Clinical Trial Summary

Study to learn about the safety of the medicine called Sym021 when given alone and in combination with either Sym022 or Sym023 or both Sym022 and Sym023 to participants with solid tumors or lymphomas.

Full scientific title: A Phase 1, open-label, multicenter trial investigating the safety, tolerability, and preliminary antineoplastic activity of Sym021 (anti-PD-1) as monotherapy, in combination with either Sym022 (anti-LAG-3) or Sym023 (anti-TIM-3), and in combination with both Sym022 and Sym023 in patients with advanced solid tumor malignancies or lymphomas.

We thank all the participants who took part in the study. Clinical study participants are very important for making progress in science, for the benefit of patients.

This document is a summary of the study. It is written for a general audience.

Researchers need many studies to decide which medicines work the best and are the safest for patients. For medical science to progress, many studies involving patients are being conducted all around the world. This summary only shows the results from this one study. Other studies, testing the same drug, may find different results. You should not change your current treatment based on the results of this single study. If you have any questions about this study, please talk to your doctor.

Therapeutic area:
Oncology

Disease:
Solid Tumors or Lymphomas

Study phase:
Phase 1

Final version
22/06/2023

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1 Why was this study done?

This study was done to test new cancer drugs called Sym021, Sym022 and Sym023 in participants with advanced solid tumors cancers or with lymphomas.

Cancers fall into two categories: solid tumor cancers and blood cancers. Solid tumor cancers are abnormal growths of cells in organ(s) of the body such as the lung, breast, or prostate. In advanced stages of disease, solid tumors may spread in the body. Blood cancers affect cells of your blood. Lymphoma is a type of blood cancer.

Sym021, Sym022, and Sym023 are proteins (called antibodies) that could help immune cells (cells that help the body fight diseases) to kill cancer cells. The ways Sym021, Sym022 and Sym023 interact with immune cells are slightly different from each other. It is hoped that by combining them, their actions on the cancer cells may be more effective.

The study was done in 3 parts.

- Part 1, Sym021 was tested alone.
- Part 2, Sym021 was tested in combination with either Sym022 or Sym023.
- Part 3, Sym021 was tested in combination with Sym022 and Sym023.

The main goals of this study were:

- To look at the safety of Sym021 when given alone and when given in combination with Sym022 and/or Sym023. The safety of Sym022 and Sym023, each given alone, was also looked at but in separate studies.
- Part 1: to find the highest dose (amount) of Sym021 that participants could take without too much risk (this is known as the highest tolerated dose) and to choose the selected dose for Part 2. The selected dose is the one that is both safe and potentially effective against cancer cells.
- Part 2 (two groups): to find the highest dose and choose the selected dose of Sym022 when given in combination with the selected dose of Sym021 (Group A) and to find the highest dose and choose the selected dose of Sym023 when given in combination with the selected dose of Sym021 (Group B).
- Part 3: To further research the highest dose of Sym023 and choose the selected dose of Sym023 when given in combination with selected doses of Sym021 and Sym022.

2 When and where did this study take place?

When did the study take place?

- This study started in November 2017.
- It ended in March 2022.

Where did the study take place?

The study took place in North America.

3 Who participated in the study?

Which participants were included in the study?

To take part, participants had to meet specific criteria, including:

- Be at least 18 years of age or older.
- Have a solid tumor cancer that had spread locally or had spread to other parts of the body or have lymphoma.
- Have one of the above cancers for which standard treatments were no longer effective or not suitable.

As it turned out, all the participants who took part had solid tumor cancer. None of the participants had lymphoma, although lymphoma patients were allowed to participate.

How many participants took part in the study?

A total of 89 participants took part in the study:
52 women and 37 men.

- 17 participants in Part 1 of the study.
- 53 participants in Part 2 of the study (26 participants in Group A and 27 participants in Group B).
- 19 participants in Part 3 of the study.

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How old were the participants?

The average age of the participants was 58 years in Part 1, 62 years in Group A of Part 2, 60 years in Group B of Part 2, and 57 years in Part 3. The youngest participant was 19 years old and the oldest was 83 years old.

4 Which treatments did the participants receive?

Participants received treatment as follows:
In Part 1, participants received Sym021.

In Part 2, participants received two drugs, depending on their group:Group A: Sym021 and Sym022.

- Group B: Sym021 and Sym023.

In Part 3, participants received three drugs: Sym021, Sym022 and Sym023.

Participants received the drugs through infusion (an injection given slowly, usually over 30 to 60 minutes) into a vein. Study drugs were given every 2 weeks. Two dosing periods of 4 weeks was considered one cycle.

These 4-week cycles were repeated for as long as the cancer did not progress (worsen), and the participant did not have side effects that were too severe. The participant could also decide to stop the treatment at any time.

5 How was the study carried out?

The study was an “open-label” and “dose escalation” study:

- “Open-label” means that participants and doctors knew which treatment was given to the participant.
- “Dose escalation” means that different increasing doses of the study drug were tested.

Part 1

In Part 1, 3 different doses of Sym021 were tested: 1 mg, 3 mg or 10 mg per kilogram (mg/kg) of body weight. “mg/kg” means that the dose was based on the weight of the participant.

To find the highest tolerated dose, the doctors tested different doses of Sym021 in small groups of participants. The first group received the lowest dose, then each new group received a higher dose.

For each dose of Sym021, doctors checked the participants to determine if the drug was safe. Then, the researchers decided whether to increase the dose in the next group of participants.

Once the highest tolerated dose was found, the researchers could define the selected dose (dose that is both safe and potentially effective against cancer cells).

Part 2

Other participants joined the study for Part 2.

- In Group A, they received Sym021 at the selected dose of 3 mg/kg of body weight in combination with Sym022. Sym022 was tested at 4 different doses: 0.3, 1, 3, or 10 mg/kg.
- In Group B, they received Sym021 at the selected dose of 3 mg/kg of body weight in combination with Sym023. Sym023 was tested at 5 different doses: 0.3, 1, 3, 10, or 20 mg/kg.

Researchers defined selected doses for each combination.

Part 3

Other participants joined the study for Part 3. They received Sym021 at the selected dose of 3 mg/kg in combination with Sym022 and Sym023. Sym022 and Sym023 were each tested at 3 doses.

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The five different combinations tested in Part 3 are shown in the table below. Researchers defined the selected doses for the combinations.

	Sym021 (mg/kg)	Sym022 (mg/kg)	Sym023 (mg/kg)
Combination 1	3	1	1
Combination 2	3	3	1
Combination 3	3	3	3
Combination 4	3	5	3
Combination 5	3	5	10

The participants visited the doctor regularly. During the visits, the doctors collected information about the participants' health.

6 What were the side effects?

Side effects are unwanted medical events that the doctors think may be caused by the treatments in the study.

In this summary, we describe unwanted medical events thought to be caused by Sym021, Sym022 and Sym023.

The results may be presented differently in other documents related to the study.

The tables below show the number of participants who had side effects during each part of the study.

	Part 1 (Sym021) (out of 17 participants)
Participants who had side effect(s)	9 (53%)
Participants who had serious* side effect(s)	2 (12%)
Participants who stopped the treatment because of side effect(s)	2 (12%)

**See definition of serious side effects below*

	Part 2: Group A (Sym021, Sym022) (out of 26 participants)	Part 2: Group B (Sym021, Sym023) (out of 27 participants)
Participants who had side effect(s)	19 (73%)	18 (67%)
Participants who had serious* side effect(s)	6 (23%)	6 (22%)
Participants who stopped the treatment because of side effect(s)	4 (15%)	3 (11%)

**See definition of serious side effects below*

	Part 3 (Sym021, Sym022 and Sym023) (out of 19 participants)
Participants who had side effect(s)	14 (74%)
Participants who had serious* side effect(s)	3 (16%)
Participants who stopped the treatment because of side effect(s)	0

**See definition of serious side effects below*

What were the types of side effects?

Only the most common side effects (defined as being reported by at least 4 participants) are presented in this summary.

In Part 1, each side effect was reported by less than 4 participants. The most frequent side effect was tiredness reported by 3 participants out of 17 participants (18%).

In Part 2

The table below shows the most common side effects reported during Part 2.

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	Part 2: Group A (Sym021, Sym022) (out of 26 participants)	Part 2: Group B (Sym021, Sym023) (out of 27 participants)
Increase in a pancreas enzyme called amylase	4 (15%)	0
Increase in CPK, an enzyme found mainly in muscle, heart and brain	4 (15%)	0
Joint pain	0	5 (18%)
Tiredness	7 (27%)	7 (26%)

= *participants*

In Part 3, the most frequent side effect was low activity of a gland called the thyroid. This was reported by 4 participants out of 19 participants (21%).

What were the serious side effects?

As presented below, a side effect (event thought caused by the study treatment) is considered serious when:

- the participant needs to be hospitalised,
- it causes lasting damage or death,
- the participant's life is in danger or,
- it is medically important in the doctor's opinion.

During Part 1 (Sym021), serious side effects were:

- pain and inflammation of the joints caused by overactivity of the immune system (the body system and its cells that fight diseases) (1 participant)
- inflammation of the intestine caused by overactivity of the immune system (1 participant)

During Part 2:
In Group A (Sym021 and Sym022) serious side effects were:

- lung disease caused by overactivity of the immune system (1 participant)
- inflammation of the pituitary gland (a gland that releases several hormones and controls many other glands) (1 participant)
- kidney disease (1 participant)
- increase in CPK, an enzyme found mainly in muscle, heart and brain (in 2 participants)
- inflammation of the thyroid gland (1 participant)

In Group B (Sym021 and Sym023), serious side effects were:

- red raised skin rash (1 participant)
- tiredness (1 participant)
- lung disease caused by overactivity of the immune system (3 participants)
- inflammation of the liver caused by overactivity of the immune system (1 participant)
- diarrhea (1 participant)

During Part 3 (Sym021, Sym022 and Sym023), serious side effects were:

- inflammation of the thyroid gland (1 participant)
- inflammation of the thyroid gland caused by overactivity of the immune system (1 participant)
- lung disease caused by overactivity of the immune system (1 participant)

No participants died because of an event thought to be caused by the treatments in the study.

7 What were the study results?

The study was completed as planned.

This document presents only the results for the main goals of the study as detailed in Section 1. Other results are available in documents listed in Section 10.

The safety of the treatments in the study is described in Section 6 of this summary.

Highest tolerated doses were not reached for any of the treatments in the study as all doses and dose combinations tested were considered well tolerated.

During Part 1, one participant had a dose limiting toxicity (DLT, severe medical event that doctors took into consideration when deciding if they should increase the dose or not). The DLT was inflammation of the intestine caused by overactivity of the immune system. This participant received Sym021 10.0 mg/kg.

The selected dose of Sym021 for Parts 2 and 3 was defined as 3 mg/kg.

During Part 2:

In Group A (Sym021 and Sym022), two participants had DLTs:

- One participant had increase in CPK, an enzyme which is mainly found in muscle, heart and brain. This participant received Sym021 3 mg/kg and Sym022 0.3 mg/kg.
- Another participant had kidney disease. This participant received Sym021 3 mg/kg and Sym022 3 mg/kg.

The selected doses of Sym022 for combination treatment in Part 3 were 1.0, 3.0 and 5.0 mg/kg. The selected dose of Sym022 for future studies was defined as 5 mg/kg.

In Group B (Sym021 and Sym023), one participant had a DLT of tiredness. This participant received Sym021 3 mg/kg and Sym023 0.3 mg/kg.

During Part 3: no participant had a DLT.

The selected doses of Sym023 for combination treatment in Part 3 were 1.0, 3.0 and 10.0 mg/kg. The selected dose of Sym023 for future studies was defined as 10 mg/kg.

8 How has this study helped research?

This study helped researchers find the safety of Sym021 when given alone and when given in combination with Sym022 and Sym023.

This study also helped researchers in their understanding of the study drugs in the cancers tested.

This summary shows only the main results from this one study. Other studies, evaluating the same drugs, may find different results.

9 Are there plans for further studies?

Clinical studies with Sym021, Sym022 and Sym023 are on-going.

10 Further information

What are the identification numbers of the study?

- Protocol code: Sym021-01
- US NCT number: NCT03311412

Who did the study?

The company that organised and funded the research, called the “sponsor”, is Symphogen A/S, located at: Pederstrupvej 93 DK-2750 Ballerup Denmark.

How can you contact us?

Contact us on the SERVIER website (Symphogen A/S is a SERVIER company) https://servier.com/en/.

Where can you learn more about this study?

You can find more information about this study on these websites:

- https://clinicaltrials.servier.com/find-clinical-trials
- www.clinicaltrials.gov

In this document we translated medical terms into lay terms. You can find the corresponding medical terms in the Servier glossary at https://clinicaltrials.servier.com/glossary/

You can find general information about clinical trials on https://clinicaltrials.servier.com/