

# CLINICAL TRIALS

# LAY SUMMARY



## SHORT STUDY TITLE

**Study that tested the combination of 2 medicines for people with glioblastoma, a kind of brain cancer: a new drug called S49076 with a marketed drug called bevacizumab.**

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# CLINICAL TRIALS LAY SUMMARY

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## Welcome

This summary explains how the study was done. It also explains what the results are. Researchers need many studies to decide which medicines work best and are safest. It takes lot of people in many studies all around the world to advance medical science. This summary only shows the results from this one study. However, other studies may find different results.

### 1 WHAT WAS THE OBJECTIVE OF THE STUDY?

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

Both belong to targeted therapy. This is a type of treatment that uses drugs to more precisely attack cancer cells.

- S49076 is called a tyrosine kinase inhibitor. It blocks the growth of cancer cells.
- Bevacizumab is a drug that slows the growth of a tumor. It blocks the blood vessels which provide blood to the tumor.

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

The main objectives of the phase 1 were:

- To test the safety of the treatment combination.
- To find the highest tolerated dose of treatment.

In addition, this phase checked efficacy of the treatment.

The main objective of the phase 2 was to assess how the treatment was effective.

Researchers want to know if the study drug (S49076) combined with bevacizumab worked better than bevacizumab alone.

Thanks to phase 1, researchers learned that the combined treatment of bevacizumab and S49076 was not more effective than bevacizumab alone. This is why the study was stopped. The phase 2 was then not performed.

### 2 WHEN AND WHERE DID THIS STUDY TAKE PLACE?

#### When was it performed?

- This trial started in October 2014.
- It ended in November 2016.

After the end of the participation in the study, the research doctor continued to get news of patients.

#### Where the clinical trial took place?

The study included 17 patients in the following countries:

Country	Number of patients
France	14
Switzerland	3

### 3 WHO PARTICIPATED IN THE STUDY?

#### What patients were included in the study?

Patients in the clinical trial had to meet the following criteria:

- 18 years older
- Diagnosed with a brain cancer called glioblastoma
- Whose cancer came back after a first treatment

#### How many men and women were in the clinical trial?

FEMALE	MALE
5 patients (29 %)	12 patients (71 %)

#### How old were the patients?

34 to 64 years	65 to 72 years
12 patients (71 %)	5 patients (29 %)

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## 4 WHAT TREATMENTS DID PATIENTS RECEIVE?

Each patient received the 2 drugs together:

- The study drug (S49076) in oral capsules. Patients had to take them once daily during 28 days cycles.
- The bevacizumab in solution for injection into veins. It was injected on the 1<sup>st</sup> day and 15<sup>th</sup> day of each cycle.

## 5 WHAT WERE THE SIDE EFFECTS?

### What about side effects?

Like all medicines, these drugs can cause side effects although not everybody gets them.

Among 17 included patients:

- 16 patients were treated.
- 1 patient stopped the study before receiving the treatment.

The table below shows the number of patients who experienced side effects. In this study, side effects were unwanted events thought to be related to the study drug or to bevacizumab or to the study drug and bevacizumab.

	Related to study drug	Related to bevacizumab	Related to study drug and bevacizumab
Patients who had side effects	16 patients (100%)	10 patients (63%)	8 patients (50%)
Patients who had serious* side effects	1 patient (6%)	1 patient (6%)	1 patient (6%)
Patients who had withdrew because of a side effect	-	-	1 patient (6%)

\*See definition below

### How many serious side effects occurred?

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, 3 patients (19%) experienced serious side effects. The serious side effects reported were:

- Decrease in the percentage of blood leaving the heart at each contraction found in a heart test. It can be a sign of weakness of the heart muscle. It occurred in 1 patient.
- Blood clotting within veins in 1 patient.
- Inflammation of bowel wall, perforation of the gut and belly infection in one patient. This led to withdrawal of the patient.

No death occurred during the treatment period. After the treatment was stopped, and for up to 6 months after participation in the study, 7 patients died. Patients died because of the progression of the brain cancer.

### What were the other side effects?

The table below shows the other side effects found in the study. Only the most common (reported by more than 2 patients) are presented. No side effects thought to be related to both drugs were reported by more than 2 patients. This is why they are not reported in the table below.

	Related to study drug	Related to bevacizumab
Swelling of the ankles, feet or fingers	8 patients (50%)	-
Diarrhoea	4 patients (25%)	-
Dry skin	4 patients (25%)	-
Yellow skin coloration	3 patients (19%)	-
Nosebleed	-	7 patients (44%)
High blood pressure	-	3 patients (19%)

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## What was the effect on blood?

The table below shows the side effects found on blood tests.

	Related to study drug	Related to bevacizumab
Decrease of a blood protein called albumin	5 patients (31%)	-
Problem with liver blood test called AST	5 patients (31%)	-
Problem with liver blood test called ALT	5 patients (31%)	-
Decrease in number of platelets, cells that help the blood to clot	3 patients (19%)	-

## 6 WHAT WERE THE STUDY RESULTS?

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

### What are the results of the clinical trial?

- The highest dose tested for S49076 was 600 mg.
- The combination of S49076 with bevacizumab was well tolerated. The most frequent side effect was swelling of the ankles, feet or fingers.
- The first results showed that the treatment was not more effective than bevacizumab alone.

### What does it mean?

This means that the combined treatment of bevacizumab and S49076 was well tolerated. However, the combination seems not to work better than bevacizumab alone in patients with glioblastoma. This is the reason why the study was stopped prematurely.

## 7 HOW HAS THIS STUDY HELPED PATIENTS AND RESEARCHERS?

- This trial helped researchers in their search for new therapeutic options. Unfortunately, this combination does not give additional benefits for glioblastoma.
- These results are only for people with glioblastoma.

## 8 ARE THERE PLANS FOR FURTHER STUDIES?

No other studies with S49076 are foreseen in glioblastoma to date. A study with S49076 is ongoing in patients with lung cancer.

## 9 FURTHER INFORMATION

### What is the full title name of the clinical trial?

The full title of this study is "Phase I/II study of S 49076, a multi-target inhibitor of c-MET, AXL, FGFR in combination with bevacizumab in patients with recurrent glioblastoma multiform".

### What is the identification number of the clinical trial?

- Protocol Number: CL1-49076-002
- EudraCT Number: 2013-003079-37
- ISRCTN Number: ISRCTN11619481

### 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](http://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](http://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