Clinical Trial Results

Research Sponsor: Eisai Ltd.
Drug Studied: Lenvatinib, also called E7080
Short Trial Title: A trial to learn how safe lenvatinib was in people with advanced thyroid cancer

Thank you!

You took part in this clinical trial for the trial drug lenvatinib, also called E7080. You and all of the participants helped researchers learn more about lenvatinib to help people with a type of cancer known as advanced thyroid cancer. Advanced thyroid cancer starts in the thyroid gland and gets worse, or spreads to other parts of the body.

Eisai Co., Ltd, a Japanese pharmaceutical company and the sponsor of this trial, thanks you for your help. Eisai is committed to improving health through continuing research in areas of unmet need and sharing with you the results of the trial you participated in. Eisai prepared this summary with a medical and regulatory writing organization called Synchrogenix.

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

What has happened since the trial started?

The trial started in September 2012.

The sponsor of the trial reviewed the data collected up to June 2014 and created a report of the results. This is a summary of that report.

The trial included 43 participants from 3 sites in Japan.

Why was the research needed?

Researchers were looking for a different way to treat people who have advanced thyroid cancer. The standard treatment for this type of cancer is surgery. Certain types of thyroid cancer can also be treated with radioactive iodine, thyroid hormone therapy, radiation, or other treatments that help stop tumor growth. But these treatments may not help all people with later stages of the disease.

The researchers in this trial wanted to find out how safe lenvatinib is to use in a small number of people with different types of advanced thyroid cancer who could not be treated with surgery. Lenvatinib is made to block the growth of new blood vessels that cancer cells need in order to grow and spread.

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

- What adverse events did participants taking lenvatinib have?

  An adverse event is a medical problem that may or may not be caused by the trial drug.

- What was the progression-free survival for participants in this trial?

  Progression-free survival, also called PFS, is the length of time participants had without their cancer getting worse after taking lenvatinib.

- What was the overall survival for participants in this trial?

  Overall survival, also called OS, is the length of time that half of the participants stayed alive after taking lenvatinib.

- What was the objective response rate for participants in this trial?

  Objective response rate, also called ORR, is the number of participants who had their tumors completely disappear or get smaller after taking lenvatinib.

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

What kind of trial was this?

To answer these questions, researchers asked for the help of men and women like you. The people in the trial were 21 to 79 years old. 42% of the people were male, and 58% of the people were female.

All of the people in this trial had thyroid cancer that:

- Was advanced or had spread to other parts of the body
- Could not be cured with surgery or radiation
- Had gotten worse in the 12 months before joining the trial in people with differentiated thyroid cancer and medullary thyroid cancer described below

All of the people in this trial had 1 of 3 types of advanced thyroid cancer:

- Differentiated thyroid cancer, also known as DTC. This type of thyroid cancer usually grows in cells of the thyroid gland called follicular cells. DTC is the most common type of thyroid cancer, and happens in at least 90% of people with thyroid cancer.
- Medullary thyroid cancer, also known as MTC. This type of thyroid cancer grows from cells of the thyroid gland called C cells. MTC is less common than DTC, and happens in about 5% of people with thyroid cancer.
- Anaplastic thyroid cancer, also known as ATC. This type may grow from other types of thyroid cancer, such as DTC. ATC is a very rare form of thyroid cancer, and tends to spread quickly to other parts of the body. ATC happens in less than 5% of people with thyroid cancer.

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

You took lenvatinib by mouth. The figure below shows how treatment was given in your trial.

What happened during the trial?

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

The doctors also:

- Asked what medications each participant was taking
- Took blood and urine samples
- Scanned each participant's tumors to see how advanced their cancer was
- Checked each participant's heart health using an electrocardiogram, also called an ECG

During the trial, the participants took lenvatinib for a total dose of 24 milligrams (also known as mg) every day for each treatment cycle. A treatment cycle was 28 days long.

Throughout the trial, the doctors:

- Continued to check the participants' health, asked what medications they were taking, and took blood and urine samples
- Checked participants' heart health
- Asked the participants every 1 to 2 weeks how they were feeling and if they had any adverse events
- Scanned the tumors of participants with DTC and MTC every 8 weeks to see if their cancer was improving or getting worse
- Scanned the tumors of participants with ATC every 4 weeks for the first 16 weeks, and then every 8 weeks after that to see if their cancer was improving or getting worse

The doctors also checked each participant's heart health again after their second cycle of treatment.

Each participant could continue taking lenvatinib until:

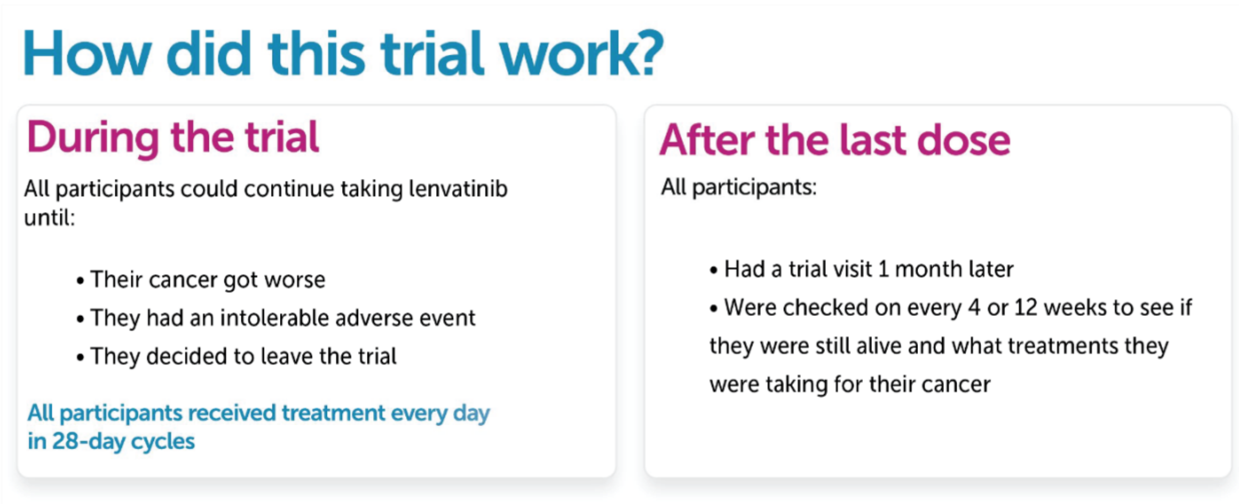
- Their cancer got worse
- They had an intolerable adverse event
- They decided to leave the trial

Their cancer was considered worse if their existing tumors got bigger or new tumors grew.

After their last dose, all participants:

- Had a trial visit 1 month later
- Who had DTC or MTC were checked on by the doctors every 12 weeks
- Who had ATC were checked on by the doctors every 4 weeks

The figure below shows how the trial was done.



What were the results of the trial?

This is a summary of the main results of this trial up to June 2014. The results each person had might 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 website listed at the end of this summary. If a full report of the trial results is available, it can also be found on this website.

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

What was the progression-free survival for participants in this trial?

The PFS is measured as a median. The median is the length of time that passed from the start of the trial to when half of the participants did not have their cancer get worse. When the median PFS was looked at in this trial, most of the participants did not have their cancer get worse. That means that the median PFS could not be determined at that time.

What was the overall survival for participants in this trial?

When the OS was looked at in this trial, most of the participants were still alive. That means that the OS could not be determined at that time.

What was the objective response rate for participants in this trial?

The ORR was 47.6%. That means that 20 participants either had their tumors completely disappear or get smaller after taking lenvatinib.

What medical problems did participants have?

Medical problems that happen in clinical trials are called “adverse events”. An adverse event is called “serious” when it is life-threatening, 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 trial. These medical problems may or may not be caused by the trial drug. The website listed at the end of this summary may have more information about the medical problems that happened in this trial. A lot of research is needed to know whether a drug causes a medical problem.

How many participants had adverse events?

In this trial, all 43 participants (100.0%) had adverse events. The table below shows how many participants had adverse events in this trial.

Adverse Events in This Trial

	Out of 43 participants who took lenvatinib
How many participants had adverse events?	100.0% (43)
How many participants had serious adverse events?	44.2% (19)
How many participants stopped taking lenvatinib because of adverse events?	0.0% (0)

What were the most common serious adverse events?

In this trial, 19 out of 43 participants (44.2%) had serious adverse events.

The table below shows the serious adverse events that happened in 2 or more of participants. There were other serious adverse events, but these happened in fewer participants.

Most Common Serious Adverse Events in This Trial

	Out of 43 participants who took lenvatinib
Loss of appetite	11.6% (5)
Infection in lungs	4.7% (2)
Nausea	4.7% (2)
Worsening of cancer	4.7% (2)

In this trial, 2 participants died. One participant died from liver failure, and one participant died due to their cancer getting worse. The trial doctors did not believe that either of these events were related to the trial drug.

What were the most common adverse events?

In this trial, all 43 participants (100.0%) had adverse events.

The most common adverse events were high blood pressure, loss of appetite, and redness, swelling, and pain on the palms of the hands and/or the soles of the feet.

The table below shows the adverse events that happened in 20% or more of participants. There were other adverse events, but these happened in fewer participants.

Most Common Adverse Events in This Trial

	Out of 43 participants who took lenvatinib
High blood pressure	86.0% (37)
Loss of appetite	83.7% (36)
Redness, swelling, and pain on the palms of the hands and/or the soles of the feet	81.4% (35)
Feeling tired	76.7% (33)
Protein in the urine	58.1%% (25)
Inflamed and sore mouth	55.8% (24)
Diarrhea	51.2% (22)
Nausea	44.2% (19)
Hoarse voice	41.9% (18)
Joint pain	39.5% (17)
Common Cold	23.3% (10)
Low numbers of platelets, which are blood cells that help with clotting	23.3% (10)
Pain in abdomen	23.3% (10)
Rash	23.3% (10)
Vomiting	23.3% (10)
Hair loss	20.9% (9)
Headache	20.9% (9)
Nosebleed	20.9% (9)
Weight loss	20.9% (9)

How many participants had adverse reactions?

Adverse reactions are medical problems that the trial doctors thought were caused by the trial drug. An adverse reaction is called “serious” when it is life-threatening, causes lasting problems, or the participant needs to be admitted to a hospital. This section is a summary of the adverse reactions that happened during this trial.

In this trial, all 43 participants (100.0%) had adverse reactions.

The table below shows how many participants had adverse reactions.

Adverse Reactions in This Trial

	Out of 43 participants who took lenvatinib
How many participants had adverse reactions?	100.0% (43)
How many participants had serious adverse reactions?	37.2% (16)
How many participants stopped receiving the trial drug because of adverse reactions?	0.0% (0)

What were the most common serious adverse reactions?

In this trial, 16 out of 43 participants (37.2%) had a serious adverse reaction.

The table below shows the serious adverse reactions that happened in 2 or more of participants. There were other serious adverse reactions, but these happened in fewer participants.

Most Common Serious Adverse Reactions in This Trial

	Out of 43 participants who took lenvatinib
Loss of appetite	9.3% (4)
Infection in lungs	4.7% (2)
Nausea	4.7% (2)

In this trial, no participants died due to a serious adverse reaction.

What were the most common adverse reactions?

In this trial, all 43 participants (100.0%) had an adverse reaction. The most common adverse reactions were high blood pressure, redness, swelling, and pain on the palms of the hands and/or soles of the feet, and loss of appetite.

The table below shows the adverse reactions that happened in 20% or more of participants. There were other adverse reactions, but these happened in fewer participants.

Most Common Adverse Reactions in This Trial

	Out of 43 participants who took lenvatinib
High blood pressure	86.0% (37)
Redness, swelling, and pain on the palms of the hands and/or the soles of the feet	79.1% (34)
Loss of appetite	76.7% (33)
Feeling tired	72.1% (31)
Inflamed and sore mouth	55.8% (24)
Protein in the urine	58.1% (25)
Diarrhea	51.2% (22)
Nausea	39.5% (17)
Hoarse voice	39.5% (17)
Joint pain	34.9% (15)
Low numbers of platelets, which are blood cells that help with clotting	23.3% (10)
Hair loss	20.9% (9)
Nosebleed	20.9% (9)
Vomiting	20.9% (9)

How has this trial helped patients and researchers?

In this trial, researchers learned more about how lenvatinib may have helped people with certain types of advanced thyroid cancer.

Researchers look at the results of many trials to decide which treatment options may work best and are well tolerated. This summary shows only the main results from this one trial. Other trials may provide new information or different results.

Further clinical trials with lenvatinib are planned.

Where can I learn more about the trial?

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

- http://www.clinicaltrials.gov - Once you are on the website, type **NCT01728623** into the search box and click "**Search**".

Full trial title: A Phase 2 Study of E7080 in Subjects With Advanced Thyroid Cancer

Protocol number: E7080-J081-208

Eisai, the sponsor of this trial, has headquarters in Tokyo, Japan, and regional headquarters in Woodcliff Lake, New Jersey, USA and Hatfield, Hertfordshire, UK. The phone number for general information is 44-845-676-1400.

Thank you

Eisai would like to thank you for your time and interest in participating in this clinical trial. 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 their families 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 http://www.eisai.com.

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