Clinical Study Results

Research Sponsor: Eisai Inc.
Drug Studied: E7080, also called lenvatinib
Short Study Title: A study to compare the effectiveness and safety of a 14 mg dose of lenvatinib plus everolimus with an 18 mg dose of lenvatinib plus everolimus in participants with kidney cancer

Thank you

You took part in this clinical study for the study drug E7080, also called lenvatinib, given together with another drug called everolimus. Everyone who participated helped researchers learn more about lenvatinib, given together with everolimus, and how it may help people with kidney cancer called renal cell carcinoma (also called RCC). Participants in this study had RCC that got worse during or after their previous cancer treatment.

Eisai, a Japanese pharmaceutical company that was 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 study results with participants.

Eisai has prepared this summary of the study and its results with a medical and regulatory writing organization called Certara.

If you participated in this 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?

It started in October 2017 and ended in June 2024.

The study included 343 participants from 82 sites in the following countries:

Australia	Canada	Czech Republic	Finland
Greece	Italy	Netherlands	Poland
Portugal	Romania	Russia	South Korea
Spain	Taiwan	United Kingdom	United States

Of the 343 participants, 341 took lenvatinib and everolimus at least once.

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

Why was the research needed?

Researchers were looking for a different way to treat people with RCC whose cancer got worse during or after their previous cancer treatment. The standard treatments for people with RCC include surgery, chemotherapy such as everolimus, and other treatments that may help shrink tumors.

The researchers in this study wanted to find out whether lenvatinib 14 mg (new starting dose) with everolimus can work as well as the approved lenvatinib 18 mg with everolimus in people with RCC. They also wanted to find out if people had any medical problems during the study.

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

- Does lenvatinib 14 mg plus everolimus work as well as lenvatinib 18 mg plus everolimus after 24 weeks of treatment?
- How safe was lenvatinib 14 mg plus everolimus for treating participants with RCC compared with lenvatinib 18 mg plus everolimus?
- What adverse events did participants receiving lenvatinib with everolimus have? An adverse event is a medical problem that may or may not be caused by the study drugs.

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, given together with everolimus, works, but these were not the main questions the study was designed to answer.

What kind of study was this?

To answer the main questions above, researchers asked for the help of adult participants with RCC whose cancer got worse during or after their previous cancer treatment.

Of these participants, 76% were men and 24% were women. The participants in the study were 28 to 87 years old.

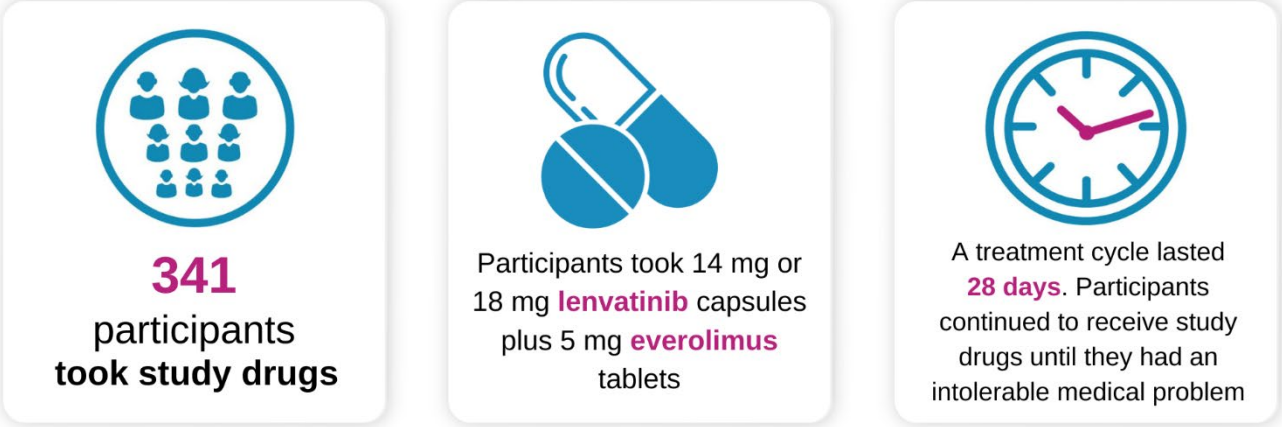
In this study, the participants were divided into 2 groups:

- **Group A**: Participants took lenvatinib 14 mg plus everolimus.
- **Group B**: Participants took lenvatinib 18 mg plus everolimus.

This study was "open label". This means that the participants, the study doctors and staff, and the sponsor knew which dose of lenvatinib the participants took until the study was over.

Participants took lenvatinib capsules and everolimus tablets by mouth once every day in a 28-day period called a treatment cycle. All participants took a fixed dose (5 mg) of everolimus in the study.

The figure below shows how treatment was given in the 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 RCC whose cancer got worse during or after their previous cancer treatment
- Took each participant's blood and urine samples
- Checked each participant's heart health
- Took scans of each participant's body to assess their tumor

During the treatment period, participants took their assigned dose of lenvatinib and everolimus.

Throughout the study, the study doctors or staff:

- Took each participant's blood and urine samples
- Took scans of each participant's body, as needed, to assess their tumor
- Asked about medical problems participants were experiencing and medicines participants were taking

Each participant could continue receiving the lenvatinib and everolimus until:

- Their cancer got worse
- They had intolerable medical problems
- They chose to leave the study
- The sponsor decided to end the study

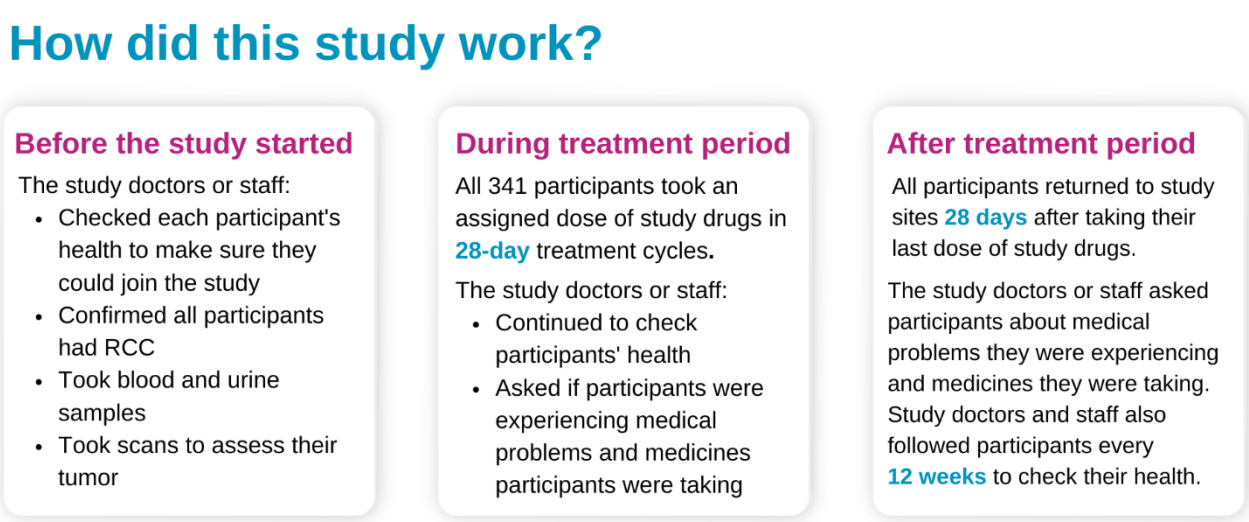
After 28 days since their last dose, all participants returned to the study site.

During this visit, the study doctors or staff:

- Took each participant's blood and urine samples
- Asked about medical problems participants were experiencing and medicines participants were taking

After this visit, study doctors or staff followed up participants every 12 weeks to check on their health.

The figure below shows how the study was done.



What were the results of the study?

This is a summary of the main results of this study. Each participant's individual results were different and unique to them. Individual results are not given separately in this summary, but all participants' results are summarized together here. 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 by patients. Other studies may provide new information or different results. Always talk to a doctor before making any treatment decisions.

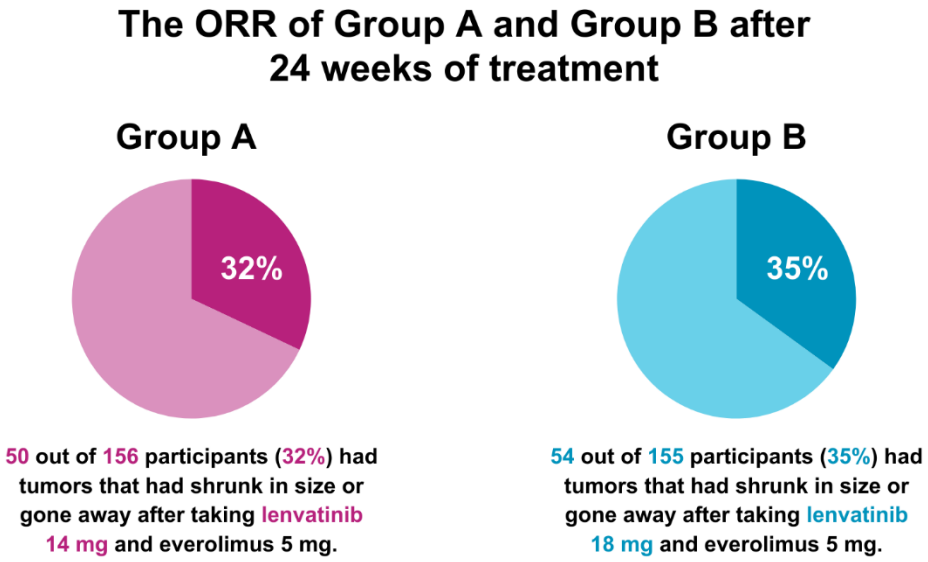
Does lenvatinib 14 mg plus everolimus work as well as lenvatinib 18 mg plus everolimus after 24 weeks of treatment?

To answer this question, the study doctors looked at the scan results and compared each participant's tumor before and after 24 weeks of taking lenvatinib and everolimus.

Study doctors checked the number of participants whose tumors had a partial (shrunk in size) or complete (gone away) response to lenvatinib and everolimus. This is called objective response rate (also called ORR).

Researchers then compared the ORR results of **Group A** (participants who received lenvatinib 14 mg plus everolimus) and **Group B** (participants who received lenvatinib 18 mg plus everolimus).

The chart below shows the ORR of **Group A** and **Group B** after 24 weeks of treatment.



Researchers did statistical tests on the ORR results. They found that the 14 mg starting dose of lenvatinib plus everolimus was not proven to work as well as the 18 mg dose.

How safe was lenvatinib 14 mg plus everolimus for treating participants with RCC compared with lenvatinib 18 mg plus everolimus?

To answer this question, researchers counted the number of participants who had intolerable Grade 2 medical problems or at least Grade 3 medical problems that happened within 24 weeks of treatment.

Medical problems that the participants had in the study were classified into Grades 1 to 5, depending on how severe they were.
A higher grade means more severe medical problem: Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe), Grade 4 (life-threatening), and Grade 5 (fatal).

Researchers then compared the results of **Group A** (participants who received lenvatinib 14 mg plus everolimus) and **Group B** (participants who received lenvatinib 18 mg plus everolimus).

The table below shows the number of participants in **Group A** and **Group B** who had intolerable Grade 2 medical problems or at least Grade 3 medical problems that happened within 24 weeks of treatment.

Intolerable Grade 2 or At Least Grade 3 Medical Problems Within 24 Weeks of Treatment

	Out of 157 participants in Group A	Out of 152 participants in Group B
How many participants had intolerable Grade 2 or at least Grade 3 medical problems that happened within 24 weeks of treatment?	130 (83%)	121 (80%)

What medical problems did participants have?

Medical problems that happen to participants in clinical studies are called “adverse events”. If the study doctors thought an adverse event was caused by the study drugs, it is called an “adverse reaction”. Adverse events or reactions are considered “serious” if the participant needs to be admitted to a hospital, if they are life-threatening, or if they cause lasting health problems.

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 these. A lot of research is needed to know whether a drug may cause a particular medical problem.

How many participants had adverse events?

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

Adverse Events in This Study

	Out of 173 participants in Group A	Out of 168 participants in Group B
How many participants had adverse events?	173 (100%)	167 (99%)
How many participants had serious adverse events?	92 (53%)	87 (52%)
How many participants stopped receiving lenvatinib and everolimus because of adverse events?	43 (25%)	43 (26%)

What were the most common serious adverse events?

The most common serious adverse events were:

- Infection of the lungs
- Diarrhea
- Worsening or spreading of cancer

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

Most Common Serious Adverse Events in This Study

	Out of 173 participants in Group A	Out of 168 participants in Group B
Infection of the lungs	13 (8%)	7 (4%)
Diarrhea	11 (6%)	6 (4%)
Worsening or spreading of cancer	5 (3%)	5 (3%)
Sudden kidney damage	3 (2%)	6 (4%)
Vomiting	6 (4%)	2 (1%)
Increased level of a chemical in the body called creatinine	2 (1%)	4 (2%)
Stomach flu	4 (2%)	1 (1%)
Fever	4 (2%)	1 (1%)
Pain in the abdomen	3 (2%)	2 (1%)
Low blood pressure	3 (2%)	2 (1%)
A life-threatening reaction to an infection that spreads through the body	3 (2%)	2 (1%)
Fluid around the lungs	2 (1%)	3 (2%)

In this study,

- 24 out of 173 participants (14%) in **Group A** died due to serious adverse events.
- 17 out of 168 participants (10%) in **Group B** died due to serious adverse events.

The most common adverse events that led to the participant's death were:

- Worsening or spreading of cancer – 10 participants (3%)
- Infection of the lungs – 4 participants (1%)
- Death – 3 participants (1%)

What were the most common adverse events?

The most common adverse events were:

- Diarrhea
- Decreased appetite
- High blood pressure

The table below shows the adverse events that happened in 25% or more of participants overall. There were other adverse events, but these happened in fewer participants.

Most Common Adverse Events in This Study

	Out of 173 participants in Group A	Out of 168 participants in Group B
Diarrhea	120 (69%)	123 (73%)
Decreased appetite	64 (37%)	58 (35%)
High blood pressure	54 (31%)	60 (36%)
Inflammation of the lining of the mouth	61 (35%)	49 (29%)
Feeling sick	54 (31%)	52 (31%)
Excess protein in the urine	40 (23%)	66 (39%)
Tiredness	52 (30%)	50 (30%)
Vomiting	43 (25%)	43 (26%)

How has this study helped patients and researchers?

In this study, researchers learned more about how lenvatinib, given with everolimus, may have helped people RCC. 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 ongoing.

Where can I learn more about the study?

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

- https://www.clinicaltrialsregister.eu/ - Once you are on the website, click "**Home and Search**", then type **2016-002778-11** in the search box and click "**Search**".
- https://clinicaltrials.gov/ - Once you are on the website, type **NCT03173560** into the search box and click "Search".

Full study title: A Randomized, Open-Label (formerly Double-Blind), Phase 2 Trial to Assess Safety and Efficacy of Lenvatinib at Two Different Starting Doses (18 mg vs 14 mg QD) in Combination With Everolimus (5 mg QD) in Renal Cell Carcinoma Following One Prior VEGF-Targeted Treatment

Protocol number: E7080-G000-218

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 numbers for general information are +1-888-274-2378 (USA) and +44-845-676-1400 (UK).

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

Eisai Co., Ltd. is a global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "to give first thought to patients and the people in the daily living domain, and increase the benefits that health care provides to them as well as meet diverse healthcare needs worldwide", 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.

CERTARA

Certara is a worldwide medical and regulatory writing organization and is not involved in recruiting participants or in conducting clinical studies.
Certara Headquarters 4 Radnor Corporate Center Suite 350 Radnor, PA 19087
https://www.certara.com • 1-415-237-8272