Novel gene therapy shows promise in sickle cell patient clinical trial

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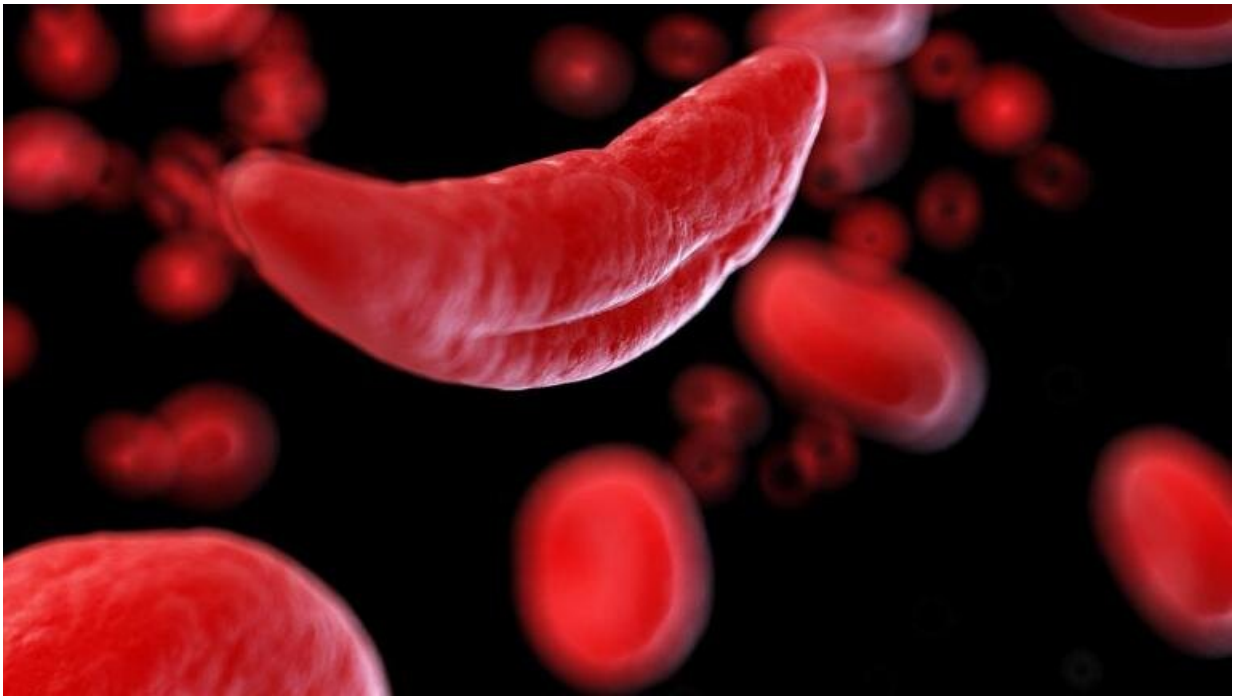

Credit: National Institutes of Health

Researchers presenting preliminary data from a clinical trial aimed at discovering a cure for sickle cell disease reveal positive results among its first patients.

Sickle cell disease, a genetic blood disorder, is a painful and debilitating condition for which there are few approved therapies.

Researchers involved in the multi-center Ruby Trial presented an update on the safety and effectiveness of a single dose of EDIT-301, an experimental one-time gene editing cell therapy that modifies a patient's own blood-forming stem cells to correct the mutation responsible for sickle cell disease. Results are being presented at the European Hematology Association Hybrid Congress in Frankfurt, Germany.

The first four patients, two of whom were treated at Cleveland Clinic Children's, had their stem cells collected for gene editing. The patients then underwent chemotherapy treatment to destroy their remaining bone marrow, making room for the repaired cells that were later infused back into their body.

This is the first time a novel type of CRISPR gene-editing technology—known as CRISPR/CA12—is being used in a human study to alter the defective gene. This technology is a highly precise tool to modify blood stem cells genomes to enable robust, healthy blood cell production.

The data showed new white blood cells in all four patients at about four weeks with no severe adverse effects. Patients also achieved a normal level of hemoglobin, which is the most important component of red blood cells that carry oxygen throughout the body. The patients also have been free of sickle cell disease's associated pain attacks for a period of 11 months and seven months following therapy.

"New treatments like this are critical for people who have sickle cell disease," said principal investigator Rabi Hanna, M.D., director of the pediatric blood and bone marrow transplant program at Cleveland Clinic Children's Hospital. "These initial results provide hope that this new technology will continue to show progress as we work toward creating a possible functional cure for this devastating and life-threatening disease."

While there are an estimated 1 million to 3 million people in the United States who have the sickle cell trait, there are only about 100,000 people with sickle cell disease. Sickle cell trait and the disease are found more often in certain ethnic groups, including African Americans. In the United States, about one in 365 African American babies have sickle cell disease.

Sickle cell disease is an inherited blood disorder that leads to the production of abnormal hemoglobin, which is a red protein responsible for transporting oxygen in the blood. Normal red blood cells are round and can move through small blood vessels to deliver oxygen. However, in people with sickle cell disease, the genetic change in DNA causes a chemical alteration in hemoglobin and alters the shape of red blood cells into a sickle, blocking them from passing through narrow blood vessels. They can clog or break apart which also leads to decreased red blood cell life, and increased iron storage in the liver and heart. This can cause conditions such as liver fibrosis, liver failure, stroke, cardiomyopathy and heart failure along with severe pain.

For most people with the condition, medications can modify disease severity and treat symptoms. However, despite current therapies, the average life of a sickle cell patient, is in the mid 40s. A blood or marrow transplant can cure sickle cell disease, but the transplant often requires a sibling donor and has the potential for severe graft-versus-host disease, which is when donor bone marrow or stem cells attack the recipient.

The Ruby Trial aims to enroll 40 adult patients, ages 18 to 50, with severe sickle cell disease. Patients will be monitored closely after treatment for up to two years.

Provided by Cleveland Clinic