

# Modified killer T-cells wipe out leukemia: study

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Three US cancer patients were brought back from the brink by a new therapy that turned their own immune cells into tumor killers, wiping out an advanced form of leukemia, researchers said Wednesday.

The breakthrough stunned scientists and although the gene transfer therapy technique is still in development, it could offer hope one day to people who suffer from ovarian, lung, breast and skin cancers.

"We saw amazing results," said Michael Kalos, lead author of the study that appeared in *Science Translational Medicine* and was published simultaneously in the *New England Journal of Medicine*.

"These were nasty tumors that were late-stage, a lot of mutations that had bad prognosis," he said. "We saw massive reduction in tumor burden. One patient had over seven pounds (three kilograms) of tumor and it all disappeared."

Two of the three men in the study with chronic lymphocytic leukemia (CLL) have remained cancer-free for almost a year, while the third has seen a slight recurrence of disease.

"Within three weeks, the tumors had been blown away, in a way that was much more violent than we ever expected," said senior author Carl June, who like Kalos is a researcher at the University of Pennsylvania.

"It worked much better than we thought it would."

Scientists removed a sample of the patients' T-cells and genetically modified them to attack all cells that express a certain kind of protein, CD19, which includes tumor cells.

They altered them using a lentivirus vector that encodes an antibody-like protein known as a chimeric antigen receptor and expressed. The protein is expressed on the surface of T-cells and designed to bind to CD19.

The scientists also engineered the T-cells to start triggering other T-cells to multiply as soon as they attached to a cancer cell, bringing on a faster death for the tumor but avoiding the side-effects of cancer drugs.

"We saw at least a 1,000-fold increase in the number of modified T-cells in each of the patients. Drugs don't do that," said June, describing the infused T-cells as "serial killers."

"On average, each infused T-cell led to the killing of thousands of tumor cells."

In one case, a 64-year-old man had blood and marrow "replete with tumor cells."

He saw little change for the first two weeks after treatment, but then started experiencing nausea, chills and fever. Tests showed he was undergoing a huge rise in T-cell count, and a condition known as tumor lysis syndrome that can arise when cancer cells are dying off.

By day 28, his blood showed no evidence of leukemia.

A 65-year-old patient saw similar results, with no trace of leukemia after a year, but a 77-year-old patient saw a slight recurrence of cancer after he was treated with steroids for the symptoms of tumor lysis syndrome.

However, his tumor load remains far below what it was before the treatment.

Steven Rosenberg, chief of the surgery branch at the National Cancer Institute, described it as "important" and "impressive." He was not involved with the study but has published research on similar approaches to eradicating B-cell lymphomas and melanoma.

"You are taking advantage of the body's immune system by creating outside the body T-cells that can act against the cancer," he told AFP.

"You have to select the particular gene modification for each type of cancer but when you pick it wisely it can be very effective."

The other main form of treatment, bone marrow transplants, carries a minimum 20 percent risk of dying from the procedure and cure rates hover at around 50 percent.

While it remains unknown how long the treatment may keep cancer at bay, researchers were excited to see that "memory" T-cells remained months after the cancer disappeared, indicating the body is retaining some protection.

The next step is to try the technique in two children and at least 13 adults with CD19-positive leukemia.

They are also looking to determine whether the approach could target non-Hodgkin's lymphoma and acute lymphocytic leukemia, mesothelioma cancer cells, ovarian and pancreatic cancer cells.

Chronic lymphocytic leukemia is the second most common type of adult leukemia after acute myeloid leukemia, according to the National Cancer Institute.

"I'm healthy and still in remission," said a statement by one of the three patients, who declined to be named. "I know this may not be a permanent condition, but I decided to declare victory."

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