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Clinical Trial Summary

Study of orally administered AG-120 in subjects with advanced solid tumors, including glioma, with an IDH1 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-120 in Subjects with Advanced Solid Tumors, Including Glioma, with an IDH1 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 single 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
18/11/2024

In this summary:

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1 Why was this study done?

The study was done to test a cancer drug called ivosidenib (also called AG-120 or TIBSOVO) in participants with advanced solid tumors, including chondrosarcoma, cholangiocarcinoma and 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. Chondrosarcoma is a rare type of cancer that starts in the bones. Cholangiocarcinoma is a cancer of the bile ducts. Bile ducts are tiny tubes carrying bile (a fluid produced in the liver that helps to break down fats during digestion) from liver to the intestine.

In several types of cancer such as gliomas, chondrosarcoma and cholangiocarcinoma, an abnormal form of a protein called Isocitrate dehydrogenase 1 (IDH1) is present in the tumor cells due to changes called mutations. When IDH1 is present in mutated form, it produces an excess amount of 2-hydroxyglutarate (2-HG), which is a substance that is normally present in cells in low levels. When 2-HG is present in excessive amounts, it impairs normal cell functioning and may cause them to become tumor cells.

Ivosidenib is a drug that blocks the activity of abnormal IDH1 proteins and may reduce 2-HG levels in tumor cells back to normal levels. Ivosidenib has already been approved in many countries to treat people who have cholangiocarcinoma and acute myeloid leukaemia, a type of cancer in the blood and bone marrow (the spongy tissue inside bones where blood cells are made).

The main objectives of the study were:

- To look at the safety of ivosidenib.
- To find the highest dose of ivosidenib 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 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 March 2014.
- It ended in January 2024.

Where did the study take place?

The study took place in the following countries:

Country	Number of participants
United States	159
France	15

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 advanced solid tumor:
  - With an IDH1 mutation.
  - That worsened despite treatment or came back after treatment (recurred) or did not respond to standard cancer treatments.

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How many participants took part in the study?

A total of 174 participants took part in the study. Among them, 6 participants stopped the study before receiving ivosidenib. In all, 168 participants took part in the study and received ivosidenib: 88 women and 80 men.

How old were the participants?

The average age of the participants was 52 years. The youngest participant was 21 years old and the oldest was 88 years old.

4 Which treatments did the participants receive?

The participants received ivosidenib (the test drug) during time periods called "cycles". Each cycle was of 28 days. 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.

Ivosidenib was taken as tablets by mouth.

The table below shows how the participants took the ivosidenib.

	Ivosidenib once a day (164 participants)	Ivosidenib twice a day (4 participants)
Dose	• from 300 mg to 1200 mg • Once a day	• 100 mg • Twice a day

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.

The participants started with a first period called a screening period that could last up to 28 days. This period allowed doctors to check if the participant fulfilled all the criteria to take part in the study.

Then, the study was carried out in 2 parts. Part 1, the dose escalation part was done so the researchers could find the highest tolerated dose and/or the recommended dose to give to the participants in Part 2, the dose expansion part. In Part 2, participants had to take the recommended dose of ivosidenib defined by the results from Part 1, to further evaluate the safety of ivosidenib.

To find the highest tolerated dose, the doctors tested different doses of ivosidenib in small groups of participants. The first group received the lowest dose, then each new group received a higher dose.

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 average duration of treatment was about 15 months for 168 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 ivosidenib.

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 168 participants)
Participants who had side effect(s)	109 (65%)
Participants who had serious* side effect(s)	3 (2%)
Participants who stopped the treatment because of side effect(s)	0

**See definition of serious side effects below*

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).

	Ivosidenib (out of 168 participants)
Tiredness	33 (20%)
Feeling sick	30 (18%)
Diarrhoea	25 (15%)
Vomiting	15 (9%)
Decrease in the number of red blood cells	11 (6%)
Abnormal electrical activity of the heart that affects its rhythm (QT prolonged)	11 (6%)
Lower appetite	11 (6%)
Increase in liver enzyme called AST	9 (5%)

= *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, 3 (2%) participants had serious side effects.

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

	Ivosidenib (out of 168 participants)
Decrease in the number of red blood cells	1 (below 1%)
Extra heart beats, which interrupt the normal regular rhythm of the heart (supraventricular extrasystoles)	1 (below 1%)
Inflammation of the large bowel	1 (below 1%)

= *participants*

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

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.

The highest tolerated dose of ivosidenib was not reached at doses up to 1200 mg once daily.

The recommended dose of ivosidenib was defined as 500 mg once daily. This dose was defined based on the overall results observed from part 1 of this study and from AG120-C-001 study in participants with blood cancers.

8 How has this study helped research?

The study helped researchers gather more information on the safety of the ivosidenib. This study also helped researchers learn more about ivosidenib in the treatment of cancer.

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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 ivosidenib are on-going and further studies are planned.

10 Further information

What are the identification numbers of the study?

- Protocol code: AG120-C-002
- NCT number: NCT02073994

Who did the study?

The company that organised and funded the research, called the "sponsor", is the Institut de Recherches Internationales Servier based in Suresnes, 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
- https://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/