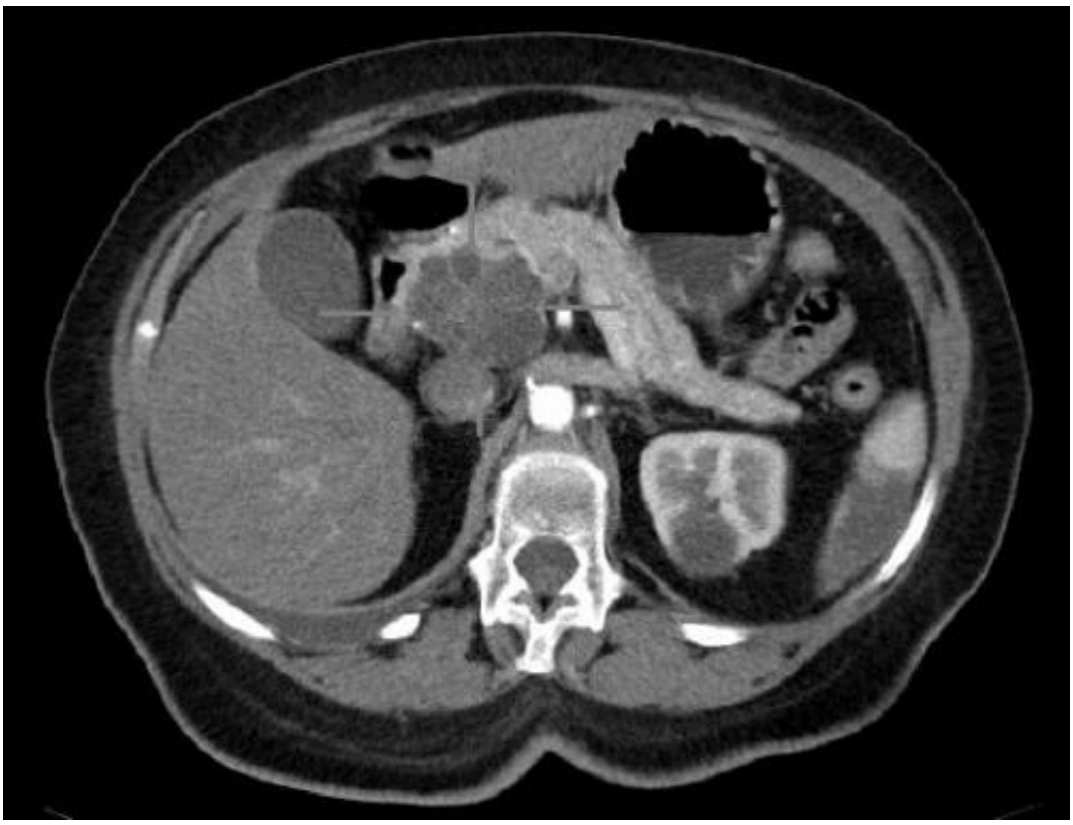
# Study finds immunotherapy combination before surgery improves outcomes for patients with pancreatic cancer

April 5 2024



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

A pilot study led by UCLA Health Jonsson Comprehensive Cancer Center investigators suggests that for people with borderline resectable

pancreatic cancer, administrating an immunotherapy drug in combination with chemotherapy before surgery is safe and may improve long-term outcomes.

The findings showed that treating patients with the combination therapy prior to surgery resulted in a higher rate of successful tumor removal, increased the period of time before the cancer worsened, and extended overall survival when compared to historical controls.

The researchers also found that adding the immunotherapy component did not increase significant adverse side effects and led to no significant post-operative complications.

"This is one of the first trials reported with a PD1-inhibitor in neoadjuvant pancreatic cancer and we found this novel approach was associated with positive outcomes, including enhancing the function of cytolytic T cells, a key component of the immune system responsible for attacking cancer cells," said Dr. Zev Wainberg, co-director of the UCLA Health GI Oncology Program and first author of the study abstract.

"Additionally, the observed increase in immunosuppressive adenosine indicates a potential resistance mechanism that we can target in a follow-up study to enhance the body's ability to fight the cancer even better."

"This trial uniquely integrated UCLA research teams with expertise in pancreatic adenocarcinoma, allowing access to patient tumor tissue beyond what is typically accessible," said Jason Link, associate professor of surgery and an author on the study.

"With these resources available, we were able to identify granular changes in anti-tumor immunity that may have contributed to positive outcomes in this novel trial."

Pancreatic cancer is one of the most challenging cancers to treat. Only 12% of people diagnosed with this particularly aggressive disease live beyond five years, and most therapies—including conventional chemotherapies, targeted therapies and immunotherapies—are unsuccessful in treating it.

Previous studies combining chemotherapy and PD1-inhibitors, a type of immunotherapy drug that helps the immune system recognize and destroy cancer cells more effectively, have not shown improvements in treating people with pancreatic cancer. However, prior to this study, using the combination of chemotherapy with immunotherapy has not been tested in the neoadjuvant setting.

The study included 28 patients (16 male, 12 female) with borderline resectable pancreatic cancer. Twenty-six (93%) of the participants completed at least three cycles of the combination therapy and 24 (86%) underwent surgery. Genetic sequencing was performed on 21 post-treatment resected tumors, six patient-matched diagnostic pre-treatment biopsies, and nine resected tumors from non-trial patients treated with chemotherapy alone.

At a median follow-up of 24 months, the median progression-free survival was 34.8 months, and the median overall survival was 35.1 months. For patients who underwent a pancreatectomy, the 18-month overall survival rate was 90%. There were two pathologic complete responses and two near complete responses.

Compared to pre-treatment biopsies, RNA sequencing from resected specimens revealed higher CD8 and Granzyme A expression. In patients with pathologically node negative disease, elevated Granzyme A expression was associated with significantly improved progression-free survival. Adenosine-related gene expression increased in 50% of post-treatment samples and correlated with expression of adenosine-

generating CD73.

This research opens up new avenues for exploring the role of immunotherapy in earlier stages of pancreatic cancer, potentially offering more effective treatment options for patients with borderline resectable pancreatic cancer. This Phase II trial is currently ongoing.

"This was a real team effort. By treating patients before surgery, not only were we able to see whether the drug combination worked but by collecting surgical resection tissues, we went back to the lab to study why this combination does not always work," said Dr. Timothy Donahue, chief of surgical oncology and professor of surgery at the David Geffen School of Medicine at UCLA and senior author of the study.

"We've identified some leads that will be the basis for subsequent studies, again in the preoperative setting by our transdisciplinary group. Through these efforts, we are working to redefine the standard of care for pancreatic cancer."

**More information:** Wainberg presents the findings at the annual American Association for Cancer Research (AACR) meeting on Monday, April 8 in the Clinical Trials Minisymposium Session titled, "Advances in Immunotherapy," from 2:30 to 4:30pm.

Provided by University of California, Los Angeles

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