Summary of Clinical Trial Results

A study to find out whether a new medicine (DHES0815A) was safe and effective in patients with breast cancer

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a "study" in this document).

This summary is written for:

- Members of the public
- People who took part in the study

This summary is based on information known at the time of writing.

The study started in April 2018 and stopped early – in April 2021 – because too many people had side effects and the Sponsor decided to stop the development of this medicine.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary.**
- **Always speak to your doctor before making any decisions about your treatment.**

Contents of the summary

Thank you to the people who took part in this study

The people who took part have helped researchers answer important questions about refractory metastatic HER2+ breast cancer and the study medicine, "DHES0815A".

Key information about this study

- This study was done to find out how safe was it to treat patients with a new medicine called, "DHES0815A".
- Patients with a certain type of breast cancer called "HER2+ breast cancer" were treated with the study medicine.
- This study included 14 patients in two countries.
- The main finding was that the investigators decided it was not safe enough to continue to give this medicine to patients above a certain dose level.
- Eleven patients had side effects and one patient had a serious side effect. The side effect and serious side effect were thought to be related to the study medicine.
- This study was stopped early because too many patients had side effects.

1. General information about this study

Why was this study done?

Patients whose cancer reappears are considered to have **relapsed**. Cancer that has spread to other tissues in the body has **metastasized**.

While there is no cure for patients with metastasized breast cancer (MBC), available treatments can extend the patient's life.

Patients with "**HER2+ breast cancer"** have a form of breast cancer that contains a protein called "HER2".

One important therapy for treating patients with metastasized HER2+ breast cancer is "**HER2-targeted therapy**". There is greater risk of relapsing and having a shorter lifespan if HER2+ breast cancer that has metastasized is not treated with a HER2-targeted therapy.

"**DHES0815A**" is a new medicine, and it is a HER2-targeted therapy. That means DHES0815A has an effect on and kills cells that have the HER2 protein.

It is possible that DHES0815A could be used to treat patients with HER2+ breast cancer. Investigators wanted to learn about the side effects of this medicine. They also wanted know if this medicine could be effective for HER2+ breast cancer.

This study was done to find a dose of DHES0815A that was safe for patients, and that was effective for treating HER+ MBC.

What was the study medicine?

The study medicine was "**DHES0815A**".

- DHES0815A is a medicine known as an "antibody-drug-conjugate" because it contains an antibody that is linked (conjugated) to the medicine.
- Antibodies are proteins that bind to a single target. The target for the antibody in DHES0815A is the HER2 protein.
- The medicine in DHES0815A is called "pyrrolo[2,1-c][1,4]benzodiazepine monoamide", which binds to the DNA inside cells and eventually causes cell death.
- The antibody directs DHES0815A to bind to its target, the HER2 protein found in cancer tissue, in patients who have HER2+ breast cancer. This way, the medicine is delivered to cancerous cells, thereby killing these cells.

What did researchers want to find out?

The main questions that researchers wanted to answer were:

1. Was there a dose of DHES0815A that was safe for treating patients?
2. Were there signs that showed that DHES0815A was useful to patients?

What kind of study was this?

This was a "**Phase 1 Study**", which means that this was one of the first studies for DHES0815A. A small number of patients with breast cancer were treated with DHES0815A. The researchers performed medical tests and examined the patients to find out more about DHES0815A.

This was an "**Open-Label Study**". That means that researchers and patients knew which treatment the patients were getting.

This was a "**Dose-Escalation Study**". Each new group of patients received a higher dose of the DHES0815A. The decision to administer the next higher dose level – "dose-escalation" – was made after reviewing results from all previously dosed people at the lower dose levels.

When and where did the study take place?

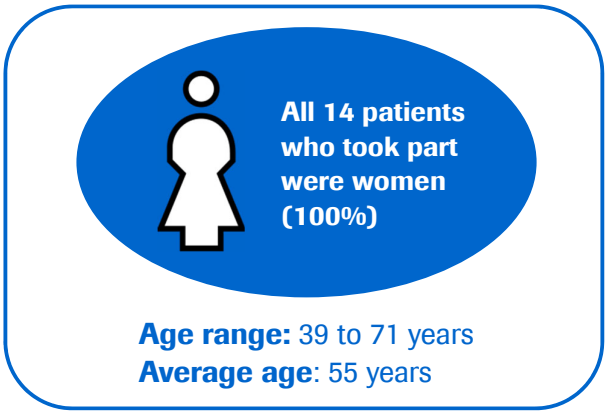
The study started in April 2018 and stopped early in July 2021 because there were too many side effects from the study treatment. This summary presents the results of the study up until it was stopped.

The study took place at 6 study centers across 2 countries:

- South Korea
- United States

2. Who took part in this study?

Fourteen patients with HER2+ breast cancer took part in this study.



People could take part in the study if:

1. They were at least 18 years old.
2. They were going to live for at least 12 weeks (life expectancy).
3. They had HER2+ breast cancer confirmed through lab tests. The cancer had relapsed, or could not be treated with available medicines (refractory cancer).
4. They had sufficient functioning blood system, liver, and kidney.
5. They were not experiencing side effects from other prior treatments.
6. They were not pregnant and could not get pregnant.

People could not take part in the study if:

1. They received certain other treatments for cancer in the last 4 weeks.
2. They had been exposed to certain other medicines during their lifetime that exceeded a certain dose.
3. They had a history of having severe allergic reactions to antibody therapies.
4. They had major surgery within the last 4 weeks.
5. They had diseases other than cancer in one or more organs.

3. What happened during the study?

Each patient was assigned to a dose group in the order in which he or she joined the study. Patients received DHES0815A via intravenous (IV) infusion once every 21 days.

Three patients received the lowest dose. When all three had completed a 21-day observation period, results for the group were reviewed. If it was safe do so, the next higher dose group started their treatment.

Patients continued to receive treatment once every 21 days at their assigned dose level. Treatment could be stopped at any time if the patient decided to do so or under advice of the doctor.

Here are the dose levels, the number of patients, and the number of treatment cycles:

Group	Dose	Number of patients	Number of treatment cycles within the group
1	0.6 mg/kg	3 patients	3 to 22 cycles
2	1.2 mg/kg	3 patients	4 to 44 cycles
3	2.4 mg/kg	3 patients	2 to 3 cycles
4	4.0 mg/kg	3 patients	3 to 6 cycles
5	6.0 mg/kg	2 patients	2 cycles

The study stopped early because too many patients had side effects. After stopping their treatments, patients were asked to go back to their study center to check their overall health.

4. What were the results of the study?

Question 1: Was there a dose of DHES0815A that was safe for treating patients?

Researchers looked at side effects from the study medicine.

None of the 14 patients had side effects of any concern during the first 21 days following their treatments. However, side effects became a problem after further treatment at higher doses. In particular, after all three patients in Group 4 received 3 cycles of treatments, they experienced swelling (edema) and problems with their skin, mostly rashes.

At the time these side effects appeared in Group 4, two patients had already been treated in Group 5. The study doctors decided to stop enrolling any new patients, and the dose of DHES0815A was reduced to a safe dose that had not caused any concerning side effects. This safe dose was 2.4 mg/kg that had been tested in Group 3.

Question 1: Were there signs that showed that DHES0815A was useful to patients?

- One patient had a “complete response” (her cancer was gone) at the beginning of the sixth treatment cycle. This response lasted until the patient discontinued from the study after 44 cycles of treatment (992 days since her first dose).
- Ten patients (71%) had “stable disease” upon treatment with the study medicine, which means their cancer did not worsen or improve while being treated with DHES0815A.
- Two patients had “progressive disease”, which indicated that the DHES0815A was not useful for them.
- One patient could not be evaluated for response to treatment.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8).

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happened during the study.

- They are described in this summary because the study doctors believe the side effects were related to the treatment in the study.
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very serious and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study.
- Serious and common side effects are listed in the following sections.

Serious side effects

A side effect is considered "serious" if it is life-threatening, needs hospital care, or causes lasting problems.

During the study, one patient in Group 5 had a headache that was considered to be a serious side effect and which the doctors thought was caused by the study medicine.

There were no deaths during the study.

Most common side effects

During the study, 11 of 14 patients (79%) reported 65 side effects that were not serious, but the study doctors thought these side effects were caused by the study medicine.

The most frequently reported side effects thought to be caused by DHES0815A, seen in two or more patients, are shown. Some patients had more than one side effect, which means the same patient can be represented on more than one line in the table below.

Side effect thought to be caused by DHES0815A	Number of patients
Rash (pruritus)	5 (36%)
Feeling tired (fatigue)	4 (29%)
Dark spots on skin (hyperpigmentation)	3 (21%)
Feeling sick to the stomach (nausea)	3 (21%)
Sensitive to light (photophobia)	3 (21%)
Abnormal blood test (alkaline phosphatase increased)	2 (14%)
Anemia	2 (14%)
Diarrhea	2 (14%)
Dry eye	2 (14%)
Eye pain	2 (14%)
Inflammation of the eye (conjunctivitis)	2 (14%)
Inflammation of the lungs (pneumonitis)	2 (14%)

During the study, four patients (29%) stopped their treatment because of side effects. They were two patients with pneumonitis, one patient with photophobia, and one patient with eye pain.

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

The information presented here is from a single study of 14 patients with HER2+ breast cancer. These results helped researchers learn more about the disease and DHES0815A.

Researchers were concerned about the side effects seen with the study medicine. Therefore, they decided not to develop DHES0815A for HER2+ metastatic breast cancer any further.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

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7. Are there plans for other studies?

At the time of writing this summary, there were no other studies planned for studying DHES0815A in HER+ breast cancer any further.

8. Where can I find more information?

You can find more information about this study on the websites listed below:

https://clinicaltrials.gov/ct2/show/results/NCT03451162

https://forpatients.roche.com/en/trials/cancer/bc/safety--tolerability--and-pharmacokinetic--pk--study-of-dhes0815.html

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/About.html
- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organized and paid for this study?

This study was organized and paid for by Genentech, Inc., South San Francisco, CA, USA. Genentech is part of F. Hoffmann-La Roche Ltd., with headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “A Phase 1, Open-Label Study Evaluating The Safety And Tolerability Of Escalating Doses Of A-HER2-DS-PBD Monoamide TDC In Patients With Refractory Metastatic HER2+ Breast Cancer.”.

- The protocol number for this study is GO39869.
- The ClinicalTrials.gov identifier for this study is NCT03451162.