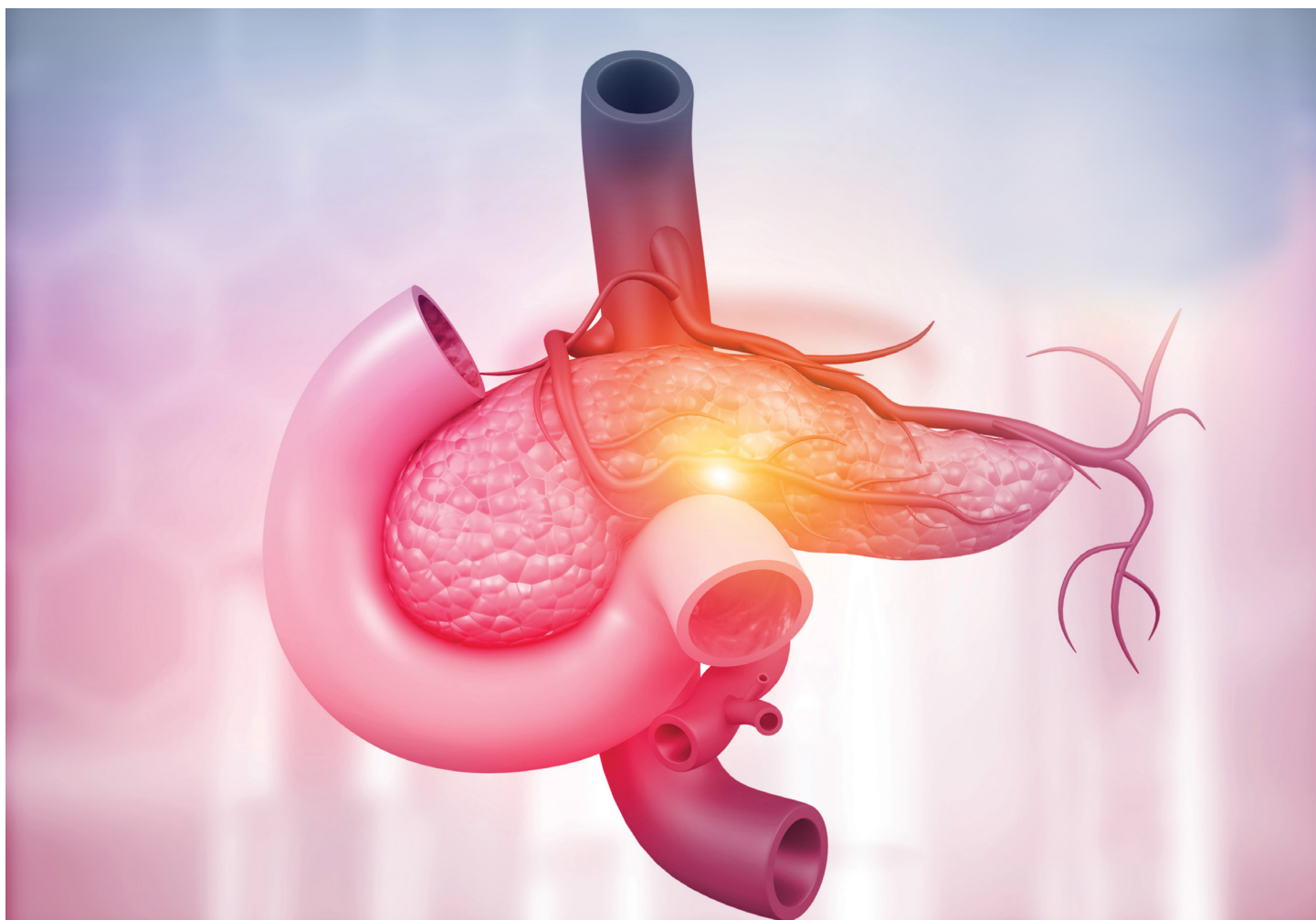




WHAT IS THE BUZZ ABOUT A NEW PANCREATIC CANCER THERAPY?

By Hardeep Phull, MD, MS

There is a novel, recently approved pancreatic cancer therapy, daraxonrasib (RASONQUE™), for adults with metastatic pancreatic adenocarcinoma who have received at least one prior systemic therapy or are not candidates for multiagent systemic therapy.¹

It was developed by Revolution Medicines, and it is revolutionizing the field, as demonstrated by pivotal phase 3 data from the RASolute-302 trial, recently published in *The New England Journal of Medicine*.²

WHY THIS WAS A HIGHLIGHT AT ASCO 26

This data was presented at the recent American Society



Hardeep Phull

of Clinical Oncology (ASCO) conference on May 31, 2026, by Brian M. Wolpin, MD.³ The presentation received a standing ovation, because we have never been able to achieve such dramatic outcomes in this deadly disease, especially in the relapsed setting. This breakthrough was delivered through the power of using precision medicine to target a known driver of disease, with patience, diligence, and a little thinking outside of the box.

WHY HAS PANCREATIC CANCER BEEN SUCH A DIFFICULT DISEASE TO TREAT?

Pancreatic cancer has historically been one of the hardest cancers to treat because:

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PANCREATIC CANCER

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1. It grows silently, with symptoms showing up typically after it has spread and become advanced;
2. It forms a physical barrier in the body with a hostile zone to keep out blood flow and immune cell infiltration; and
3. Pancreas cancer cells typically grow and mutate rapidly, becoming treatment resistant.⁴

WHAT IS THE MECHANISM OF ACTION OF DARAXONRASIB?

What makes this drug, daraxonrasib, unique is that it is an oral RAS multiselective, tricomplex inhibitor, working on multiple common RAS mutations (G12D, G12V, and G12R).⁵ The RAS pathway is a key driver of this disease, with RAS mutations present in more than 90% of cases.²

Traditionally, RAS proteins were thought to be “undruggable” because their smooth spherical structure essentially lacks any crevices for molecules or drugs to latch onto. RAS also binds tightly to GTP, which is its natural cellular fuel, making it hard to break this interaction.⁵

Daraxonrasib acts like a molecular glue, binding both the active, GTP-bound “ON” state of both mutant and wild-type RAS proteins, creating a complex with RAS and cyclophilin A, which stops RAS from pairing up with downstream cellular growth and proliferation proteins.⁵ In doing so, this targeted inhibition essentially shuts down the cancer’s power supply.

WHAT ARE THE KEY TAKEAWAYS FROM THE TRIAL?

The most important takeaway from this study was that the overall survival in the population of 500 enrolled patients was 13.2 months with the novel oncolytic as compared to 6.7 months with traditional chemotherapy.²

There was also a nearly threefold increase in objective response rates (31% as compared to 11%).²

Daraxonrasib was also associated with improved patient-reported quality

For patients, this breakthrough provides a novel targeted medication that they can take orally, overcoming the harsh side effects and logistics of chemotherapy, while achieving superior outcomes and disease control.

of life, with expected side effects of a targeted oncolytic drug: rash, diarrhea, stomatitis, nausea, fatigue, vomiting, abdominal pain, edema, decreased appetite, and hemorrhage.²

However, there were fewer overall grade 3 or higher adverse events (61%) as compared to chemotherapy (69%) resulting in only 1% of patients discontinuing the oral oncolytic as compared to 11% with chemotherapy.²

WHAT QUESTIONS AND FUTURE STUDIES STILL NEED TO BE ADDRESSED TO CHANGE PRACTICE?

The rapid FDA approval of daraxonrasib is already making this oncolytic a potential game changer in clinical practice.¹

However, as this trial had an open-label design and use of monotherapy, future studies are needed, including studies of combinations with other agents such as oncolytics, immunotherapy and chemotherapy.²

It could potentially even be studied in the frontline setting soon where it could replace or delay the need for toxic chemotherapy or even prevent therapy resistance.²

Lastly, daraxonrasib has incredible promise in other RAS-mutated and -driven cancers such as lung cancer and colon cancer, where it could replace or be combined with conventional therapies including immunotherapy.⁶

WHAT ARE THE IMPLICATIONS OF THIS DATA FOR PATIENTS WITH PANCREATIC CANCER?

For patients, this breakthrough provides a novel targeted medication that they can take orally, overcoming the harsh side effects and logistics of chemotherapy, while achieving superior outcomes and disease control. This can help restore a sense of hope, purpose, and dignity in human beings who are typically devastated by the grave diagnosis of pancreatic cancer.

▲ **Hardeep Phull**, MD, MS, is a physician-scientist, educator, author and speaker involved with cancer care, personalized medicine and innovation in healthcare, including clinical AI. He is president of Hematology Oncology Partners in Excellence, a firm dedicated to empowering doctors with medical education and opportunities. He also serves in a leadership alumni role at the Cleveland Clinic Foundation and serves as a Clinical Instructor at the University of California San Diego.

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