

Clinical Trial Results



Research Sponsor: Eisai

Drug Studied: Lenvatinib or E7080

National Clinical Trial #: NCT00784303

EudraCT #: 2007-005933-12

Protocol #: E7080-G000-201

Trial Period: November 2008 to April 2011

Short Trial Title: A trial to see if lenvatinib helps reduce tumors in people with thyroid cancer and to see how lenvatinib works in the body

Thank you!

As a clinical trial participant, you belong to a large community of participants around the world who help researchers answer important health questions and discover new medical treatments.

Eisai, 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 an independent non-profit organization called CISCRP and a medical and regulatory writing organization called Synchrogenix.

If you have questions about the results, please speak with the doctor, research nurse, or other team member at your trial site.

What has happened since my trial ended?

You were in this trial for up to 10 months, but the trial took about two and a half years to complete. When the trial ended in April 2011, the research sponsor reviewed the data and created a report of the results. This is a summary of that report.

Your trial included 117 participants from 30 sites in Australia, France, Italy, Poland, the United Kingdom, and the United States.

Why was the research needed?

Researchers were looking for a different way to treat people with advanced thyroid cancer.

Some participants in this trial had the most common form of thyroid cancer, called differentiated thyroid cancer, or DTC. People with DTC are first treated with radioactive iodine, or radioiodine. This type of treatment may not help all people with DTC, so researchers are developing new treatments.

Other participants had a less common form called medullary thyroid cancer, or MTC. Radioiodine treatment does not work on MTC.

Researchers in this trial were interested in a drug called lenvatinib. This drug is not radioactive and works in a different way from radioiodine treatment. Researchers wanted to see how well lenvatinib shrunk tumors in people with DTC or MTC.

The main questions researchers asked in the trial were:

- Did lenvatinib reduce tumors in patients with advanced thyroid cancer?
- How did lenvatinib act in the body?
- How many participants had their tumors shrink or stay about the same?
- How long did participants live before their cancer got worse?
- How long did participants' cancer respond to lenvatinib?
- How many participants survived their cancer 1 year after starting treatment in the trial?
- 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.

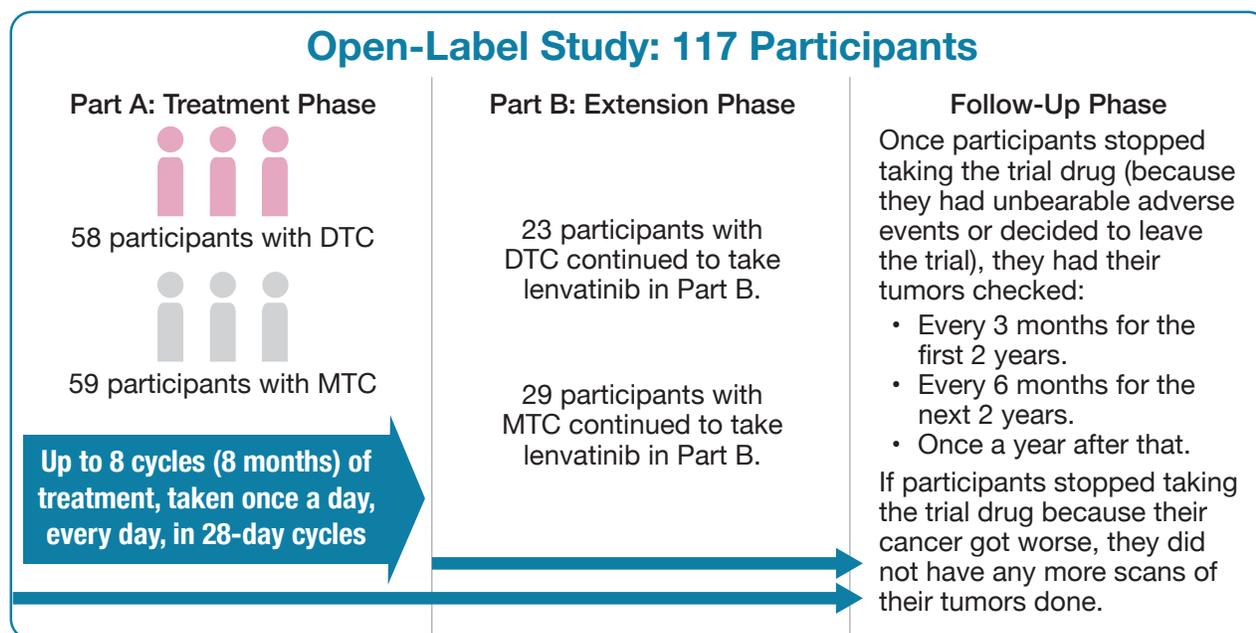
To answer these questions, researchers asked for the help of men and women like you. Participants in this trial were 22 to 77 years old. They all had either DTC that did not get better with radioiodine treatment or they had MTC.

What kind of trial was this?

This trial was “open-label”. That means participants, trial doctors and staff, and the sponsor knew what drugs participants were getting. During this study, all participants took lenvatinib.

What happened during the trial?

This trial had 2 parts. The figure below shows how the trial was done.



Before the trial started, trial doctors did a full check-up, including taking blood and urine samples, of all participants to make sure they could join the trial. The trial doctors also did scans to see how advanced each participant's cancer was. They also checked the electrical activity of the heart of each participant using an electrocardiogram (ECG) and took pictures of the heart using an echocardiogram.

During Part A, each participant took a pill containing 24 milligrams (mg) of lenvatinib by mouth once a day for up to 8 cycles. Each cycle lasted 28 days, so Part A lasted about 8 months. Participants came to the trial clinic on Days 1, 8, 15, and 22 of the treatment cycles. Participants continued in Part A of the trial for 8 cycles of treatment, or until they decided to leave the trial.

At different points, trial doctors:

- Did a physical check-up of participants and took blood and urine samples
- Did an ECG and an echocardiogram to check participants' heart health
- Scanned participants' tumors to see if the cancer was responding to lenvatinib
- Scanned participants' bones to see if they were affected by cancer

During Part B, participants could continue in the trial until their cancer got worse, they had an unbearable adverse event, they decided to leave the trial, or the sponsor stopped the trial. Participants' cancer was considered worse if it spread to other areas or new tumors grew.

If participants stopped taking the trial drug because they had unbearable adverse events or decided to leave the trial, they had their tumors checked every 3 months for the first 2 years and then every 6 months during years 3 and 4, and once a year after that. If participants stopped taking the trial drug because their cancer got worse, they did not have any more scans of their tumors done.

What were the results of the trial?

This is a summary of the overall results of this trial, not your individual results. The results for each participant may have been different. Other trials may provide new information or different results. You should not make changes to your treatment based on the results of a single trial without first talking to your doctor.

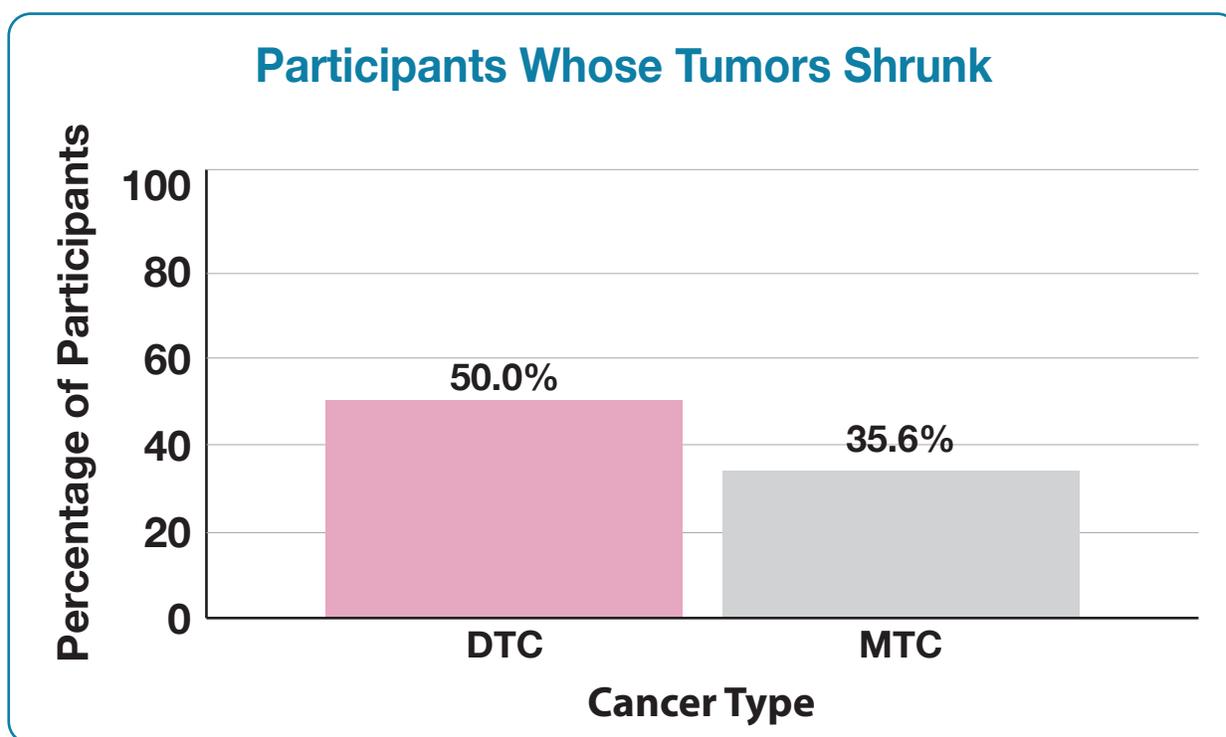
Did lenvatinib reduce tumors in patients with advanced thyroid cancer?

Yes. Researchers looked at whether participants' tumors completely went away or if they at least shrunk by 30% of their original size.

Researchers found that:

- **Participants with DTC:** 29 out of 58 participants (50.0%) had their tumors shrink.
- **Participants with MTC:** 21 out of 59 participants (35.6%) had their tumors shrink.
- No participants had tumors that completely disappeared.

The chart below shows the number of participants whose tumors shrunk during the trial.



How did lenvatinib act in the body?

Researchers used blood tests to see how much lenvatinib was in the participants' blood.

Knowing this helped researchers better understand how the drug acts in the body. They learned that:

- The amount of lenvatinib in the blood and how quickly it left the blood were different from participant to participant.
- The amount of time it took for lenvatinib to leave the blood depended on participants' weight, but not on their age, gender, or amount of certain liver and kidney proteins.

How many participants had their tumors shrink or stay about the same?

Researchers also looked at how many participants had their tumors shrink or stay about the same. They found the following:

- **Participants with DTC:** 93.1% of participants had their tumor shrink or stay about the same.
- **Participants with MTC:** 79.7% of participants had their tumor shrink or stay about the same.

How long did participants live before their cancer got worse?

Researchers looked at how long participants lived before their cancer got worse. Cancer was considered worse if participants' tumors from the start of the study grew bigger or spread to other areas. They found the following:

- **Participants with DTC** lived for about 13 months before their cancer got worse.
- **Participants with MTC** lived for about 9 months before their cancer got worse.

How long did participants' cancer respond to lenvatinib?

Researchers looked at how long participants' cancer continued to respond to lenvatinib treatment. They found the following:

- **Participants with DTC:** Their cancer responded to lenvatinib for about 13 months.
- **Participants with MTC:** It is too soon to tell for participants with MTC.

How many participants survived their cancer 1 year after starting treatment in the trial?

After 1 year in the trial, researchers wanted to see how many participants survived their cancer. They found the following:

- **Participants with DTC:** 85.8% of participants survived their cancer 1 year after starting treatment in the trial.
- **Participants with MTC:** 76.1% of participants survived their cancer 1 year after starting treatment in the trial.

What medical problems did participants have?

A lot of research is needed to know whether a drug causes an adverse event. So when new drugs are being studied, researchers keep track of all adverse events that patients have.

How many participants had adverse events during the trial?

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

Adverse Events in This Trial

| | Participants with DTC (Out of 58 participants) | Participants with MTC (Out of 59 participants) |
|--|---|---|
| How many participants had adverse events? | 58 participants (100.0%) | 59 participants (100.0%) |
| How many participants stopped taking lenvatinib because of adverse events? | 15 participants (25.9%) | 14 participants (23.7%) |

Did any participants have serious 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.

In this trial, 28 participants (48.3%) with DTC and 30 participants (50.8%) with MTC had serious adverse events after treatment with lenvatinib. Some patients experienced more than one serious adverse event. The table below shows the serious adverse events that happened to at least 2 participants in this trial.

Serious Adverse Events in This Trial

| Serious Adverse Event | Participants with DTC (Out of 58 participants) | Participants with MTC (Out of 59 participants) |
|-------------------------|---|---|
| Dehydration | 4 participants (6.9%) | 2 participants (3.4%) |
| Low blood pressure | 3 participants (5.2%) | 1 participant (1.7%) |
| Decreased appetite | 1 participant (1.7%) | 3 participants (5.1%) |
| Blood clot in the lungs | 2 participants (3.4%) | 2 participants (3.4%) |
| High blood pressure | 2 participants (3.4%) | 1 participant (1.7%) |
| Pneumonia | 1 participant (1.7%) | 2 participants (3.4%) |
| Abdominal pain | 0 participants (0.0%) | 2 participants (3.4%) |
| Early menopause | 0 participants (0.0%) | 2 participants (3.4%) |
| Heart failure | 2 participants (3.4%) | 0 participants (0.0%) |
| Lower abdominal pain | 2 participants (3.4%) | 0 participants (0.0%) |
| Lung infection | 0 participants (0.0%) | 2 participants (3.4%) |

In this trial, there were 7 deaths: 3 participants with DTC and 4 participants with MTC. Out of the 7 deaths, 2 participants died directly due to their cancer getting worse. The other participants died from the following serious medical problems:

- Cardiac arrest (sudden loss of heart function)
- Sudden failure to breathe
- Failure of the respiratory system, resulting in the inability to breathe
- Paraneoplastic syndrome (a rare disease in cancer patients when the immune system reacts to tumors in an abnormal way)
- Bleeding from the carotid artery (an artery that carries blood from the heart to the brain)

What were the most common non-serious adverse events?

The table below shows the most common non-serious adverse events in this trial. A non serious adverse event was considered “common” if it happened in at least 40% of participants.

Most Common Non-Serious Adverse Events in This Trial

| Non-Serious Adverse Event | Participants with DTC (Out of 58 participants) | Participants with MTC (Out of 59 participants) |
|----------------------------------|---|---|
| Diarrhea | 39 participants (67.2%) | 44 participants (74.6%) |
| High blood pressure | 44 participants (75.9%) | 30 participants (50.8%) |
| High protein levels in urine | 37 participants (63.8%) | 35 participants (59.3%) |
| Decreased weight | 40 participants (69.0%) | 25 participants (42.4%) |
| Tiredness | 35 participants (60.3%) | 31 participants (52.5%) |
| Decreased appetite | 30 participants (51.7%) | 29 participants (49.2%) |
| Nausea | 29 participants (50.0%) | 28 participants (47.5%) |
| Headache | 25 participants (43.1%) | 24 participants (40.7%) |
| Cough | 26 participants (44.8%) | 21 participants (35.6%) |
| Hoarse voice | 25 participants (43.1%) | 19 participants (32.2%) |

Where can I learn more about the study?

You can learn more about your trial online at:

- www.clinicaltrials.gov/show/results/NCT00784303
- www.clinicaltrialsregister.eu/ctr-search/search?query=2007-005933-12

Official trial title: Phase 2, Multicenter, Open-label, Single Arm Trial to Evaluate the Safety and Efficacy of Oral E7080 in Medullary and Iodine-131 Refractory, Unresectable Differentiated Thyroid Cancers, Stratified by Histology

The results presented here are for a single trial. Other studies may provide new information or different results. You should not make changes to your treatment based on the results of a single trial without first talking to your doctor.

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.



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