Fact Sheet

DAWN-303: A Study for Patients with Metastatic Pancreatic Cancer Whose Tumors are Positive for a Specific Gene Change Called KRAS G12D

Global, randomized, double-blind, phase 3 study to evaluate the efficacy and safety of chemotherapy with or without INCB161734 (KRAS G12D inhibitor) in patients with metastatic pancreatic ductal adenocarcinoma

Why is this study being done?

KRAS G12D is the most common KRAS alteration in pancreatic ductal adenocarcinoma and is present in roughly 35%–40% of cases. Outcomes with current treatment for metastatic disease remain limited, highlighting the need for more effective targeted therapies.

DAWN-303 is a Phase 3 clinical study testing whether adding a new investigational medicine called INCB161734 to standard chemotherapy can help patients with metastatic pancreatic ductal adenocarcinoma (PDAC) and KRAS G12D mutations live longer and have better outcomes compared to chemotherapy alone.[1]

Who is conducting this study?

This study is being conducted and sponsored by Incyte, a global biopharmaceutical company focused on discovering and delivering medicines for patients with unmet medical needs in Oncology and Inflammation and Autoimmunity.

Where is this study being conducted?

This study is being conducted at approximately 214 sites across North America, Europe and the Asia-Pacific region. The study is registered on ClinicalTrials.gov under identifier NCT07522073, where you can find study site locations.[1]

What is KRAS G12D and why does it matter?

KRAS is a gene that helps control how cells grow and divide. The G12D mutation is a specific genetic alteration in the KRAS gene that can cause cells to grow out of control, leading to cancer. The G12D change is the most common type of KRAS mutation in pancreatic cancers and is found in more than 40 percent of PDAC.[2] There is no approved medicine that targets this specific mutation.

What is INCB161734?

INCB161734 is an investigational medicine (not yet approved) that is designed to block the KRAS G12D protein directly. It is a pill taken by mouth. In early studies (Phase 1), INCB161734 showed encouraging signs of tumor shrinkage in patients with pancreatic cancer, both when used alone and in combination with standard chemotherapy.[3]

What is each phase of clinical development designed to demonstrate?

Clinical trials are usually conducted in 4 phases:

- Phase 1 is designed to demonstrate safety and preliminary effectiveness
- Phase 2 is designed to show effectiveness, if additional evidence is needed
- Phase 3 compares an investigational treatment to existing treatment
- Phase 4 studies are conducted after approval to monitor long-term safety and effectiveness

Who may be eligible to participate?

You may be eligible for this study if you:

- ✓ You have been diagnosed with pancreatic cancer that has spread to other parts of the body (metastatic)
- ✓ Your tumor has been tested and is positive for a KRAS G12D mutation
- ✓ You have not yet received treatment for metastatic disease (prior surgery or treatment before cancer spread may be acceptable)
- ✓ You are able to carry out most daily activities
- ✓ Your cancer can be measured on imaging scans
- ✓ Your organs (such as your liver or kidneys) are functioning adequately based on lab tests

The above criteria represent a partial list. The full list may be found at ClinicalTrials.gov. Final eligibility is determined by the study doctors.[1]

How does this study work?

This is a randomized, double-blind study, meaning you will be randomly assigned (like flipping a coin) to one of two groups. Neither you nor your doctor will know which group you are in during the study. Everyone in the study receives standard chemotherapy. You and your doctor will choose which chemotherapy regimen is best for you before you are assigned to a group.

- **Group 1:** Standard chemotherapy (mFOLFIRINOX or gemcitabine/nab-paclitaxel) **plus INCB161734 (the study drug)**
- **Group 2:** Standard chemotherapy (same regimen) **plus a placebo** (an inactive pill that looks like the study drug)

Treatment continues until the disease progresses or side effects become intolerable. The study plans to enroll approximately 590 patients worldwide. You may discontinue the study at any time.[1]

What are the possible benefits of study participation?

- You will receive standard metastatic pancreatic cancer treatment regardless of study group
- You may or may not benefit from the investigational drug
- Information learned from this study may help future patients with pancreatic cancer
- You may have additional tests and closer monitoring in the setting of a clinical trial

Because this is a research study, benefit cannot be guaranteed. This is an investigational compound – the efficacy and safety have not been fully established.

What are the possible risks and side effects?

All treatments can cause side effects. In early studies of INCB161734 alone, the most common side effects were gastrointestinal in nature. They included:

- Nausea, vomiting, diarrhea, and fatigue
- Vomiting was mainly limited to the first cycle and improved over time
- Serious side effects were seen in some patients including: low blood platelets, lowered number of infection fighting white blood cells, and lowered red blood cells. Your study team will monitor you closely and explain all known risks before you decide to participate.

When combined with chemotherapy, the side effects tracked were from both the study drug and the chemotherapy. Gastrointestinal symptoms and blood count changes were manageable with standard medications to treat these side effects, and doctors could adjust doses as needed.[3]

Talk to your doctor about potential risks and side effects associated with the medicines used in this study.

What factors could make me ineligible to participate?

Certain conditions may prevent you from joining this study. These include, but are not limited to:

- You have already received systemic treatment (chemotherapy, immunotherapy, etc.) for metastatic pancreatic cancer
- You received treatment for non-metastatic disease less than 6 months before the first dose in this study
- You have another active cancer that requires treatment
- You still have significant side effects from previous cancer treatment that have not improved
- You have significant heart disease or certain liver conditions (such as cirrhosis or uncontrolled fluid buildup in the abdomen)
- You have had gastrointestinal surgery that may affect how the study drug is absorbed

Your doctor and/or the study team will review your full medical history to determine if you are eligible. The above list is not exhaustive.[1]

What are the main goals of this study?

The study measures three main things:

- **Overall survival:** How long patients live
- **Progression-free survival:** How long the cancer stays under control without getting worse
- **Objective response rate:** How many patients see their tumors shrink some or completely [1]

What tests, visits and procedures are required and how often?

Expect a structured schedule with frequent visits early on, then regular monitoring throughout treatment, and long-term follow-up to ensure safety and assess how well the treatment works.

General Timeline:

- **Before treatment:** Screening tests, baseline labs, imaging, and genomic testing
- **Early treatment (first month):** Most frequent and intensive monitoring
- **Ongoing treatment:** Visits every 2–4 weeks, scans every 6–8 weeks
- **After treatment:** Long-term follow-up for up to 2+ years

How long will the study last?

It is estimated the study treatment will continue for an average of 6-12 months, but this will vary between participants. After you complete all study treatment, you will have a follow-up visit approximately 30 days later. After the follow-up visit, you will be contacted from time to time to check on your health unless you decide to withdraw from follow up.

What happens if the treatment does not work or I want to stop?

Everyone in the study receives standard chemotherapy. Treatment continues until the disease progresses or side effects become intolerable. You may discontinue the study at any time.

What study expenses do I need to cover? What expenses are covered by the sponsor?

The study sponsor will pay for all study tests and procedures performed for the purpose of this study only. You and your caregiver may be reimbursed for travel expenses directly related to your participation, such as parking, mileage, meals and hotel expenses. The study sponsor will not pay for your routine medical care, such as tests, procedures, and drugs that you would get if you were not in this study.

If I benefit, can I stay on treatment after the study ends?

If you have ongoing benefit when the study ends, there may be an opportunity to join a “rollover study” or participate in a post study access program. The Sponsor will determine, in conjunction with Health Authorities and local ethics committees, what the appropriate post-study access program is available.

Questions to ask your doctor

- Has my tumor been tested for a KRAS G12D mutation? If not, can it be tested?
- Am I eligible for this clinical study based on my current health and treatment history?
- What are the potential benefits and risks of joining this study compared to standard treatment alone?
- Is there a study site near me?

Important things to know

- This is a research study, not standard treatment. In this study you'll receive the investigational treatment or placebo in addition to standard treatment
- The study drug is investigational
- You may leave the study at any time
- Your regular medical care will not be affected if you choose not to participate

Have questions?

Talk with your doctor or care team to learn whether this study may be an option for you. You can also ask the study team any questions before deciding.

For more information please visit:

- **ClinicalTrials.gov:** Search for NCT07522073 at www.clinicaltrials.gov for the full listing and participating sites https://clinicaltrials.gov/study/NCT07522073
- IncyteClinicalTrials.com: https://incyteclinicaltrials.com/about-clinical-trials

The efficacy and safety of the investigational compound discussed have not been established. There is no guarantee that INCB161734 will become commercially available. This fact sheet is for informational purposes only and is not a substitute for professional medical advice. Always talk to your doctor about your treatment options.

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[1] ClinicalTrials.gov – NCT07522073, *A Study to Evaluate Chemotherapy With or Without INCB161734 in Previously Untreated, KRAS G12D-Mutated Metastatic Pancreatic Ductal Adenocarcinoma (DAWN-303)*

[2] Cells. 2022 Oct 10;11(19):3175. doi: 10.3390/cells11193175

[3] Wainberg Z, et al. ASCO-GI 2026. Oral presentation 654