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Clinical Trial Summary

Study of orally administered AG-881 in patients with advanced solid tumors, including gliomas, with an IDH1 and/or IDH2 mutation

Full scientific title: A Phase 1, Multicenter, Open-Label, Dose Escalation and Expansion, Safety, Pharmacokinetic, Pharmacodynamic, and Clinical Activity Study of Orally Administered AG-881 in Patients with Advanced Solid Tumors, Including Gliomas, with an IDH1 and/or IDH2 Mutation

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:
Solid tumors

Study phase:
Phase 1

Final version
03/06/2025

In this summary:

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1 Why was this study done?

This study was done to test a new cancer drug called vorasidenib (also called AG-881) in patients with advanced solid tumors, including glioma.

Solid tumor cancers are abnormal growths of cells in organ(s) of the body such as the lung, breast, or brain. In advanced stages of the disease, solid tumors may spread in other parts of the body.

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 of 2-hydroxyglutarate (2-HG), which is a substance that is normally present in cells in 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 IDH proteins.

The study included participants with glioma and participants with non-glioma solid tumors (solid tumors other than glioma).

The main objectives of this study were:

- To look at the safety of vorasidenib.
- To find the highest dose of vorasidenib that participants could take without too much risk (highest tolerated dose). This highest tolerated dose helps to find the recommended dose (the one that is be both safe and effective for patients).

2 When and where did this study take place?

When did the study take place?

- This study started in June 2015.
- It ended in June 2024.

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 a solid tumor:
    - with an IDH1 and/or IDH2 mutation.
    - that worsened despite treatment or came back after treatment (recurred) or did not respond to standard cancer treatments and/or medicines that block the activity of IDH proteins, or for which the doctor believed that there is no suitable treatment.
- Have been able to care for themselves and spend more than half the day out of bed or chair.
- Have good blood, kidney and liver function.
- Have not received prior anticancer medicines or radiation therapy within 21 days before starting the study.

How many participants took part in the study?

93 participants took part in the study:

- 52 participants (26 women and 26 men) with glioma.
- 41 participants (27 women and 14 men) with non-glioma solid tumors.

How old were the participants?

The average age of the participants was 42 years for the participants with glioma and 58 years for the

participants with non-glioma solid tumors. The youngest participant was 16 years old (16-year-old participant was allowed to take part in the study as an exception) and the oldest was 89 years old.

4 Which treatments did the participants receive?

The participants received vorasidenib 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.

Participants took vorasidenib tablets by mouth daily over 28-day cycles at a dose ranging from 10 milligrams (mg) to 400 mg.

5 How was the study carried out?

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

To find the highest tolerated dose, the doctors tested different doses of vorasidenib in small groups of participants.

The first group received the lowest dose, then each new group received a higher dose. After testing the highest dose, one or more lower doses may have been tested.

For each dose, the doctors checked the safety of the study drug. Then, the researchers decided whether to increase the dose in the next group of participants. Once the highest tolerated dose was found, the researchers defined the recommended dose (dose that is both safe and effective for participants).

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 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.

	Vorasidenib (out of 52 participants with glioma)
Participants who had side effect(s)	39 (75%)
Participants who had serious* side effect(s)	4 (8%)
Participants who stopped the treatment because of side effect(s)	2 (4%)

**See definition of serious side effects below*

	Vorasidenib (out of 41 participants with non-glioma solid tumors)
Participants who had side effect(s)	26 (63%)
Participants who had serious* side effect(s)	0
Participants who stopped the treatment because of side effect(s)	0

**See definition of serious side effects below*

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What were the types of side effects?

The table below shows the most common side effects reported in the study (reported by at least 5% of participants with glioma or non-glioma solid tumors).

	Vorasidenib (out of 52 participants with glioma)
Increase in liver enzyme called ALT	23 (44%)
Increase in liver enzyme called AST	21 (40%)
Tiredness	13 (25%)
Feeling sick	9 (17%)
Headache	9 (17%)
Low number of white blood cells called neutrophils	7 (14%)
Low number of white blood cells	6 (12%)
Constipation	4 (8%)
Diarrhoea	4 (8%)
Increase in liver enzyme called GGT	4 (8%)
Decrease in the number of red blood cells	3 (6%)
Vomiting	3 (6%)
High blood sugar	3 (6%)
Increase in an enzyme called lactic acid dehydrogenase	3 (6%)

= participants

	Vorasidenib (out of 41 participants with non-glioma solid tumors)
Tiredness	10 (24%)
Feeling sick	7 (17%)
Lower appetite	7 (17%)
Increase in liver enzyme called AST	6 (15%)
Vomiting	6 (15%)
Increase in liver enzyme called ALT	5 (12%)
Diarrhoea	4 (10%)

= 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, 4 participants (8%) had at least 1 serious side effect (serious unwanted medical events thought to be caused by the treatments in the study). All of these were reported in the participants with glioma.

The table below shows all the serious side effects reported in the study.

	Vorasidenib (out of 52 participants with glioma)
Increase in liver enzyme called ALT	3 (6%)
Increase in liver enzyme called AST	2 (4%)

= participants; one participant had increase in both ALT and AST and is only counted once. Therefore, number of participants is 4.

In the study, no participants died because of an unwanted event thought to be caused by vorasidenib.

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 safety results of the study drug are described in section 6 of this summary.

Participants with glioma tolerated vorasidenib doses of less than 100 mg daily. The recommended dose of vorasidenib was defined as 50 mg once daily.

The highest tolerated dose of vorasidenib in participants with non-glioma solid tumors was not reached and the recommended dose could not be determined.

8 How has this study helped research?

The study helped researchers gather more information on the safety of the vorasidenib. This study also helped researchers learn more about vorasidenib in the treatment of glioma and non-glioma solid tumors.

Results of this study were used to design other studies with vorasidenib. These results along with results from other studies with the same drug are now being used to get approvals for vorasidenib to treat patients with glioma that has an IDH mutation.

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?

Clinical studies with vorasidenib in participants with glioma are ongoing and further studies are planned

10 Further information

What are the identification numbers of the study?

- Protocol code: AG881-C-002
- US NCT number: NCT02481154

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/