After a year of turmoil, cancer researchers see promising signs for mRNA vaccines

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Vita Sara Blechner's life changed on a Saturday afternoon. The middle school librarian was home in Oceanside, New York, when she felt shooting pains in her back. After an acid reflux pill couldn't soothe the fiery feeling, her husband suggested a trip to the emergency room.

It was March 7, 2020, just days before Covid-19 would turn New York City's hospitals into something approaching a war zone. If the doctors knew what was coming, they didn't let on. They were cool and collected as they put Blechner, then 67, through a sonogram and a CT scan. But the pictures turned her world upside-down.

"They said I have a tumor on my pancreas. And I said, 'No, it can't be. This can't be happening to me. I don't drink. I don't smoke. I'm leading a healthy life.'"

After an anxious two days in the hospital, Blechner headed home and weighed her options. There weren't many. Pancreatic cancer is notoriously unforgiving: Just 1 in 4 patients lives a year after their diagnosis. Just 1 in 10 makes it two years.

Blechner felt the numbers in the pit of her stomach as she, her husband and their three adult sons made calls and pored over the internet, deciding her next move. They settled on a path that would land Blechner in a fast-moving and often misunderstood realm of cancer research.

Messenger RNA, or mRNA, is a single-stranded molecule that delivers genetic information from DNA to direct the formation of proteins. It's known to most people from high school science classes or for its use in Covid vaccines. But long before anyone had heard of Covid, mRNA was generating intense excitement in the cancer research community. BioNTech,

the German company that designed the Covid vaccine for Pfizer, adapted that vaccine from a platform it had been using to develop cancer treatments for nearly a decade.

The mRNA-based Covid vaccines produced by Pfizer and Moderna helped blunt the impact of the pandemic but also sparked political backlash that, in the past year, has threatened to slow or derail dozens of potential cancer treatments. Now, after a tumultuous 12 months, there are signs that the mRNA train is still on track.

“It’s exciting,” said Elizabeth Jaffee, deputy director of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University. “There’s been a number of successes in early-stage, positive trials.”

Dr. Catherine Wu, a professor of medicine at Dana Farber Cancer Institute and Harvard Medical School, says the recent stretch of positive real-world results helped drive the recent announcement by the National Cancer Institute that it would help raise $200 million specifically for novel cancer vaccines.

“We’re getting a lot of support from NCI in terms of developing and promoting cancer vaccines, and mRNA vaccines are a major part of that portfolio,” she said.

An unforgiving enemy

To guide her treatment, Blechner turned to doctors at Memorial Sloan Kettering Cancer Center, including Dr. Vinod Balachandran, director of MSK’s Olayan Center for Cancer Vaccines.

It’s more challenging to make a vaccine against cancer than it is to create a vaccine against a virus or bacteria, Balachandran says. “That’s because our body’s immune systems are hard-wired to recognize viruses and pathogens as foreign, so a vaccine is teaching our body to do something it already wants to do. In contrast, cancer is ourselves. It’s derived from our own tissues.”

Much of Balachandran’s work the past two decades has focused on pancreatic tumors because the disease is such a tough nut to crack. “It’s a cancer where nothing had really worked,” he said.

When Blechner arrived at MSK, he was just launching a trial of an experimental mRNA-based vaccine against pancreatic cancer, in combination with standard immunotherapy and chemotherapy. He felt like a successful vaccine would also have the potential for wider application. “If we could break through and crack the toughest one, it could unlock how to crack the other [types of cancer], because it would provide a blueprint.”

To develop the vaccine, he began by studying “super-survivors”: the fewer than 10% of pancreatic cancer patients who live more than five years from the time of diagnosis. He found that their immune systems were especially good at spontaneously recognizing cancer cells as foreign. In fact, Balachandran says, these patients had about 12 times as many T-cells - a specialized type of immune cell - inside their tumors as average patients. The same T cells were circulating for more than a decade, in some cases.

Balachandran also realized that these weren’t generic cancer-fighters. “These T cells were recognizing mutations,” he said, “but each person’s immune system was recognizing their cancer as foreign in a very specific way. To replicate this would require us to teach each individual person’s immune system how to recognize their individual cancer. It would be an individualized vaccine. And we felt the best technology for rapid custom cancer vaccination was to use RNA.”

Taking a chance as a research volunteer

After Blechner signed on for the trial, the first step was surgery. She underwent what’s known as a Whipple procedure to remove the tumor in the head of her pancreas. In a lab at MSK, the tumor was preserved and sliced into fine pieces, each thinner than a human hair. In less than 72 hours, the package was en route to Germany, where technicians at BioNTech took steps to process the material into a clear liquid: a personalized vaccine, custom-made for Vita Sara Blechner.

A little more than two months after her diagnosis, the vaccine concoction from Germany arrived back in New York. By that time, she had been given a dose of an immune checkpoint inhibitor, an immunotherapy drug designed to make her immune cells more effective in fighting cancer. For weekly infusions of the vaccine, her husband, Simon, would drive Blechner from Oceanside to the MSK hospital on Manhattan’s East Side. It was the height of the Covid pandemic, so instead of running

errands or visiting friends after dropping her off, he would drive through empty streets and wait back home on Long Island. Blechner would lie in a hospital bed for eight hours while the vaccine coursed through her body, until Simon returned to pick her up.

After nine weeks, she was done and ready for the next step in her treatment: chemotherapy. But chemo was a fiasco. Blechner suffered mightily, with side effects so severe that doctors had to halt treatment. “I got very sick,” she recalled.

“I only had three sessions before they had to stop, and I was in and out of the hospital three or four times. I was down to 90 pounds. I had no appetite. I was constantly nauseous, and my liver was damaged,” she said. “My doctor said to me she never thought she’d see me again.”

By the time she felt strong enough to try again, her doctors felt it would be unsafe to resume. She hoped that stopping early wouldn’t make a difference. But she would have to wait and see.

She tells this story more than six years later: Blechner not only survived longer than anyone expected, she’s still doing well and showing no sign of cancer.

And she’s no singular exception. Of 16 patients in Balachandran’s trial, eight showed a dramatic immune response to the mRNA-based vaccine. Seven of the eight are alive and well six years after the trial began, a finding that was to be presented Monday at the American Association of Cancer Research meeting in San Diego.

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