# Precision medicine improves treatment outcomes for some pancreatic cancer patients

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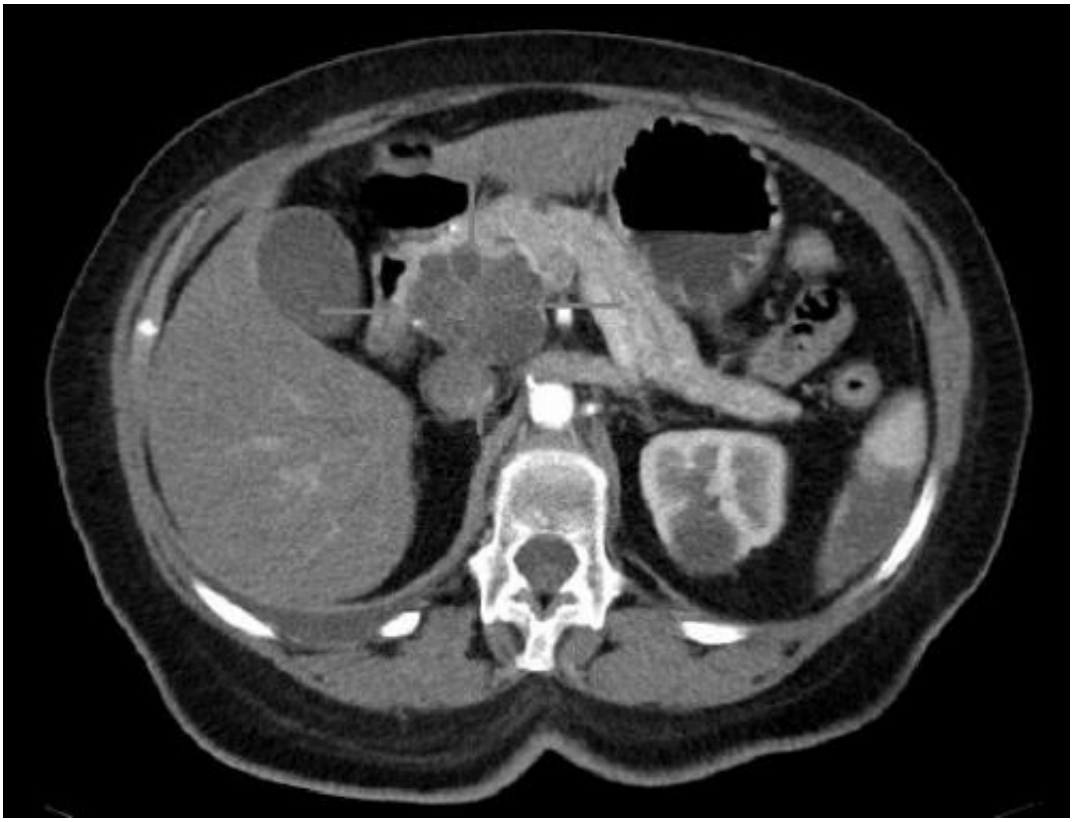

Axial CT image with i.v. contrast. Macrocystic adenocarcinoma of the pancreatic head. Credit: public domain

University of Pittsburgh and UPMC researchers are paving the way for genome-targeted treatments in pancreatic cancer, an especially deadly form of cancer with few existing therapeutic options, according to a pair

of recent studies.

The first study used genomic profiling to identify targeted therapies that resulted in benefits for patients with pancreatic cancer, including one whose tumor contained a mutation in the anaplastic lymphoma kinase (ALK) gene. In the second study, researchers used existing drugs already treating other types of ALK-mutated cancers to improve outcomes in pancreatic cancer patients with the same genetic alterations.

"Together, these two findings begin to capture the promise of precision medicine in pancreatic cancer, which has so far not experienced the same success with targeted treatments as other cancer types," said the senior author of both studies, Nathan Bahary, M.D., Ph.D., associate professor of medicine at Pitt, and co-director of the UPMC Pancreatic Cancer Center of Excellence. "The assessment of these actionable alterations is now part of routine pancreatic cancer care at UPMC."

As the third-leading cause of cancer deaths in the United States, and with a five-year survival rate of just 8 percent, pancreatic cancer is one of the most lethal forms of the disease. Currently available treatments are largely ineffective, so there is a desperate need for better therapeutic options, explained Bahary.

In the first study, published in the January issue of *Cancer Medicine*, first author Mashaal Dhir, M.D., an oncologic surgical fellow at UPMC, and colleagues used DNA sequencing to look for gene changes in over 100 patient samples of advanced gastrointestinal cancers, including colorectal and pancreatic tumors.

They identified several mutations in each cancer type and used that information to make treatment recommendations in 38 percent of cases. Approximately 14 percent of patients could receive the recommended therapy due to rapid decline in the other patients. However, half of those

who received genomic-guided therapy experienced significant clinical benefit with improvement in overall survival, which would not have been possible on standard-of-care therapies. This suggests that mutational analyses done earlier during therapy may provide benefit to more patients, the authors said.

One patient's pancreatic tumor had a mutation in the ALK gene. Genetic mutations involving ALK have been identified in several different types of cancer, including those of the breast, colon and lung, and drugs targeting this pathway have been successfully used for treatment of these tumors.

The second study, published online this month in the Journal of the National Comprehensive Cancer Network (JNCCN), took a closer look at ALK mutations in pancreatic cancer. Co-lead authors Aatur Singhi, M.D., Ph.D., assistant professor of pathology at UPMC, and Siraj Ali, M.D., Ph.D., director of clinical development and medical affairs, Foundation Medicine Inc., Cambridge, Massachusetts, performed comprehensive genomic profiling of more than 3,000 pancreatic cancers .

Alterations in the ALK gene were present in five patients (.2 percent). Four of these five were treated with drugs that inhibit ALK, and three experienced a positive response, as evidenced by either stable disease, tumor shrinkage or a reduction in levels of a pancreatic cancer biomarker.

Patients with pancreatic cancer are typically diagnosed late in life, at an average age of 71. Patients with ALK mutations averaged just 38 years at diagnosis. The prospect of having an effective and clinically available treatment to offer a small subset of pancreatic cancer patients, a population with so few options, is extremely encouraging, said Bahary. The new work also highlights the importance of ALK mutation

screening in young pancreatic cancer patients.

The new studies also have much broader implications for pancreatic cancer.

"Modern DNA sequencing techniques have brought with them the hope of targeting anti-cancer therapies to a particular cancer's vulnerabilities," Bahary said. "However, the potential of these precision medicine initiatives has not yet been achieved in pancreatic cancer. Beyond ALK mutations, our two studies describe some of the initial steps needed to utilize targeted therapies more generally in pancreatic cancer."

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