



HEALTH | NYT NOW

Patient's Cells Deployed to Attack Aggressive Cancer

By DENISE GRADY MAY 8, 2014

Doctors have taken an important step toward a long-sought goal: harnessing a person's own immune system to fight cancer.

An article published Thursday in the journal *Science* describes the treatment of a 43-year-old woman with an advanced and deadly type of cancer that had spread from her bile duct to her liver and lungs, despite chemotherapy.

Researchers at the National Cancer Institute sequenced the genome of her cancer and identified cells from her immune system that attacked a specific mutation in the malignant cells. Then they grew those immune cells in the laboratory and infused billions of them back into her bloodstream.

The tumors began "melting away," said Dr. Steven A. Rosenberg, the senior author of the article and chief of the surgery branch at the cancer institute.

The woman is not cured: Her tumors are shrinking, but not gone. And an experiment on one patient cannot determine whether a new treatment works. But the report is noteworthy because it describes an approach that may also be applied to common tumors — like those in the digestive tract, ovaries, pancreas, lungs and breasts — that cause more than 80 percent of the 580,000 cancer deaths in the United States every year.

Dr. Rosenberg's patient, Melinda Bachini, now 45, a paramedic in

Billings, Mont., who is the mother of six children, said that without the cell treatment, “honest, I don’t know that I would be here.”

Dr. Rosenberg agreed, saying that in April 2012, when Ms. Bachini received the first immune treatment, her life expectancy was probably a matter of months.

Related techniques involving immune cells have brought lasting remissions for people with leukemia, a blood cancer, and the aggressive skin cancer melanoma. But until now researchers had not found a way to use the cells against the so-called solid tumors that cause so many deaths.

Other researchers said the treatment used by Dr. Rosenberg’s team, known as adoptive cell therapy, had promise for these common cancers. But they also cautioned that the report was early and based on just one patient.

Dr. Carl June, who directs similar research at the University of Pennsylvania, said the research addressed an important issue by showing that adoptive cell therapy could have an effect on commonly lethal solid tumors.

Another expert, Dr. Michel Sadelain of the Memorial Sloan-Kettering Cancer Center in New York, said the report showed that carefully selected immune cells could be a powerful tool against bile-duct cancer. But he also said it was too soon to tell if the same approach would work for other patients or could be scaled up to treat all those who might need it.

Dr. Rosenberg acknowledged that there were limitations: The technique required highly sophisticated techniques in immunology, and produced a treatment tailored to only one patient. He said his team was working around the clock to streamline the process, and added, “Potentially, if we could reduce the complexity, it’s something that could get out into common usage eventually.”

Researchers have hoped for decades to find some unique marker on cancer cells, something not present on healthy cells, that could be used as a target so that cells of the immune system could home in on it and leave the good ones alone.

The goal has been elusive, but Dr. Rosenberg's team has helped some patients with melanoma by treating them with immune cells — a type of T cell called a tumor-infiltrating lymphocyte — that were extracted from samples of the patients' tumors. The team decided to study whether this type of T cell could help people with other types of cancer.

Ms. Bachini learned in 2009 that she had bile-duct cancer, or cholangiocarcinoma. It had already spread to her liver. She had surgery to remove about two-thirds of her liver, but within a few months the disease had turned up in her lungs. She went through one grueling regimen of chemotherapy, then another. She had nerve damage, nausea and hearing loss from the drugs. Her tumors began growing again. She started to cough.

“I knew chemotherapy was not going to kill this,” she said. She quit the drugs.

Searching the Internet for clinical trials, she came across Dr. Rosenberg's T cell study.

“I looked at my husband and said, ‘This is what I want to do,’ ” Ms. Bachini said.

In March 2012, Dr. Rosenberg's team removed tumors from her lungs to extract tumor-infiltrating T cells, then cultured the cells in a lab. A month later, Ms. Bachini was given chemotherapy to wipe out her immune system, and more than 42 billion T cells were infused through an intravenous line. She was also given a drug called interleukin-2, which helps activate T cells.

The treatment was arduous: The chemotherapy left her vomiting, weak and bald, and the interleukin-2 made her swell up with fluid.

By the end of April 2012, her cough was gone and her strength returning. She went back to the cancer institute once a month for checkups. The study, paid for by the government, was free, even including her airfare.

“Life was good,” she said. “Everything kept shrinking.”

But by last summer, the lung tumors were growing again.

By then, the team had sequenced the genome of her cancer, and done extensive studies on her immune system. And it had found what researchers had long hoped for: a mutation in the cancer that was unique to it and not found in normal cells, and a type of T cell that would attack the mutation. Tests revealed that only 25 percent of the T cells that had been given to Ms. Bachini were of this specialized type.

Again, the team cultured Ms. Bachini's T cells, but this time it used only the ones that would go after the mutation. In October, she received more than 120 billion T cells, 95 percent of which were the highly specific ones.

Her tumors quickly began shrinking, and have continued to do so for the past six months, Dr. Rosenberg said.

Ms. Bachini said she was grateful for every day. She walks her dog, a 140-pound Labrador, two miles a day, and said she was constantly on the run with three teenage daughters still at home.

"I pretty much can do anything I want," she said.

Dr. Rosenberg said that his team would check up on her every two months, and that if the tumors started growing, it might be possible to treat her again. As for her long-term outlook, he said, "We'll just have to wait and see."

In the meantime, he said, the team has identified unique mutations and T cells ready to attack them in two of three other patients with cancer in the gastrointestinal tract. Treatment plans are underway.

Correction: May 8, 2014

An earlier version of this article misstated the number of other cancer patients in which Dr. Steven A. Rosenberg's team has identified unique mutations and T-cells. It is two of three patients, not three of four.

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