Clinical trial SUMMARY

SHORT STUDY TITLE

Phase I dose-escalation study of oral administration of S55746 in patients with Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)

Full scientific title

Phase I dose-escalation study of the orally administered selective Bcl-2 inhibitor S55746 as monotherapy for the treatment of patients with Acute Myeloid Leukaemia (AML) or high or very high risk Myelodysplastic Syndrome (MDS)

Therapeutic area:
Oncology

Indications:
Acute Myeloid Leukaemia and Myelodysplastic Syndrome

Study phase:
Phase I

Date:
16 April 2019
Final version

IN THIS SUMMARY:

CLINICAL TRIAL SUMMARY

Phase I dose-escalation study of oral administration of S55746 in patients with Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)

Welcome

This summary explains how the study was performed as well as its results. Researchers need many studies to decide which medicines work best and are safest for the patient. It takes a lot of people in many studies all around the world to advance medical science. This summary only shows the results from this one study. Other studies may find different results.

1 WHAT WAS THE OBJECTIVE OF THE STUDY?

This study is called a "phase 1 study". Its main objectives were:

- To test the safety of the study drug
- To find the highest tolerated dose of treatment, called "maximum tolerated dose (MTD)"

Bcl-2 is a protein that promotes tumor cells survival.
The current name of the study drug is S55746. It is a new anticancer drug that blocks the Bcl2 protein.
Researchers thought that S55746 could be effective in Acute Myeloid Leukaemia and Myelodysplastic Syndrome, kinds of blood cancers. The MTD helps to find the dose that could be effective.

2 WHEN, WHERE AND HOW WAS THIS STUDY DONE?

When was it performed?

- This study started in January 2015.
- It ended in 24 May 2018.

Where did the study take place?

The study included 48 patients in 2 countries:

Country	Number of patients
Australia	21
France	27

How the study was done?

To find the highest tolerated dose, different increasing doses of S55746 were tested one after the other in small groups of patients (2 to 12 patients).
During the study, 11 different dose levels were tested from 100 mg to 1300 mg.

Doctors checked certain severe medical events, called "dose limiting toxicity (DLT)" that could be caused by S55746 at the beginning of the treatment. Doctors increased the dose only if few of these severe medical events occurred.
The maximum tolerated dose (MTD) is finally the dose at which less than a third of patients have some of these severe medical events.

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

- "Open label" means that patients and doctors knew which treatment was given
- "Dose escalation" means that different increasing doses of S55746 were tested

3 WHO PARTICIPATED IN THE STUDY?

Which patients were included in the study?

Patients in the study had to meet notably the following criteria:

- 18 years older
- Diagnosed with a kind of blood cancer called Acute Myeloid Leukaemia or another kind of blood cancer called Myelodysplastic syndrome
- Whose cancer came back after previous treatment and for whom standard treatment couldn't be used anymore
- Whose cancer did not respond to the standard treatment
- Not previously treated for acute myeloid leukaemia if they were more than 65 years old and too frail to support intensive treatment

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How many men and women were in the study?

WOMEN	MEN
18 patients (38 %)	30 patients (62 %)

All patients stopped the treatment, most of them because of the progression of the cancer.

How old were the patients?

Less than 65 years	65 to 80 years
16 patients (33%)	32 patients (67 %)

4 WHICH TREATMENTS DID PATIENTS RECEIVE?

All of the patients took the same study drug, S55746, available as oral 100 mg tablets.
Patients took the study drug during time periods called “cycles”.
Patients took oral tablets of S55746 once daily during 21-days cycles. There was no interruption of treatment between cycles.
The treatment was maintained as long as the cancer did not progress and if the patient had not too severe side effects.

The design of the study planned that some patients would receive the treatment in fasting condition (at least 30 minutes prior to the meal, or at least 2 hours after the meal) and some others in fed condition (during the meal).

5 WHAT WERE THE SIDE EFFECTS?

What about side effects?

Like all medicines, this drug can cause side effects although not everybody gets them.
Side effects are unwanted events thought to be related to the study drug, S55746.
The table below shows the number of patients who experienced side effects.

No patient had dose limiting toxicity (severe medical events that doctors checked in order to decide if they could increase the dose or not).

	Related to study drug
Patients who had side effect(s)	15 patients (31%)
Patients who had serious* side effect(s)	4 patients (8%)
Patients who withdrew because of side effect(s)	2 patients (4%)

**See definition below*

How many patients experienced serious side effects?

A side effect is serious when:

- The patient needs to be hospitalized
- The patient’s life is in danger
- It causes permanent damage or death
- Or it may put at risk the patient and requires a medical intervention to prevent the situations listed above

In this study, 4 patients (8%) had serious side effects.
The serious side effects reported were:

- Kidney failure
- Unusual weakness. This event led to withdrawal of the patient
- Heart failure and Hepatic failure - Both events led to withdrawal of the patient
- Lack of platelets, cells that help the blood to clot
- Decrease in the number of white blood cells called neutrophils
- Decrease in the number of red blood cells

Each of them occurred once.

Among the 48 patients who participated in the study, 34 patients died: 11 patients during the treatment period and 23 after the treatment was stopped.
Most of them died because of progression of the cancer. For one patient, the death was due to a heart failure thought to be related to the study drug.

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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 2 patients) are presented.

	Related to study drug
Diarrhoea	3 patients (6%)
Decrease in the number of red blood cells	2 patients (4%)
Decreased appetite	2 patients (4%)
Involuntary contraction of muscle	2 patients (4%)

6 WHAT WERE THE STUDY RESULTS?

Despite dose escalation up to 13 oral tablets of 100 mg, the study drug was not sufficient in the blood to be possibly effective. For that reason, the study was discontinued. The maximum tolerated dose (MTD) was not found: all doses tested were well tolerated in most of the patients.

7 HOW HAS THIS STUDY HELPED PATIENTS AND RESEARCHERS?

The results of this study showed that it was not possible to use this drug with an oral form. Findings from this study allowed researchers to decide to stop testing this new anticancer drug.

8 ARE THERE PLANS FOR FURTHER STUDIES?

No other studies with S55746 are foreseen to date.

9 FURTHER INFORMATION

What is the identification number of the clinical study?

- Protocol Number: CL1-55746-002
- EudraCT Number: 2014-002559-24

What is the name of the Sponsor?

The company organizing and funding the research, called sponsor, is the Institut de Recherches Internationales Servier based in Suresnes, France.

How can you contact the Sponsor?

Contact us on Servier website (www.servier.com).

Where can you learn more about this study?

- The scientific summary is also available on 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 Servier Clinical Trial Data website