Clinical trial SUMMARY

Short study title

Phase I/II trial of S81694 plus paclitaxel in metastatic Breast Cancer

Full scientific title:

Phase I/II trial of S81694 administered intravenously in combination with paclitaxel to evaluate the safety, pharmacokinetic and efficacy in metastatic breast cancer

Therapeutic area:
Oncology

Indication:
Breast Cancer

Study phase:
Phase I/II

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Final version

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CLINICAL TRIAL SUMMARY

Phase I/II trial of S81694 plus paclitaxel in metastatic Breast Cancer

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 the 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 talk 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 breast cancer that had spread to other parts of the body.
The current name of the study drug is S81694. MPS1 kinase is an enzyme that controls cell multiplication. S81694 blocks the MPS1 kinase. This leads to the death of cancer cells.
The marketed drug is called paclitaxel. Paclitaxel is used to treat patients who have different types of cancer, including breast cancer.
Researchers had expected that S81694 combined with paclitaxel would work better in patients with breast cancer.
The study combined phase 1 and phase 2 studies.

The main objectives of the phase 1 were:

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

The main objective of phase 2 was to assess how the study drug combined with paclitaxel was effective.

During phase 1, first results suggested that the difference between the helpful dose and the harmful dose is probably very small. At this time, newly available anticancer drugs showed more effectiveness in breast cancer. Therefore, the sponsor decided to stop the development of S81694.
The phase 2 study was then not carried on.

2 When and where did this study take place?

When was it performed?

- This study started in January 2018.
- It ended in June 2020.

Where did the study take place?

The study took place in the following countries:

Country	Number of patients
Belgium	7
The Netherlands	3
France	8
Japan	4

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.
- Be diagnosed with any type of breast tumour that had spread to other parts of the body.
- Be patients for whom standard treatments were no longer effective or not suitable.

How many patients participated in the study?

Overall, 22 patients joined the study, all were women. All patients stopped the treatment before the end of the study, most of them because of the progression of their disease.

How old were the patients?

The average age of the patients was 52 years. The youngest patient was 37 years old and the oldest one was 67 years old.

4 Which treatments did patients receive?

All patients received the same study drug called S81694. In this study, it was combined with a marketed drug called paclitaxel.

Each patient received the study drug and paclitaxel by intravenous (into a vein) infusions during time periods called "cycles".

A cycle lasted 28 days:
The first 13 patients had one infusion of the study drug and one infusion of paclitaxel per week during the 3 first weeks of the cycle.

During the study, the researchers observed a low number of white blood cells called neutrophils in a third of patients. For this reason, they decided to cancel the second infusion of the study drug. The last 9 patients received the study drug on the first week and the third week of the cycle.

This 28-day cycle was repeated 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 phase I 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.

To find the Maximum Tolerated Dose, different increasing doses of the study drug were tested in small groups of patients (3 to 6 patients). The first group received the lowest dose, then each new group received a higher dose.
During the study, 4 different doses of the study drug were tested.

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

The maximum tolerated dose is the highest dose at which no more than a third of patients had DLT.

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 or to paclitaxel, or to the combination of the study drug and paclitaxel.

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

	Related only to S81694 Out of 22 patients	Related only to paclitaxel Out of 22 patients	Related to S81694 and paclitaxel Out of 22 patients
Patients who had side effect(s)	4 patients (18.2%)	15 patients (68.2%)	20 patients (90.9%)
Patients who had serious* side effect(s)	0 patient	0 patient	2 patients (9.1%)
Patients who stopped the treatment because of side effect(s)	0 patient	3 patients (13.6%)	3 patients (13.6%)

**See definition below*

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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.
- It may put the patient at risk and requires a medical intervention to prevent the situations listed above.

In this study, 2 patients (9.1%) had serious side effects:

- One patient had a lack of white blood cells called neutrophils twice, and a lung infection, that led to the stopping of treatment.
- Another patient had a decrease in the number of red blood cells, a high blood potassium level, a high blood uric acid level that can cause pain in the joints, called gout, and sudden kidney failure.

Those serious side effects were related to both the study drug and paclitaxel.

During the study, 7 patients died. All of them died because of the progression of the breast cancer.

What were the other side effects?

The table below shows the other side effects reported in the study. Only the most common* are presented.

	Related only to S81694 Out of 22 patients	Related only to paclitaxel Out of 22 patients	Related to S81694 and paclitaxel Out of 22 patients
Tiredness	0 patient	2 patients (9.1%)	10 patients (45.5%)
Decrease in the number of red blood cells	0 patient	1 patient (4.5%)	9 patients (40.9%)
Low number of white blood cells called neutrophils	1 patient (4.5%)	1 patient (4.5%)	9 patients (40.9%)
Diarrhoea	1 patient (4.5%)	1 patient (4.5%)	4 patients (18.2%)
Feeling sick	2 patients (9.1%)	0 patient	3 patients (13.6%)
Decreased appetite	0 patient	0 patient	3 patients (13.6%)
Hair loss	0 patient	7 patients (31.8%)	2 patients (9.1%)
Difficulty in breathing	0 patient	1 patient (4.5%)	2 patients (9.1%)
Flu-like illness	0 patient	1 patient (4.5%)	2 patients (9.1%)
Inflamed and sore mouth	0 patient	1 patient (4.5%)	2 patients (9.1%)
Generally feeling unwell	0 patient	0 patient	2 patients (9.1%)

**Side effects related to S81694 or to both S81694 and paclitaxel reported by at least 2 patients*

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7 What were the study results?

Because the study was stopped early, this is a summary of the phase 1 only.

The most frequent side effects were tiredness, decrease in the number of red blood cells and decrease in the number of white blood cells called neutrophils.

During dose escalation, 1 patient had a Dose Limiting Toxicity (severe medical event that doctors checked in order to decide if they could increase the dose or not). The patient had sudden kidney failure, decrease in the number of red blood cells, high blood potassium level, and high blood uric acid level that can cause pain in the joints, called gout.

The sponsor decided to stop the development of S81694 combined with paclitaxel. The study was discontinued, and the maximum tolerated dose was not found. The decision to discontinue the study was not due to any safety reason.

8 How has this study helped patients and researchers?

This study helped researchers in their understanding of the study drug. Unfortunately, the use of S81694 combined with paclitaxel does not seem to be effective in breast tumours that had spread to other parts of the body.

Patients included in the study had close medical follow-up with experts in cancer.

9 Are there plans for further studies?

A clinical study with the study drug in liver cancer is currently conducted by Nerviano, a partner of Servier.

10 Further information

What is the identification number of the clinical study?

- Protocol Number: CL1-81694-003
- EudraCT Number: 2017-002459-27
- ClinicalTrials.gov ID: NCT03411161

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's website (servier.com).

Where can you learn more about this study?

- The scientific summary is also available on Servier's Clinical Trial Data website. (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's 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 the Clinical Cancer Research Patients Committee of La Ligue Nationale contre le Cancer.