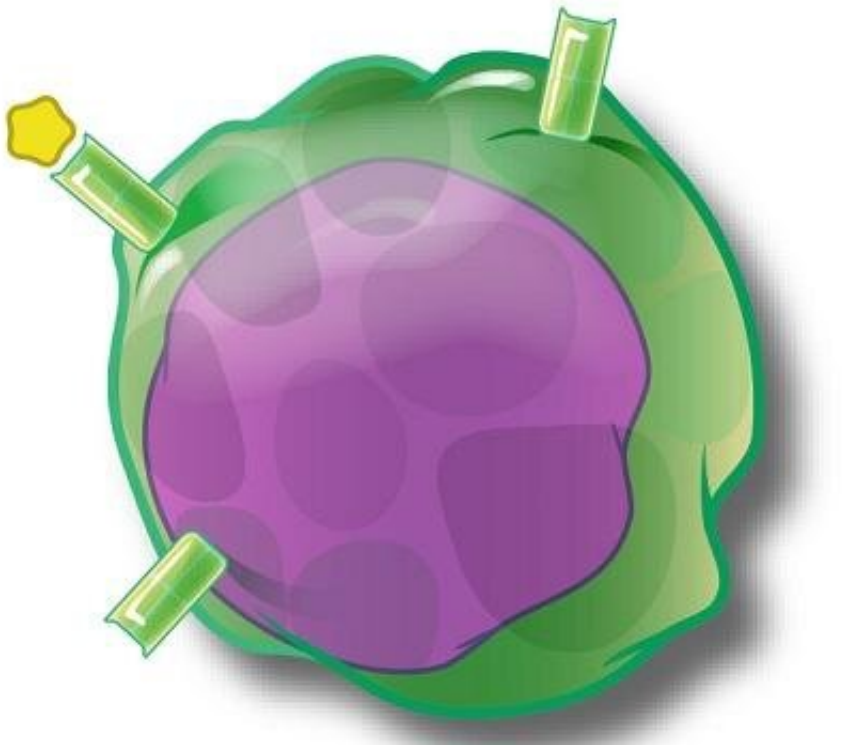
MedicalXpress

Children with resistant leukemia given CRISPR-edited T cells: Phase 1 study results reported

October 27 2022



An artist's depiction of a T cell. Credit: NIAID

Researchers at Great Ormond Street Hospital for Children (GOSH) and UCL Great Ormond Street Institute of Child Health (UCL GOS ICH) have used CRISPR/Cas9 technology to engineer donor T cells to try to treat seriously ill children with resistant leukemia who had otherwise

exhausted all available therapies.

This Phase I trial, published in *Science Translational Medicine*, is the first use of "universal" CRISPR-edited cells in humans and represents a significant step forward in the use of gene-edited cells for cancer treatment. As part of the trial the research team, built and applied a new generation of "universal" genome-edited T cells, which builds on previous work that had used older, less accurate technology.

T cells were modified using CRISPR, which makes a cut in the cells' DNA and inserts a genetic code. In this case this piece of genetic code allows the T cells to express a receptor—called a chimeric antigen reception (CAR)—that can recognize a marker on the surface of cancerous B cells and then destroy them. The T cells were then gene-edited using CRISPR so that they could be used "off the shelf" without any donor matching needed.

While a number of CAR T-cell therapies are now being provided by the NHS, they rely on collecting and engineering a patient's own cells. This is expensive and is not always feasible or possible in a short period of time. Genome editing is being investigated to allow donated cells to be pre-manufactured and used in multiple patients, aiming to reduce costs and make the treatments more accessible.

In specialist clean rooms at GOSH, researchers manufactured their banks of donor CAR T cells using a single disabled virus to transfer both the CAR and a CRISPR guidance system, and then applied cutting-edge mRNA technology to activate the gene editing steps. Donors were all healthy volunteers from the UK and provided by the Anthony Nolan Registry.

The trial

Six children aged 14 months to 11 years with relapsed and treatment-resistant B-ALL have been treated up to February 2022. All of the children had previously been through standard UK treatments for B-ALL but had sadly seen their disease return multiple times.

Patients were infused with the edited cells that were expected to be active for around four weeks. This is long enough to hopefully achieve deep remission, a state where their cancer is dramatically reduced or undetectable. When successful, patients were then eligible to follow through with a bone marrow stem cell transplant to help re-establish a healthy immune system.

Four of the first six children treated entered remission within 28 days, which allowed them to receive a stem cell transplant. Of those four children, two children remain in ongoing remission, 9 months and 18 months after treatments respectively, while sadly two relapsed following their stem cell transplant.

In this study, overall side effects were within expectations and were managed in hospital, with one patient requiring a short period of intensive care.

Professor Waseem Qasim, Consultant Immunologist at GOSH and Professor of Cell and Gene Therapy at UCL GOS ICH and the lead author, said, "This kind of unresponsive leukemia is thankfully very rare, but we are pleased to be able to bring new therapies into play for some of the most difficult to treat childhood leukemias, especially when all other options have been exhausted. Whilst there are challenges to overcome, this study is a promising demonstration of how emerging genome-editing technologies can be used to tackle unmet health needs in some of the sickest children we see."

Professor Ajay Vora, Consultant Hematologist and Leukemia specialist

at GOSH, said, "The children treated in this study were facing the worst possible prognosis with their disease. It is only possible for us to save more young lives though clinical trials, and we are forever grateful to all the families who have been involved in this study that will help more children in the future."

Dr. Kanchan Rao, Consultant in Bone Marrow Transplant at GOSH, said, "This study adds to the growing body of evidence that genome-edited T cells can be a viable alternative to currently available treatments. Whilst this hasn't been successful in all cases, for some children in this study it has been life-saving."

The next step is for researchers to offer the treatment to more children, earlier in their treatment pathways, when their cancers have not progressed so far.

More information: Giorgio Ottaviano et al, Phase 1 clinical trial of CRISPR-engineered CAR19 universal T cells for treatment of children with refractory B cell leukemia, *Science Translational Medicine* (2022). DOI: 10.1126/scitranslmed.abq3010

Provided by University College London

Citation: Children with resistant leukemia given CRISPR-edited T cells: Phase 1 study results reported (2022, October 27) retrieved 9 April 2024 from https://medicalxpress.com/news/2022-10-children-resistant-leukemia-crispr-edited-cells.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.