Clinical Study Results

Research Sponsor: Eisai Inc.
Drug Studied: Lenvatinib
Short Study Title: A study of lenvatinib in participants with advanced or unresectable liver cancer

Thank you!

You took part in this clinical study for the study drug lenvatinib. All of the participants helped researchers learn more about lenvatinib and how it may help people with advanced or unresectable liver cancer. Liver cancer refers to the uncontrolled growth of abnormal cells in the liver. Advanced cancer is a cancer that has spread to other parts of the body. Unresectable cancer is a cancer that cannot be removed by surgery.

Eisai, a Japanese pharmaceutical company and the sponsor of this study, thanks you for your help. Eisai is committed to improving health through continuing research in areas of unmet need and sharing the results of the study with you.

Eisai prepared this summary with a medical and regulatory writing organization called Certara Synchrogenix.

If you participated in the study and have questions about the results, please speak with the doctor or staff at your study site.

What has happened since the study started?

The study started in April 2021 and ended in December 2023.

The study included 316 participants from 44 study sites in the following countries:

Australia	Austria	Germany	Italy
Portugal	Russia	Spain	Sweden
United Kingdom	United States		

The sponsor of the study reviewed the data collected and created a report of the primary results. This is a summary of that report.

Why was the research needed?

The researchers in this study wanted to find out the effect of lenvatinib on the liver in participants with liver cancer. They did this by looking at all medical problems that participants may have had during the study.

The main questions the researchers wanted to answer in this study were:

- What was the effect of lenvatinib on the liver?
- What medical problems did participants who took lenvatinib have?

It is important to know that this study was designed to get accurate answers to the questions listed above. There were other questions the researchers wanted to answer to learn more about how lenvatinib works. However, these were not the main questions the study was designed to answer.

What kind of study was this?

To answer the main questions, researchers asked for the help of participants with advanced or unresectable liver cancer. Of these participants, 80% were men, and 20% were women. The youngest was 28 years old, and the oldest was 88 years old.

This was a "Phase 4" study. This means that the study treatment has been approved and is available for use by the public.

In this study, researchers and study doctors followed participants with liver cancer who were taking lenvatinib or sorafenib. All treatment decisions, including dose and duration, were made by participants' doctors based on the approved product information.

This study was also "open-label." This means that the participants, the study doctors and staff, and the sponsor knew which treatment participants were taking.

The figure below shows how the treatment was given in your study.

What happened during the study?

Before the study started, the study doctors did a full check-up to make sure each participant could join the study.

The study doctors or staff also:

- Confirmed that participants had liver cancer and were taking lenvatinib or sorafenib
- Took blood and urine samples for analyses

During the treatment period, the participants continued to take lenvatinib or sorafenib.

Throughout the study, the study doctors or staff:

- Took blood and urine samples for analyses
- Asked about medicines participants were taking and medical problems participants had experienced

After their last dose, all participants returned to the study site.

The participants:

- Had their blood and urine samples taken
- Were asked about medicines participants were taking and medical problems participants had experienced

The figure below shows how the study was done.

How did this study work?

Before the study started

The study doctors or staff:

- Did a full check-up to make sure each participant could join the study
- Confirmed participants had liver cancer and were taking lenvatinib or sorafenib
- Took blood and urine samples

During treatment period

All 316 participants continued to take lenvatinib or sorafenib.

The study doctors or staff:

- Took blood and urine samples
- Asked about medical problems participants had and medicines participants were taking

After treatment period

All participants returned to study sites after taking their last dose of study treatment.

The study doctors or staff took blood and urine samples and asked participants about medical problems participants had and medicines participants were taking.

What were the results of the study?

This is a summary of the main results of this study. The results each person had individually may be different and are not in this summary. But the results each person had are part of the summary of results. A full list of the questions researchers wanted to answer can be found on the websites listed at the end of this summary. If a full report of the study results is available, it can also be found on these websites.

Researchers look at the results of many studies to decide which treatment options may work best and are well tolerated. Other studies may provide new information or different results. Always talk to a doctor before making any treatment decisions.

What was the effect of lenvatinib on the liver?

To answer this question, researchers looked at all medical problems that happened during the study, including medical problems related to the liver.

Overall, participants tolerated treatment with lenvatinib. Generally, medical problems in the study, including those related to the liver, were effectively managed.

More information on the safety of lenvatinib is shown below.

What medical problems did participants have?

Medical problems that happen in clinical studies are called “adverse events.” An adverse event may or may not be caused by the study drug. An adverse event is called “serious” when it is life-threatening or fatal, causes lasting problems, or the participant needs to be admitted to a hospital.

This section is a summary of the adverse events that happened during this study. The websites listed at the end of this summary may have more information about the medical problems that happened in this study. A lot of research is needed to know whether a drug causes a medical problem.

Results in this section were from participants who received at least 1 dose of any study treatment.

How many participants had adverse events?

The table below shows how many participants had adverse events in this study.

Adverse Events in This Study

	Lenvatinib Out of 193 participants	Sorafenib Out of 123 participants
How many participants had adverse events?	164 (85%)	104 (85%)
How many participants had adverse events related to the liver?	52 (27%)	41 (33%)
How many participants had serious adverse events?	74 (38%)	42 (34%)
How many participants died because of adverse events	22 (11%)	6 (5%)
How many participants stopped taking lenvatinib or sorafenib because of adverse events?	57 (30%)	25 (20%)

What were the most common adverse events?

The most common adverse events in this study were the following:

- Decreased appetite
- Diarrhea
- Tiredness

The table below shows the adverse events in 10% of participants or more in either group. There were other adverse events, but these happened in fewer participants.

Most Common Adverse Events in the Study

	Lenvatinib Out of 193 participants	Sorafenib Out of 123 participants
Decreased appetite	55 (29%)	32 (26%)
Diarrhea	50 (26%)	39 (32%)
Tiredness	47 (24%)	26 (21%)
Underactive thyroid gland	30 (16%)	5 (4%)
Feeling sick	29 (15%)	16 (13%)
Decreased weight	28 (15%)	12 (10%)
Weakness	24 (12%)	26 (21%)
Changes in the sound or tone of the voice	23 (12%)	6 (5%)
High blood pressure	23 (12%)	7 (6%)
Abdominal pain	21 (11%)	9 (7%)
A build-up of fluid in the abdomen	13 (7%)	14 (11%)
Hand foot syndrome[a]	6 (3%)	14 (11%)

[a] Rash and numbness on the palms and soles.

What were the most common adverse events related to the liver?

The most common adverse events related to the liver in this study were the following:

- Brain damage caused by liver problems
- A build-up of fluid in the abdomen
- Increased level of bilirubin (a breakdown product of red blood cells)

The table below shows the adverse events in 5% of participants or more in either group. There were other adverse events, but these happened in fewer participants.

Most Common Adverse Events Related to the Liver in the Study

	Lenvatinib Out of 193 participants	Sorafenib Out of 123 participants
Brain damage caused by liver problems	15 (8%)	10 (8%)
A build-up of fluid in the abdomen	13 (7%)	14 (11%)
Increased level of bilirubin	10 (5%)	8 (7%)
Increased level of AST[a]	5 (3%)	11 (9%)
Increased level of ALT[a]	4 (2%)	8 (7%)
Increased level of GGT[a]	4 (2%)	8 (7%)
Increased level of ALP[a]	3 (2%)	9 (7%)

Abbreviations: ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; GGT = gamma-glutamyl transferase.

[a] ALP, ALT, AST, and GGT are enzymes in the liver that doctors use to check the liver's health. An increase in levels of these enzymes could mean there is a problem with liver function.

What were the most common serious adverse events?

The most common serious adverse events in this study were the following:

- Brain damage caused by liver problems
- Short-term kidney problem
- Heart and lungs stopped working
- Overall health getting worse

The table below shows the adverse events in 2% of participants or more in the lenvatinib group. There were other adverse events, but these happened in fewer participants in either group.

Most Common Serious Adverse Events in the Study

	Lenvatinib Out of 193 participants	Sorafenib Out of 123 participants
Brain damage caused by liver problems	13 (7%)	6 (5%)
Short-term kidney problem	9 (5%)	1 (1%)
Heart and lungs stopped working	5 (3%)	0 (0%)
Overall health getting worse	5 (3%)	1 (1%)
Abdominal pain	4 (2%)	1 (1%)
Diarrhea	4 (2%)	2 (2%)
Infection of the lungs	4 (2%)	0 (0%)
COVID-19	3 (2%)	0 (0%)
Infection of the parts of the body that collect and pass out urine	3 (2%)	1 (1%)

Abbreviations: COVID-19 = coronavirus disease 2019.

How many participants had adverse reactions?

Adverse reactions are adverse events that the study doctors thought were caused by the study drugs.

The table below shows how many participants had adverse reactions in this study.

Adverse Reactions in This Study

	Lenvatinib Out of 193 participants	Sorafenib Out of 123 participants
How many participants had adverse reactions?	134 (69%)	86 (70%)
How many participants had adverse reactions related to the liver?	32 (17%)	23 (19%)
How many participants had serious adverse reactions?	35 (18%)	15 (12%)
How many participants died because of adverse reactions	3 (2%)	0 (0%)

The table below shows the adverse reactions in 10% of participants or more in either group. There were other adverse reactions, but these happened in fewer participants.

Most Common Adverse Reactions in the Study

	Lenvatinib Out of 193 participants	Sorafenib Out of 123 participants
Diarrhea	45 (23%)	30 (24%)
Decreased appetite	40 (21%)	21 (17%)
Tiredness	36 (19%)	23 (19%)
Underactive thyroid gland	25 (13%)	2 (2%)
Feeling sick	23 (12%)	12 (10%)
Changes in the sound or tone of the voice	21 (11%)	3 (2%)
Decreased weight	21 (11%)	8 (7%)
Weakness	13 (7%)	14 (11%)

How has this study helped participants and researchers?

In this study, researchers learned more about how lenvatinib may have helped people with liver cancer. Researchers look at the results of many studies to decide which treatment options may work best and are well tolerated. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Further clinical studies with lenvatinib are planned.

Where can I learn more about the study?

You can find more information about this study on the website listed below. If a full report of the study results is available, it can also be found here:

- https://www.clinicaltrials.gov - Once you are on the website, type **NCT04763408** into the search box and click "**Search**."

Full study title: A Multicentre, Observational, Phase 4 Study to Evaluate the Safety and Tolerability of Lenvatinib in Patients with Advanced or Unresectable Hepatocellular Carcinoma (STELLAR)

Protocol number: E7080-M000-508

Eisai, the sponsor of this study, has headquarters in Tokyo, Japan, and regional headquarters in Nutley, New Jersey, USA and Hatfield, Hertfordshire, UK. The phone number for general information is 44-845-676-1400 (UK) and 1-888-274-2378 (USA).

Thank you

Eisai would like to thank you for your time and interest in participating in this clinical study. Your participation has provided a valuable contribution to research and improvement in health care.

Eisai Co., Ltd. is a global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "giving first thought to patients and the people in the daily living domain and to increasing the benefits health care provides," which we call our human health care (hhc) philosophy. With over 10,000 employees working across our global network of R&D facilities, manufacturing sites, and marketing subsidiaries, we strive to realize our hhc philosophy by delivering innovative products in multiple therapeutic areas with high unmet medical needs, including Oncology and Neurology. For more information, please visit https://www.eisai.com.

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