Targeted Meds Improve Pancreatic Cancer Survival

Daraxonrasib and elraglusib significantly extended survival time for people with hard-to-treat metastatic disease.

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Two experimental targeted therapies extended survival for people with metastatic pancreatic cancer in clinical trials. Revolution Medicines' daraxonrasib pill doubled overall survival time compared with standard chemotherapy in a Phase III study, while patients treated with Actuate Therapeutics' elraglusib were twice as likely to be alive at one year in a Phase II trial.

Pancreatic cancer is often detected late, when it is difficult to treat, and it has one of the lowest survival rates of all cancer types. Standard treatment may include surgery, radiation, chemotherapy, targeted medications and immunotherapy, but disease progression and relapse are common. Five-year survival is around 10%, and some 50,000 people die from this aggressive cancer each year.

"For patients with metastatic pancreatic cancer, new treatment options are urgently needed to increase survival time and improve quality of life," Brian Wolpin, MD, MPH, of Harvard Medical School and Dana-Farber Cancer Institute, principal investigator for the daraxonrasib study, said in a news release. "I believe that this new approach is a very important advance for the field that I expect will be practice-changing for physicians and improve the care for patients with previously treated metastatic pancreatic cancer."

Daraxonrasib

Daraxonrasib is a RAS(ON) inhibitor that targets mutations in a family of RAS oncogenes (KRAS, NRAS and HRAS) that regulate cell growth and drive cancer development. Long considered "undruggable," RAS mutations are implicated in around a third of all cancers and some 90% of pancreatic cancers. The Food and Drug Administration (FDA) has approved two drugs that block a specific KRAS mutation—Lumakras (sotorasib) and Krazati (adagrasib) for lung and colorectal cancer—but daraxonrasib has broader activity.

The international RASolute 302 trial (NCT06625320) is evaluating the efficacy and safety of

daraxonrasib alone in 501 patients with previously treated metastatic pancreatic ductal adenocarcinoma. It enrolled people whose tumors harbored a range of RAS variants as well as those without an identified RAS mutation (wild-type). Participants were randomly assigned to receive either once-daily oral daraxonrasib or the investigator's choice of standard IV chemotherapy.

Topline results showed that daraxonrasib "demonstrated statistically significant and clinically meaningful improvements" in progression-free survival (PFS) and overall survival (OS) compared with chemotherapy, Revolution Medicines announced on April 13. In the full study population, people treated with daraxonrasib had a median OS of 13.2 months versus 6.7 months for those on chemotherapy, a 60% improvement.

Daraxonrasib was described as "generally well tolerated, with a manageable safety profile," but the drug can sometimes cause severe side effects. The most common adverse events included skin rash, mouth sores and gastrointestinal symptoms. Former Nebraska senator Ben Sasse, who announced he had Stage IV pancreatic cancer in December, was a participant in the trial. In a recent video interview with the New York Times—in which he appear with sores covering his face—Sasse said daraxonrasib had shrunk his tumors and relieved his pain, but he called it a "nasty drug."

The study results, which have not yet been published in a peer-reviewed journal, have been submitted for presentation at the American Society of Clinical Oncology Annual Meeting in May. The PFS and OS endpoints from this first interim analysis are considered final and will be submitted to the FDA and other regulatory authorities, according to the Revolution Medicines. The company has a new type of FDA priority voucher intended to shorten review time to just one to two months. Daraxonrasib is also being studied for previously untreated pancreatic cancer and for non-small-cell lung cancer.

"We are standing at the threshold of groundbreaking treatments for patients with pancreatic cancer," said PanCAN Chief Scientific and Medical Officer Anna Berkenblit, MD, MMSc. "[Monday's] announcement represents a real opportunity to bring new hope for people facing this disease: hope for more time with family, hope for better quality of life and hope that ongoing and future research may ultimately lead to a cure."

[Update 4/22/26: Based on the latest results from a Phase I/II trial, presented at the American Association for Cancer Research Annual Meeting, daraxonrasib also shows promise for pancreatic cancer patients starting treatment for the first time. First-line daraxonrasib, either alone or in combination with chemotherapy, demonstrated early signs of durable antitumor activity with manageable safety and tolerability profiles, according to a Revolution Medicines news release. The objective response rates were 47% for daraxonrasib monotherapy and 58% for daraxonrasib plus chemotherapy.]

[Update 5/2/26: On May 1, the Food and Drug Administration issued a "safe to proceed"

letter allowing Revolution Medicines to start an expanded access treatment protocol for daraxonrasib. also known as compassionate use. This means physicians can request the drug from the company for eligible patients.]

Elraglusib

Further back in the pipeline, an international Phase II trial (NCT03678883) is testing elraglusib for people with previously untreated metastatic pancreatic ductal adenocarcinoma. The targeted drug is a GSK-3-beta inhibitor, which blocks a protein that plays a role in tumor growth and immune suppression. Early studies suggest that elraglusib alters the tumor microenvironment, which typically promotes disease progression in people with pancreatic cancer.

Participants in this open-label study were randomly assigned to receive IV infusions of elraglusib plus gemcitabine/nab-paclitaxel chemotherapy or chemotherapy alone. Results were reported this week in Nature Medicine.

In a modified intention-to-treat analysis of 233 patients, elraglusib plus chemotherapy improved median overall survival by 2.9 months and decreased the risk of death by 38% compared with chemotherapy alone. The median OS time was 10.1 months versus 7.2 months, respectively, and one-year survival rates were 44% versus 22%. What's more, patients treated with the combination regimen showed increases in cancer-fighting immune cells in their tumors.

Here, too, the safety profile of elraglusib was described as "manageable." The most common severe treatment-emergent adverse events were neutropenia, anemia and fatigue, all of which occurred more in the combination group compared with the chemotherapy monotherapy group.

"While these results will need to be confirmed in Phase III trials, observing survival benefit in such a difficult-to-treat cancer is encouraging," lead study author Devalingam Mahalingam, MD, PhD, of Northwestern University Feinberg School of Medicine, said in a university news release. "Given the novel mechanism of this drug, these findings raise the possibility that it could have broader application across other tumor types."

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