Doctors hail world first as woman's advanced breast cancer is eradicated

Immune cells from the woman's own body used to wipe out tumours

Ian Sample *and* **Jessica Glenza**

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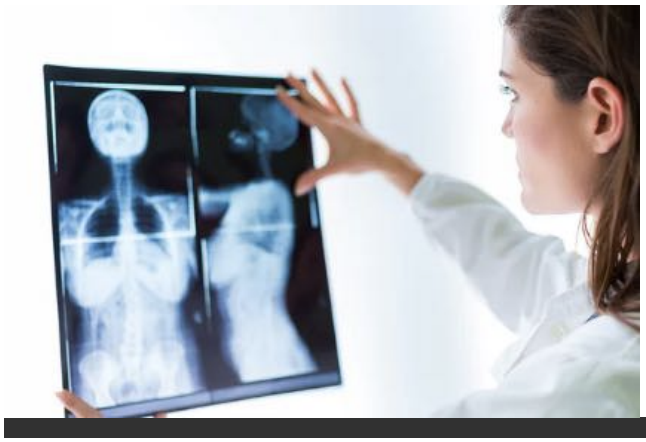

A leading cancer researcher said the experiment was proof that we are on the 'cusp of a major revolution' in being able to target cancer with immunotherapy. Photograph: ilbusca/Getty Images

A woman with advanced breast cancer which had spread around her body has been completely cleared of the disease by a groundbreaking therapy that harnessed the power of her immune system to fight the tumours.

It is the first time that a patient with late-stage breast cancer has been successfully treated by a form of immunotherapy that uses the patient's own immune cells to find and destroy cancer cells that have formed in the body.

Judy Perkins, an engineer from Florida, was 49 when she was selected for the radical new therapy after several rounds of routine chemotherapy failed to stop a tumour in her right breast from growing and spreading to her liver and other areas. At the time, she was given three years to live.

Doctors who cared for the woman at the US National Cancer Institute in Maryland said Perkins's response had been "remarkable": the therapy wiped out cancer cells so effectively that she has now been free of the disease for two years.

"My condition deteriorated a lot towards the end, and I had a tumour pressing on a nerve, which meant I spent my time trying not to move at all to avoid pain shooting down my arm. I had given up fighting," Perkins said. "After the treatment dissolved most of my tumours, I was able to go for a 40-mile hike."

Laszlo Radvanyi, scientific director of the Ontario Institute for Cancer Research, who was not involved in Perkins's treatment, said it was "an unprecedented response in such advanced breast cancer."

Judy Perkins says her condition had deteriorated a lot and she was planning her death. But since the treatment she has been on a 40 mile hike. Photograph: Courtesy of Judy Perkins

The dramatic success has raised hopes that the therapy will work in more patients with advanced breast cancer and other difficult to treat cancers, such as ovarian and prostate. Researchers are now planning full scale clinical trials to assess how effective the treatment could be.

"We are now at the cusp of a major revolution in finally realising the elusive goal of being able to target the plethora of mutations in cancer through immunotherapy," Radvanyi said.

But experts caution that the treatment has only proved itself in one woman and that the clinical trials are needed to see how effective the therapy could be in other cancer patients. Researchers point out that while the treatment could in principle work for many different kinds of

cancer, it will not help everyone.

To create the treatment, doctors first cut small pieces of tissue from Perkins's tumours and studied the DNA to find mutations specific to her cancer. They focused on mutations that disrupted four genes which produced an array of abnormal proteins in the tumours.

Next, the doctors extracted immune cells known as tumour infiltrating lymphocytes, or TILs, from the tumour biopsies. These are cells from the patient's immune system that have invaded the tumour in a bid to kill it, but which failed in the task by being either too weak or too few in number.

After growing billions of these immune cells in the lab, the researchers screened them to find which ones would most effectively find and destroy the woman's cancer cells by recognising their abnormal proteins.

The doctors treated Perkins by injecting 80 billion of the carefully-selected immune cells into her body. The therapy was given alongside pembrolizumab, a standard drug that can help the immune system to attack cancers. Tests after 42 weeks showed Perkins was completely cancer free. She has remained so ever since.

"It feels miraculous, and I am beyond amazed that I have now been free of cancer for two years," Perkins said.

"I had resigned my job and was planning on dying. I had a bucket-list of things I needed to do before the end, like going to the Grand Canyon," she added. "Now, I have gone back to normal everyday life."

While the US doctors who developed the therapy cannot be sure how much the infused immune cells contributed to her recovery, the use of pembrolizumab alone has not been very effective for advanced breast cancer in the past. The infused T cells were found in Perkins's system for at least 17 months after her treatment began.

The success, reported in the journal Nature Medicine, is all the more remarkable because breast cancers, like prostate and ovarian cancer, have relatively few mutations, which makes them harder for the immune system to spot amid the body's healthy tissues.

Alan Melcher, professor of translational immunotherapy at the Institute of Cancer Research in London, who was not involved in the study said: "The work shows that even cancers like breast cancer, which don't have many antigens, are amenable to this sort of treatment. It would certainly be applicable in principle to a range of tumours, and even those in which immunotherapy hasn't worked so well yet."

But Melcher points out that the therapy is complex and expensive and more importantly, requires doctors to find enough infiltrating immune cells in a patient's tumour to make the treatment effective. "The case with other TIL therapies in the past is that they've not been able to expand enough T cells in many patients, there aren't enough to start with."

Simon Vincent, director of research at Breast Cancer Now, added: "This is a remarkable and extremely promising result, but we need to see this effect repeated in other patients before giving hope of a new immunotherapy for incurable metastatic breast cancer.

"Metastatic breast cancer remains incurable, and if we are to finally stop women dying we urgently need to find new ways to target and stop the spread of the disease. We are thrilled by this early finding, but we must remember that this type of immunotherapy remains an experimental approach that has a long way to go before it might be routinely available to patients."

There's a miraculous chance to cure cancer. But we'll have to pay for it.

Floridian Judy Perkins is free of advanced breast cancer after undergoing a novel therapy that used her immune cells to target her tumors. (Scott McIntyre/For The Washington Post)

By Megan McArdle
Columnist
June 5 at 7:02 PM

In 1971, when Richard M. Nixon declared war on cancer, "conquering this dread disease" must have seemed like an ambitious but reasonable goal. Within his lifetime, man had split the atom and walked on the moon; now it was time to turn our wealth and our growing knowledge inward, to expand our control over our bodies.

But 40 years later, we were still pinned down by a wily enemy, advancing by millimeters through hostile terrain. In 1975, the U.S. mortality rate for all cancers stood at 199 per 100,000 people. In 2015, after decades of money and human effort had been poured into research, that figure stood at 159 .

But it's no longer unreasonable to hope that the battle might finally turn our way, thanks to therapies based on the patient's own immune system. Drugs such as Opdivo and Yervoy can weaken restraints on our immune cells that prevent them from attacking our bodies (or, unfortunately, our tumors). And a technique known as CAR T-cell therapy lets scientists modify those cells and release them back into the body to hunt down cancer cells. Some of the results achieved with these new weapons look positively miraculous.

These miracles have so far largely been confined to relatively rare cancers with lots of mutations. The techniques haven't been as effective against the cancers that start in the epithelial cells lining organs, which account for the overwhelming majority of deaths. Until now, that is.

A team led by Steven Rosenberg at the National Cancer Institute is working on a new method: sequencing the genes in the patient's tumor, then finding immune cells that are already primed to look for the tumor's unique mutations. These are grown in a lab, and then infused back into the patient's body in massive numbers. A new paper reports that adoptive cell therapy has kept a 52-year-old Florida woman named Judy Perkins, who had advanced metastatic breast cancer, completely free of the disease for 2½ years. Earlier papers reported equally striking recoveries in patients with colon and liver cancer.

Miraculous? Yes. A cure for cancer? Not quite. As with other immunotherapies, not all patients have responded to treatment; in this case, it's only about 15 percent. And because it's a small study, where one or two outliers can skew results either way, we'll have to see what larger trials bring.

But then, no "medical miracle" actually comes to us in a single, brilliant flash of insight; George Orwell died of tuberculosis more than 20 years after the discovery of penicillin, awaiting an antibiotic that could kill the disease without killing him. And so with cancer, which is many diseases lurking under a single name. If adoptive cell therapy can be refined to make it more

effective, and simplified so that ordinary hospitals can administer it, it will join a growing arsenal that might just beat cancer back to a fraction of its former territory.

Rosenberg is hopeful that the new therapy will be a key player in that fight: “The development of this approach holds the best opportunities for finding effective immunotherapies for patients with the solid cancers that last year caused over 500,000 deaths in this country.” And his lab, he says, is “working around the clock” to develop it further: identifying more tumor mutations to target, extracting more of the tumor-fighting cells from lab cultures. Then the biotech industry will need to figure out how to turn this into a standardized process that can be deployed outside of a research center.

Which brings us to the only bad news in this amazing story: We’re going to have to find some way to pay for our massive new expeditionary force. Antibiotics, our last medical revolution, were relatively cheap, and often eliminated long and costly hospital stays to boot. But immune-based therapies are unlikely to ever be available for a few cents a dose, especially not the personalized ones. Of the immunotherapies we already have, Opdivo and Yervoy combination drug therapy can cost a quarter of a million dollars; CAR T-cell almost double that.

Eventually those prices will surely fall. But how far? And what about other weapons we discover in the meantime? Thanks to earlier technological advances, health-care spending is already approaching 20 percent of our national income. How much is too much?

That’s not an idle question. Over a lifetime, 1 in 3 Americans will be diagnosed with cancer; 1 in 5 will die from it. That’s why Rosenberg’s work is such a hopeful development — and also why it would be so expensive to make treatments like this widely available. Fighting a total war on cancer, one that might approach something like victory, will require an open, clear commitment to meeting those expenses.

So ask yourself: If you were diagnosed with cancer, what object do you own, what public service do you enjoy, that you’d rather have than a tumor-killing treatment? Frankly, I find it hard to name *anything* more worthy of investment than beating cancer — which is to say, extra years of life, liberty and the pursuit of happiness. But if you agree, you should get ready to put your money where your mouth is.

'Remarkable' therapy beats terminal breast cancer

By James Gallagher
Health and science correspondent, BBC News
4 hours ago

Image copyright
JUDY PERKINS

The life of a woman with terminal breast cancer has been saved by a pioneering new therapy, say US researchers.

It involved pumping 90 billion cancer-killing immune cells into her body.

Judy Perkins had been given three months to live, but two years later there is no sign of cancer in her body.

The team at the US National Cancer Institute says the therapy is still experimental, but could transform the treatment of all cancer.

Judy - who lives in Florida - had spreading, advanced breast cancer that could not be treated with conventional therapy.

She had tennis ball-sized tumours in her liver and secondary cancers throughout her body.

She told the BBC: "About a week after [the therapy] I started to feel something, I had a tumour in my chest that I could feel shrinking.

"It took another week or two for it to completely go away."

She remembers her first scan after the procedure when the medical staff "were all very excited and jumping around".

It was then she was told that she was likely to be cured.

Now she's filling her life with backpacking and sea kayaking and has just taken five weeks circumnavigating Florida.

Living therapy

The technology is a "living drug" made from a patient's own cells at one of the world's leading centres of cancer research.

Dr Steven Rosenberg, chief of surgery at the National Cancer Institute, told the BBC: "We're talking about the most highly personalised treatment imaginable."

It remains experimental and still requires considerably more testing before it can be used more widely, but this is how it works: it starts by getting to know the enemy.

A patient's tumour is genetically analysed to identify the rare changes that might make the cancer visible to the immune system.

Out of the 62 genetic abnormalities in this patient, only four were potential lines of attack.

Next researchers go hunting. A patient's immune system will already be attacking the tumour, it's just losing the fight between white blood cells and cancer.

The scientists screen the patient's white blood cells and extract those capable of attacking the cancer.

These are then grown in huge quantities in the laboratory.

Around 90 billion were injected back into the 49-year-old patient, alongside drugs to take the brakes off the immune system.

Dr Rosenberg told me: "The very mutations that cause cancer turn out to be its Achilles heel."

'Paradigm shift'

These are the results from a single patient and much larger trials will be needed to confirm the findings.

The challenge so far in cancer immunotherapy is it tends to work spectacularly for some patients, but the majority do not benefit.

Dr Rosenberg added: "This is highly experimental and we're just learning how to do this, but potentially it is applicable to any cancer.

"At lot of works needs to be done, but the potential exists for a paradigm shift in cancer therapy - a unique drug for every cancer patient - it is very different to any other kind of treatment."

Image copyright
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Image caption
Around 90 billion cancer-killing cells were infused back into Judy

The details were **published in journal Nature Medicine**:

https://www.nature.com/articles/s41591-018-0040-8

Commenting on the findings, Dr Simon Vincent, director of research at Breast Cancer Now, said the research was "world class".

He told the BBC: "We think this is a remarkable result.

"It's the first opportunity to see this sort of immunotherapy in the most common sort of breast cancer at the moment it has only been tested in one patient,

"There's a huge amount of work that needs to be done, but potentially it could open up a whole new area of therapy for a large number of people."

Letter | Published: 04 June 2018

Immune recognition of somatic mutations leading to complete durable regression in metastatic breast cancer

Nikolaos Zacharakis, Harshini Chinnasamy, Mary Black, Hui Xu, Yong-Chen Lu, Zhili Zheng, Anna Pasetto, Michelle Langhan, Thomas Shelton, Todd Prickett, Jared Gartner, Li Jia, Katarzyna Trebska-McGowan, Robert P. Somerville, Paul F. Robbins, Steven A. Rosenberg, Stephanie L. Goff & Steven A. Feldman

Nature Medicine (2018) |

Abstract

Immunotherapy using either checkpoint blockade or the adoptive transfer of antitumor lymphocytes has shown effectiveness in treating cancers with high levels of somatic mutations—such as melanoma, smoking-induced lung cancers and bladder cancer—with little effect in other common epithelial cancers that have lower mutation rates, such as those arising in the gastrointestinal tract, breast and ovary[1,2,3,4,5,6,7]. Adoptive transfer of autologous lymphocytes that specifically target proteins encoded by somatically mutated genes has mediated substantial objective clinical regressions in patients with metastatic bile duct, colon and cervical cancers[8,9,10,11]. We present a patient with chemorefractory hormone receptor (HR)-positive metastatic breast cancer who was treated with tumor-infiltrating lymphocytes (TILs) reactive against mutant versions of four proteins—SLC3A2, KIAA0368, CADPS2 and CTSB. Adoptive transfer of these mutant-protein-specific TILs in conjunction with interleukin (IL)-2 and checkpoint blockade mediated the complete durable regression of metastatic breast cancer, which is now ongoing for >22 months, and it represents a new immunotherapy approach for the treatment of these patients.