MedicalXpress

Triplex vaccine reduces rate of CMV complications in transplant recipients

February 11 2020

Patients who underwent a stem cell transplant and received the Triplex vaccine to prevent a type of herpes virus—cytomegalovirus (CMV) - from duplicating out of control were 50% less likely to develop health complications related to the virus than patients who did not take Triplex, according to a City of Hope-led study published today in *Annals of Internal Medicine*.

The phase 2 randomized, placebo-controlled clinical trial, which took place at City of Hope, Dana-Farber Cancer Institute and MD Anderson Cancer Center, is the first time a viral anti-CMV vaccine has been tested in patients. The trial enrolled 102 people who underwent an allogeneic hematopoietic stem cell transplant (HSCT), which can cure blood cancers such as lymphoma and leukemia. Half of the patients were randomly assigned to receive Triplex, developed by City of Hope scientists to enhance CMV-specific T cells, create immunity in patients against CMV and prevent it from causing such severe complications as pneumonia, gastroenteritis and retinitis.

In the trial, patients who received at least the first of two planned injections of Triplex on day 28 and day 56 after HSCT had 50% fewer CMV complications (virus reactivation, antiviral treatment and disease) through day 100 (primary endpoint) than those who received the placebo. There were five subjects with CMV complications in the vaccine arm versus 10 in the placebo arm.

In addition, patients who received Triplex developed immunity against

CMV that was 212% higher than those in the placebo group. Prior to undergoing a transplant, patients received high-dose chemotherapy to obliterate the hematopoietic system, which produces blood and is part of the immune system. Despite having weakened immune systems, patients who received Triplex developed immunity against CMV, and the immunity endured a year after the trial took place.

"It is unprecedented that we can measure the response to the vaccine so early after the transplant procedure," said Don J. Diamond, Ph.D., City of Hope professor in the Department of Hematology & Hematopoietic Cell Transplantation and the study's senior author. "That is significant because we believe that immunity is the key to controlling CMV's negative effects."

Furthermore, the number of patients who developed serious health problems in both groups was low. No Triplex-related infections or deaths occurred in the study.

"Our study represents hope for transplant patients who already have weakened immune systems and can develop serious, life-threatening CMV-related complications," Diamond said. "Triplex spurs immunity in patients and prevents CMV-related complications from occurring in stem cell patients. Our vaccine has the potential to become yet another powerful therapy for transplant recipients who are fighting for a cure."

Triplex could also eventually be used in patients who receive solid organ transplants.

One finding that needs further examination is patients who received high-dose steroids to prevent graft- versus-host disease (GVHD) did not have as strong of a response to the vaccine as patients who did not take steroids.

"Steroids are the standard treatment for GVHD but we are looking at other ways to overcome or avoid steroids," Diamond added.

One trial underway at City of Hope vaccinates the patient's donor with Triplex. That could provide the patient with earlier and greater immunity against CMV, which is particularly important for patients undergoing high-risk transplants in which they have a haploidentical donor (a half-matched bone marrow donor.)

Ryotaro Nakamura, M.D., director of City of Hope's Center for Stem Cell Transplantation, served as the overall principal investigator of the trial, and Ibrahim Aldoss, M.D., assistant clinical professor in the Department of Hematology & Hematopoietic Cell Transplantation, was City of Hope's site principal investigator.

Over half of adults by the age of 40 have been infected with CMV, according to the Centers for Disease Control and Prevention. While symptoms of the virus do not show up in healthy individuals because the immune system is able to fight off CMV infection, it can cause severe, life-threatening disease in those with weakened immune systems such as transplant patients.

Triplex is a best-in-class, universal recombinant viral vector vaccine that can be given without restrictions to all eligible transplant recipients and/or their donors, scientifically called modified vaccinia Ankara, engineered to induce a robust and durable virus-specific T cell response to three immuno-dominant proteins linked to CMV complications in stem cell transplant recipients.

More information: *Annals of Internal Medicine* (2020). http://annals.org/aim/article/doi/10.7326/M19-2511

Provided by City of Hope