Clinical Study Results

Research Sponsor: Eisai Inc.
Drug Studied: H3B-6545
Short Study Title: A study of H3B-6545 in participants with HR-positive and HER2-negative breast cancer

Thank you!

You took part in this clinical study for the study drug H3B-6545. All of the participants helped researchers learn more about H3B-6545 and how it may help people with HR-positive and HER2-negative breast cancer.

Breast cancer refers to the uncontrolled growth of abnormal cells in the breast. Different types of breast cancer depend on the presence of hormone receptors (or HR) and human epidermal growth factor receptor 2 (or HER2). The receptor is a part of a cell that attaches to a substance and triggers a particular response. The presence of HR and HER2 in breast cancer defines the treatment that can be used.

In this study, participants had HR-positive and HER2-negative breast cancer. They also had either advanced breast cancer or breast cancer that had spread to other parts of the body (metastatic).

Eisai, a Japanese pharmaceutical company and 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 the results of the study with you.

Eisai prepared this summary with a medical and regulatory writing organization called Certara Synchrogenix.

If you participated in the 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?

The study started in August 2017 and ended in October 2023.

The study included 206 participants from 39 study sites in France, the United Kingdom, and the United States. Out of 206 participants, 151 took at least 1 dose of H3B-6545.

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

Why was the research needed?

In this study, researchers were looking for a different way to treat people who have HR-positive and HER2-negative breast cancer. The standard treatments for people with this type of cancer include chemotherapy and other treatments that may help shrink tumors. However, these treatments may not help all people with this type of breast cancer.

Researchers thought that H3B-6545 might help participants with HR-positive and HER2-negative breast cancer by targeting and blocking specific proteins that help cancer cells survive and grow.

The researchers in this study wanted to find out whether H3B-6545 can help treat participants with HR-positive and HER2-negative breast cancer. They also wanted to find out if participants had any medical problems during the study.

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

- What was the highest dose of H3B-6545 with manageable side effects that could be given to participants in Part 1?
- How effective was H3B-6545 in treating participants with HR-positive and HER2-negative breast cancer?
- What medical problems did participants who took H3B-6545 have that study doctors thought were caused by the study drug?

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 H3B-6545 works. However, these were not the main questions the study was designed to answer.

What kind of study was this?

To answer the main questions, researchers asked for the help of women with HR-positive and HER2-negative breast cancer. The participants in the study were 31 to 87 years old.

This study had 2 parts:

- **Part 1**: The researchers wanted to learn about the safety of different doses of H3B-6545. They also wanted to find out the highest dose of H3B-6545 with manageable side effects that could be given to participants. They do this by looking at the dose-limiting toxicities (also called DLTs). **DLTs** are medical problems that would prevent participants from taking a higher dose.
- **Part 2**: Using the selected dose of H3B-6545 from Part 1, the researchers wanted to learn how H3B-6545 works in shrinking the tumor.

All participants took H3B-6545 capsules once per day.

This study was "open-label." This means that the participants, the study doctors and staff, and the sponsor know that all participants took H3B-6545.

The figure below shows how the treatment was given in your 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 did the following:

- Confirmed that participants had HR-positive and HER2-negative breast cancer
- Checked participants' heart health
- Took blood and urine samples for analyses
- Took scans of each participant's bone, chest, and body to assess their tumor

During treatment in Parts 1 and 2, the participants took H3B-6545 once per day.

Throughout the study, the study doctors or staff did the following:

- Checked participants' heart health
- Took blood and urine samples for analyses
- Took scans of each participant’s bone, chest, and body to assess their tumor
- Asked about medicines participants were taking and medical problems participants had experienced

The participants could continue taking H3B-6545 until:

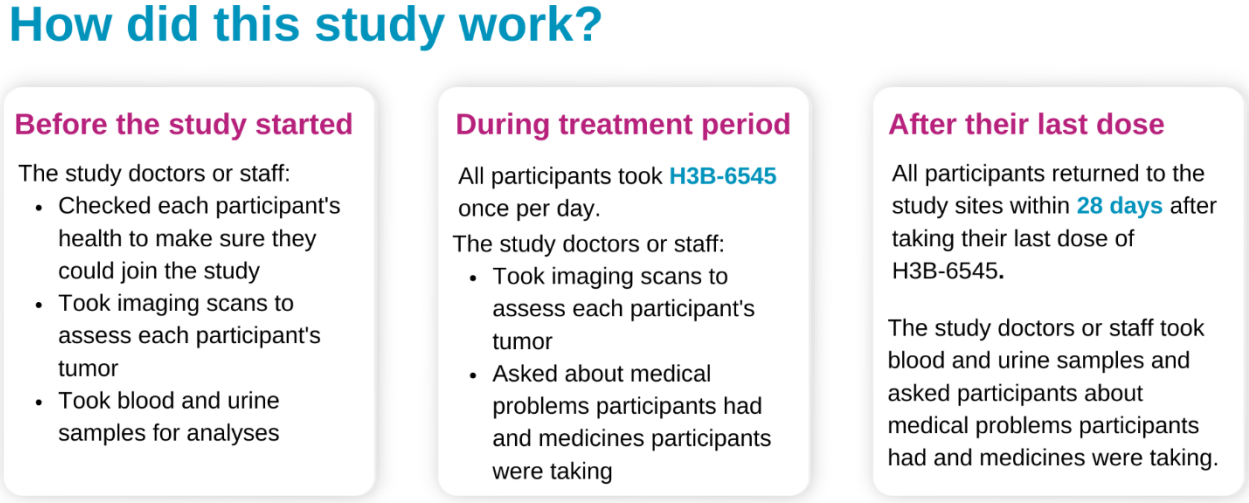
- Their cancer got worse
- They had intolerable medical problems
- They chose to leave the study or withdrew their consent
- The sponsor chose to end the study

Within 28 days after their last dose, all participants who discontinued treatment returned to the study site.

During this visit, the participants had the following:

- Physical examination
- Heart health checked
- Blood and urine samples taken for analyses
- Answered questions about medicines they were taking and medical problems they had experienced

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. The results each person had individually may be different and are not in this summary. But the results each person had are part of the summary of results. 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. Other studies may provide new information or different results. Always talk to a doctor before making any treatment decisions.

What was the highest dose of H3B-6545 with manageable side effects that could be given to participants in Part 1?

To answer this question, researchers checked whether participants had DLTs after taking different dose levels of H3B-6545.

Overall, 2 participants who took 600 mg H3B-6545 had DLTs of skin reaction to the study drug and tiredness. No participants who took H3B-6545 at dose levels of 450 mg or less had DLTs.

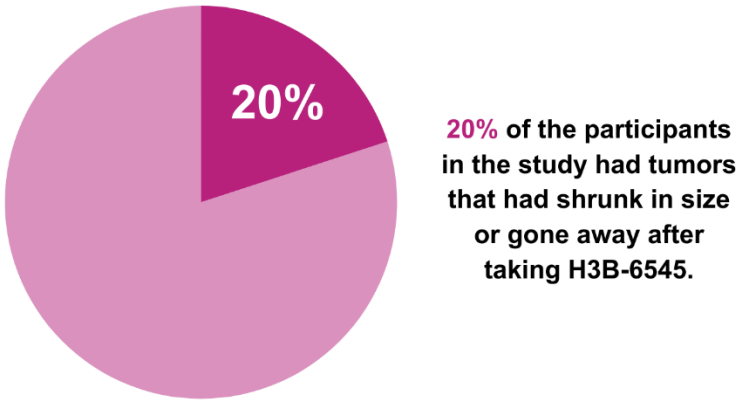
Based on the safety results from Part 1, H3B-6545 450 mg once per day was used in Part 2 of the study.

How effective was H3B-6545 in treating participants with HR-positive and HER2-negative breast cancer?

To answer this question, the study doctors looked at the scan results and compared the size of each participant's tumor before and after taking H3B-6545. Study doctors then checked the number of participants whose tumors had a partial (shrunk in size) or complete (gone away) response to H3B-6545. This is called objective response rate (also called ORR).

The chart below shows the ORR from participants after taking H3B-6545.

The ORR from participants after taking H3B-6545



Of the participants whose tumors had partial or complete responses to H3B-6545, the midpoint time their tumors continued to respond was **9 months**.

The midpoint time is called median duration of response. This means that for participants whose tumors responded to H3B-6545, half continued to respond for 9 months or more, while the other half continued to respond for less than 9 months.

What medical problems did participants have?

Medical problems that happen in clinical studies are called “adverse events”. An adverse event that the study doctors thought may have been caused by the study drug is called an “adverse reaction”. An adverse reaction is called “serious” when it is life-threatening, causes lasting problems, or the participant needs to be admitted to a hospital.

This section is a summary of the adverse reactions that happened during this study. The websites listed at the end of this summary may have more information about the medical problems that happened in this study. A lot of research is needed to know whether a study drug causes a medical problem.

Results in this section were from participants who received at least 1 dose of H3B-6545.

How many participants had adverse reactions?

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

Adverse Reactions in This Study

	Total Out of 151 participants
How many participants had adverse reactions?	135 (89%)
How many participants had serious adverse reactions?	6 (4%)
How many participants had died because of adverse reactions?	0 (0%)
How many participants stopped taking H3B-6545 because of adverse reactions?	10 (7%)

What were the most common adverse reactions?

The most common adverse reactions in this study were the following:

- Abnormally slow heartbeat
- Feeling sick
- Diarrhea
- Tiredness

The table below shows the adverse reactions in 10% of participants or more overall in the study. There were other adverse reactions, but these happened in fewer participants.

Most Common Adverse Reactions in the Study

	Total Out of 151 participants
Abnormally slow heartbeat	61 (40%)
Feeling sick	49 (33%)
Diarrhea	36 (24%)
Tiredness	36 (24%)
Low levels of red blood cells	23 (15%)
Vomiting	22 (15%)
Itching	15 (10%)

What were the most common serious adverse reactions?

All serious adverse reactions happened in 1 participant each.

How has this study helped participants and researchers?

In this study, researchers learned more about how H3B-6545 may have helped people with HR-positive and HER2-negative breast cancer. 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 H3B-6545 are not planned.

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:

- http://www.clinicaltrialsregister.eu - Once you are on the website, click "**Home and Search**", then type **2018-000570-29** in the search box and click "**Search**".
- https://www.clinicaltrials.gov - Once you are on the website, type **NCT03250676** into the search box and click "**Search**."

Full study title: A Phase 1-2 multicenter, open-label trial of H3B-6545, a covalent antagonist of estrogen receptor alpha, in women with locally advanced or metastatic estrogen receptor-positive, HER2 negative breast cancer

Protocol number: H3B-6545-A001-101

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 number for general information is 44-845-676-1400 (UK) and 1-888-274-2378 (USA).

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 "giving first thought to patients and the people in the daily living domain 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 https://www.eisai.com.

CERTARA

Certara Synchrogenix is a worldwide medical and regulatory writing organization and is not involved in recruiting participants or in conducting clinical studies.
Certara Synchrogenix Headquarters 100 Overlook Center, Suite 101, Princeton, NJ 08540
https://www.certara.com • 1-415-237-8272