Clinical Trial Results

Trial Sponsor:	Eisai
Drug Studied:	Lenvatinib or E7080
National Clinical Trial #:	NCT01321554
EudraCT Number:	2010-023783-41
Protocol #:	E7080-G000-303
Trial Period:	July 2011 to November 2013
Short Trial Title:	A trial to see if lenvatinib helps slow down the worsening of advanced thyroid cancer

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.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

What has happened since my trial ended?

You were in this trial for about 2 years, but the trial took about 2½ years to collect enough data to complete the analysis. When the trial ended in November 2013, the research sponsor reviewed the data and created a report of the results. This is a summary of that report.

The trial included 392 participants from 117 trial sites around the world. Trial sites were located in:

Australia	France	Russian Federation
Austria	Germany	South Korea
Belgium	Italy	Spain
Brazil	Japan	Sweden
Canada	Poland	Thailand
Chile	Portugal	United Kingdom
Denmark	Romania	The United States

Why was the research needed?

Researchers were looking for a better way to treat people with advanced thyroid cancer. People with this type of cancer are first treated with radioactive iodine, or radioiodine. But, this type of treatment may not help all people with advanced thyroid cancer, so researchers are developing new treatments.

Researchers in this trial wanted to compare the effect of lenvatinib with no treatment at all in slowing the worsening of advanced thyroid cancer. The main questions researchers asked in the trial were:

- Did lenvatinib slow down participants' cancer from getting worse compared to no treatment at all?
- Did lenvatinib help in other ways?
- How did lenvatinib act in the body?
- What adverse events did people taking lenvatinib have? An adverse event (AE) 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. The participants in this trial were 21 to 89 years old and had advanced thyroid cancer that did not get better with previous radioiodine treatment.

What kind of trial was this?

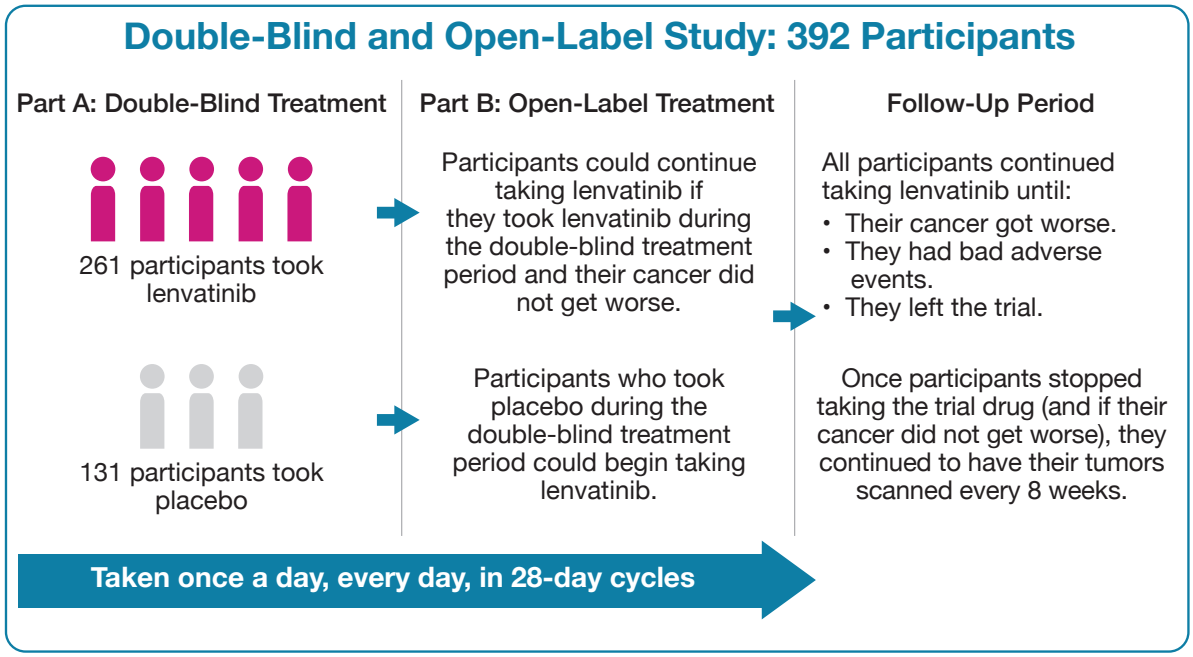
This trial had 2 main parts.

Part A was "double-blind". This means none of the participants, trial doctors, or staff knew what treatment each participant received. During Part A, participants took either lenvatinib or a placebo. A placebo looks like the trial drug but has no real medicine in it. When the trial was still ongoing, the research sponsor found out which treatment participants took so they could make a report of the trial results.

Part B was "open-label". This means that the participants, the trial doctors, and the staff knew what drugs the participants were getting. During Part B, all participants took lenvatinib.

What happened during the trial?

The figure below shows how the trial was done.



Before the trial started, the trial doctors did a full check-up, physical exam, and took blood and urine samples to make sure participants could join the study. Doctors also did scans to see how advanced each participant's cancer was before the trial began, and checked participants' heart health using an electrocardiogram (ECG) and an echocardiogram. An ECG checks the electrical activity of the heart, while an echocardiogram takes pictures of the heart using sound waves.

During Part A, participants were randomly assigned to take either 24 milligrams (mg) of lenvatinib or placebo once a day. For every 2 participants who took lenvatinib, 1 participant took placebo. If participants had an adverse event (AE) from lenvatinib, they were given a lower dose of lenvatinib.

During Part B, all participants took lenvatinib once a day.

- Participants who took lenvatinib in Part A and whose cancer did not get worse continued to take lenvatinib. If participants had an AE from lenvatinib, then they were given a lower dose of lenvatinib.
- Participants who took a placebo in Part A started taking lenvatinib.

Participants could continue in the trial until their cancer got worse, they had an AE, or they decided to leave the trial. Participants' cancer was considered getting worse if their tumors started growing larger or if there was growth of new tumors.

Every 8 weeks, trial doctors:

- Scanned participants' tumors to see if the cancer was improving, and
- Scanned participants' brains to see if the cancer was affecting the brain.

Every 16 weeks, trial doctors:

- Checked participants' heart health using an echocardiogram.

Every 24 weeks, trial doctors:

- Scanned participants' bones to see if the cancer was affecting their bones.

Throughout the trial, trial doctors took blood and urine samples and checked participants' weight, height, temperature, blood pressure, heart rate, and respiratory rate.

During the follow-up period, participants continued to have their tumor size and bones scanned. All participants had a final trial visit within 30 days of their last dose of lenvatinib. If participants left Part A or Part B early, but their cancer did not get worse, they entered the follow-up Period.

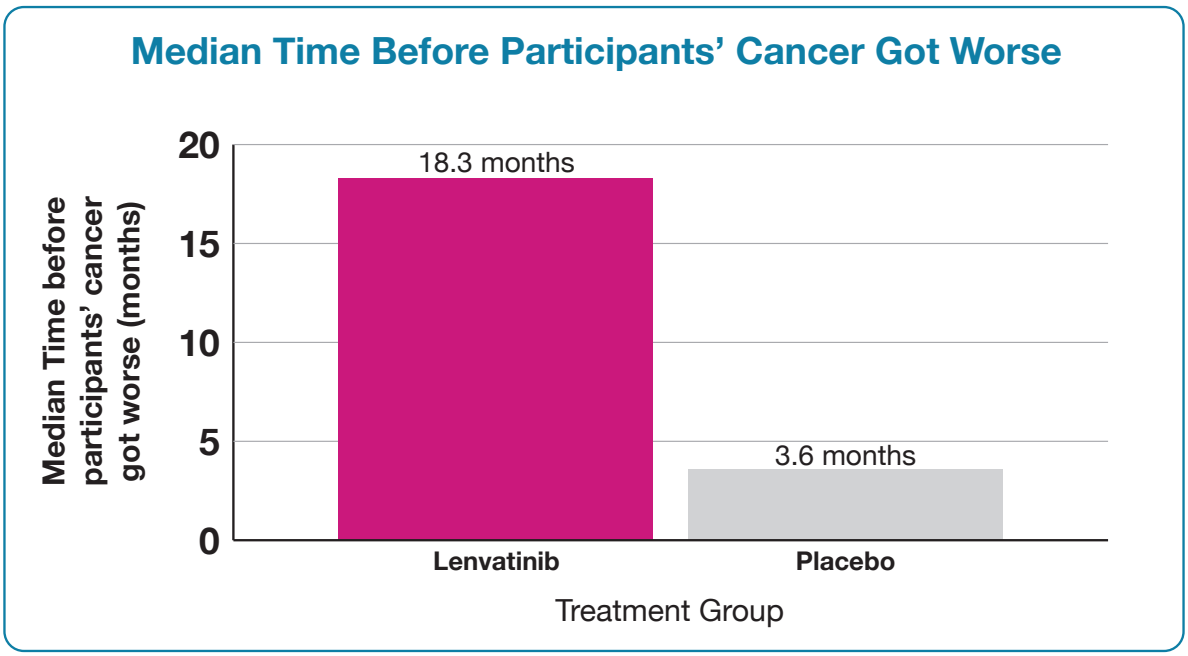
What were the results of the trial?

This is a summary of the overall results of this trial, not your individual results. The results for each participant may have been different. Researchers look at results of many studies to decide which drugs work best and are safest for patients. Other trials may provide new information or different results. You should not make therapeutic changes to your treatment based on the results of a single trial without first talking to your doctor.

Did lenvatinib slow down participants' cancer from getting worse compared to no treatment at all?

Yes. Researchers looked at the median time participants survived before their cancer got worse. The median is the amount of time halfway between the shortest time and the longest time it took for participants' cancer to get worse. Half of the participants took more than the median time for cancer to get worse, and half of the participants took less than the median time for cancer to get worse. Researchers found that it took a median time of about 18.3 months for cancer to get worse in the participants who took lenvatinib, compared to a median time of about 3.6 months for participants who took a placebo. This means that it took longer for the cancer to get worse in participants taking lenvatinib than in patients taking placebo.

The chart below shows the average amount of time before participants' cancer got worse.



Did lenvatinib help in other ways?

Yes. Researchers looked at how many participants either had all of their cancer disappear ("complete response"), or their tumors got smaller and no new tumors appeared ("partial response"). Researchers then added the participants who had a complete response to those who had a partial response to get the "objective response". More participants who took lenvatinib got better compared to participants who took placebo. Researchers found that:

- Out of 261 participants who took lenvatinib, 169 participants (64.8%) had an objective response.
- Out of 131 participants who took placebo, 2 participants (1.5%) had an objective response.

How did lenvatinib act in the body?

Researchers tested participants' blood to see how much of the trial drug was in the blood. Knowing this amount helps researchers understand better how the trial drug acts in the body. They found the following:

- The amount of lenvatinib in the blood was different from participant to participant.
- The amount of time it took for lenvatinib to leave the blood slightly depended on participants' weight and the level of certain liver proteins.

What medical problems did participants have?

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

How many participants had adverse events during the trial?

Out of the 261 participants who took lenvatinib, 260 participants (99.6%) had AEs, and 43 participants (16.5%) stopped taking lenvatinib because of an AE.

Out of the 131 participants who took the placebo, 118 participants (90.1%) had AEs, and 6 participants (4.6%) stopped taking the placebo because of an AE.

Adverse Events in This Trial

	Lenvatinib (Out of 261 participants)	Placebo (Out of 131 participants)
How many participants had adverse events?	260 participants (99.6%)	118 participants (90.1%)
How many participants stopped taking the trial drug because of adverse events?	43 participants (16.5%)	6 participants (4.6%)

Did any participants have serious adverse events?

An AE is called "serious" when it is life-threatening, causes lasting problems, or the participant needs to be admitted to a hospital.

Out of the 261 participants who took lenvatinib, 133 participants (51.0%) experienced serious AEs.

Out of the 131 participants who took placebo, 31 participants (23.7%) experienced serious AEs. The table below shows the most common serious AEs that happened in at least 2% of participants.

Serious Adverse Events in This Trial

Serious Adverse Event	Lenvatinib (Out of 261 participants)	Placebo (Out of 131 participants)
Pneumonia	10 participants (3.8%)	3 participants (2.3%)
Difficulty swallowing	3 participants (1.1%)	3 participants (2.3%)
Difficulty breathing	3 participants (1.1%)	5 participants (3.8%)
Coughing up blood	0 participants (0.0%)	3 participants (2.3%)
General worsening of physical health	6 participants (2.3%)	0 participants (0.0%)
Dehydration	7 participants (2.7%)	0 participants (0.0%)
High blood pressure	9 participants (3.4%)	0 participants (0.0%)

In this trial, 71 participants (27.2%) died in the lenvatinib group, and 47 participants (35.9%) died in the placebo group. Most of the deaths in this trial were due to participants' cancer getting worse.

What were the most common non-serious adverse events?

The table below shows the most common non-serious AEs in this trial that happened in at least 30% of participants.

Most Common Non-Serious Adverse Events in This Trial

Adverse Event	Lenvatinib (Out of 261 participants)	Placebo (Out of 131 participants)
High blood pressure	181 participants (69.3%)	19 participants (14.5%)
Diarrhea	173 participants (66.3%)	22 participants (16.8%)
Decreased appetite	139 participants (53.3%)	24 participants (18.3%)
Decreased weight	132 participants (50.6%)	19 participants (14.5%)
Nausea	121 participants (46.4%)	33 participants (25.2%)
Tiredness	110 participants (42.1%)	32 participants (24.4%)
Headache	100 participants (38.3%)	15 participants (11.5%)
Stomatitis (inflammation and sores inside the mouth)	93 participants (35.6%)	9 participants (6.9%)
Vomiting	92 participants (35.2%)	19 participants (14.5%)
Hand-foot syndrome (pain, redness, and swelling on the palms of hands and/or soles of feet)	84 participants (32.2%)	1 participant (0.8%)
High levels of protein in the urine	84 participants (32.2%)	4 participants (3.1%)
Hoarse voice	82 participants (31.4%)	7 participants (5.3%)

Where can I learn more about the study?

You can find more information about the results of your trial online at:

- www.clinicaltrialsregister.eu/ctr-search/trial/2010-023783-41/results
- www.clinicaltrials.gov/show/results/NCT01321554.

Official trial title: A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial of Lenvatinib (E7080) in 131I-Refractory Differentiated Thyroid Cancer

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 its 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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CISCRP
One Liberty Square, Suite 510
Boston, MA 02109

1-877-MED-HERO

www.ciscrp.org

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Synchrogenix Headquarters
2 Righter Parkway, Suite 205
Wilmington, DE 19803

1-302-892-4800

www.synchrogenix.com