaltrials.gov/ct2/show/NCT04954469