Clinical Study Protocol Synopsis

A study of E7386 taken with E7080 (also called lenvatinib) in people with solid tumors

Full Study Title:	An Open-Label Study of E7386 in Combination With Other Anticancer Drug(s) in Subjects With Solid Tumors		
EU Clinical Study Number:	2023-510275-64-00	**US Clinical Study Number:**	NCT04008797
Study Sponsor:	Eisai, Inc., Nutley, NJ, USA	Telephone number:	+1 201-692-1100

Why is this research needed?

Researchers are looking for a different way to treat people who have solid tumors. A **solid tumor** is an uncontrolled growth that forms an abnormal mass of tissue. Standard treatments for people with solid tumors include surgery and other treatments that help shrink the tumors.

E7386 may help people with solid tumors by blocking the proteins responsible for the formation and growth of the tumors. In this study, researchers want to learn about the safety profile and the optimal dose of E7386. They also want to learn how effective E7386 is when taken with the targeted therapy, lenvatinib, by participants with solid tumors and to compare the optimal dose of the combination of E7386 with lenvatinib with the chemotherapy treatment of physician's choice (TPC) in participants with endometrial cancer (EC). The TPC in this study is doxorubicin or paclitaxel.

What treatment is being studied?

Participants will take E7386 tablets once or twice daily with lenvatinib capsules by mouth.

Some participants will take lenvatinib alone, and some participants will receive doxorubicin or paclitaxel as an injection through the vein (also called IV injection).

Doses of both E7386 and lenvatinib are measured in milligrams (also called mg).

Doses of TPC are measured in mg per participant's body surface area measured in meters squared (m^2).

Study doctors will give study treatment in 28-day periods called treatment cycles.

Everyone involved in the study will know which treatment participants will receive.

What are the goals of this study?

The primary objectives of this study are to investigate the safety and tolerability of E7386 and when taken with lenvatinib by participants with solid tumors and to learn the optimal dose of the combination of E7386 with lenvatinib in participants with EC.

The secondary objectives are to investigate the movement of E7386 and lenvatinib within the body and how effective E7386, when taken with lenvatinib, is in shrinking the size of solid tumors of participants. Researchers will also investigate how effective the optimal dose of E7386 when taken with lenvatinib and compare the combination of E7386 with lenvatinib with lenvatinib or TPC alone in participants with EC.

What are the measurements in this study?

1. **Main measurement:** To investigate the primary objectives, researchers will collect information on any medical problems and symptoms that participants may have during the study. Researchers will also find the recommended Phase 2 dose, dose-limiting toxicities, how participants respond (Parts 1 and 2), and the optimal dose of E7386 when taken with lenvatinib (Part 3).

2. **Secondary measurements:** To investigate the secondary objectives, researchers will use the following measurements (see Page 3 for definitions of terms):

Pharmacokinetics/ Pharmacodynamics	Best overall response	Objective response rate	Disease control rate
Clinical benefit rate	Progression-free survival	Overall survival	Duration of response

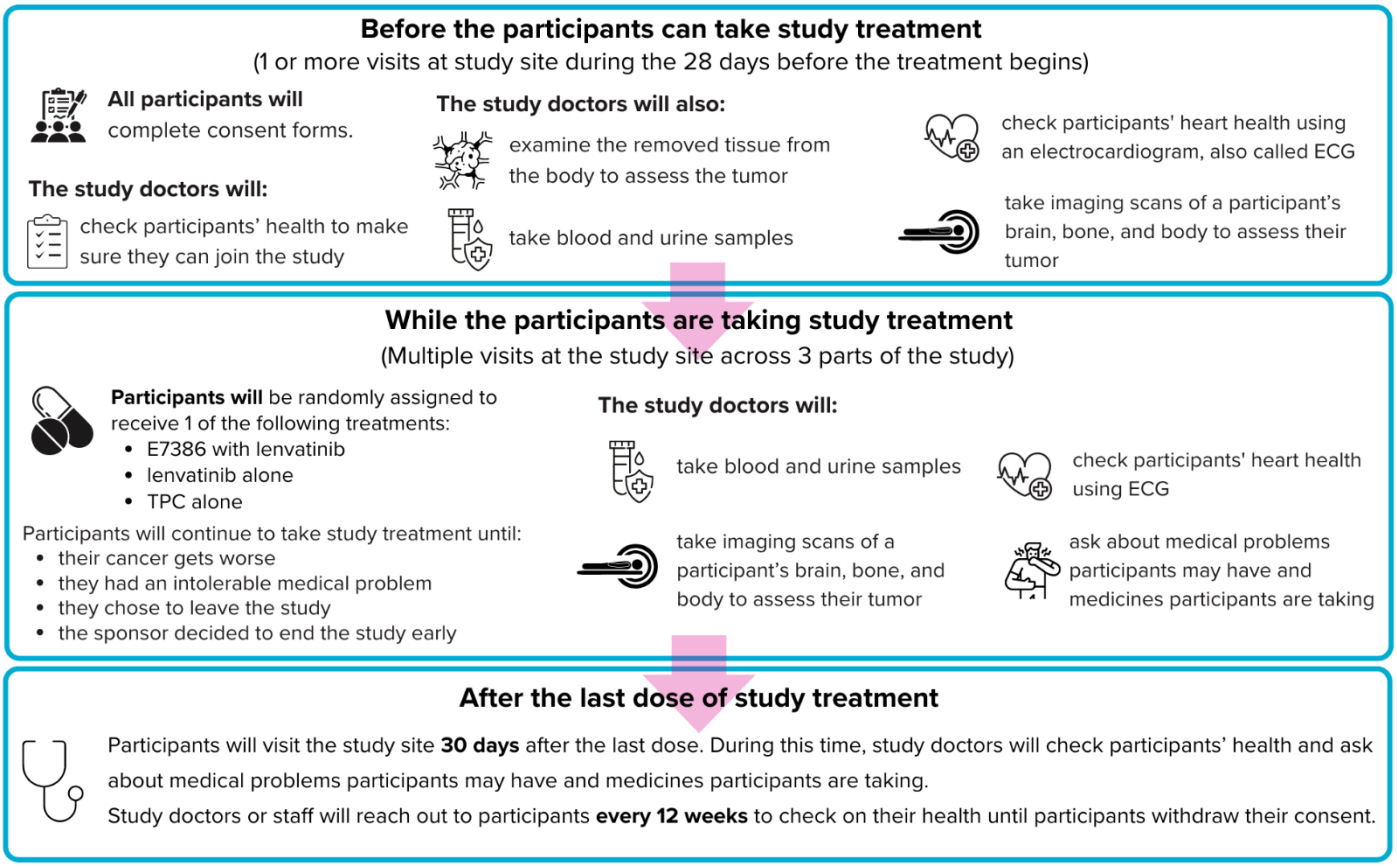
The researchers will also collect other information about E7386 and lenvatinib, but the measurements described above are the most important for this study.

What will happen during the study?

This study has 3 parts:

- **Part 1:** Researchers want to learn the safety and tolerability of E7386 when taken with lenvatinib by participants with liver cancer or with certain solid tumors.
- **Part 2:** Researchers want to learn the safety and effectiveness of E7386 when taken with lenvatinib by participants with certain kinds of tumors.
- **Part 3:** Researchers want to find the optimal dose of the combination of E7386 with lenvatinib for participants with EC and compare the combination with lenvatinib or TPC alone.

The chart below shows what will happen in 3 parts of the study.



Who can and cannot take part in this study?

People can take part in this study if they have solid tumors that:

- have spread to another part of the body
- do not respond to or have come back since the previous treatment

People cannot take part in this study if they have:

- certain heart problems
- planned surgery before the study starts
- any allergy to the study drugs
- previously taken lenvatinib (Part 3 only)

These are just some of the main guidelines. Study doctors will check all guidelines to see if a person can join this study. Participation in this study is voluntary. Participants can leave the study at any time.

What are the potential benefits and risks of taking part in this study?

Potential Benefits (Advantages): The information collected in this study may help doctors learn more about E7386 when taken with lenvatinib, which could help the participants and other people with solid tumors.

Potential Risks (Disadvantages): Participants' solid tumors might get worse, or they might have a side effect from E7386 or lenvatinib. There may be additional risks that are unknown and unexpected.

Definition of Terms

Term	Definition
Best overall response (or BOR)	Participant's best response to treatment. It can be complete (tumor gone away), partial (tumor shrunk in size), or stable (no change in tumor size) response
Clinical benefit rate (or CBR)	The proportion of participants who have a complete (tumor gone away), partial (tumor shrunk in size), or stable (no change in tumor size) response to treatment
Disease control rate (or DCR)	The proportion of participants who will have reduced (shrunk) or stable (no change) tumor size
Dose-limiting toxicity (or DLT)	Medical problems related to the study drug that would prevent participants from taking a higher dose
Duration of response (or DOR)	How long from the first improvement (tumor shrunk in size) until it starts to get worse (tumor increased in size)
Endometrial cancer (or EC)	Cancer of the lining of the womb
Objective response rate (or ORR)	The proportion of participants who have a partial (tumor shrunk in size) or complete (tumor gone away) response to treatment
Overall survival (or OS)	How long participants live after the start of treatment
Pharmacodynamics (or PD)	A medicine's effects in the body
Pharmacokinetics (or PK)	How a medicine is absorbed, modified, and removed from the body
Progression-free survival (or PFS)	How long participants live without their tumor getting worse after the start of treatment
Recommended Phase 2 dose (or RP2D)	Dose of the study drug that will be used in the next part of the study
Treatment cycle	A period of treatment followed by a period of rest (no treatment) that is repeated on a regular schedule
Treatment of physician's choice (or TPC)	The treatment that a physician decided to use to treat the participant's condition