SERVIER

Clinical Trial Summary

Study of AG-120 and AG-881 in subjects with low grade glioma

Full scientific title: A Phase 1, multicenter, randomized, controlled, open-label, perioperative study of AG-120 and AG-881 in subjects with recurrent, non-enhancing, IDH1 mutant, low-grade glioma

We thank all the participants who took part in the study. Clinical study participants are very important for making progress in science, for the benefit of 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 patients. For medical science to progress, many studies involving patients are running 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 study. If you have any questions about this study, please talk to your doctor.

Therapeutic area:
Oncology

Disease:
Glioma

Study phase:
Phase 1

Final version 1
21/04/2026

In this summary:

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1 Why was this study done?

This study was done to test two cancer drugs called ivosidenib (also called AG-120) and vorasidenib (also called AG-881) in patients with slow-growing brain tumors called low-grade glioma.

Glioma is a type of brain cancer that begins in 'glial' cells (the cells that surround and support nerve cells). It is a serious and rare disease with few effective treatment options.

In several types of cancer such as gliomas, an abnormal (mutated) form of a protein called isocitrate dehydrogenase (IDH) is present in the tumor cells due to changes called mutations. In the body, there are two types of IDH proteins: IDH1 and IDH2. When IDH1 or IDH2 is mutated, it produces too much 2-hydroxyglutarate (2-HG), which is a substance that is normally present in cells at low levels. When there is too much 2-HG, it impairs normal cell functioning and may cause the cells to become tumor cells.

Vorasidenib blocks the activity of abnormal IDH1 and IDH2 proteins. Ivosidenib blocks the activity of abnormal IDH1 protein. Vorasidenib and ivosidenib may reduce 2-HG levels in tumor cells back to normal levels.

The main objective of this study was to measure the level of 2-HG in surgically removed tumors after being treated with ivosidenib or vorasidenib compared with untreated (no treatment) tumors.

2 When and where did this study take place?

When did the study take place?

- This study started in March 2018.
- It ended in March 2025.

Where did the study take place?

The study took place in the United States.

3 Who participated in the study?

Which participants were included in the study?

To take part, participants had to:

- Be at least 18 years old.
- Have low grade glioma:
  - with a specific type of IDH1 mutation.
  - that can be removed with surgery in the next 2 to 4 months.
- Have good blood, kidney, and liver function.

Participants were not included in the study if they:

- Had already taken medicines that block the activity of IDH proteins.
- Had radiation therapy within 6 months before starting the study.

How many participants took part in the study?

A total of 49 participants took part in the study and received at least one dose of a study drug: 16 women and 33 men.

How old were the participants?

The average age of the participants was 42 years in the ivosidenib group and 48 years in the vorasidenib group. The youngest participant was 19 years old and the oldest was 75 years old.

4 Which treatments did the participants receive?

Before surgery, participants received no treatment or treatment with ivosidenib or vorasidenib for at least 28 days, including the day of surgery.

Participants took ivosidenib or vorasidenib tablets by mouth:

- Ivosidenib as 250 milligrams (mg) twice daily or 500 mg once daily.
- Vorasidenib as 10 mg or 50 mg once daily.

After surgery, all participants had the option to receive treatment with ivosidenib or vorasidenib (at the same dose or at the dose assessed by the doctor) during time periods called "cycles". Each cycle was 28 days long. The 28-day cycles were repeated for as long as the cancer did not progress and if the participant did not have too severe side effects. The participant could also decide to stop the treatment at any time.

5 How was the study carried out?

The study is called a "randomised" study. This means that the participants were put by chance into one of the three groups of treatment **prior to surgery**:

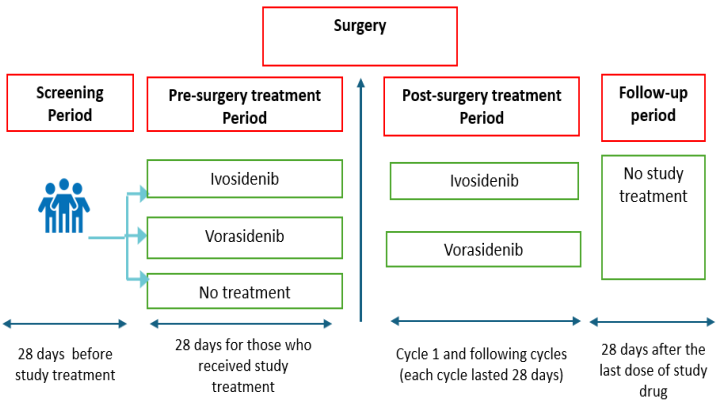
- Ivosidenib (22 participants)
- Vorasidenib (22 participants)
- No treatment (5 participants)

After surgery, 46 participants received ivosidenib or vorasidenib. Among the 46 participants who received the drug after surgery:

- 22 participants took ivosidenib (including 3 participants who were untreated prior to surgery).
- 24 participants took vorasidenib (including 2 participants who were untreated prior to surgery).

The study is called an "open-label" study. This means that both the participants and the research doctors knew which treatment was taken.

The study design is presented in the image below.



The study was conducted in 4 parts (periods): a screening period, a pre-surgery treatment period, a post-surgery treatment period, and a follow-up period.

The screening period lasted up to 28 days. During this period, the doctors checked if the volunteers who wanted to enter the study met all necessary requirements. After the screening period, participants entered the pre-surgery treatment period, which was followed by surgery. After the surgery, participants entered a post-surgery treatment period.

Once the treatment ended, participants had a follow-up period (up to 28 days after the last dose of study drug). During this period, participants were contacted to check on their health and well-being.

The participants visited the doctors regularly. During the visits, the doctors collected information about the participants' health.

6 What were the side effects?

Side effects are unwanted medical events that the doctors think may be caused by the treatments in the study.

In this summary, we describe unwanted medical events thought to be caused by ivosidenib and vorasidenib.

The results may be presented differently in other documents related to the study.

The table below shows the number of participants who had side effects.

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	Ivosidenib (out of 25 participants)	Vorasidenib (out of 24 participants)
Participants who had side effect(s)	18 (72%)	16 (67%)
Participants who had serious* side effect(s)	0	1 (4%)
Participants who stopped the treatment because of side effect(s)	0	0

**See definition of serious side effects below*

What were the types of side effects?

The table hereafter shows the most common side effects reported in the study (reported by at least 10% of participants in either treatment group).

	Ivosidenib (out of 25 participants)	Vorasidenib (out of 24 participants)
Decrease in the number of red blood cells	8 (32%)	4 (17%)
Headache	5 (20%)	2 (8%)
Cough	4 (16%)	0
Diarrhoea	4 (16%)	6 (25%)
Feeling sick	3 (12%)	3 (13%)
Vomiting	3 (12%)	0
Increase in liver enzyme called AST	3 (12%)	4 (17%)
Low blood potassium level	3 (12%)	0
Tiredness	2 (8%)	6 (25%)
Constipation	2 (8%)	3 (13%)
Increase in liver enzyme called ALT	0	7 (29%)

= *participants*

What were the serious side effects?

A side effect is considered serious when:

- the participant needs to be hospitalised,
- it causes lasting damage or death,
- the participant's life is in danger or,
- it is medically important in the doctor's opinion.

In this study, 1 participant (4%) had serious side effects (serious unwanted medical events thought to be caused by the treatments in the study). The serious side effect reported was an increase in a liver enzyme called ALT.

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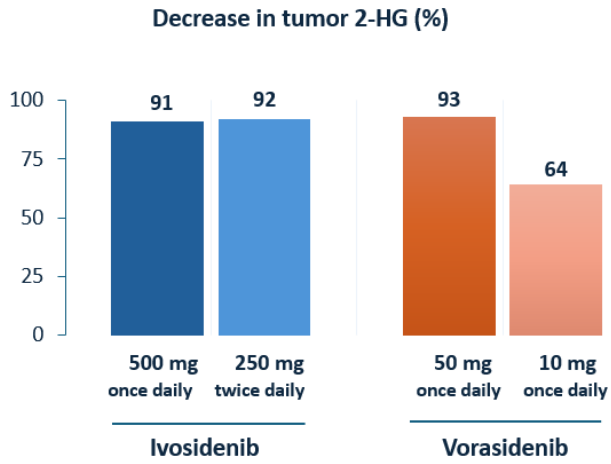
7 What were the study results?

The study was completed as planned.

This document presents only the results for the main goal of the study. Other results are available in other documents listed in section 10.

The researchers wanted to see how well ivosidenib or vorasidenib reduced the 2-HG levels in surgically removed tumors compared with untreated tumors.

To answer this question, the researchers measured the level of 2-HG in surgically removed tumors after being treated with ivosidenib or vorasidenib as well as in untreated tumors. Results are shown below.



Researchers compared the results to the group that did not receive any treatment before surgery.

Researchers found that participants taking ivosidenib (500 mg once daily or 250 mg twice daily) or the higher dose of vorasidenib (50 mg once daily) had a decrease in tumor 2-HG level by at least 90%. Participants taking the lower dose of vorasidenib (10 mg once daily) had a smaller decrease in tumor 2-HG level of about 64%.

8 How has this study helped research?

The study found that ivosidenib and vorasidenib successfully reduced the level of the harmful substance 2-HG in surgically removed tumors.

This study also helped researchers learn more about ivosidenib and vorasidenib in the treatment of cancer.

This summary shows only the main results from this one study. Other studies, evaluating the same drug, may find different results.

9 Are there plans for further studies?

No other studies are planned with ivosidenib in patients with glioma. Clinical studies with vorasidenib are on-going.

10 Further information

What are the identification numbers of the study?

- Protocol code: AG120-881-C-001
- US NCT number: NCT03343197

Who did the study?

The company that organised and funded the research, called the “sponsor”, is the Institut de Recherches Internationales Servier based in Gif-Sur-Yvette, France.

How can you contact the sponsor?

Contact us on the Servier website
https://servier.com/en/

Where can you learn more about this study?

You can find more information about this study on these websites:

- https://clinicaltrials.servier.com/find-clinical-trials
- www.clinicaltrials.gov

In this document we translated medical terms into lay terms. You can find the corresponding medical terms in the Servier glossary at https://clinicaltrials.servier.com/glossary/

You can find general information about clinical trials on https://clinicaltrials.servier.com/