Clinical trial SUMMARY

Short study title

Phase I/II study to evaluate safety and activity of oral administration of S49076 in combination with gefitinib in adult patients with EGFR mutated advanced non-small cell lung cancer who have progressed while on treatment with EGFR tyrosine kinase inhibitor (TKI) therapy.

Full scientific title:

Phase I/II study of oral administration of S 49076 given in combination with gefitinib in patients with EGFR mutated advanced non-small-cell lung cancer who have progressed after treatment with EGFR tyrosine kinase inhibitor.

Therapeutic area:
Oncology

Indication:
Lung cancer

Study phase:
Phase 1/2

22 October 2019
Final Version

In this summary:

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Phase I/II study to evaluate safety and activity of oral administration of S49076 in combination with gefitinib in adult patients with EGFR mutated advanced non-small cell lung cancer who have progressed while on treatment with EGFR tyrosine kinase inhibitor (TKI) therapy

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?

The study was done to assess a new anticancer drug combined with a marketed drug in patients who had a specific kind of lung cancer – "EGFR mutated advanced non-small cell lung cancer".

The new anticancer drug is called S49076.
The marketed drug is called "gefitinib".

EGFR (Epidermal Growth Factor Receptor inhibitor) is a protein found on the surface of certain cells. EGFR normally allows the cells to grow and divide. Changes in EGFR result in tumour growth.

Gefitinib belongs to a family of anticancer drugs called EGFR inhibitors. EGFR inhibitors block the protein EGFR. This helps to stop the growth of cancer cells.
This drug family is used to treat patients who have a cancer with changes in EGFR: "EGFR mutated advanced non-small cell lung cancer".

Some patients have specific information on their cancer cells: high levels of MET and AXL proteins. In those patients, the cancer progresses again after initial efficacy of EGFR inhibitor treatment. Researchers thought that the combination of S49076 with gefitinib could be effective in those patients for whom EGFR inhibitor alone has stopped working.

This study combined Phase 1 and phase 2 studies. It is called a phase 1-2 study.

The main objective of the phase 1 study was:

- To test the safety of S49076 given in combination with gefitinib.
- To find the best dose of S49076 to be given in combination with gefitinib.

The main objective of the phase 2 study was to assess how effective S49076 given in combination with gefitinib was in patients with this type of lung cancer.

Unfortunately, towards the end of phase 1, the results did not suggest an added value of the combination of S49076 and gefinitib. This is why the phase 2 study was finally not performed.

2 When and where did this study take place?

When was it performed?

- This study started in January 2016.
- It ended in November 2018.

Where did the study take place?

The study took place in the following countries:

Country	Number of patients
Italy	3
Spain	3
Korea	2
Taiwan	3
Singapore	3

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3 Who participated in the study?

Which patients were included in the study?

To take part, patients had to:

- Be 18 years of age or older
- Diagnosed with a kind of lung cancer called non-small cell lung cancer.
- Have a lung cancer that was advanced or had spread to other parts of the body.
- Have a lung cancer that had specific abnormalities on a protein called EGFR (Epidermal Growth Factor Receptors).
- Have a cancer that had progressed again whereas EGFR inhibitor had previously been effective.
- Have high levels of MET and AXL proteins (specific information on the cancer cells).

How many patients participated in the study?

Overall 14 patients joined the study: 8 women and 6 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 was 61 years. The youngest patient was 35 years old and the oldest one was 72 years old.

4 Which treatments did patients receive?

The study drug is called S49076. In this study it was combined with a marketed drug called gefitinib.

All patients took the same treatment. Each patient received the 2 drugs together:

- S49076 in 100 mg tablets.
- Gefitinib in 250 mg tablets

Patients took the tablets orally once daily.

Patients took the drugs during time periods called “cycles”. A cycle lasted 28 days. There was no interruption between cycles.

These 28-day cycles were maintained as long as the cancer did not progress and if the patient did not have too severe side effects.

5 How was the study done?

The study is called an “open-label” study. This means that patients and doctors knew which treatment was given.

To find the best dose to treat lung cancer, doctors tested increasing doses of S49076 one after the other in small groups of patients.
During the study 2 different dosage levels of S49076 were tested: 4 patients received 500 mg per day and 10 patients received 600 mg per day.
For both doses, doctors checked certain medical events. These events called “dose limiting toxicity (DLT)” could be caused by the study treatment during the first treatment cycle.
Doctors were allowed to increase the dose of S49076 for the next group of patients only if few of these DLT occurred.
The best dose was defined according to the safety results.

6 What were the side effects?

What about side effects?

Like all medicines, these drugs can cause side effects although not everybody gets them.
Side effects are unwanted events thought to be related to the study drug (S49076) or gefitinib.

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

	Related to S49076	Related to gefitinib	Related to S49076 and gefitinib
Patients who had side effect(s)	12 patients (86%)	8 patients (57%)	8 patients (57%)
Patients who had serious* side effect(s)	3 patients (21%)	2 patients (14%)	2 patients (14%)
Patients who withdrew because of side effect(s)	2 patients (14%)	-	-

**See definition below*

How many patients had serious side effects?

A side effect is considered "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, 3 patients (21%) had serious side effects related to S49076.

The serious side effects thought to be related to S49076 were:

- Fever with lack of white blood cells called neutrophils.
- Irregular heartbeat.
- Diarrhoea.
- Inflamed and sore mouth.
- Unusual weakness.

In the study, each of them occurred once.

The following side effects were also thought to be related to gefitinib:

- Fever with lack of white blood cells called neutrophils.
- Diarrhoea.
- Inflamed and sore mouth.

Overall, 2 patients withdrew because of a side effect but none of the side effects was serious.

In the study, 6 patients died: 1 during the treatment period and 5 after the treatment period. Most of them died because of the cancer. No patient died because of side effect 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 3 patients) are presented.

	Related to S49076	Related to gefitinib	Related to S49076 and gefitinib
Diarrhoea	6 patients (43%)	3 patients (21%)	3 patients (21%)
Infection of the skin around the nail	6 patients (43%)	4 patients (29%)	4 patients (29%)
Feeling sick	5 patients (36%)	1 patient (7%)	1 patient (7%)
Decreased appetite	4 patients (29%)	1 patient (7%)	1 patient (7%)
Problem with liver blood test called ALT	4 patients (29%)	0	0
Unusual weakness	4 patients (29%)	3 patients (21%)	3 patients (21%)
Decrease in the number of red blood cells	3 patients (21%)	3 patients (21%)	3 patients (21%)
Inflamed and sore mouth	3 patients (21%)	2 patients (14%)	2 patients (14%)
Problem with liver blood test called AST	3 patients (21%)	2 patients (14%)	1 patient (7%)
Swelling of the ankles, feet or fingers	3 patients (21%)	0	0
Yellow skin coloration	3 patients (21%)	0	0

7 What were the study results?

Because phase 2 was not done, this is a summary of phase 1 study only.

- The best dose for S49076 was 600 mg in combination with 250 mg of gefitinib.
- The most frequent side effects thought to be related to S49076 were diarrhoea and infection of the skin around the nail.
- Phase 1 results did not suggest a better effectiveness by adding S49076 to gefitinib.

8 How has this study helped patients and researchers?

This study helped researchers in their search for new treatments. The study also brought better understanding of the non-small cell lung cancer. Unfortunately, the addition of S49076 to gefitinib does not seem to restore the activity of gefitinib.

9 Are there plans for further studies?

No other studies with S49076 are foreseen to date.

10 Further information

What is the identification number of the clinical study?

- Protocol Number: CL1-49076-003
- EudraCT Number: 2015-002646-31

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 study 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.