Treatments Offer Hope On Pancreatic Cancer

By Brianna Abbott

Pranathi Perati was running out of time to treat her stage-four pancreatic cancer when she found out she would get another shot: a clinical trial testing a new experimental drug.

Perati's odds were slim—only 3% of late-stage pancreatic cancer patients are still alive after five years. And half of all pancreatic cancer patients live for less than a year after their diagnosis. For Perati, the drug, daraxonrasib from Revolution Medicines, has helped keep her alive for 17 months and counting.

"Someone told me once that I hit the clinical-trial lottery, and I definitely feel that way," said Perati, a 54-year-old molecular biologist in Cupertino, Calif., who is fighting pancreatic cancer a second time. "I see a lot of hope."

Pancreatic cancer is one of the toughest cancers to treat. Often caught late, it kills nearly 52,000 people in the U.S. each year, making it the country's third leading cause of cancer death, behind lung and colorectal. Case rates have gradually increased, particularly among younger women, in part because of rising obe-

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New Hope For Cancer Of Pancreas

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sity rates. Researchers estimate that by 2030, deaths will overtake those for colorectal cancer, as other cancers have become more treatable and are caught earlier.

But doctors in the field have newfound optimism, thanks to a wave of newer therapies that are in development. Many, including Revolution Medicines' drug, target a gene called KRAS, which helps control cell growth.

Some 90% of pancreatic cancer cases have KRAS mutations, making their tumors potentially vulnerable. Companies including Pfizer and Eli Lilly now also have KRAS-blocking drugs in early-stage human trials.

"That is the main foot-on-the-gas pedal for pancreas cancer," said Dr. Sunil Hingorani, director of the Pancreatic Cancer Center of Excellence at the University of Nebraska Medical Center. "And we haven't been able to find drugs until the last couple of years that actually hit it."

Targeted drugs and immunotherapies that have revolutionized the outlook for other cancers have yet to make a significant dent for pancreatic cancer. The organ itself is hard to reach, and a bulky microenvironment of fibrous tissue and cells creates a fortress around the cancer.

Some 480 early-phase and 85 late-phase clinical trials for advanced pancreatic cancer have resulted in five new drug approvals since 2000, according to the American Cancer Society.

"Pancreatic cancer has been the graveyard for drug discovery," said Dr. Benjamin Weinberg, a gastrointestinal medical oncologist at the Lombardi Comprehensive Cancer Center at Georgetown University.

Researchers believe that could change with newer therapies, particularly those that target KRAS. The gene acts as a switch for cellular growth, and KRAS mutations can cause cells to proliferate uncontrollably and become cancerous. Researchers considered KRAS "undruggable" for decades, until a breakthrough in the 2010s cracked open the field.

Two therapies have since been approved for lung and colorectal cancer patients with some KRAS mutations. The drugs, called inhibitors, turn off that growth switch.

At California-based Revolution Medicines, patients are now enrolling in the company's late-stage trial for pancreatic cancers with mutations including KRAS. In an earlier-stage trial, 27% of pancreatic cancer patients had a partial or full response, according to the data released so far. Patients were able to fend off the disease for a median of 8.5 months before it progressed. More than a third of patients harboring KRAS mutations in a category called G12 responded.

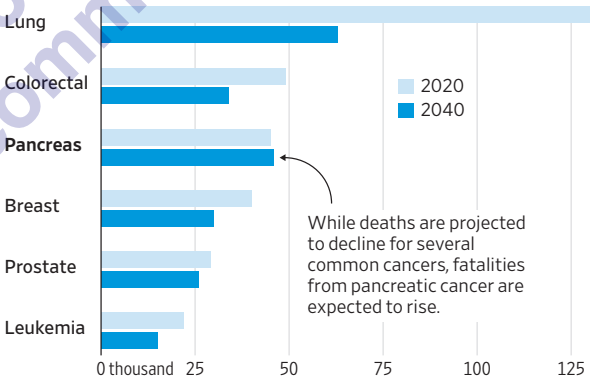
"The hope really in the field is that these drugs will have some effectiveness and give us a foothold," said Dr. Brian Wolpin, director of the Gastrointestinal Cancer Center at Dana-Farber Cancer Institute in Boston, one of the cancer centers working with Revolution Medicines. "If that works, it gives us something to build on."

Perati was first diagnosed with pancreatic cancer in 2016, at stage two, and surgery and chemotherapy put it into remission. When Perati's cancer re-emerged in the summer of 2020 in her lung, the mother of three worried she wouldn't live to see Christmas.

HELYNN OSPINA FOR WSJ

Pranathi Perati has been fighting pancreatic cancer since 2016.

Estimated U.S. cancer deaths



Note: Projections based on demographic changes and average annual change in death rates
Source: Journal of the American Medical Association

"I couldn't sleep at night. I couldn't do very much," she said. "What if I'm not around?"

Perati underwent more surgeries. Knowing she had a KRAS G12 mutation, Perati reached out to cancer centers across the U.S., hunting for clinical trials. In 2023, Perati got a spot on the Revolution Medicines trial. Twenty-five other patients treated by Perati's doctor were waiting for the same chance.

The pill has given her some fatigue and mouth ulcers, but she feels better than she did with chemo. A lesion in her lung started progressing this past winter and was radiated, but her disease has been stable otherwise.

"Seventeen months is a lot of good time to buy," she said. Still, Perati worries that her time on the drug might soon run out. She has started looking for more options. Her son is set to graduate high school this summer.

Eli Lilly is enrolling pancreatic cancer patients in initial studies for two KRAS inhibitors, and Pfizer's trial started last year. Companies Bristol-Myers Squibb, Verastem Oncology and Jacobio Pharmaceuticals have reported positive preliminary results in their own early studies. Side effects have included rashes, fatigue and gastrointestinal problems.

Others are seeing promise with different therapies: Researchers last week said that a small number of pancreatic cancer patients who received a personalized vaccine after surgery still had an immune response years later. The Food and Drug Administration approved a drug called Bizengri in late 2024 that targets a rare gene fusion called NRG1.

Still, people like Perati remain outliers. Many pancreatic tumors don't respond to KRAS drugs or grow resistant within months. Bristol-Myers Squibb discontinued a study of one of its KRAS inhibitors because of disappointing data.

"We know they are not going to come in and work on every single patient forever," said Gregory Lesinski, associate director for basic research at Emory University's Winship Cancer Institute. "But moving the needle even a little bit will have a tremendous impact."