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 to evaluate novel immunotherapy combinations in participants with advanced non-small cell lung cancer (NSCLC)

Full scientific title: A Phase 1b/2, multicenter, open-label platform study of select immunotherapy combinations in adult participants with previously untreated advanced non-small cell lung cancer (NSCLC) with high PD-L1 expression (EU trial number: 2023-508730-34)

1 Why is this study needed?

The study aims to test three drugs in combination with an approved drug called cemiplimab in people who have non-small cell lung cancer (NSCLC). NSCLC is the most common type of lung cancer.

In our immune system, there are immune cells that can kill cancer cells. However, some cancer cells can turn off these immune cells, making it harder for the body to fight the cancer.

Cemiplimab and the three drugs, called S095018, S095024, and S095029 (collectively called "S-compounds"), are designed to help immune cells stay turned on and prevent cancer cells from turning them off. These drugs are types of immunotherapies (a treatment that helps the immune system fight cancer). They are made to recognize and stick to specific proteins on the surface of immune cells.

This 2-part study aims to test if each of the S-compounds in combination with cemiplimab works well and is safe for patients with NSCLC. The hope is that by keeping the immune cells turned on, they will be better able to move into tumors and kill the cancer cells. Since cemiplimab and the S-compounds work in different ways to affect immune cells, combining the S-compounds with cemiplimab might increase the effect cemiplimab has on the cancer.

This research is important because it aims to improve current lung cancer treatments, potentially leading to better outcomes and longer survival for patients.

2 What are we mainly looking for?

What are the main goals of the study?

- To see how safe each of the S-compounds is in combination with cemiplimab and to confirm the recommended doses for each combination (the doses that are both safe and effective) (Part A).
- To test how well each of the three treatment combinations work in treating the cancer, compared to using cemiplimab alone (Part B).

What are the main study endpoints?

A study endpoint is the criteria used to decide whether a study goal is reached or not. One of the main endpoints of the study is to observe how many participants experience unwanted medical events (Part A). Another main endpoint is to check how many participants had their cancer get smaller or go away based on medical scans (Part B).

3 What about the other goals of the study?

What are the other goals of this study?

The other goals are:

- To learn more about the safety and effectiveness of each treatment combination.
- To understand how S095018, S095024, and S095029 are processed in the body (pharmacokinetics).
- To learn how the body's immune system responds to S095018, S095024, and S095029.

What are the other study endpoints?

The other study endpoints are:

- The length of time the participant's cancer continues to respond to the treatments without their cancer getting worse.
- The number of participants whose cancer did not get worse for at least 6 months.
- The number of participants whose cancer got smaller or went away and stayed that way for 6 months.
- The length of time from the start of the treatment that a participant lives without the cancer getting worse.
- The length of time a participant lives after starting the treatments.
- The number of unwanted medical events and other findings related to safety during the study.
- The levels of S095018, S095024, and S095029 in the blood.
- The number of participants who develop antibodies against S095018, S095024, and S095029.

4 Who is participating in the study?

Overall, up to 176 participants are expected to take part in the study.

To take part, participants have to:

- Be at least 18 years old.
- Have advanced NSCLC that has spread within the lungs (locally advanced) or to other parts of the body (metastatic).
- Have tumors with high levels of PD-L1 (a protein present on the surface of cells).
- Have not received any previous treatment for their NSCLC.
- Have no specific mutations/genetic changes in their tumor cells that can already be treated by approved targeted therapies. Targeted therapy is a type of cancer treatment that targets proteins that control how cancer cells grow, divide, and spread.

5 How is the study carried out?

The study is called an "open-label" study. This means that both the participants and the research doctors will know which treatments are taken.

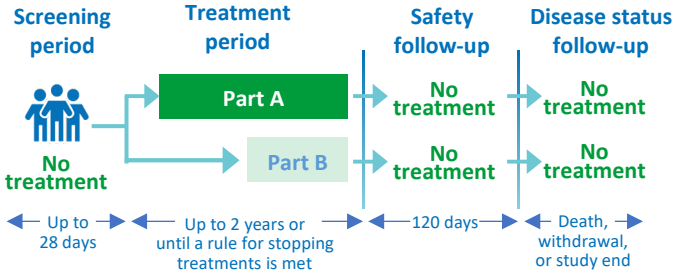
The study is split into two parts. Participants can only join one part of the study.

In **Part A**, participants will be assigned to one of three treatment groups: S095018, S095024, or S095029, each in combination with cemiplimab. Doctors will study the safety of each treatment combination. Doctors will also work out the best doses of S095018, S095024, and S095029 to use in Part B of the study.

In **Part B**, participants will be assigned by chance (or "randomised") to one of four treatment groups:

- S095018 in combination with cemiplimab
- S095024 in combination with cemiplimab
- S095029 in combination with cemiplimab
- Cemiplimab only

The study design is presented in the image below:



6 What are the treatments and tests used in the study?

Each study treatment will be given as an injection into a vein under the care of the study doctors.

- S095018, S095024, and S095029 are still being tested and have not yet been approved for use outside of research studies.
- Cemiplimab given alone is approved in several countries worldwide for patients with NSCLC.

Study treatments will be given on Day 1 of each cycle, where one cycle lasts 21 days. These 21-day cycles are repeated for up to 2 years, as long as the cancer does not worsen, and the participant does not have too severe side effects. The participant can also decide to stop the treatment at any time.

The participants will visit the doctors regularly. During the visits, doctors will collect information about the participants' health. Doctors will also take medical scans and blood samples at scheduled times.

7 What are the possible benefits and risks?

As NSCLC is a complex disease, safer and more effective treatments are needed. This study may help to develop new treatment combinations that work better for patients. The NSCLC may or may

not improve with the study treatments. But participants will have close monitoring.

As for all drugs, the study treatments may cause some unwanted events, called side effects. Every care will be taken to avoid and treat side effects if they occur.

Like any other medicine, the study treatments may cause allergic reactions. As with any new treatment affecting the immune system, there is a risk that immune-related side effects occur when taking S095018, S095024, S095029 or cemiplimab. Other risks may include infusion-related reactions, infections, or harm to a developing baby (embryofoetal toxicity). Based on the data collected so far, the study treatments can cause side effects, but they have been manageable.

There may be other risks that are unknown and unexpected. All side effects will be collected and regularly reviewed by the study doctors to make sure the benefits outweigh the risks.