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Clinical Trial Summary

A study to evaluate S65487 (a BCL-2 inhibitor) in patients with previously treated Acute Myeloid Leukemia, Non-Hodgkin Lymphoma, Multiple Myeloma or Chronic Lymphocytic Leukemia

Full scientific title: Phase I, open label, non-randomised, non-comparative, multicenter study, evaluating S65487, a BCL-2 inhibitor intravenously administered, in patients with Relapsed or Refractory Acute Myeloid Leukemia, Non-Hodgkin Lymphoma, Multiple Myeloma or Chronic Lymphocytic Leukemia

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 running all around the world. This summary only shows the results from this one study. Other studies, evaluating 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:
Acute Myeloid Leukemia (AML), Non-Hodgkin lymphoma (NHL), Multiple Myeloma (MM) or Chronic Lymphocytic Leukemia (CLL)

Study phase:
Phase 1

Final Version
25/10/2024

In this summary:

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1 Why was this study done?

This study was done to see if a new cancer drug called S65487 is safe and could be beneficial for treating the following types of blood cancers:

- Acute Myeloid Leukemia (AML): a cancer of the blood and bone marrow (the spongy tissue inside bones where blood cells are made).
- Non-Hodgkin Lymphoma (NHL): a cancer that starts in the lymphatic system. This system is a part of the body's defence system that fights against infections.
- Multiple Myeloma (MM): a cancer that affects a type of white blood cells called plasma cells.
- Chronic Lymphocytic Leukemia (CLL): a cancer that starts from white blood cells (called lymphocytes).

In these types of blood cancers, cancer cells have higher amounts of certain proteins. One of these proteins is BCL-2 (B-cell lymphoma-2). This protein protects cancer cells from death, allowing them to survive and multiply.

S65487 is a drug that blocks BCL-2 proteins. By blocking BCL-2 proteins, this drug could cause cancer cells to die.

The main objectives of the study were:

- To look at the safety of S65487.
- To find the highest dose of S65487 that participants could take without too much risk (highest tolerated dose). This highest tolerated dose helps to find the recommended dose (the one that is both safe and effective for patients).

2 When and where did this study take place?

When did the study take place?

- This study started in July 2019.
- It ended in November 2023.

Where did the study take place?

The study took place in the following countries:

Country	Number of participants
Spain	32
France	20
United Kingdom	6
Australia	2

3 Who participated in the study?

Which participants were included in the study?

To take part, participants had to:

- Be at least 18 years old.
- Have one of the following cancers that returned after improvement (relapsed) or did not respond to any treatment (refractory):
  - Acute Myeloid Leukemia (AML)
  - Non-Hodgkin Lymphoma (NHL)
  - Multiple Myeloma (MM)
  - Chronic Lymphocytic Leukemia (CLL)
- Had adequate organ function.

How many participants took part in the study?

A total of 60 participants took part in the study: 21 women and 39 men.

How old were the participants?

The average age of the participants was 66 years. The youngest participant was 28 years old and the oldest was 87 years old.

4 Which treatments did the participants receive?

The participants received the drug S65487 during time periods called "cycles". Each cycle lasted

21 days. The 21-day cycles were repeated for as long as the cancer did not get worse and if the participant did not have too severe side effects. The participant could also continue the treatment if the doctor considered that it was really beneficial despite the worsening of the cancer. The participant could also decide to stop the treatment at any time.

The participants received S65487 through infusion (injection given slowly) into a vein, in one of the following treatment schedules:

- S65487 was given once every week in cycles of 21 days at weekly doses ranging from 25 milligrams (mg) to 1200 mg.
- S65487 was given on Days 1, 3, 5, 8 and 15 in each 21-day cycle at weekly doses ranging from 200 mg to 3000 mg.

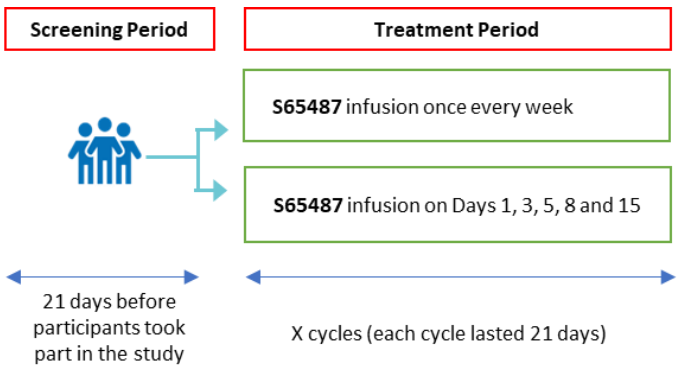
Infusion time was about 30 minutes and could be increased to more than 1 hour if clinically indicated.

5 How was the study carried out?

The study is called an "open-label" study. This means that both the participants and the research doctors knew the treatment taken.

The participants started with a first period called a screening period that could last up to 21 days. This period allowed doctors to check if the participant fulfilled all the criteria to take part in the study.

The study design is presented in the image below.



To find the highest tolerated dose, the doctors tested different doses of S65487 in small groups of participants. The first group received the lowest dose, then each new group received a higher dose.

For each dose, the doctors checked the safety of the study drug. Then, the researchers decided whether to increase the dose of S65487 in the next group of participants.

Once the highest tolerated dose was found, the researchers defined the recommended dose (the dose that is both safe and effective for participants).

The participants visited the doctors 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 S65487.

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

The table below shows the number of participants who had side effects.

	S65487 (out of 60 participants)
Participants who had side effect(s)	27 (45%)
Participants who had serious* side effect(s)	12 (20%)
Participants who stopped the treatment because of side effect(s)	6 (10%)

**See definition of serious side effects below*

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What were the types of side effects?

The table below shows the most common side effects reported in the study (reported by at least 2 participants).

	S65487 (out of 60 participants)
Strong unwanted body reaction to the treatment given intravenously (leading to fever, vomiting, shortness to breath, etc.)	5 (8%)
Increase in liver enzyme called ALT	4 (7%)
Low level of platelets (needed for blood clotting)	4 (7%)
Increase in liver enzyme called AST	3 (5%)
Feeling sick	3 (5%)
Low level of neutrophils, a type of white blood cells	3 (5%)
Decrease in the number of red blood cells	2 (3%)
Unusual weakness	2 (3%)
Increase in an enzyme called lactic acid dehydrogenase	2 (3%)
Headache	2 (3%)

= *participants*

What were the serious side effects?

Serious side effects are serious unwanted medical events thought to be caused by S65487 in the study.

A side effect 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.

In this study, 12 participants (20%) had serious side effects.

The table below shows the serious side effects reported in this study (by at least 2 participants).

	S65487 (out of 60 participants)
Strong unwanted body reaction to the treatment given intravenously (leading to fever, vomiting, shortness to breath, etc.)	3 (5%)

In the study, no participants died because of an unwanted event thought to be caused by the treatment.

7 What were the study results?

This document presents only the results for the main goal of the study. Other results are available in other documents listed in section 10.

The study was stopped earlier than planned. The sponsor (the company that organised and funded the research) stopped including new participants because the study drug showed limited effectiveness based on first results. This decision was not due to any safety problem with the study drug.

As the study was stopped earlier than planned, the highest tolerated dose of S65487 was not reached, and the recommended dose could not be determined.

The safety results of the study drugs are described in section 6 of this summary.

8 How has this study helped research?

The study helped researchers to gather more information on the safety of the S65487. This study also helped researchers in their understanding of the study drug for the treatment of blood cancers such as AML, NHL, MM.

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9 Are there plans for further studies?

Another study (CL1-65487-003) with S65487 is on-going at the time of writing this summary and no further studies are planned.

10 Further information

What are the identification numbers of the study?

- Protocol code: CL1-65487-002
- US NCT number: NCT03755154

Who did the study?

The company that organised and funded the research, called the "sponsor", is the Institut de Recherches Internationales Servier based in Gif-Sur-Yvette, France.

How can you contact the sponsor?

Contact us on the Servier website 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/
- https://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/