Daiichi-Sankyo

Clinical Results Summary

A clinical study to learn about the effects of HER3-DXd in participants with advanced or metastatic colorectal cancer

Protocol number: U31402-A-U202

Thank You!

Daiichi Sankyo, Inc., the sponsor of this study, would like to thank the participants who took part in this study for HER3-DXd, also known as patritumab deruxtecan or U3-1402. Each participant helped to advance medical research for people affected with colorectal cancer. Their contribution to medicine and healthcare is greatly appreciated.

Important note: This summary only shows the results of a single study. Other studies may have different findings. Researchers and health authorities look at the results of many studies to understand which treatments work and how they work. It takes a lot of people in many studies around the world to advance medical science and healthcare.

Do not use the results of this study to make health decisions. Please talk to a doctor before changing any treatment you are taking or if you have any questions about these study results.

What was the main purpose of this study?

Advanced or metastatic colorectal cancer

Colorectal cancer is a type of cancer that affects the colon (large intestine) or the rectum (final part of the intestine). Advanced or metastatic means that the cancer has spread to other parts of the body.

Current treatment options for advanced colorectal cancer are surgery, radiation therapy, and chemotherapy. Radiation therapy is a type of cancer treatment that uses radiation to kill cancer cells. Chemotherapy uses medicine to kill cancer cells or stop them from growing and dividing. However, these treatment options do not work in all patients. Less than 20% of patients with advanced colorectal cancer are expected to survive for up to 5 years. The expectation of survival is particularly poor for patients with previously treated advanced or metastatic colorectal cancer. Therefore, new methods for treating colorectal cancer are needed.

Some people with colorectal cancer have increased levels of a protein called HER3, which makes their cells grow and divide too fast. This is called HER3 positive colorectal cancer. If the cancer does not have increased levels of HER3, it is called HER3 negative colorectal cancer.

U3-1402, also known as patritumab deruxtecan or HER3-DXd, binds to HER3-expressing cells to inhibit the cell growth and target the death of cancer cells.

In this study, researchers wanted to learn about the effects of HER3-DXd in people with HER3 positive or HER3 negative colorectal cancer in whom at least 2 other therapies were not effective.

Treatment given in this study

HER3-DXd

(Study drug)

Drug being studied for the treatment of advanced or metastatic colorectal cancer.

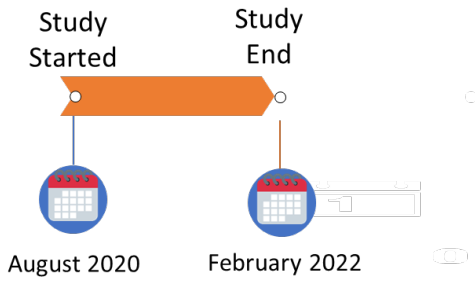
Main goal of this study

The main question the researchers wanted to answer in this study was:

How many participants had tumors* that completely disappeared or became at least 30% smaller after treatment?

**When the cancer cells form a lump or growth, it is called a cancerous tumor.*

How long was this study?



An individual participant could have been in this study for around 2 years and 3 months. The sponsor ended this trial early because the initial results indicated that not enough participants responded to treatment with HER3-DXd. The study started in August 2020 and ended in February 2022.

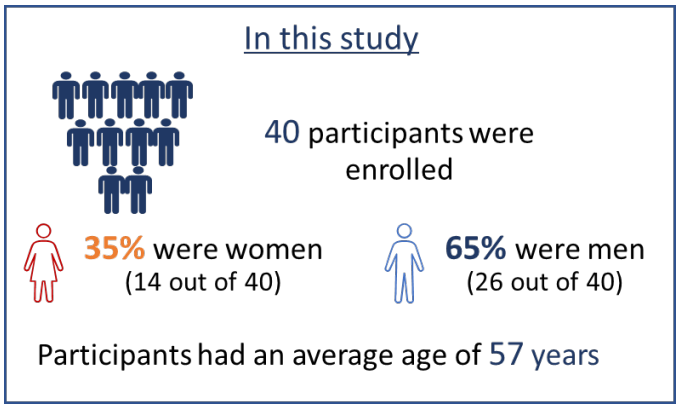
The results were collected up to February 2022 and a study report was created. This summary is based on that report.

Who was in this study?

This study included 40 participants from the United States (30 participants) and Japan (10 participants).

Participants could take part in this study if they:

- were at least 18 years of age and had confirmed advanced or metastatic colorectal cancer,
- had previous treatment with at least 2 therapies to which the cancer was resistant or came back, OR were intolerant to the therapy,
- had at least one tumor that could be measured,
- were willing to provide a tumor biopsy to test for HER3 levels before receiving treatment. A biopsy is a procedure to remove cells, tissue, or fluid from the tumor for examination,
- were either fully active OR unable to do hard physical activity but able to walk and do light housework or office work,
- had a life expectancy of at least 3 months, and
- had adequate liver, kidney, bone marrow and blood clotting function, as measured by blood tests.



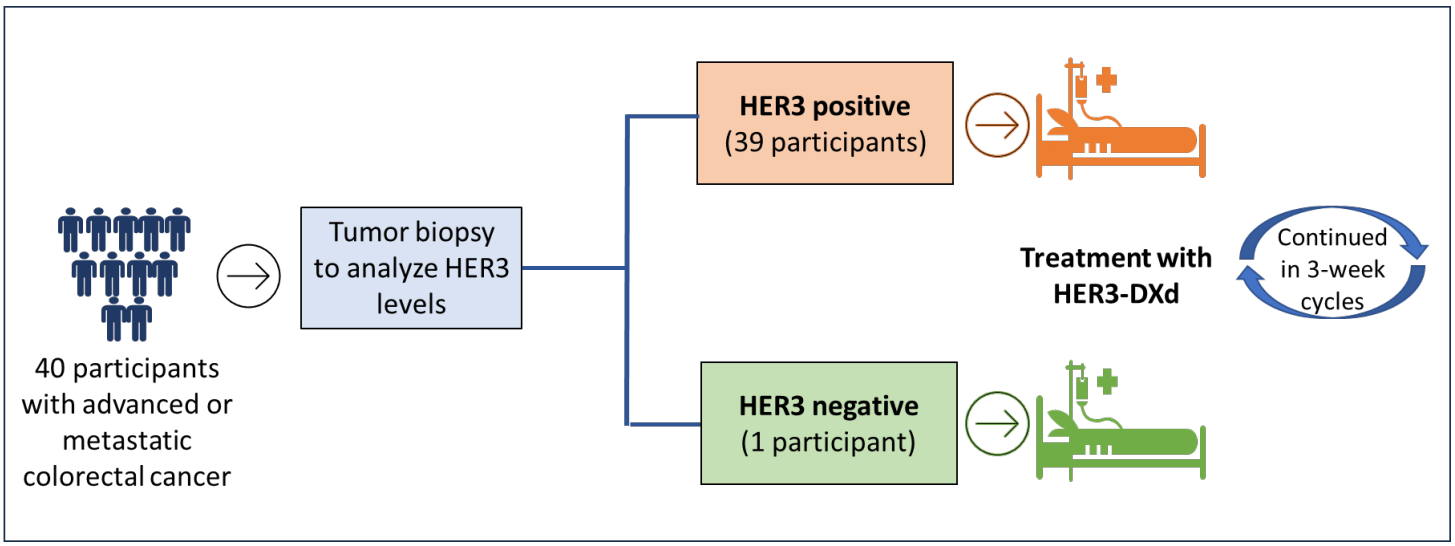
What happened during this study?

This was a Phase 2 study. In Phase 2 studies, the study treatment is given to a small number of participants with the disease condition to gather information about the effects of the study treatment in patients.

This study was "open label". This means that both the researchers and the participants knew which treatment was given to which participants.

40 participants underwent a tumor biopsy to check the levels of HER3. Participants were then divided into 2 groups, depending on whether their tumors were HER3 positive or HER3 negative. All participants received a dose of 5.6 milligrams (mg) of HER3-DXd per kilogram (kg) of body weight. It was given as an infusion into blood vessels called veins, once every 3 weeks.

Participants continued to receive treatment until all participants had the opportunity to complete 2 tumor evaluations, and as long as they did not show worsening of cancer, have serious side effects, or ask to be removed from the study. The participants' health was monitored throughout the study.



What was the key result of this study?

The key result from this study is shown for the total group of participants as an average. This summary does not show the results from each individual participant. An individual participant's results could be different from the total group of participants. A full list of the questions the researchers wanted to answer and a detailed presentation of the results can be found on the websites listed at the end of this summary.

How many participants had tumors that completely disappeared or became at least 30% smaller after treatment?

To answer this question, researchers measured the tumors from imaging (scans). Results for the 39 participants with HER3 positive colorectal cancer are presented in the figure below.

Number of participants (percentage) with tumors that completely disappeared or became at least 30% smaller

HER3 positive
2 out of 39 participants (5%)

For the 1 participant with HER negative colorectal cancer, the tumor did not completely disappear or become at least 30% smaller.

The response expected was not achieved and the study was terminated early. However, 2 participants treated with HER3-DXd had their tumors completely disappear or become at least 30% smaller.

What side effects did the study participants have?

Side effects are medical problems (such as a feeling tired) that happened during the study which the study doctor (investigator) thought could be related to the treatments in the study.

Side effects are considered serious if they cause death, are life-threatening, cause lasting problems, or require hospitalization. The website listed at the end of this summary has more information about the side effects that happened in this study.

How many participants had serious side effects?

During the study **23% (9 out of 40)** participants had serious side effects.

The serious side effects that occurred were:

Serious side effects	HER3-DXd (40 participants)
Low levels of neutrophils* with fever	5% (2 out of 40)
Nausea	5% (2 out of 40)
Kidney damage	3% (1 out of 40)
Anemia	3% (1 out of 40)
Scarring of the lungs	3% (1 out of 40)
Decreased platelet** count	3% (1 out of 40)
Inflammation in the lungs	3% (1 out of 40)
Bleeding from the bottom	3% (1 out of 40)

*Neutrophils are a type of white blood cell that fight bacteria.
**Platelets are a type of blood cell that prevent or stop bleeding.

There were no deaths due to study treatment.

How many participants had side effects?

All side effects, both serious and non-serious, are presented in this section.

During the study **(93%) 37 out of 40** participants had side effects.

The most common side effects that occurred in at least 10% (1 out of 10) of participants were:

Side effects	HER3-DXd (40 participants)
Feeling tired	45% (18 out of 40)
Nausea	45% (18 out of 40)
Decrease in appetite	40% (16 out of 40)
Decreased neutrophil* count	33% (13 out of 40)
Diarrhea	33% (13 out of 40)
Decreased platelet** count	30% (12 out of 40)
Anemia	23% (9 out of 40)
Vomiting	20% (8 out of 40)
Hair loss	18% (7 out of 40)
Decreased white blood cell count	15% (6 out of 40)
Decreased lymphocyte*** count	13% (5 out of 40)
Low levels of neutrophils* with fever	10% (4 out of 40)
Constipation	10% (4 out of 40)
Rash	10% (4 out of 40)
Inflammation of the mouth and lips	10% (4 out of 40)

*Neutrophils are a type of white blood cell that fight bacteria.
**Platelets are a type of blood cell that prevent or stop bleeding.
***Lymphocytes are a type of white blood cell that help the body fight infection and disease.

How many participants had to stop treatment because of side effects?

During the study **(10%) 4 out of 40** of participants stopped treatment early because of side effects.

How was this study useful for patients and researchers?

This study helped researchers learn about the effects of HER3-DXd in participants with advanced or metastatic colorectal cancer who did not respond to at least 2 prior therapies. The researchers could not conclude the effects of HER3-DXd in participants as the study was stopped earlier than planned. The study was stopped early because the number of participants who responded to treatment was lower than expected during the initial part of the study.

This study also helped researchers learn about the safety of HER3-DXd when given to participants with advanced or metastatic colorectal cancer. HER3-DXd at the current dose was found to have acceptable and manageable safety similar to what is found in other types of cancer.

Other studies of HER3-DXd are ongoing.

Please remember, this summary only shows the results of a single study. Other studies may have different findings. Please talk to a doctor before changing any treatment you are taking or if you have any questions about these study results.

Where can I learn more about this study?

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

- www.clinicaltrials.gov: Use the NCT identifier NCT04479436 in the search field.
- www.clinicaltrialsregister.eu/ctr-search/search: Use the EudraCT identifier 2019-004418-32 in the search field.

Please remember that the results on these websites may be presented in a different way. If you were a study participant and have questions about the results of this study, please speak with the doctor or staff at your study site.

Full study title: A multicenter, open-label, phase 2 study to evaluate safety and efficacy of U3-1402 in subjects with advanced or metastatic colorectal cancer (CRC)	**Sponsor:** Daiichi Sankyo, Inc. **Sponsor contact information:** 211 Mount Airy Road, Basking Ridge, NJ 07920 **Email:** CTRInfo@dsi.com **Phone number:** 1-908-992-6640 **Date of this summary:** 11 January 2024

This summary was prepared by Syneos Health.