Immunotherapy Plus Chemotherapy Before Surgery Shows Promise for Pancreatic Cancer

UCLA study finds treatment is safe, helps more patients reach surgery and reveals new insights into the tumor’s immune response.

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A new UCLA investigator-initiated study sponsored by the UCLA Health Jonsson Comprehensive Cancer Center has found that adding immunotherapy to standard chemotherapy before surgery is safe and shows promise for some patients with borderline-resectable pancreatic cancer, a disease that has historically been difficult to treat.

The findings, published in Nature Communications, show that while the combination did not produce a clear survival advantage for most patients, a notable subset experienced unusually deep and durable responses. It also helped some patients live long enough to reach surgery, shrank tumors and produced encouraging survival outcomes. The study also revealed immune changes that may limit how well immunotherapy works in pancreatic cancer, offering important clues for how future treatment strategies could be refined to further improve patient outcomes.

Why it matters

Pancreatic cancer remains one of the deadliest cancers, with few effective treatment options and limited benefit from immunotherapy, which has transformed care for many other cancer types. In diseases such as lung and breast cancer, giving immunotherapy alongside chemotherapy before surgery has significantly improved outcomes, but this strategy has rarely been tested in pancreatic cancer.

By focusing on patients with borderline-resectable disease, a group for whom surgery is possible but technically challenging, this study provides an opportunity to evaluate whether immunotherapy can improve surgical success and survival, while also revealing how the tumor’s immune environment responds. These insights could help guide the development of more effective, tailored treatment strategies for a cancer that urgently needs better options.

What the study did

Researchers conducted a single-arm Phase 1b/2 clinical trial in 28 patients with borderline-resectable pancreatic cancer. Patients received modified FOLFIRINOX chemotherapy combined with the immunotherapy drug nivolumab [Opdivo] before surgery. This approach allowed investigators to directly analyze tumor tissue removed during surgery and compare it with pretreatment biopsies and historical samples from patients who received chemotherapy alone. The team used advanced techniques, including gene expression analysis, immunohistochemistry and spatial transcriptomics, to examine how the treatment altered the tumor's immune landscape.

What they found

Most patients tolerated the combination treatment well and were able to proceed to surgery, with no serious immune-related side effects or treatment-related delays.

- 79% of patients went on to surgical resection.
- All patients who underwent surgery had their tumors successfully removed.
- 86% had clean margins.
- 50% had no cancer detected in their lymph nodes.

While overall survival outcomes were similar to those typically achieved with chemotherapy alone, a subset of patients experienced unusually strong and durable responses:

- 9% had complete disappearance of detectable cancer at the time of surgery.
- Another 9% had near-complete responses.

Immune analyses showed that immunotherapy increased immune activity within tumors, including higher levels of cancer-killing CD8 T cells. At the same time, treatment was associated with changes in the tumor immune environment marked by disorganized immune cell clusters and an accumulation of plasma cells and exhausted T cells, which are immune cells that are activated but less effective at attacking cancer. These findings may help explain why immunotherapy often triggers immune activation without translating into long-term tumor control in pancreatic cancer and point to strategies for improving future combination therapies.

The impact

While adding immunotherapy to standard chemotherapy did not produce a clear survival advantage for most patients with borderline-resectable pancreatic cancer, a subset of patients experienced unusually deep and durable responses, including complete tumor regression and long-term disease control, suggesting that immunotherapy may benefit select individuals.

The study also provides important insight into why immune-based treatments have shown limited success in pancreatic cancer, revealing that while immunotherapy activates immune cells within tumors, it may also disrupt immune organization and promote immune exhaustion. Future research will focus on identifying patients most likely to benefit and developing strategies that better support effective, sustained anti-tumor immune responses.

“By testing this novel drug combination in the preoperative setting, we were able to directly compare pre-treatment biopsies with surgical resection specimens to better understand why the therapy works in some patients, and, just as importantly, why it does not in others, and what additional strategies might improve responses,” said senior author Dr. Timothy Donahue, chief of surgical oncology and professor of surgery at the David Geffen School of Medicine at UCLA. “Establishing this platform within the Agi Hirshberg Center for Pancreatic Diseases positions us to evaluate multiple new therapeutics in a systematic and translationally integrated way in the future.”

About the research team

The study’s first authors are Dr. Zev Wainberg, co-director of the UCLA Health GI Oncology Program, and Dr. Jason Link, associate professor of surgery at the David Geffen School of Medicine at UCLA. The senior author is Dr. Donahue, who is also the director of the UCLA Agi Hirshberg Center for Pancreatic Diseases. All are members of the UCLA Health Jonsson Comprehensive Cancer Center. Other authors, all from UCLA, are Alykhan Premji, Serena Zheng, Michael Srienc, McKensie Hammons, Shineui Kim, Luyi Li, Zeyu Liu, Olga Tsvetkova, Evan Abt, Lee Rosen, Stephen Kim, Jonathan King, O. Joe Hines, Mark Girgis, Saeed Sadeghi, Olga Olevsky, Deborah Wong, Lisa Yonemoto, Ann Marie Siney, Kim Kelly, Christine Kivork, Chi-Hong Tseng, Caius Radu and David Dawson.

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