Clinical trial SUMMARY

Short study title

Dose-escalation Study of Oral Administration of S 55746 in Patients With Chronic Lymphocytic Leukaemia and B-Cell Non-Hodgkin Lymphoma

Full scientific title:

Phase I dose-escalation study of oral administration of the selective Bcl2 inhibitor S55746 in patients with refractory or relapsed Chronic Lymphocytic Leukaemia and B-Cell Non-Hodgkin Lymphoma

Therapeutic area:
Oncology

Indication:
Chronic Lymphocytic Leukaemia
and
B-Cell Non-Hodgkin Lymphoma

Study phase:
Phase 1

16 September 2019
Final version

In this summary:

CLINICAL TRIAL SUMMARY

Dose-escalation Study of Oral Administration of S 55746 in Patients With Chronic Lymphocytic Leukaemia and B-Cell Non-Hodgkin Lymphoma

We would like to thank all the patients who participated in the study. As clinical study participants, they help researchers to 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 the patients. It involves a lot of people in many studies all around the world for medical science to progress. This summary only shows the results from this 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 on this study, please speak to your doctor.

1 Why was this study done?

This study is called a "first-in-human phase 1" study. It means that it was the first time the test drug was given to human beings.

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 different kinds of blood cancers.
The MTD helps to find the dose that could be both safe and effective.

2 When and where did this study take place?

When was it performed?

- This study started in March 2014.
- It ended in October 2018.

Where did the study take place?

The study took place in 5 countries:

Country	Number of patients
France	49
Germany	6
Hungary	1
Poland	2
Singapore	7

3 Who participated in the study?

Which patients were included in the study?

Patients in the study had to meet at least the following criteria:

- 18 years and older.
- Diagnosed with a group of blood cancer called B-Cell Non-Hodgkin Lymphoma (NHL) or another kind of blood cancer called Chronic Lymphocytic Leukaemia (CLL).
- Whose cancer came back after standard treatment or whose cancer did not respond to the standard treatment.

How many patients participated in the study?

Overall 65 patients joined the study. There were 49 patients with NHL (25 women and 24 men) and 16 patients with CLL (3 women and 13 men).

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

How old were the patients?

The average age of the patients with NHL was 59 years. The average age of patients with CLL was 65 years.

The youngest patient was 22 years old and the oldest patient was 85 years old.

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4 Which treatments did patients receive?

All of the patients took the same study drug, S55746, available as 100 mg tablets.
Patients took the study drug during time periods called "cycles".
A cycle lasted 21 days as follows: patients took tablets of S55746 once daily. 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.

Some patients received the treatment in fasting condition (at least 30 minutes prior to the meal, or at least 2 hours after the meal) and others in fed condition (during the meal).

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 S55746 were tested.

To find the highest tolerated dose, different increasing doses of S55746 were tested one after the other in small groups of patients (2 to 13 patients).
During the study, 10 different dose levels were tested ranging from 100 mg to 1300 mg.
For each dose, doctors checked certain severe medical events, called "dose limiting toxicity (DLT)" that could be caused by S55746 at the beginning of the treatment (during the first cycle).
Doctors were able to increase 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.

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, S55746.

The table below shows the number of patients who experienced side effects.

	Related to study drug
Patients who had side effect(s)	21 patients (32%)
Patients who had serious* side effect(s)	4 patients (6%)
Patients who withdrew because of side effect(s)	3 patients (5%)

**See definition below*

How many patients had 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 (6%) had serious side effects.
The serious side effects reported were:

- Increase in liver blood test called GGT
- Increase in liver blood test called bilirubin
- Increase in liver blood test called AST
- Lack of white blood cells called neutrophils
- Decrease in the number of white blood cells called neutrophils
- Increase in liver and bone blood test called alkaline phosphatase
- Yellowing of the skin or whites of the eyes caused by liver or blood problems.

Each of them occurred once except decrease in the number of white blood cells called neutrophils which occurred in 2 patients.

Among the 3 patients who withdrew because of side effects, 2 patients withdrew because of serious side effects.

Among the 65 patients who participated in the study, 25 patients died: 4 during treatment period and 21 during follow up period. Most of them died because of progression of the cancer. None of them died due to an event thought to be related to the study drug.

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
Feeling sick	4 patients (6%)
Feeling tired	3 patients (5%)
Lack of platelets, cells that help the blood to clot	3 patients (5%)
Unusual weakness	2 patients (3%)
Diarrhoea	2 patients (3%)
Decrease in the number of white blood cells called neutrophils	2 patients (3%)

7 What were the study results?

Despite dose escalation up to 13 tablets of 100 mg once daily, there was not enough study drug in the blood to be possibly effective. For that reason, the study was discontinued. The maximum tolerated dose (MTD) was not found.

8 How has this study helped patients and researchers?

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

9 Are there plans for further studies?

No other studies with S55746 are foreseen to date.

10 Further information

What is the identification number of the clinical study?

- Protocol Number: CL1-55746-001
- EudraCT Number: 2013-003779-36

Who did the study?

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 the Servier Clinical Trial Data website