Study Aims to Cure Blood Cancers With Transplants That Could Block HIV, Too

Ten HIV-positive cancer patients to receive donated cord blood with rare resistance gene.

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Thanks to a new federal grant, Fred Hutchinson Cancer Research Center is about to lead a clinical trial offering cord blood transplants to a small group of especially vulnerable patients with blood cancers: those who also have HIV, the virus that causes AIDS.

Cord blood transplants, which use stem cells from a newborn's umbilical cord, are a lifesaving option for patients who cannot find a suitable match in their family and from the global network of bone marrow registries. Transplants are a potential cure for many advanced blood cancers, because they replace a patient's damaged immune system of blood-forming cells with a healthy one from a donor with a compatible tissue type.

Although lymphomas are the most common blood cancers faced by HIV-positive patients taking antiviral drugs, they usually have options other than a transplant to treat their cancer. It is much less common for people with HIV to have leukemia, but these patients typically have no option but a transplant. The participants in this trial are therefore most likely to come from that group.

A shot at cure for cancer — and HIV?

For 10 HIV-positive patients enrolled over the next three years, the trial design offers more than a chance for stopping their cancer. It offers a long-shot possibility of an HIV cure. The study team will sift through global cord blood inventories to find units of cord blood that carry a natural mutation that blocks HIV from infecting immune cells — potentially suppressing HIV without a need for antiviral drugs.

Filippo Milano, MD, PhD, associate director of the Cord Blood Program at the Hutch, was awarded the $1 million grant for the trial from the National Heart, Lung, and Blood Institute.

For gravely ill leukemia patients, a transplant may be their best hope. However, Milano said that because blood cancer patients with HIV are deemed to have active infections that put them at a higher risk of complications, they have difficulty qualifying at many centers for conventional bone marrow or blood stem cell transplants.

Milano's pioneering cord blood program at Fred Hutch is accustomed to finding options for blood

cancer patients who cannot find a suitable donor for a bone marrow or blood stem cell transplant. Cord blood, which contains immature blood cells less likely to attack the patient's own tissues, could turn out to be an alternative for HIV-positive leukemia patients.

"We are not conducting this trial to cure HIV," Milano said. "We are doing it to cure patients with hematological malignancies and concomitant HIV infection."

Mutation seals a molecular doorway to HIV

Yet this trial also offers a tantalizing bonus: The researchers plan to offer these patients cord blood from roughly one in 100 donors who are naturally resistant to HIV. In effect, these leukemia patients will emerge with the immune system of a person who would not be susceptible to the virus. The hope is that this HIV-resistant immune system will eventually scrub out the remaining pockets of HIV, which can roar back without an uninterrupted course of antiretroviral drugs.

To date, there is only one person in the world generally recognized to be cured of HIV: Seattle-born Timothy Ray Brown. While living in Germany in 2007, Brown — whose HIV was controlled by antiviral drugs — received the first of two bone marrow transplants for leukemia. On a hunch, his doctor used cells from donors who carried an HIV-resistance mutation in a gene that affects a protein called CCR5.

In most people, CCR5 operates as a kind of molecular doorway. HIV can pry this doorway open and enter an immune cell. But 0.8 percent of the world population inherits from both their mother and father a genetic mutation that effectively seals this doorway, and these lucky few are naturally resistant to HIV. It was from such donors that Brown received his new immune system, and 11 years later, he still has no trace of HIV and his leukemia remains in remission. To date, no other patient receiving such a transplant has successfully remained HIV negative. Milano's trial will try to replicate Brown's experience using cord blood.

Experimental cord blood product is key to trial

In this trial, patients will receive only one unit of cord blood, which has a very small number of immature blood cells. However, each patient will also receive a dose of a still-experimental product, dilanubicel, from Nohla Therapeutics. The Seattle company was founded by Fred Hutch researcher Colleen Delaney, MD, holder of the Madeline Dabney Adams Endowed Chair in AML Research and director of the Hutch's Cord Blood Program.

Derived from cord blood cells that are multiplied in the lab, the experimental drug is administered with the transplant cells to protect the patient from infection until the transplanted cord blood cells have time to set up shop as a functioning immune system.

"The number of stem cells in cord blood is very limited, especially for adults, because they come from a baby's umbilical cord," Milano said. "Colleen's product buys time for the cord blood to engraft and protect the patient."

By including the Nohla drug in the trial, cells from only one donated umbilical cord are needed

instead of the two ordinarily required in cord blood transplants. As a result, it is necessary to find only one donor carrying the mutation, improving the odds of meeting the needs of a patient seeking an HIV-blocking mutation in the transplant. Milano calculates that there are roughly 6,500 such units stored in cord blood banks throughout the world. The hope is to find several dozen units, stored at the Cleveland Cord Blood Center, that might be perfect fits for this trial.

The plan calls for patients to be treated at one of five U.S. cancer centers that also have expertise in HIV care.

“We will have world-class cancer doctors working with world-class HIV experts,” Milano said.

Participating hospitals working with the Hutch include UW Medicine and Seattle Children’s Hospital; Case Western Reserve University / University Hospitals Cleveland Medical Center; Children’s Research Institute / Children’s National Medical Center, Washington, D.C.; Memorial Sloan Kettering Cancer Center, New York; and the University of California, San Francisco Medical Center.

Note: Scientists at Fred Hutch played a role in developing these discoveries, and Fred Hutch and certain of its scientists may benefit financially from this work in the future.

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