Protocol Summary

of Clinical Trial

The protocol of a clinical study is a document that explains why and how a study will be carried out.

A Study of S241656 in Patients With KRAS, BRAF and Other Selected RAS/MAPK Mutation-Positive Malignancies

Full scientific title: *A Phase 1/2, Open-label Study of Oral S241656 (BDTX-4933) as Monotherapy and in Combination with Other Anti-Cancer Therapies in Patients with KRAS, BRAF and Other Selected RAS/MAPK Mutation-Positive Malignancies (EU Study Number: 2025-523474-16-00)*

1 Why is this study needed?

This study is needed to find new treatments for certain types of cancer that are difficult to treat. These cancers have changes in their genes (hereditary material), called mutations, which can affect signals in cells that help cells grow and survive. This causes uncontrolled cell growth and cancer. The study focuses on certain mutations in five genes: KRAS, NRAS, HRAS, BRAF and CRAF. These mutations are common in cancers like lung cancer, pancreatic cancer, colorectal cancer, biliary tract cancer (the biliary tract consists of the gallbladder and the bile ducts, which produce, store, and release bile), and others.

The study drug, S241656, is designed to block the effect of these mutations, which may stop cancer cells from growing.

Researchers hope that by giving this new drug alone or combined with other anti-cancer treatments, they can find better treatments for these cancers and improve the lives of people who have them. This research is crucial because current treatments don't work well enough for these cancers, and patients need better options.

2 What are we mainly looking for?

What are the main goals of the study?

Part 1:

- To look at the safety and tolerability of S241656 (at different increasing doses) alone or in combination with other anti-cancer treatments.

Part 2:

- To see how well S241656 works in treating the tumor, alone or in combination with other anti-cancer treatments.

What are the main study endpoints?

A study endpoint is the measurement used to decide whether a study goal is reached or not.

Part 1:

- The number and type of dose-limiting toxicities (DLT) during the first treatment period. A DLT is a side effect that is severe enough to prevent an increase in dose of the study drug(s). Side effects are unwanted medical events that the doctors think may be caused by the study treatment(s).
- The number of unwanted medical events that occur during Part 1 and how serious they are.

Part 2:

- The percentage of patients whose cancer shrinks or disappears after treatment, known as the overall response (OR).

3 What about the other goals of the study?

What are the other goals of this study?

- To understand how the body processes S241656. Scientists call this pharmacokinetics (PK).
- To further see how well S241656 works in treating the tumor, alone or in combination with other anti-cancer treatments.
- To find and confirm the effective dose(s) of S241656 alone or in combination with other anti-cancer treatments. The effective dose is the one that produces the desired effect in the body without causing too many side effects.

What are the other study endpoints?

Other study endpoints include:

- PK measurements, including the levels of S241656 and its breakdown product in the blood at different times.
- Changes in the size of the tumor(s), how quickly the tumor(s) shrink or disappear, and how long they remain smaller or gone.
- How long participants live after the start of the treatment and how long they live without their cancer getting worse.
- The number of unwanted medical events occurring during the study and how serious they are.

4 Who is participating in the study?

Overall, approximately 554 participants are expected to join the study.

To take part, participants have to:

- Be adults aged 18 years or older.
- Have a tumor with a specific mutation in the KRAS, NRAS, HRAS, BRAF and/or CRAF genes.
- Not have a tumor with mutation in MEK1/2 genes.
- Have received at least one anti-cancer treatment before starting the study.
- Have adequate organ and bone marrow function.

5 How is the study carried out?

The study is called an open-label study. This means that the research doctors and the participants know which treatment is given. Participation in the study is completely voluntary. The participants can change their mind and withdraw from the study at any stage, for any reason.

The study has two parts. In Part 1, small groups of participants will receive different doses and/or dose schedules of S241656 alone or in combination with other anti-cancer treatments to determine the best and safest dose. This part is called dose escalation.

Part 2 of the study will evaluate the best doses observed in Part 1 in a larger number of participants. Groups of participants will receive the best doses of the study drug(s) to better determine the safety and effectiveness of S241656 alone or in combination with other anti-cancer treatments. This part is called dose optimization and dose expansion.

6 What are the treatment(s) and tests used in the study?

Participants will take the study drug, S241656, as capsules or tablets by mouth. The drug will be taken during periods called "cycles". One cycle lasts 28 days.

These 28-day cycles will be repeated for as long as the cancer does not progress and if the participant does not have too severe side effects. The participant can also decide to stop the treatment at any time.

Some participants will also receive other cancer treatments, like chemotherapy, along with the study drug. If participants receive chemotherapy, it will be given through a drip into a vein.

Participants will visit the study doctors regularly for check-ups to closely monitor the safety of the study treatments and how well they work. These check-ups will include blood and urine tests, scans to look at the tumors, and other health checks.

7 What are the possible benefits and risks?

The participant's disease may or may not improve with the study treatment. Participants will receive close medical follow-up. The results of this study will help the researchers learn more about the study drugs. Studies such as this one could lead to better treatments for people with similar medical conditions in the future.

Researchers designed the study to be safe, with minimal risk or discomfort for participants. The study has strict safety rules and regular check-ups. As with all medicines, S241656 treatment may cause side effects. If side effects occur, the study doctors will take care of the participants until they are resolved.

The study doctors will tell the participants about the known and possible risks and side effects of S241656 alone or in combination with other anticancer treatments. Based on the information collected from the study drug or similar drugs, side effects may include gut issues, skin rash and changes to certain blood and liver measurements.

Before enrolling in the study, participants will be provided with an informed consent document, and they will have the opportunity to ask questions and discuss any concerns with their healthcare provider. The informed consent document will contain detailed benefits, risks and side effects. This is a document that provides people with the information they need to decide if they want to join the study.