Clinical trial SUMMARY

Short study title

Efficacy and safety trial with S44819 after recent ischemic cerebral event.

Full scientific title:

Randomized Efficacy and Safety Trial with Oral S44819 after Recent ischemic cerebral Event. International, multi-centre, randomized, double-blind placebo-controlled phase II study.
RESTORE BRAIN study

Therapeutic area:
Neurology

Indication:
Post stroke recovery

Study phase:
2

27 February 2020
Final version

In this summary:

CLINICAL TRIAL SUMMARY

Efficacy and safety trial with S44819 after recent ischemic cerebral event.

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.

If you have any questions on this study, please speak to your doctor.

1 Why was this study done?

This study was done to test a new drug called S44819 (study drug), in patients who had a recent ischemic stroke.
An ischemic stroke is a sudden lack of blood in the brain. It is caused by the blockage of a blood vessel called artery. Without blood, the brain tissue is damaged. Symptoms include dizziness, numbness, weakness on one side of the body, and problems with talking, writing, or understanding language. Stroke is also called cerebrovascular accident.

The main objective of the study was to test if S44819 works better than a placebo on recovery after a stroke. A placebo is a medicine that contains no active ingredients.
This study is called a phase 2 study.

2 When and where did this study take place?

When was it performed?

- This study started in December 2016.
- It ended in March 2019.

Where did the study take place?

The study took place in the following countries:

Country	Number of patients
Australia	40
Belgium	20
Brazil	34
Canada	9
Czech Republic	1
France	52
Germany	33
Hungary	101
Italy	16
Republic of South Korea	25
Netherlands	3
Poland	58
Spain	121
United Kingdom	72

3 Who participated in the study?

Which patients were included in the study?

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

- Be aged from 18 to 85 years
- Have a recent ischemic stroke. Recent meant between 3 and 8 days before starting the study.
- Do not have a previous disability.

How many patients participated in the study?

Overall 585 patients joined the study: 264 women and 321 men.

119 patients did not complete the study: most of them because of medical events.

How old were the patients?

The average age of the patients was 67 years. The youngest patient was 22 years old and the oldest patient was 86 years old.

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4 Which treatments did patients receive?

The study drug was called S44819. It was powder in a sachet of 150 mg. It was compared to placebo that looked identical to the S44819. Placebo does not contain the active drug.

The sachets of powder were put in a glass of water. Patients took the treatment orally in the morning and in the evening.

Patients received either:

- 150 mg of S44819 twice a day
- 300 mg of S44819 twice a day
- Placebo twice a day.

5 How was the study done?

The study is called a "randomized" study.
It means that patients were put by chance into one of the 3 groups:

- 195 patients took S44819 150 mg twice a day
- 194 patients took S44819 300 mg twice a day
- 193 patients took Placebo.

Among 585 patients enrolled, 3 stopped the study before receiving the treatment.

The study is called a "double-blinded" study. It means that neither patients nor doctors knew who was given which treatment. This enables to not influence the results in any way.
Patients took the treatment for 3 months.

All patients received also the usual medical cares for their stroke.

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 treatment in the study.

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

	Group S44819 150 mg twice a day	Group S44819 300 mg twice a day	Group placebo
Patients who had side effect(s)	22 patients (11%)	20 patients (10%)	29 patients (15%)
Patients who had serious* side effect(s)	2 patients (1%)	2 patients (1%)	11 patients (6%)
Patients who withdrew because of side effect(s)	5 patients (3%)	3 patients (2%)	11 patients (6%)

**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.

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The table below shows all the serious side effects reported by the patients treated with S44819. Patients treated with placebo reported other serious side effects which are not listed in this table.

	Group S44819 150 mg twice a day	Group S44819 300 mg twice a day	Group placebo
Feeling sick	1 patient (0.5%)	0	0
Evolution of the stroke	1 patient (0.5%)	0	0
Vomiting	1 patient (0.5%)	0	0
Disease of brain which causes repeated fits or convulsions, called epilepsy.	0	1 patient (0.5%)	0
Low blood pression	0	1 patient (0.5%)	0

Among the patients who withdrew from the study because of a side effect, 8 patients withdrew because of a serious one. The 8 patients were all in the placebo group.

During the study, no people died of side effects thought to be related to the S44819.

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 in one of the S44819 groups) are presented.

	Group S44819 150 mg twice a day	Group S44819 300 mg twice a day	Group placebo
Feeling sick	1 patient (0.5%)	4 patients (2.1%)	0
Diarrhoea	2 patients (1.0%)	2 patients (1.0%)	1 patient (0.5%)
Vomiting	1 patient (0.5%)	2 patients (1.0%)	2 patients (1.0%)
Headache	1 patient (0.5%)	2 patients (1.0%)	1 patient (0.5%)
Increase in liver blood test called GGT	0	2 patients (1.0%)	3 patients (1.6%)
Difficulty in sleeping	0	2 patients (1.0%)	1 patient (0.5%)
Increase in blood test called acid uric. It can cause pain in the joints, called gout.	2 patients (1.0%)	1 patient (0.5%)	0
Increase in waste body product in blood called urea. It occurs in kidney failure.	2 patients (1.0%)	0	0
Confusion	2 patients (1.0%)	0	0

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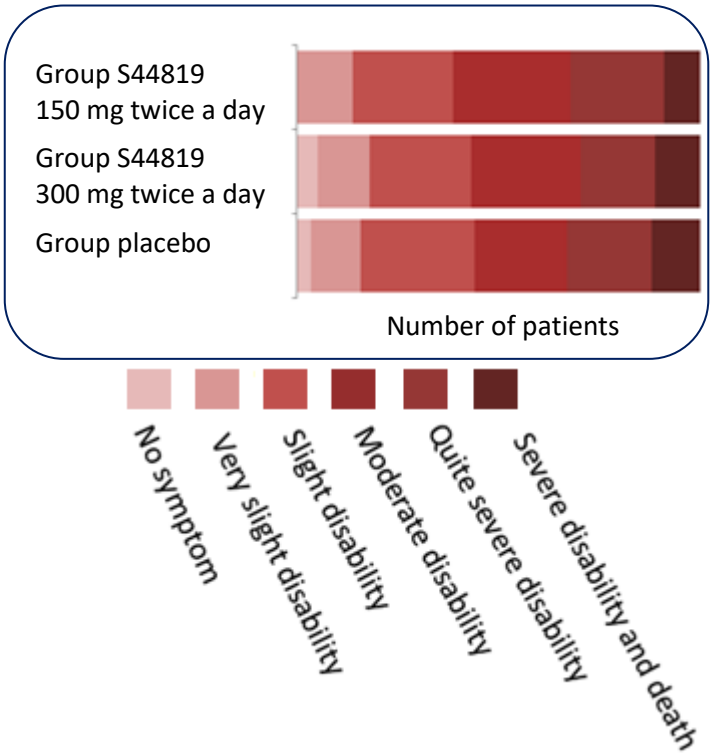
7 What were the study results?

The study was completed as planned.
To test the effectiveness, the doctors quoted the disability of the patients due to the stroke in their daily activities.
They quoted the disability after 3 months of treatment compared to the patient's activities before the stroke. For that, doctors used a scale, called modified Rankin Scale (mRS).
On this scale, the scores ranged from 0 (no disability) to 5-6 (severe disability and death).

The figure below shows the results of the study.

Distribution of patients by mRS score



The distribution of patients by score was similar in patients treated with S44819 and in patients treated with placebo. It means that recovery after a stroke was not better in patients treated with S44819 than in patients treated with placebo.

8 How has this study helped patients and researchers?

This study helped researchers to know more on ischemic stroke. Unfortunately, the study did not show that S44819 works better than placebo in recovery after a stroke.

9 Are there plans for further studies?

The sponsor has decided to stop testing S44819. No other studies with S44819 are foreseen to date.

10 Further information

What is the identification number of the clinical study?

- Protocol Number: CL2-44819-004
- EudraCT Number: 2016-001005-16

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 Servier Clinical Trial Data website.