

# Multi-Selective RAS(ON) Inhibitor Nearly Doubles Survival Time in People With Metastatic Pancreatic Cancer

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## ASCO Perspective Quote

"These results are landscape-changing for metastatic pancreatic cancer patients with a *KRAS* mutation. We are seeing unprecedented survival and efficacy in second-line treatment with an expected safety profile. The RAS revolution is here, and this study is proof of principle that targeting *KRAS* in pancreatic cancer is feasible and effective," said Rachna Shroff, MD, MS, FASCO, Chief of the Division of Hematology/Oncology at the University of Arizona Cancer Center and an ASCO Expert in gastrointestinal cancers.

## Study at a Glance

Focus	New second-line treatment for previously treated metastatic
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## Key Details

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	pancreatic ductal adenocarcinoma (mPDAC)
<b>Population</b>	500 participants from North America, Europe, and Asia
<b>Main Takeaway</b>	The multi-selective RAS(ON) inhibitor daraxonrasib can improve progression-free survival and overall survival in people with mPDAC, whether the tumor has a <i>RAS</i> mutation or not.
	<ul style="list-style-type: none"><li>• Pancreatic cancer accounts for about 3% of cancer diagnoses in the United States. The American Cancer Society estimates that 35,160 men and 32,340 women will be diagnosed with it in 2026. About 95% of cases will be pancreatic ductal adenocarcinoma (PDAC).</li><li>• More than half of pancreatic cancers are diagnosed after they have already metastasized. The 5-year relative survival rate for metastatic</li></ul>

## Significance

pancreatic cancer is about 3%.

Chemotherapy is typically given as first-line treatment, and as second-line treatment when needed. But with second-line chemotherapy, median progression-free survival (PFS) is 3 to 4 months and median overall survival is 6 to 7 months.

- More than 90% of mPDACs are caused by a mutation in the *KRAS* gene, called a *RAS* G12 variant, that results in an overactive *KRAS* protein. Previously available drugs that turn off this protein, called *RAS* inhibitors, are specific to one of the altered versions of the protein.
- Daraxonrasib is a new kind of *RAS* inhibitor called a *RAS(ON)* multi-selective inhibitor. It can turn off the *KRAS* protein to stop cancer growth whether

there is a *KRAS* variant or not, and regardless of which variant it is.

*ALEXANDRIA, Va.* — Results from the first phase 3 trial of a RAS(ON) multi-selective inhibitor show that daraxonrasib is effective for *RAS*-mutant and *RAS*-wild-type metastatic pancreatic ductal adenocarcinoma (mPDAC). In people who have received treatment, daraxonrasib nearly doubles survival with fewer side effects compared to chemotherapy. The research will be presented at the 2026 American Society of Clinical Oncology (ASCO) Annual Meeting, taking place May 29 to June 2 in Chicago.

#### **About the Study**

"Few therapies are available for patients with previously treated metastatic pancreatic cancer, and these therapies have modest efficacy and substantial toxicities. The RASolute 302 trial was designed to assess a RAS(ON) multi-selective inhibitor as a second-line treatment for patients with metastatic pancreatic cancer, looking to define a new standard of care for these patients that works better and has less side effects than currently available chemotherapies," said Brian Wolpin, MD, MPH, Hale Family Center for Pancreatic Cancer Research and Gastrointestinal Cancer Center, Dana-Farber Cancer Institute, Boston, Massachusetts.

A previous phase 1/2 study found that daraxonrasib is safe and effective for people with advanced pancreatic ductal adenocarcinoma (PDAC) with a *KRAS* gene variant who have previously received treatment. However, the [RASolute 302 clinical trial](#) is the first phase 3 study to evaluate survival outcomes based on daraxonrasib treatment and compare it to chemotherapy in this group of patients.

The study included 500 people with mPDAC who had previously received treatment. Participants had to have an ECOG Performance Status score of 0 or 1, meaning they were able to carry out most of their usual activities. About half were men and half were women, and their median age was 66.

The participants were randomly assigned to receive either daraxonrasib (248 people) or chemotherapy (252 people). Most of the participants in both groups had tumors with a RAS G12 variant: 228 in the daraxonrasib group and 231 in the chemotherapy group. In participants without a RAS G12 variant, the tumors could have another RAS variant, called G13 or Q61, or no RAS variant.

### Key Findings

- At a median follow-up of 8.5 months, median overall survival (OS) was 13.2 months in the daraxonrasib group (both for participants with a RAS G12 variant and for the overall group). In the chemotherapy group, median OS was 6.6 months in the participants with a RAS G12 variant and 6.7 months in the total group.
- In people who had received daraxonrasib, median progression-free survival (PFS) was 7.3 months for those with a RAS G12 variant and 7.2 months for the overall group. By comparison, in people who'd gotten chemotherapy, median PFS was 3.5 months for those with a RAS G12 variant and 3.6 months for the whole group.
- For participants in the daraxonrasib group, the objective response rate (ORR) was 33.2% for those with a RAS G12 variant and 31.6% for the overall group. For participants in the chemotherapy group, the ORR was 11.8% for those with a RAS G12 variant and 11.2% for the overall group.

Daraxonrasib caused fewer serious side effects than chemotherapy. Grade 3 or

effects than chemotherapy. Grade 3 or higher adverse events occurred in 43.6% of the daraxonrasib group and 57.5% of the chemotherapy groups. Because of the side effects, 1.2% of people in the daraxonrasib group stopped treatment, compared to 11.2% of the chemotherapy group.

### **Next Steps**

The data from RASolute 302 will be submitted to the U.S. Food and Drug Administration to support assessment of daraxonrasib for approval as a new drug for pancreatic cancer. The drug is also being tested in several other clinical trials, including as a first-line treatment for pancreatic cancer and to treat other RAS-related cancers. In addition, researchers are working to understand how cancers develop resistance to daraxonrasib and to identify other therapies that can be used in combination with daraxonrasib to improve its effectiveness.

This trial was funded by Revolution Medicines.

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COVERAGE.**

**###**

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