Gene therapy trial for 'Bubble boy' disease promising

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(Medical Xpress)—Researchers reported promising outcomes data for the first group of boys with X-linked severe combined immunodeficiency syndrome (SCID-X1), a fatal genetic immunodeficiency also known as "bubble boy" disease, who were treated as part of an international clinical study of a new form of gene therapy. The mechanism used to deliver the gene therapy is designed to prevent the serious complication of leukemia that arose a decade ago in a similar trial in Europe, when one-quarter of boys treated developed the blood cancer.

Eight of the nine boys registered to date in the new trial are alive and well, with functioning immune systems and free of infections associated with SCID-X1, between nine and 36 months following treatment, according to Sung-Yun Pai, MD, a pediatric hematologist-oncologist from Dana-Farber/Boston Children's Cancer and Blood Disorders Center. She presented the findings (Abstract #715) at the 55th annual meeting of the American Society of Hematology on behalf of the Transatlantic Gene Therapy Consortium (TAGTC). The investigators continue to monitor the children for signs of treatment-associated leukemia, which developed three to five years post-treatment in the prior trial. They point to surrogate biological markers that give them hope the viral vector used to deliver the new treatment is safe.

"These results show that the new vector appears to retain efficacy and, at least in preliminary studies, may be safer," said David A. Williams, MD, a leader of Dana-Farber/Boston Children's, who is chief of the Division

of Hematology/Oncology at Boston Children's Hospital, associate chair of pediatric oncology at Dana-Farber Cancer Institute, and principal investigator for the gene therapy trial's U.S. sites.

Of the eight patients, seven are actively producing T cells, which are critical components of a healthy immune system. Six of these seven have met the trial's primary endpoint: a T-cell count greater than 300 cells per microliter of blood and T-cell proliferation in response to stimulation with phytohemagglutinin. The one patient among the seven who is producing T cells but has not yet achieved 300 cells/microliter will receive a second round of gene therapy next month.

The eighth surviving patient underwent a cord blood stem cell transplant after the gene therapy treatment failed to stimulate T-cell production. The lone fatality was caused by an overwhelming adenovirus infection present at the time the child entered the trial.

At the heart of the trial is a self-inactivating vector used to ferry the gene for the IL-2 receptor gamma subunit (IL2RG) into a patient's hematopoietic (blood-forming) stem cells. Once the gene is inserted, the cells are returned to the patient. IL2RG fuels the development and growth of immune cells and is a key component of normal immune system development. In children born with SCID-X1, the gene carries a mutation that renders it inactive.

The viral vector used in the study is a modified gammaretrovirus, a member of a family of viruses able to insert genetic cargo into the genome of mammalian cells and drive expression of the inserted genes. The vector has been engineered to avoid the leukemia that halted the previous SCID-X1 gene therapy effort.

Analyses of T cells from the participants in the current trial suggest that the new vector avoided genomic sites known to contribute to leukemia

development. The study team will continue to keep a close eye on the patients for any signs of abnormal T-cell growth.

Provided by Dana-Farber Cancer Institute