Pancreatic cancer treatments show promise in studies

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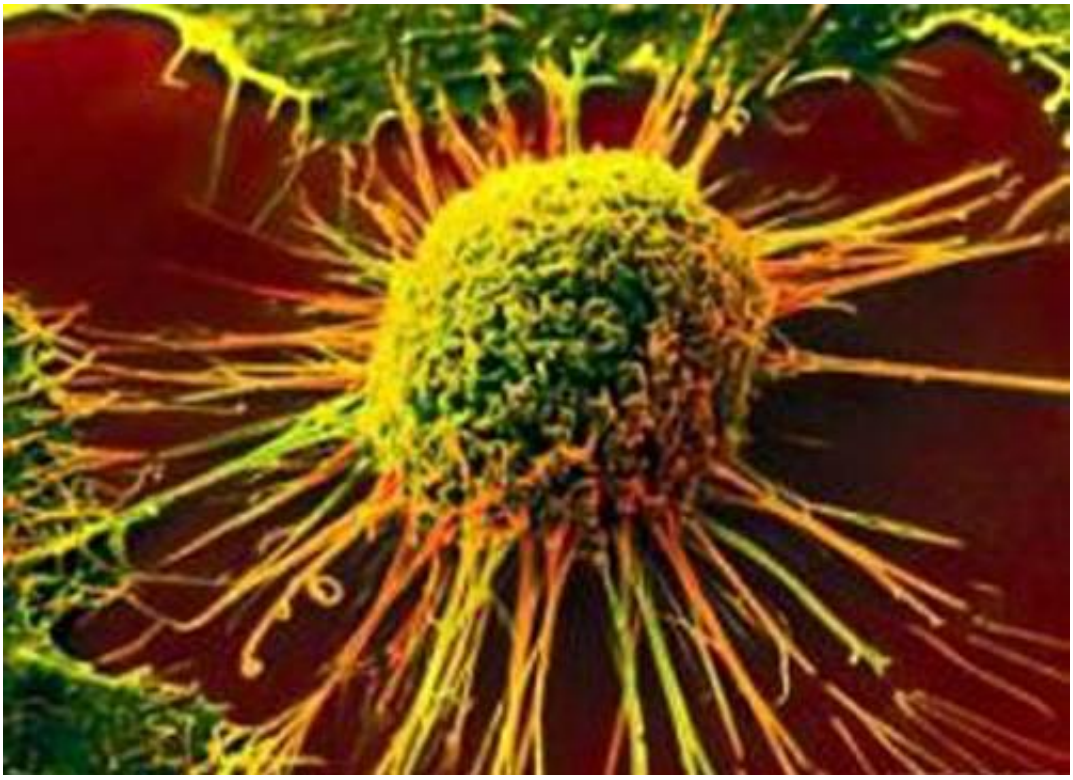

University of Pennsylvania researchers are reporting early but encouraging results from two small ongoing studies of experimental treatments for metastatic pancreatic cancer.

Pancreatic cancer is a fearsome malignancy that has long defied efforts

to find effective treatments. Only 9 percent of patients survive five years after diagnosis. The disease is now the nation's third-leading cancer killer even though it causes only 3 percent of all new cancer cases. This year, about 56,700 people will be diagnosed with pancreatic cancer, and 45,700 will die of it.

For one study, funded by the Parker Institute for Cancer Immunotherapy, researchers at Penn and seven other centers combined two standard chemotherapies with varying doses of an experimental antibody, called APX005M, being developed by Apexigen. Half the patients also received Opdivo, a "checkpoint inhibitor" drug that boosts the immune response by cutting an immune system brake. Although checkpoint inhibitors have dramatically improved survival in many solid tumor cancers, they have not worked so far in pancreatic cancer.

The experimental antibody, which binds to a particular cell surface receptor, is designed to reverse the suppression of the immune system that occurs in all cancers, but especially pancreatic. In theory, the antibody complements Opdivo's cut-the-brakes mechanism by pressing on the accelerator, explained Penn hematologist-oncologist Mark O'Hara, the study's co-leader.

The interim analysis was from 24 patients followed for a minimum of seven months and a maximum of 19 months. Of those, 14 saw their tumors shrink, and two had stable disease. All of the treatment subgroups had patients whose cancers regressed. The largest number of responses—four patients—was seen in the group that got a higher dose of the antibody plus Opdivo, but it will take a larger study to tease out whether Opdivo made the difference.

Side effects including anemia and fatigue were manageable.

"These findings give us clues that new and innovative combination

therapy can be effective against pancreatic cancer," said O'Hara.

The other study enrolled patients with a mutation in BRCA1, BRCA2 or PALB2 genes. These defects, carried by about 6 percent of pancreatic cancer patients, are known to increase the chance of developing the disease, as well as breast and ovarian cancer. The mutations interfere with the normal tumor-suppressing functions of the genes.

The patients were already responding to intensive chemotherapy, but the toxic side effects can make long-term treatment intolerable—and eventually the cancer develops resistance. The study switched the patients from chemotherapy to Rubraca, a "PARP inhibitor" drug approved a year ago as a maintenance therapy for advanced ovarian cancer patients. PARP inhibitors are believed to keep cancer cells from repairing DNA that is damaged by chemotherapy.

Of 19 patients treated with Rubraca, 17 saw their tumors shrink or stop growing. One patient had a complete response, meaning all evidence of cancer disappeared. Eight patients have been on the drug, which comes in pills, for at least six months, and two patients have been on it for more than a year. The study was supported by Clovis Oncology, which makes Rubraca.

Penn hematologist-oncologist Kim Reiss Binder, who led the study, called the results "extremely preliminary" but "very exciting."

"This is a population that doesn't have many options to treat one of the deadliest forms of cancer," she said. "To be able to offer a targeted therapy with much less toxicity, even if only for a subset of our patients, would be a wonderful thing."

Davi D'Agostino, 64, of Manassas, Va., knows just how wonderful.

In January 2018, the retired federal government executive was diagnosed with inoperable pancreatic cancer that had spread to her liver. Even though she had no medical history suggesting a genetic mutation, her oncologist at Sloan Kettering Memorial Cancer Center did molecular tests that revealed a BRCA2 defect. Such testing was recently added to treatment guidelines.

"He said this is good because it means you can get some precision medicine," D'Agostino recalled.

First, though, she had chemotherapy to shrink the cancer. The side effects—continual vomiting, diarrhea, fatigue, pain—derailed her high-energy lifestyle. "I couldn't even walk the dog because I wasn't sure I'd make it back," she recalled.

In contrast, Rubraca, which she began getting at Penn last August, had tolerable side effects that soon subsided. After barely six months, scans revealed a remarkable effect: her liver metastases were gone. Her primary pancreas tumor has not grown and is no longer causing pain, weight loss and other symptoms.

"I'm thrilled with how I'm doing," she said. "I'm back to 99 percent energy-wise. I teach painting out of my studio. I stay very busy. Friends say to me, 'We forget you have cancer.'"

The findings from both studies were presented this week at the annual meeting of the American Association for Cancer Research.