

Developing and Studying the Investigational City of Hope COVID-19 Vaccine

BY SANJEET DADWAL, MD



City of Hope is a National Cancer Institute-designated comprehensive cancer center and founding member of the National Comprehensive Cancer Network. Its mission is centered on transforming the future of healthcare through advancing research and quality patient care for people with cancer, diabetes, and other serious illnesses. In huge part, this mission is carried out in its research program, which now includes the development and study of an investigational City of Hope COVID-19 vaccine known as COH04S1.

The investigational City of Hope COVID-19 vaccine is important because it was designed with immunocompromised patients in mind, including transplant patients and those with cancer. As chief of the division of infectious diseases and co-chair of the infection control committee at City of Hope, I have seen first-hand the unique situation immuno-compromised patients face with the COVID-19 vaccines currently under emergency use authorization by the U.S. Food and Drug Administration.

The current recommendation led by the Centers for Disease Control and Prevention is for everyone to get vaccinated—regardless of patients' immune status. Though the COVID-19 pandemic is a great example of the benefits of vaccine research and development, little research has been done to show a more positive response in patients with cancer and other immuno-compromised people. This was made apparent in data released by Johns Hopkins University on the Pfizer-BioNTech and Moderna COVID-19 vaccines.¹ Researchers at Johns Hopkins conducted a multicenter

study in which they looked at the antibody response of these vaccines and found that they produce very low rates of detectable antibodies in patients with solid organ transplants and others who are immuno-compromised. These findings identified a need to study and evaluate a COVID-19 vaccine that induces a much better response in these patients.

That is not to say that patients with cancer or others who are immuno-compromised should forgo COVID-19 vaccination. Instead, those who receive a COVID-19 vaccine should be told that their chance of responding to the vaccine varies depending on their disease—those with solid tumors respond better than those with a blood cancer. All immuno-compromised patients with a history of or active cancer should be advised to continue practicing social distancing and to wear masks to stay safe even after they are vaccinated.

I work with Don J. Diamond, PhD, professor in the Department of Hematology & Hematopoietic Cell Transplantation, who leads research on vaccine development for hematologic malignancies, solid tumors, and cytomegalovirus human immunodeficiency virus and who led development of City of Hope's investigational COVID-19 vaccine. When the COVID-19 pandemic first began, Dr. Diamond and his team quickly began developing a vaccine for the virus. Based on the track record of the investigational vaccine platform, we believe that people, especially those who are immuno-compromised, may have a better response. But that hypothesis needs to be investigated.

Vaccine Design

Dr. Diamond and his team used the Modified Vaccinia Ankara (MVA)—a vaccine delivery system for antigens—as the vehicle for City of Hope's investigational COVID-19 vaccine. MVA technology has been around for a long time and has been tested extensively in patients who have received hematopoietic cell transplants. Studies have found that these MVA-based vaccines are very safe, effective, and able to induce a good immune response even in patients who are immuno-compromised. The investigational City of Hope COVID-19 vaccine is novel because it is the only one in study in the United States that uses the SARS-CoV-2 spike protein and nucleocapsid proteins to induce an immune response in the host. By using both the spike and the nucleocapsid proteins, we believe that the vaccine will be more immunogenic and will induce antibody responses and a very strong T-cell response.

T-cells are the immune cells that linger behind after vaccine injection and can be recalled by the body when you are exposed to the SARS-CoV-2 infection. So even when the antibody count decreases, these T-cells can still fight the virus. We believe the vaccine should work by inducing an immune response to two different targets and may have a lasting, more durable response in people. We also believe that side effects should be less severe and that the investigational vaccine could have a more robust and positive effect on the immune system, especially in immuno-compromised patients.

Animal studies are being done now in Dr. Diamond's lab to look at the vaccine and the COVID-19 variants we have seen so far. We have targeted the two major COVID-19 components recognized by the immune system, namely, the spike and the nucleocapsid proteins, and we believe that it could be effective against known variants (because most of the mutations are in the spike protein). But it is still too early to truly make this determination, because research data will prove the effectiveness of the vaccine on COVID-19 variants.



Josh Jenisch is executive director of content at City of Hope.



Josh Jenisch receives the investigational City of Hope COVID-19 vaccine.

City of Hope began animal studies in April 2020, in May we developed the investigational COVID-19 vaccines, and the optimal vaccine candidate was chosen in June. The animal studies showed a good antibody and cellular immune response to the vaccine candidate. Manufacture of the new investigational COVID-19 vaccine was completed by August 2020, and applications were filed with the U.S. Food and Drug Administration by October 2020 to begin the phase I clinical trial.

Our Phase I Clinical Trial: A First-Person Perspective

We are still conducting the phase I clinical trial for the City of Hope investigational COVID-19 vaccine, whose principal investigator is Dr. John Zaia, director of City of Hope's Center for Gene Therapy. This phase I study is designed to evaluate safety and optimize the effective dosage. We began with a lower dose, followed by a medium dose, and then a high dose to study the immune response with a small selection of participants. These first set of studies gave us the dosing mechanism for this vaccine: two doses per individual. Patients get the first dose at day zero and the second dose at day 28. As a co-investigator from a clinical standpoint, I help enroll patients in the study and follow up with them in the clinic.

Josh Jenisch is executive director of content at City of Hope. He often speaks with and shares the amazing stories of the patients we treat on our website and through our social media channels. As part of City of

Hope's initiative to increase trial accrual, we offered the opportunity to join the clinical trial to those who work with us, as well as those in the broader community. Jenisch was one of the first to volunteer to take part in the phase I trial.


"I had been sitting at home since March, really just frustrated with my inability to do anything about this virus," Jenisch said. "I go to work every day, and I work alongside some of the smartest folks on the planet. I was unable to help them, even in the most rudimentary way."

We sent out an email to all City of Hope staff offering the opportunity to participate in the phase I clinical trial in December 2020.

"I just had this realization that this is the one thing I could do right to push the science forward," Jenisch explained. He received the investigational COVID-19 vaccine in December and continues to come in for follow-up as we continue to study it. He experienced no symptoms himself and found the process easy and straightforward.

"It was almost exactly like getting a flu shot," he says. "I didn't have any side effects whatsoever. But the best part of this experience for me was getting to work from inside the science. I'm in communications, so I'm always hearing about these things after the fact. This was a chance for me to be in that background space with doctors like Dr. Dadwal, Dr. Zaia, and Dr. Diamond. These really smart scientists. For someone who

loves science and discovery, it was a perfect opportunity."

The situation is improving in the United States. More people are getting vaccinated, and the federal government has said that vaccinated individuals need not wear masks when indoors except where required by local guidance. However, the story is different for people who are immuno-compromised. Even after COVID-19 vaccination, these individuals are advised to continue to wear masks because it is unclear how effective the current vaccines are for them. Their treatment blunts the immune system so that it doesn't produce as many antibodies as the vaccines are designed to stimulate. The hope is that further clinical trial data on City of Hope's investigational COVID-19 vaccine will result in a viable option for patients with cancer or who are immuno-compromised. 

Sanjeet Dadwal, MD, is chief of the Division of Infectious Diseases and co-chair of the Infection Control Committee at City of Hope in Duarte, Calif.