SERVIER

Clinical Trial Summary

Study of orally administered AG-120 in subjects with advanced solid tumors, including glioma, with an IDH1 mutation

Results for participants with conventional chondrosarcoma

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 and healthy volunteers are running all around the world. **This summary shows the results of the AG120-C-002 study in participants with conventional chondrosarcoma**. The clinical trial summary presenting the results **in all participants with advanced solid tumors** is available on the Servier clinical trials website (for more, see details in section 10 at the end of the document). 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
21/03/2025

In this summary:

Clinical Trial Summary

Study of orally administered AG-120 in subjects with advanced solid tumors, including glioma, with an IDH1 mutation

Results for participants with conventional chondrosarcoma

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 to other parts of the body.

Chondrosarcoma is a rare type of cancer that starts in the cartilage, which is the tough, flexible tissue that cushions bones at the joints. The most common form, called conventional chondrosarcoma, makes up 90% of chondrosarcoma cases. The primary treatment for conventional chondrosarcoma is surgery to remove the tumor. Currently, there are no approved medications for this type of cancer. Glioma is a type of brain cancer and cholangiocarcinoma is a cancer of the bile ducts. Bile ducts are tiny tubes carrying bile from liver to the intestine.

In several types of cancer such as chondrosarcoma, gliomas and cholangiocarcinoma, an abnormal form of a protein called isocitrate dehydrogenase 1 (IDH1) is present in the tumor cells due to genetic changes called mutations. About half of the people with conventional chondrosarcoma have IDH1 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 abnormal tumor cells.

Ivosidenib is a drug that blocks the activity of abnormal IDH1 proteins and reduces 2-HG levels in tumor cells back to normal levels. Ivosidenib has already been approved in many countries to treat people with cholangiocarcinoma and acute myeloid leukaemia, a type of blood cancer.

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) to be used for Part 2.

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 United States of America and in France. Participants with conventional chondrosarcoma were all from the United States of America.

Country	Number of participants in the study	Number of participants with conventional chondrosarcoma
United states of America	159	13
France	15	0

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.

How many participants took part in the study?

A total of 174 participants took part in the study and 168 received treatment with ivosidenib.
Among these 168 participants, 13 had conventional chondrosarcoma (9 men and 4 women).

How old were the participants?

The average age of the participants with conventional chondrosarcoma was 55 years. The youngest participant was 38 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 participants with conventional chondrosarcoma took the ivosidenib.

	Ivosidenib once a day (12 participants with conventional chondrosarcoma)	Ivosidenib twice a day (1 participant with conventional chondrosarcoma)
Doses	• 400 mg, 500 mg, 800 mg and 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 were informed of the treatment taken.

The participants started with a first period called 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 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 treatment in the study.

Clinical Trial Summary

Study of orally administered AG-120 in subjects with advanced solid tumors, including glioma, with an IDH1 mutation

Results for participants with conventional chondrosarcoma

In this summary, we describe unwanted medical events which in the doctor's opinion, are believed to be caused by ivosidenib.

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

	Ivosidenib (out of 13 participants with conventional chondrosarcoma)
Participants who had side effect(s)	9 (69%)
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*

What were the types of side effects?

The table hereafter shows the most common side effects reported in participants with conventional chondrosarcoma (reported by at least 2 participants with conventional chondrosarcoma).

	Ivosidenib (out of 13 participants with conventional chondrosarcoma)
Feeling sick	5 (38%)
Diarrhoea	4 (31%)
Abnormal electrical activity of the heart that affects its rhythm (QT prolonged)	4 (31%)
Tiredness	2 (15%)
Red raised skin rash	2 (15%)
Low blood levels of phosphates	2 (15%)

= *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.

There were no serious side effects reported in participants with conventional chondrosarcoma during the study.

7 What were the study results?

The study was completed as planned.

This document presents the results for the main objectives of the study in participants with conventional chondrosarcoma (see more details on the main study objectives at the end of section 1). One of the secondary objectives, called the best response to treatment, is also presented in this summary.

Safety of ivosidenib

The safety results of the study drug in participants with conventional chondrosarcoma are described in section 6 of this summary.

Highest tolerated dose and recommended dose

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.

Clinical Trial Summary

Study of orally administered AG-120 in subjects with advanced solid tumors, including glioma, with an IDH1 mutation

Results for participants with conventional chondrosarcoma

Response to treatment

The study doctors wanted to see how well the treatment worked for each participant with conventional chondrosarcoma.

For the 13 participants, the best response to treatment observed during the study was as follows:

- 1 participant (8%) had a complete disappearance of the tumor,
- 2 participants (15%) had a partial reduction of the tumor (the tumor got smaller, but it did not completely disappear),
- 7 participants (54%) had stable disease (the size of the tumor stayed about the same),
- 2 participants (15%) had their disease get worse.
- 1 participant (8%) had no response assessment (due to stopping the study before the first scheduled imaging assessment).

The average duration of treatment was about 33 months for 13 participants with conventional chondrosarcoma.

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 the use of ivosidenib to treat cancer.

This summary shows only the results from this one study in a small number of participants with conventional chondrosarcoma. The clinical trial summary presenting the results in all participants with advanced solid tumors is available on the Servier clinical trials website. Other studies, evaluating the same drug, may find different results.

9 Are there plans for further studies?

A study involving a larger number of participants called CHONQUER (phase 3 study, CL3-95031-007) is currently ongoing at the time of writing this summary. This new study aims to see how well ivosidenib works in participants having advanced conventional chondrosarcoma with an IDH1 mutation.

Further studies with ivosidenib are also 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/