Clinical Trial Results

Trial Sponsor:	Eisai
Drug Studied:	Lenvatinib or E7080
National Clinical Trial #:	NCT01136733
EudraCT #:	2010-019484-10
Protocol #:	E7080-G000-205
Trial Period:	August 2010 to June 2014
Short Trial Title:	A trial to compare the drugs lenvatinib and everolimus alone and combined together to treat advanced kidney 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.

What has happened since my trial ended?

You were in this trial for about 1 year, but the trial is still going on. The research sponsor reviewed the data collected up to June 2014 and created a report of the results.

This trial had a Part A and a Part B. This is a summary of results from Part A. The summary from Part B will be shared when Part B is over and the summary has been written.

Part A included 20 participants from 4 trial sites in the United States and the United Kingdom.

Why was the research needed?

Researchers were looking for a different way to treat people with advanced kidney cancer. Standard treatments like chemotherapy and radiation usually do not work on this type of cancer. So, researchers were interested in a drug called lenvatinib that can stop the growth of new blood vessels that help cancer grow and spread.

Researchers in this trial wanted to find out the effects of combining lenvatinib and a drug called everolimus for the treatment of advanced kidney cancer. Everolimus works in a different way to stop cancer cells from growing and spreading. It is used to treat advanced kidney cancer and other types of cancer. Researchers wanted to see if participants could take the 2 drugs together.

The main questions researchers asked in Part A of the trial were:

- How many participants had side effects that kept them from continuing to take lenvatinib with everolimus? A side effect is a medical problem caused by the trial drug.
- What was the highest dose of lenvatinib taken with everolimus that patients could tolerate?
- What adverse events did participants taking both lenvatinib and everolimus 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 46 to 72 years old. They all had advanced kidney cancer that could not be removed by surgery or had spread outside the kidney.

What kind of trial was this?

This trial was "open-label". That means that the participants, the trial doctors, and the staff knew which drugs participants were getting. During Part A, all participants took lenvatinib and everolimus together.

What happened during the trial?

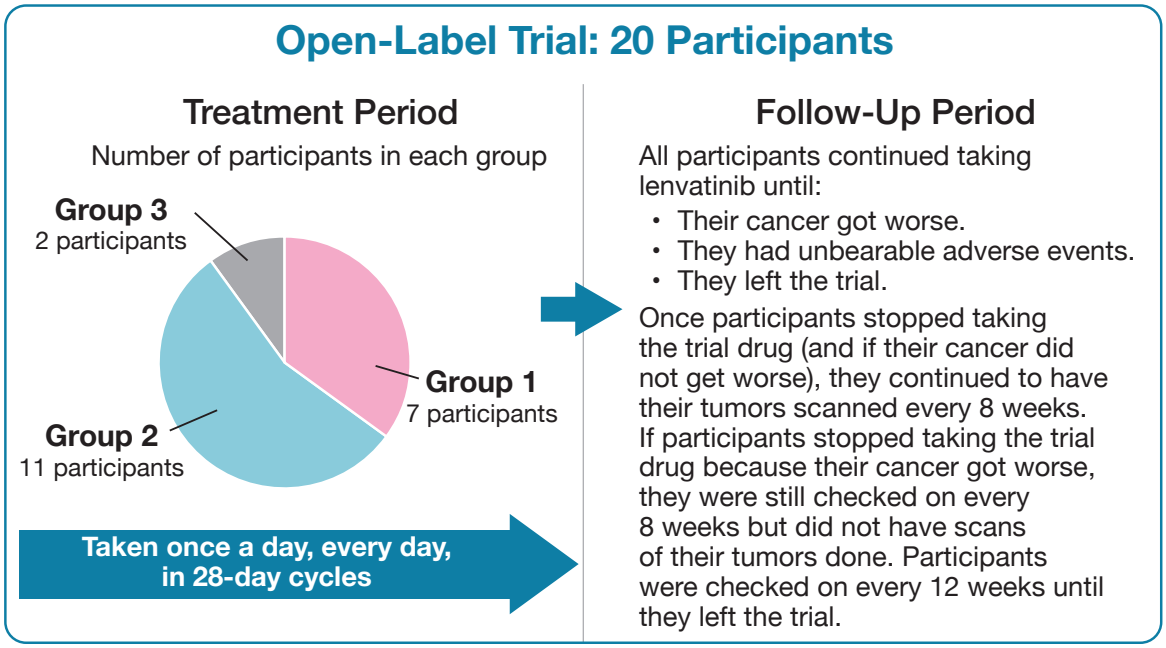
Before the trial started, trial doctors did full check-ups, including taking blood and urine samples, to make sure each participant could join the study. Then doctors did scans to see how advanced each participant's cancer was. They also checked each participant's heart health.

During the treatment period, all participants took both lenvatinib and everolimus once a day for 28-day cycles. Participants were randomly assigned to 1 of 3 groups:

- **Group 1:** 12 milligrams (mg) of lenvatinib and 5 mg of everolimus
- **Group 2:** 18 mg of lenvatinib and 5 mg of everolimus
- **Group 3:** 24 mg of lenvatinib and 5 mg of everolimus

The doses of both lenvatinib and everolimus were chosen based on the results of previous studies. If participants had any severe side effects, they were given a lower dose of lenvatinib.

The figure below shows how the trial was done.



Throughout the trial, trial doctors took blood and urine samples and checked participants' weight, height, temperature, blood pressure, heart rate, and breathing rate. Trial doctors also asked how participants were feeling and kept track of any medical problems.

Every 8 weeks, trial doctors scanned participants' tumors to see if the cancer was improving.

Participants could continue taking the trial drugs until their cancer got worse, they had an unbearable adverse event, or they decided to leave the trial. Their cancer was considered worse if their existing tumors got bigger, if they spread to other areas, or if new tumors grew.

During the follow-up period, participants who stopped taking the trial drugs and whose cancer did not get worse continued to have their tumors scanned every 8 weeks. Participants who stopped taking the trial drugs because their cancer got worse were still checked on every 8 weeks but did not have their tumors scanned. Participants were checked on every 12 weeks until they left the trial.

What were the results of the trial?

This is a summary of the overall results of Part A 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.

How many participants had side effects that kept them from continuing to take lenvatinib together with everolimus?

Researchers found that 4 out of the 20 participants had side effects that kept them from continuing to take lenvatinib together with everolimus:

- **Group 1:** One participant had abdominal pain.
- **Group 2:** One participant did not take the full dose of the trial drugs due to tiredness.
- **Group 3:** One participant had nausea and vomiting. Another participant did not take the full dose of the trial drugs due to stomatitis, a condition that causes painful swelling and sores in the mouth.

What was the highest dose of lenvatinib taken with everolimus that patients could tolerate?

Researchers decided that the dose in Group 2, 18 mg of lenvatinib and 5 mg of everolimus, was the highest dose of the trial drugs that patients could tolerate. This was the dose that was then tested in Part B of the trial. The results of Part B will be described in a separate report.

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 participants have. They may or may not be caused by the trial drug.

How many participants had adverse events during the trial?

During the trial, all 20 out of the 20 participants (100.0%) who took lenvatinib and everolimus had adverse events during the treatment period, and 6 participants stopped taking the trial drugs because of an adverse event.
The table below shows how many participants had adverse events in this trial and how many stopped taking the trial drugs because of an adverse event by treatment group.

Adverse Events in This Trial

	Group 1: 12 mg lenvatinib + 5 mg everolimus (Out of 7 participants)	Group 2: 18 mg lenvatinib + 5 mg everolimus (Out of 11 participants)	Group 3: 24 mg lenvatinib + 5 mg everolimus (Out of 2 participants)
How many participants had adverse events?	7 participants (100.0%)	11 participants (100.0%)	2 participants (100.0%)
How many participants stopped taking the trial drugs because of adverse events?	0 participants (0.0%)	5 participants (45.5%)	1 participant (50.0%)

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.

Within 30 days of the end of the trial, 2 participants (1 participant in each group) died because their cancer got worse. Beyond 30 days after the trial, 5 more participants in Group 1 and 6 more participants in Group 2 died because their cancer got worse.

In this trial, 14 out of the 20 participants who took lenvatinib with everolimus had serious adverse events:

- **Group 1:** 6 participants (85.7%)
- **Group 2:** 8 participants (72.7%)
- **Group 3:** 0 participants (0.0%)

The table below shows the serious adverse events that happened to at least 2 participants.

Serious Adverse Events in This Trial

Serious Adverse Event	Group 1: 12 mg lenvatinib + 5 mg everolimus (Out of 7 participants)	Group 2: 18 mg lenvatinib + 5 mg everolimus (Out of 11 participants)	Group 3: 24 mg lenvatinib + 5 mg everolimus (Out of 2 participants)
Severe renal failure	1 participant (14.3%)	2 participants (18.2%)	0 participants (0.0%)
Shortness of breath	1 participant (14.3%)	1 participant (9.1%)	0 participants (0.0%)
Decreased sodium	2 participants (28.6%)	0 participants (0.0%)	0 participants (0.0%)
Dehydration	0 participants (0.0%)	2 participants (18.2%)	0 participants (0.0%)

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 20% of participants.

Most Common Non-Serious Adverse Events in This Trial

Non-Serious Adverse Events	Group 1: 12 mg lenvatinib + 5 mg everolimus (Out of 7 participants)	Group 2: 18 mg lenvatinib + 5 mg everolimus (Out of 11 participants)	Group 3: 24 mg lenvatinib + 5 mg everolimus (Out of 2 participants)
Tiredness	5 participants (71.4%)	11 participants (100.0%)	2 participants (100.0%)
Stomatitis (Swelling and sores in the mouth)	4 participants (57.1%)	7 participants (63.6%)	2 participants (100.0%)
Nausea	6 participants (85.7%)	6 participants (54.5%)	1 participant (50.0%)
Vomiting	5 participants (71.4%)	6 participants (54.5%)	1 participant (50.0%)
High protein levels in urine	5 participants (71.4%)	6 participants (54.5%)	0 participants (0.0%)
Diarrhea	3 participants (42.9%)	7 participants (63.6%)	1 participant (50.0%)
Decreased appetite	3 participants (42.9%)	6 participants (54.5%)	1 participant (50.0%)
Constipation	3 participants (42.9%)	4 participants (36.4%)	1 participant (50.0%)
Decreased sodium	3 participants (42.9%)	2 participants (18.2%)	0 participants (0.0%)

Where can I learn more about the trial?

You can learn more about your trial online at:

- www.clinicaltrialsregister.eu/ctr-search/search?query=2010-019484-10
- www.clinicaltrials.gov/ct2/show/NCT01136733

Official trial title: An Open-Label, Multicenter Phase 1b/2 Study of E7080 Alone, and in Combination with Everolimus in Subjects with Unresectable Advanced or Metastatic Renal Cell Carcinoma Following One Prior VEGF-Targeted Treatment

The results presented here are for a single trial. 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.

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 participants 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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