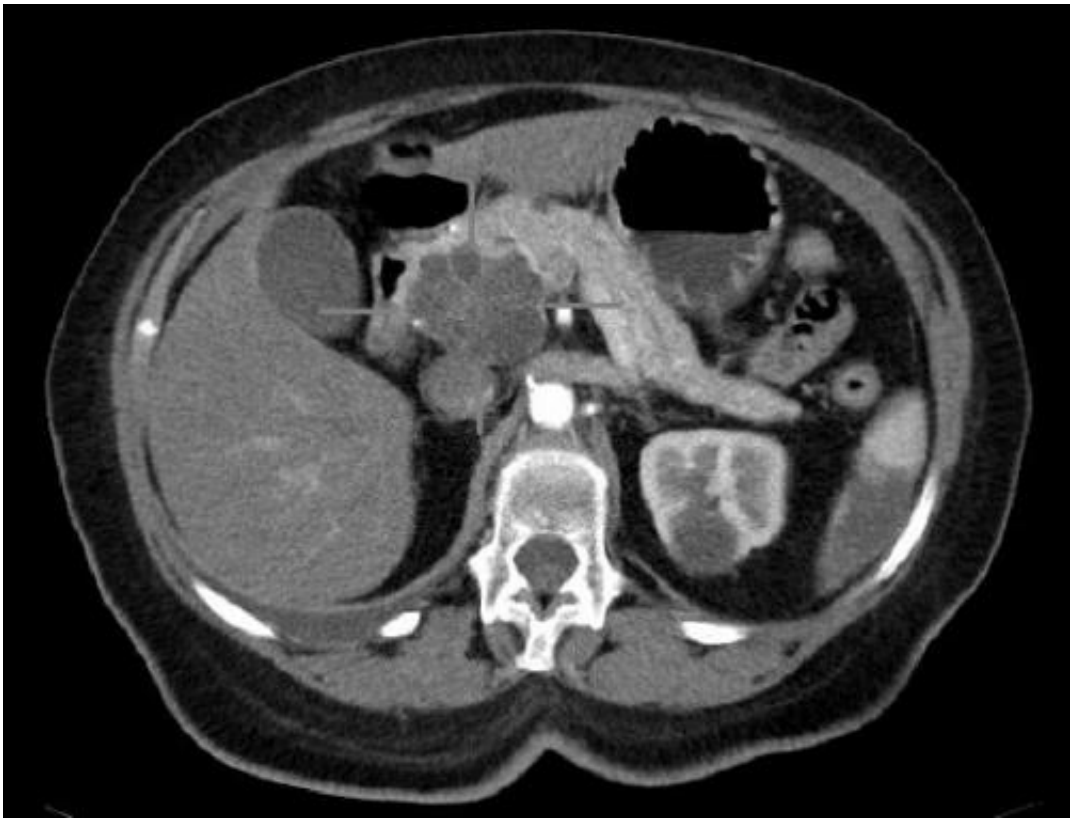
CD40 combination therapy can shrink pancreatic tumors

March 31 2019



Axial CT image with i.v. contrast. Macrocystic adenocarcinoma of the pancreatic head. Credit: public domain

A new combination of immunotherapy and chemotherapy for pancreatic cancer caused tumors to shrink in the majority of evaluable patients—20 out of 24 as of an interim analysis of the phase 1b trial data. The early

findings provide hope that this strategy involving a CD40 antibody, a checkpoint inhibitor, and standard-of-care chemotherapy could be effective for treating the nation's third deadliest type of cancer. Researchers from the Abramson Cancer Center at the University of Pennsylvania will present the findings today in a clinical trials plenary session at the American Association for Cancer Research 2019 Annual Meeting in Atlanta (Abstract #8060). The ongoing study is being conducted in collaboration with the Parker Institute for Cancer Immunotherapy and its other member institutions and partners. These are the first clinical trial data ever presented as a result of this collaboration.

"These findings give us clues that this new and innovative combination therapy can be effective against pancreatic cancer," said the study's co-lead author Mark H. O'Hara, MD, an assistant professor of Hematology-Oncology at Penn. "Although only time and further research will truly tell, our data are a reason for optimism." O'Hara will present the plenary at 12:45 p.m. in Marcus Auditorium, Bldg A-GWCC.

Pancreatic ductal adenocarcinoma (PDAC) is the most common type of pancreatic cancer, and it kills more Americans each year than any cancer type other than lung and colorectal. Despite the fact that it only accounts for about three percent of new cancer cases, it is responsible for more than seven percent of all cancer deaths, and just 8.5 percent of patients survive five years with the disease. Previous research has shown PD-1 inhibitors are ineffective on their own against PDAC, but preclinical data showed combining PD-1 inhibitors with antibodies that target a different antigen known as CD40 can trigger an immune response.

For this study, patients with metastatic PDAC who were previously untreated received combinations of four different therapies. Each patient received gemcitabine and nab-paclitaxel, which are standard-of-care chemotherapies, as well as an experimental antibody targeting CD40

called APX005M. Half the patients also received the PD-1 inhibitor nivolumab. As of the data cutoff for the interim analysis, 20 of 24 patients (83 percent) saw their tumors shrink. Overall, although the majority of the patients experienced side effects from the treatment, they were expected and manageable, with several patients continuing on treatment for more than a year, which also suggests the combination treatment can produce a durable response.

"Seeing patients continue treatment for this length of time does give us hope that this combination approach holds promise, especially when you consider that for stage 4 pancreatic cancer, the median survival is just two to six months," said senior author Robert H. Vonderheide, MD, DPhil, director of the Abramson Cancer Center and a Parker Institute member researcher. Vonderheide previously led the first-in-human clinical trial of APX005M reported in 2017 that enabled the current study.

The Parker Institute holds the Investigational New Drug application from the U.S. Federal Drug Administration. Patients on this trial were treated at seven Parker member institutions, leveraging a unique ability to develop faster and more efficient clinical studies.

"This study represents the first illustration that our unique collaborative model, which we used to bring together partners from across academia, pharma, and biotech, can help speed the process of translating laboratory findings into efficient, impactful clinical trials in areas with high unmet medical need," said Ramy Ibrahim, MD, the chief medical officer at the Parker Institute for Cancer Immunotherapy. "Based on these early but promising findings, we are excited to see results from the next phase of the study."

In addition to Penn, Parker member institutions who treated patients on this study were Memorial Sloan Kettering Cancer Center; The University

of Texas MD Anderson Cancer Center; University of California, Los Angeles; University of California, San Francisco; Stanford University; and Dana-Farber Cancer Institute.

The randomized phase two portion of the trial evaluating chemotherapy, APX005M, and/or nivolumab is currently underway. Apexigen, which manufactures APX005M, and Bristol-Myers Squibb, which manufactures nivolumab, each supplied the drugs for this study. Additional support was provided by the Cancer Research Institute.

Provided by Perelman School of Medicine at the University of Pennsylvania