Clinical trial SUMMARY

Short study title

Phase I dose-escalation study of intravenously administered S64315 in patients with Acute Myeloid Leukaemia (AML) or Myelodysplastic Syndrome (MDS)

Full scientific title:

Phase I, international, multicentre, open-label, non-randomised, non-comparative study of intravenously administered S64315, a Mcl-1 inhibitor, in patients with Acute Myeloid Leukaemia (AML) or Myelodysplastic Syndrome (MDS)

Therapeutic area:
Oncology

Indication:
Acute Myeloid Leukaemia and Myelodysplastic Syndrome

Study phase:
Phase 1

2nd February 2021
Final Version

In this summary:

CLINICAL TRIAL SUMMARY

Phase I dose-escalation study of intravenously administered S64315 in patients with Acute Myeloid Leukaemia (AML) or Myelodysplastic Syndrome (MDS)

We would like to thank all the patients who participated in the study. As clinical study participants, they help researchers discover new medicines for the benefit of all 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, a lot of people are involved in many studies 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 speak to your doctor.

1 Why was this study done?

The study was done to test a new anticancer drug.

The current name of the study drug is S64315. S64315 blocks the Mcl-1 protein, which promotes tumour-cell survival. This blocking leads to the death of the cancer cells.

Therefore, researchers have expected that S64315 could be effective in different kinds of blood cancers, including Acute Myeloid Leukaemia (AML) and Myelodysplastic Syndrome (MDS).

The main objectives of this study were:

- To look at the safety of the study drug.
- To find the highest tolerated dose of the treatment, called “Maximum Tolerated Dose”. This dose helps to find the recommended dose (dose that could be both safe and effective for patients).

2 When and where did this study take place?

When was it performed?

- This study started in March 2017.
- It ended in May 2020.

Where did the study take place?

The study took place in the following countries:

Country	Number of patients
Australia	13
France	11
Spain	10
United States of America	6

3 Who participated in the study?

Which patients were included in the study?

Patients in the study had to meet specific criteria, including:

- Be 18 years of age or older.
- Diagnosed with a kind of blood cancer called Acute Myeloid Leukaemia (AML) or Myelodysplastic Syndrome (MDS).
- Whose cancer came back after previous treatment and for whom no treatment could be used anymore, or
- Whose cancer did not respond to any treatment, or
- Not previously treated for AML if they were 65 years old or more, and too frail to support usual treatment.

How many patients participated in the study?

Overall 40 patients joined the study: 17 women and 23 men. Two patients withdrew from the study before having received the study drug. Therefore, 38 patients received the study drug.

How old were the patients?

The average age of the patients was 66 years. The youngest patient was 19 years old and the oldest patient was 85 years old. Most of the patients were between 65 and 85 years old.

4 Which treatments did patients receive?

All patients received the same study drug, called S64315, at different doses. Each patient received the same dose during the study.

Each patient received the study drug by intravenous (into a vein) infusion during time periods called "cycles". A cycle lasted 21 days: patients had one infusion of the study drug per week for 3 weeks.

This 21-day cycle was repeated as long as the cancer did not progress, and if the patient did not have too severe side effects. The patient could also decide to stop the treatment at any time.

5 How was the study done?

The study is called an "open-label, dose escalation" study:

- "Open label" means that patients and doctors knew which treatment was given to the patient.
- "Dose escalation" means that different increasing doses of the study drug were tested.

During the study, 7 different doses were tested ranging from 50 mg to the highest dose of 500 mg.

To find the Maximum Tolerated Dose, these different doses were tested one after the other in small groups of patients (3 to 6 patients).

For each dose, doctors checked the safety of the study drug, especially certain severe medical events. These events called DLT (Dose Limiting Toxicity) could be caused by the study drug during the first cycle. Doctors were allowed to increase the dose for the next group of patients only if few of these severe medical events occurred. These events allowed the doctors to define the Maximum Tolerated Dose.

6 What were the side effects?

What about side effects?

Like all medicines, the study drug can cause side effects, although not everybody gets them.
Side effects are unwanted events thought to be related to the study drug.

The table below shows the number of patients who experienced side effects related to the study drug.

	Related to study drug
Patients who had side effect(s)	34 patients (90%)
Patients who had serious* side effect(s)	13 patients (34%)
Patients who withdrew because of side effect(s)	4 patients (11%)

**See definition below*

How many patients had serious side effects?

A side effect is considered serious when:

- The patient needs to be hospitalised,
- the patient's life is in danger,
- there is permanent damage or death,
- or the patient is at risk and requires a medical intervention to prevent the situations listed above.

In this study, 13 patients (34%) had serious side effects. The table below shows the serious side effects that were reported by more than one patient.

	Related to study drug
Fever with lack of white blood cells called neutrophils	2 patients (5%)
Increase in troponin "I" possibly indicating a heart injury	2 patients (5%)
Condition called tumour lysis syndrome, which occurs when a lot of tumour cells die. This causes changes in the blood that may cause damage to organs	2 patients (5%)

Among the 4 patients who withdrew because of side effects, 3 patients withdrew because of serious side effects: one patient for lung infection and lack of white blood cells called neutrophils, one patient for serious, chronic inflammatory disease of the large intestine (colon), rectal bleeding and fever, and one patient for heart failure.

During the study, 27 patients died. None of them died because of a side effect.

What were the other side effects?

The table below shows the other side effects reported in the study. Only the most common (reported by at least 3 patients) are presented.

	Related to study drug
Feeling sick	17 patients (45%)
Vomiting	16 patients (42%)
Diarrhoea	14 patients (37%)
Increase in liver enzyme called ALT	9 patients (24%)
Increase in troponin "I" possibly indicating a heart injury*	9 patients (24%)
Increase in liver enzyme called AST	6 patients (16%)
Increase in CPK enzyme which is found mainly in muscles, heart and brain	4 patients (11%)
Increase in troponin possibly indicating a heart injury	4 patients (11%)
Increase in pancreas enzyme called amylase	3 patients (8%)
Increase in liver and bone enzyme called alkaline phosphatase	3 patients (8%)

**This side effect was considered as serious for 2 patients but not for the 9 patients for whom it did not fit the definition of a serious side effect.*

7 What were the study results?

The most frequent side effects were feeling sick, vomiting and diarrhoea.

During dose escalation, 7 patients had Dose Limiting Toxicity (DLT, severe medical events that doctors checked in order to decide if they could increase the dose or not). Among the 4 patients who were receiving the highest dose of 500 mg, 3 patients had DLT. These DLTs were related to heart problems.

Due to these DLTs detected, and the lack of effect of the study drug when used alone, the sponsor decided to stop the development of S64315 used alone. Therefore, the study was discontinued. The recommended dose was not defined.

8 How has this study helped patients and researchers?

This study helped researchers in their understanding of the study drug. Findings from this study will help to learn whether S64315 can be useful for patients in combination with other treatments.

Patients included in the study had close medical follow-up with experts in cancer. By participating in this study, patients had the opportunity to test a new drug.

9 Are there plans for further studies?

Experiments have shown better activity when S64315 was combined with other anticancer drugs. Therefore, clinical studies with S64315 in combination with another anticancer drug are on-going for patients with blood cancers. Further studies are planned.

10 Further information

What is the identification number of the clinical study?

- Protocol Number: CL1-64315-001
- EudraCT Number: 2016-003768-38
- ct.gov: NCT02979366

Who did the study?

The company organising and funding 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 (www.servier.com).

Where can you learn more about this study?

- The scientific study summary is also available on the Servier Clinical Trial Data website. (www.clinicaltrials.servier.com)
- In this document, we translated medical terms into lay terms. You can find the corresponding medical terms in the Servier glossary on the Servier Clinical Trial Data website.

In accordance with the recommendations of the Cancer Plan III (Measure 5.4), this document was submitted for review, and guidance to Clinical Cancer Research Patients Committee of La Ligue Nationale contre le Cancer.