# FDA approval of 4-drug combination for front-line treatment of metastatic pancreatic cancer

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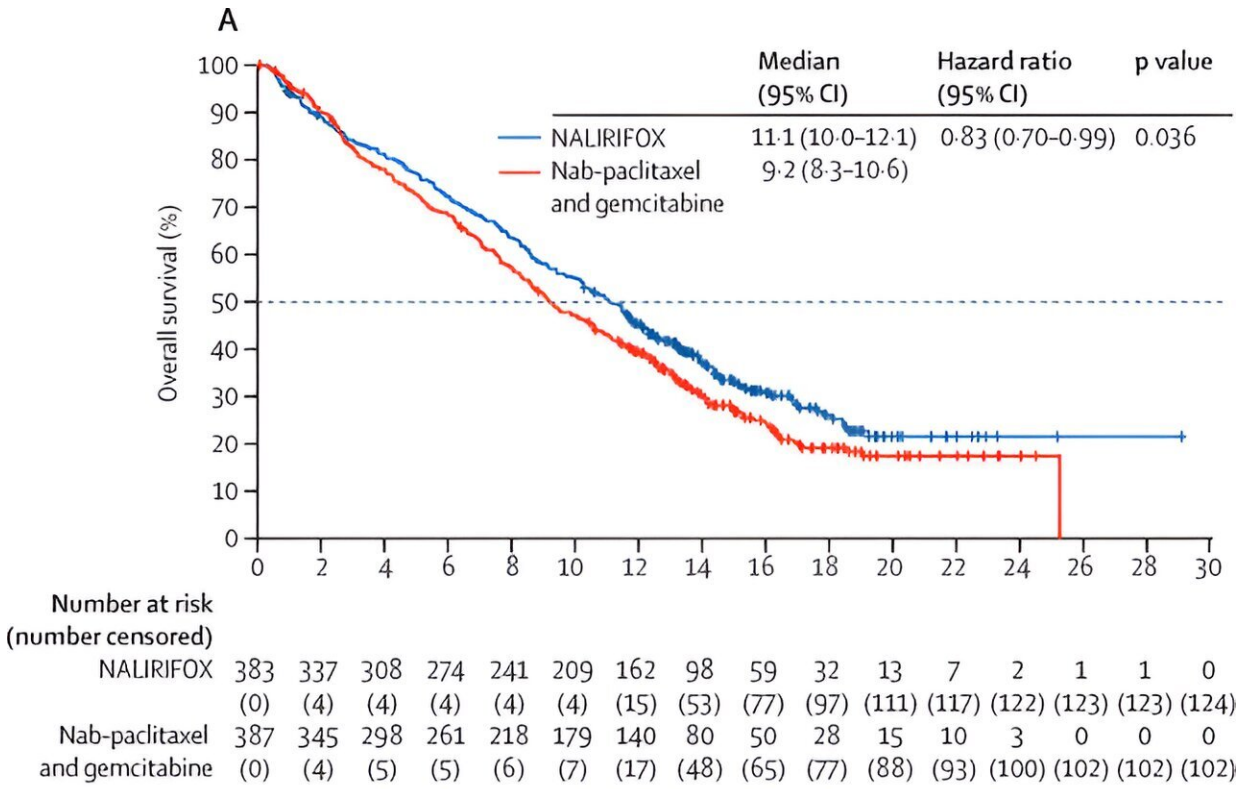


Kaplan–Meier estimates of overall survival (A) and progression-free survival (B) NALIRIFOX=liposomal irinotecan in combination with fluorouracil, leucovorin, and oxaliplatin. Credit: *The Lancet* (2023). DOI: 10.1016/S0140-6736(23)01366-1

A four-drug chemotherapy regimen of irinotecan liposome (Onivyde) in combination with oxaliplatin, leucovorin, and fluorouracil—together referred to as NALIRIFOX—has been approved by the U.S. Food and Drug Administration (FDA) for the first-line treatment of metastatic pancreatic adenocarcinoma.

The FDA approval was based on results of the NAPOLI 3 trial, a study led by Dr. Zev Wainberg, co-director of the UCLA Health GI Oncology Program and a researcher at the UCLA Health Jonsson Comprehensive Cancer Center.

Findings from the NAPOLI 3 trial were first presented at the 2023 American Society of Clinical Oncology Gastrointestinal Cancers Symposium annual meeting and published in *The Lancet* in September of 2023. Wainberg, the global principal investigator for the trial, reported NALIRIFOX resulted in longer overall survival than a two-drug protocol comprised of nab-paclitaxel (Abraxane) and gemcitabine.

"The FDA approval is significant because of how difficult it is to treat metastatic pancreatic cancer," said Wainberg, who is also a professor of medicine at the David Geffen School of Medicine at UCLA. "Metastatic pancreas cancer has long been recognized as a very difficult type of cancer to treat, but this study represents a possible new benchmark standard for current therapies and a promising avenue for ongoing research and drug development."

The phase 3 study included 770 patients with pancreatic ductal adenocarcinoma, which makes up 95% of pancreatic cancers. Participants were from 250 sites in 25 countries and were randomly assigned to NALIRIFOX or the two-drug therapy.

Patients in the NALIRIFOX group had an overall survival of 11.1 months, compared with 9.2 months for those in the two-drug arm.

Progression-free survival also increased with NALIRIFOX to 7.4 months versus 5.6 months with the two-drug regimen, which translates into a 30% reduction in the risk of disease progression or death.

The study is believed to be the first metastatic pancreatic cancer study in nearly a decade to have a positive endpoint for overall survival.

Most cases of pancreatic cancer are diagnosed at more advanced stages when the disease is more aggressive and has already started spreading to other parts of the body. There are also limited treatment options, which contributes to the high fatality rate of pancreatic cancer. Only about 13% of patients survive five or more years. In 2024 alone, the American Cancer Society estimates that around 35,000 people are anticipated to die from the disease.

The most common side effects people experienced in the trial included diarrhea, fatigue, nausea, vomiting, reduced appetite, abdominal pain, mucosal inflammation, constipation and decreased weight.

**More information:** Zev A Wainberg et al, NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial, *The Lancet* (2023). DOI: 10.1016/S0140-6736(23)01366-1

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