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Clinical Trial Summary

Phase I Dose Escalation Study of Intravenously Administered S64315 in Combination with Orally Administered Venetoclax in Patients with Acute Myeloid Leukaemia

Full scientific title: An International Phase Ib multicentre study to characterize the safety and tolerability of intravenously administered S64315, a selective Mcl-1 inhibitor, in combination with orally administered venetoclax, a selective Bcl-2 inhibitor, in patients with Acute Myeloid Leukaemia (AML)

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 Leukaemia (AML)

Study phase:
Phase Ib

Final version
07/12/2023

In this summary:

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1 Why was this study done?

This study was done to test a new anticancer drug, S64315, combined with another anticancer drug, venetoclax, in participants with Acute Myeloid Leukaemia (AML).

AML is a cancer of the blood and bone marrow. In AML, the cancer cells have higher amounts of certain proteins. These proteins are Mcl-1 (myeloid cell leukaemia 1) and Bcl-2 (B-cell lymphoma-2). They protect cancer cells from destruction by the body's defence system.

S64315 is a drug that blocks Mcl-1 proteins.

In this study, S64315 was combined with another drug called venetoclax (study drugs). Venetoclax is already approved for the treatment of AML in combination with other drugs. Venetoclax blocks Bcl-2 proteins. It was hoped that by combining S64315 and venetoclax their actions on the cancer cells may be more effective.

The main objectives of this study were:

- To look at the safety of S64315 in patients when given in combination with venetoclax.
- To find the highest dose of S64315 and venetoclax 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 November 2018.
- It ended in November 2022.

Where did the study take place?

The study took place in the following countries:

Country	Number of participants
Australia	14
United States of America	14
France	9

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 AML
  - that returned after improvement (relapsed) or did not respond to any treatment (refractory), or
  - secondary to a condition called myelodysplastic syndrome which means the bone marrow does not make enough healthy blood cells, or
  - not previously treated for AML if they were 65 years old or older and too frail to support usual treatment.

How many participants took part in the study?

A total of 37 participants took part in the study: 15 women and 22 men.

How old were the participants?

The average age of the participants was 63 years. The youngest participant was 19 years old and the oldest was 84 years old.

4 Which treatments did the participants receive?

All participants received a combination of S64315 and venetoclax.

- S64315 was given through infusion (injection given slowly) into a vein at doses ranging from 25 milligrams (mg) to 75 mg. Infusion time was about 30 minutes (and up to 3 hours if clinically indicated).
- Venetoclax was given as tablets taken orally at doses ranging from 100 mg to 400 mg.

The participants took a combination of S64315 once a week and venetoclax once a day, at the doses listed above.

The participants took the drugs during time periods called “cycles”. One cycle lasted 21 days.

These 21-day cycles were repeated for as long as:

- the cancer did not progress,
- the treatment was working for the participant,
- the participant did not have too severe side effects.

The participant could also decide to stop the treatment at any time.

5 How was the study carried out?

Among the 37 participants included in the study:

- 35 participants took a combination of S64315 and venetoclax.
- 2 participants decided not to take part in the study before receiving the treatment.

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

The participants started with a first period called a screening period. This period allowed doctors to decide if the participant was fit to take part in the study and could receive the study treatment.

Then, the participants were included in the study and started treatment.

Participants received the treatment for an average of 8 weeks.

To find the highest tolerated dose, the doctors tested different doses of S64315 and venetoclax in small groups of participants. For each dose, the doctors checked the safety of the study drugs.

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 reactions or events that the doctors think may be caused by the treatments in the study.

In this summary, we describe unwanted reactions or events thought to be caused by the S64315 or venetoclax.

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.

	Out of 35 participants
Participants who had side effect(s)	31 (89%)
Participants who had serious* side effect(s)	13 (37%)
Participants who stopped the treatment because of side effect(s)	7 (20%)

**See definition of serious side effects below*

What were the types of side effects?

The table below shows the most common side effects reported in the study (by at least 4 participants).

	Out of 35 participants
Diarrhoea	19 (54%)
Feeling sick	17 (49%)
Vomiting	13 (37%)
Increase in troponin "I" possibly indicating a heart injury	11 (31%)
Increase in liver enzyme called ALT	6 (17%)
Stomach pain	5 (14%)
Strong unwanted body reaction to the treatment given intravenously (leading to fever, vomiting, shortness to breath, etc.)	5 (14%)
Increase in the levels of a protein called BNP in blood	4 (11%)

= *participants*

What were the serious side effects?

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.

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

	Out of 35 participants
Increase in troponin "I" possibly indicating a heart injury	3 (9%)
Low blood pressure	3 (9%)
Diarrhoea	2 (6%)
Stomach and gut toxicity	2 (6%)

= *participants*

In the study, no participants died because of an unwanted event thought to be caused by S64315 or venetoclax.

7 What were the study results?

During the study, the Sponsor (the company that organised and funded the research) reassessed the clinical benefit of the S64315 and decided to stop the study and the development with the S64315. This decision was based on the fact that it was unlikely that active doses of S64315 and venetoclax could be achieved with an acceptable level of risks or side effects for patients.

This decision was not due to any safety issues, as confirmed by an independent group of experts.

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

The highest tolerated dose of the combination was not reached, and the recommended dose could not be determined.

8 How has this study helped research?

The study helped researchers to gather more information on the safety of the S64315 combined with venetoclax. This study also helped researchers in their understanding of the combination of S64315 and venetoclax for AML treatment.

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

9 Are there plans for further studies?

One clinical study with S64315 is ongoing and no further clinical studies are planned.

10 Further information

What are the identification numbers of the study?

- Protocol code: CL1-64315-002
- EudraCT number: 2018-001809-88
- NCT number: NCT03672695

Who did the study?

The company that organised and funded the research, called the “sponsor”, is the Institut de Recherches Internationales Servier based in Suresnes, 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://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/