

After Giving Up on Cancer Vaccines, Doctors Start to Find Hope

Encouraging data from preliminary studies are making some doctors feel optimistic about developing immunizations against pancreatic, colon and breast cancers.



By Gina Kolata

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It seems like an almost impossible dream — a cancer vaccine that would protect healthy people at high risk of cancer. Any incipient malignant cells would be obliterated by the immune system. It would be no different from the way vaccines protect against infectious diseases.

However, unlike vaccines for infectious diseases, the promise of cancer vaccines has only dangled in front of researchers, despite their arduous efforts. Now, though, many hope that some success may be nearing in the quest to immunize people against cancer.

The first vaccine involves people with a frightening chance of developing pancreatic cancer, one of the most difficult cancers to treat once it is underway. Other vaccine studies involve people at high risk of colon and breast cancer.

Of course, such research is in its early days, and the vaccine efforts might fail. But animal data are encouraging, as are some preliminary studies in human patients, and researchers are brimming with newfound optimism.

“There is no reason why cancer vaccines would not work if given at the earliest stage,” said Sachet A. Shukla, who directs a cancer vaccine program at MD Anderson Cancer Center. “Cancer vaccines,” he added, “are an idea whose time has come.” (Dr. Shukla owns stock in companies developing cancer vaccines.)

That view is a far cry from where the field was a decade ago, when researchers had all but given up. Studies that would have seemed like a pipe dream are now underway.

“People would have said this is insane,” said Dr. Susan Domchek, the principal investigator of a breast cancer vaccine study at the University of Pennsylvania.

Now, she and others foresee a time when anyone with a precancerous condition or a genetic predisposition to cancer could be vaccinated and protected.

“It’s super aspirational, but you’ve got to think big,” Dr. Domchek said.

A Less Grim Prognosis



Dr. Elizabeth Jaffee, deputy director of the Sidney Kimmel Cancer Center at Johns Hopkins University, in 2019. Nina Westervelt for The New York Times

Marilynn Duker knew her family tree was dotted with relatives who had cancer. So when a genetic counselor offered her testing to see if she had any of 30 cancer-causing gene mutations, she readily agreed.

The test found a mutation in the gene CDKN2A, which predisposes people who carry it to pancreatic cancer.

“They called and said, ‘You have this mutation. There really is nothing you can do,’” recalled Ms. Duker, who lives in Pikesville, Md., and is chief executive of a senior living company.

She began having regular scans and endoscopies to examine her pancreas. They revealed a cyst. It has not changed in the past several years. But if it develops into cancer, treatment is likely to fail.

Patients like Ms. Duker don’t have many options, noted Dr. Elizabeth Jaffee, deputy director of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University. A person with more advanced cysts could avoid cancer by having their pancreas removed, but that would immediately plunge them into a realm of severe diabetes and digestive problems. The drastic surgery might be worthwhile if it saved their lives, but many precancerous lesions never develop into cancer if they are simply left alone. Yet if the lesions turn into cancer — even if the cancer is caught at an early stage — the prognosis is grim.

But it also offers an opportunity to make and test a vaccine, she added.

In pancreatic cancer, Dr. Jaffee explained, the first change in normal cells on the path to malignancy almost always is a mutation in a well-known cancer gene, KRAS. Other mutations follow, with six gene mutations driving the cancer’s growth of pancreatic cancer in the majority of patients. That insight allowed Hopkins researchers to devise a vaccine that would train T cells — white blood cells of the immune system — to recognize cells with those mutations and kill them.

Their first trial, a safety study, was in 12 patients with early stage pancreatic cancer who already had been treated with surgery. Although their cancer was caught soon after it had emerged and despite the fact that they were treated, pancreatic cancer patients typically have a 70 percent to 80 percent chance of having a recurrence in the next few years. When pancreatic cancer returns, it is metastatic and fatal.

Two years later, those patients have not yet had a recurrence.

Now, Ms. Duker and another patient have been vaccinated to try to prevent a tumor from starting in the first place.

“I am really excited about this opportunity,” she said.

The vaccine seems safe, and it has elicited an immune response against the common mutations in this cancer.

“So far, so good,” Dr. Jaffee said.

But only time will tell if it prevents cancer.

‘We Have to Look at Different Patients’



Dr. Olivera Finn, a professor in the departments of immunology and surgery at University of Pittsburgh School of Medicine. Tom Altany/University of Pittsburgh

In a sense, the search for cancer vaccines started with Dr. Olivera Finn, a distinguished professor in the departments of immunology and surgery at University of Pittsburgh School of Medicine.

She began in 1993 with a vaccine directed at the core of a molecule, mucl. In normal cells, the molecule is invisible to the immune system because it is covered in a bush of sugar molecules. But in colon, breast and pancreatic cancers, it can become visible to the immune system. That made it seem like a perfect vaccine target because it could allow the immune system to attack only cancer cells.

“We had this trial, 63 patients, Stage 4 cancer. They had failed all therapies,” Dr. Finn said.

The first patient had had breast cancer and was treated with a double mastectomy. But the cancer returned.

“The tumor was on her chest, thick and red,” she said. “She had two pumps, one emptying liquid from her lungs and the other liquid from her abdomen.”

In their initial studies, it became clear to Dr. Finn and her colleagues that the cancers were too far advanced for immunizations to work. After all, she notes, with the exception of rabies, no one vaccinates against an infectious disease in people who are already infected.

“I said, ‘I don’t want to do that again,’” Dr. Finn said. “It is not the vaccines. We have to look at different patients.”

Now, she and her colleague at Pittsburgh, Dr. Robert Schoen, a gastroenterologist, are trying to prevent precancerous colon polyps with a vaccine. But intercepting cancer can be tricky.

They focused on people whose colonoscopies had detected advanced polyps — lumps that can grow in the colon, but only a minority of which turn into cancer. The goal, Dr. Schoen said, was for the vaccine to stimulate the immune system to prevent new polyps.

It worked in mice.

“I said, ‘OK, this is great,’” Dr. Schoen recalled.

But a recently completed study of 102 people at six medical centers randomly assigned to receive the preventive vaccine or a placebo had a different result. All had advanced colon polyps, giving them three times the risk of developing cancer in the next 15 years compared to people with no polyps.

Only a quarter of those who got the vaccine developed an immune response, and there was no significant reduction in the rate of polyp recurrences in the vaccinated group.

“We need to work on getting a better vaccine,” Dr. Schoen said.

Pre-empting a Pre-cancer



Dr. Mary L. Disis, director of the Cancer Vaccine Institute at the University of Washington. Kiran Dhillon

Dr. Mary L. Disis, director of the Cancer Vaccine Institute at the University of Washington, wants to prevent breast cancer in women with gene variants that put them at high risk. Her initial hopes, though, are more modest.

One goal is to help women who have ductal carcinoma in situ, which doctors call a pre-cancer. Surgery is the standard treatment, but because some women also have chemotherapy and radiation to protect themselves from developing invasive breast cancer. “Ideally, a vaccine would replace those treatments,” she said.

She began by looking at breast cancer stem cells. These cells, found in early cancers, are resistant to chemotherapy and radiation, and they can metastasize. They drive recurrences of breast cancers, said Dr. Disis, who has received grants from pharmaceutical companies and is a founder of EpiThany, a company that is developing vaccines.

Dr. Disis and her colleagues found a number of proteins in these stem cells that were normal but produced at a much higher level in cancer cells than in noncancerous cells. That offered an opportunity to test a vaccine that produced some of those proteins.

Their vaccine was tested in women with advanced cancers that were well established. It did not cure the cancers but demonstrated that the vaccine could provide the sort of immune response that might help earlier in the course of the disease.

She plans to try vaccinating patients with ductal carcinoma in situ, or another precancerous condition, atypical ductal hyperplasia. Her group has a vaccine they developed to target three proteins produced in abnormally high amounts in these lesions.

The hope, she said, is to make the lesions shrink or go away before the women have surgery to remove them.

“This would be proof the vaccine has a cleansing effect,” she said. If the vaccine succeeds, women may feel comfortable forgoing chemotherapy or surgery.

To Paint a Grand Future

“I really think we will see a few vaccines approved for clinic in the next five years,” Dr. Disis said. The first vaccines, she predicts, will be used to prevent recurrences in patients whose cancer was successfully treated.

“Then, I think we will very rapidly move on to primary prevention,” giving vaccines to healthy people at high risk, she said.

Others are similarly optimistic.

“At least we know the road map,” said Dr. Shizuko Sei, medical officer of the chemopreventive agent development research group at the National Cancer Institute.

“People may disagree, but the answer at this point is, yes, it is possible” to make vaccines to intercept cancer, she said.

Dr. Domchek said she can envision a future in which people will have blood tests to find cancer cells so early that they do not show up in scans or standard tests.

“To paint a grand future,” she said, “if we knew the tests predicted cancer we could say, ‘Here’s your vaccine.’”

Gina Kolata writes about science and medicine. She has twice been a Pulitzer Prize finalist and is the author of six books, including “Mercies in Disguise: A Story of Hope, a Family’s Genetic Destiny, and The Science That Saved Them.” @ginakolata • Facebook