AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca K.K.

Treatment Studied: Cotadutide

Study Purpose: This study was done to learn about the safety of cotadutide in Japanese participants with obesity and type 2 diabetes mellitus

Protocol Number: D5671C00003

Thank you

Thank you for taking part in the clinical study for the study drug cotadutide, also called MEDI0382.

AstraZeneca K.K. sponsored this study and believes it is important to share the results. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you.

If you participated in the study and have questions about the results, please speak with the study doctor or staff at your study site.

Who took part in this study?

The researchers asked for the help of Japanese men and women with obesity and type 2 diabetes mellitus, also called T2DM. The participants in this study were 34 to 69 years old when they joined.

The study included 16 participants in Japan.

Why was the research needed?

Researchers are looking for a different way to treat obesity and T2DM. Before a drug can be approved for people to take, researchers do clinical studies to find out how safe it is and how it works.

T2DM is a condition that causes high levels of blood sugar, also called glucose. In people with T2DM, a hormone called insulin does not work as well as it does in people without T2DM. When insulin works properly, it helps keep the blood sugar levels from getting too high. Some people with T2DM also have obesity, which can contribute to their health problems. In people with T2DM, weight loss may help to lower blood sugar levels and reduce the risk of having other health problems.

The study drug, cotadutide, was designed to lower blood sugar levels by helping the body to produce more insulin. It also slows digestion and reduces appetite, which may lead to some weight loss.

In this study, the researchers wanted to find out about the safety of cotadutide in Japanese participants with obesity and T2DM.

What was the purpose of this study?

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

- What signs and symptoms did the participants have?
- What medical problems did the participants have during the study?

The answers to these questions are important to know before other studies can be done to find out if cotadutide helps improve the health of people with obesity and T2DM.

What treatments did the participants take?

In this study, all of the participants took cotadutide or a placebo through a needle under the skin. This is also known as a subcutaneous injection.

A placebo looks like a drug but does not have any medicine in it. Researchers use a placebo to help make sure any of the effects they see in the participants who take the drug are actually caused by the drug.

This was a "double-blind" study. This means none of the participants, researchers, study doctors, or other study staff knew what treatment each participant was taking. Some studies are done this way because knowing what treatment the participants are taking can affect the results of the study. When the study ended, the research sponsor found out which treatment the participants took so they could create a report of the study results.

A computer program was used to randomly choose the treatment each participant took. This helps make sure the groups are chosen fairly. Researchers do this so that comparing the results of each treatment is as accurate as possible.

The participants who took cotadutide took increasing doses throughout the study. The doses were measured in micrograms, also known as µg.

The table below shows the treatments that the participants took during the study.

	Cotadutide	Placebo
	12 participants	4 participants
	• Injections under the skin • 50 µg to 600 µg of cotadutide in each injection	• Injections under the skin • Placebo in each injection
	1 injection every day	1 injection every day

What happened during this study?

The study started in January 2020 and ended in July 2020.

Before the participants took study treatment, they visited their study site 2 times. This part of the study lasted for 3.5 weeks. At these visits, the study doctors checked to make sure the participants could join the study. The study doctors:

- did a physical exam and asked about the participants' medications and any medical problems they were having
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG
- asked the participants to wear a device that measured their blood pressure for a period of 24 hours

The study doctors also did these tests and measurements throughout the study.

At these visits, the study doctors showed the participants how to give themselves injections of the study treatment. The participants also started wearing a device to measure sugar levels in their body. This is called continuous glucose monitoring, also known as CGM.

While the participants took study treatment, they visited their study site 17 times. This part of the study lasted 10 weeks. During this time, the participants:

- took cotadutide or the placebo every day, either by getting 1 injection from the study doctors or by giving themselves 1 injection at home
- stayed overnight at their study site for several of their study visits
- kept a diary of their symptoms and wore their CGM device

After the participants took study treatment, they visited their study site 1 time about 4 weeks after their last dose.

What were the results of this study?

This is a summary of the main results from this study overall. The results each participant had might be different and are not in this summary.

Researchers look at the results of many studies to decide which treatments work best and are safest. Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

The websites listed at the end of this summary may have a full report of the study results.

What signs and symptoms did the participants have during the study?

To answer this question, the study doctors did tests and measurements throughout the study.

The study doctors:

- did physical exams
- tested the participants' blood and urine samples
- checked the participant's heart health using ECGs

Overall, the researchers found that the participants did have some changes in their heart health during the study. The participants who took cotadutide had a slightly faster heart rate and lower blood pressure than the participants who took the placebo.

The researchers found that there were some small changes in the results of the participants' other tests and measurements during the study. But, the researchers did not consider these to be significant.

The study doctors also kept track of the "adverse events" that the participants had. An adverse event is any sign or symptom that participants have during a study. Doctors keep track of all the adverse events that happen in studies, even if they do not think the adverse events might be related to the study treatments.

Later in this document, there will be a summary of the adverse events that the study doctors thought might be related to the study treatments. This section is a summary of all the adverse events, whether they might be related to the study treatments or not. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care.

Adverse events may or may not be caused by the treatments in the study. A lot of research is needed to know whether a treatment causes an adverse event.

During the study:

- 91.7% of participants who took cotadutide had adverse events. This was 11 out of 12 participants.
- 25.0% of participants who took the placebo had adverse events. This was 1 out of 4 participants.
- None of the participants had serious adverse events or stopped taking study treatment due to adverse events.

The most common adverse events, which were seen in more than 2 participants, were:

- Nausea
- Constipation
- Pain in the abdomen
- A low number of red blood cells, which take oxygen to the whole body

What medical problems happened during this study?

This section is a summary of the medical problems the participants had during the study that the study doctors thought might be related to the study treatments. These medical problems are called "adverse reactions". An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or requires hospital care.

These adverse reactions may or may not be caused by the study treatments. A lot of research is needed to know whether a treatment causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for cotadutide.

The websites listed at the end of this summary may have other information about adverse reactions or other medical problems that happened during this study.

Did any adverse reactions happen during this study?

During the study:

- 83.3% of participants who took cotadutide had adverse reactions. This was 10 out of 12 participants.
- 25.0% of participants who took the placebo had adverse reactions. This was 1 out of 4 participants.
- None of the participants had serious adverse reactions or stopped taking study treatment due to adverse reactions.

What serious adverse reactions happened during this study?

None of the participants had serious adverse reactions during this study.

What adverse reactions happened during this study?

The most common adverse reaction was nausea.

The table below shows the adverse reactions that happened during the study.

Adverse reactions

Adverse reaction	Cotadutide (out of 12 participants)	Placebo (out of 4 participants)
Nausea	66.7% (8)	0.0% (0)
Constipation	33.3% (4)	0.0% (0)
Pain in the abdomen	25.0% (3)	0.0% (0)
Diarrhea	8.3% (1)	0.0% (0)
Feeling hot	8.3% (1)	0.0% (0)
High levels of ketones in the urine	8.3% (1)	0.0% (0)
Indigestion	8.3% (1)	0.0% (0)
Redness of the skin at the injection site	8.3% (1)	0.0% (0)
Vomiting	8.3% (1)	0.0% (0)
Soft stools	0.0% (0)	25.0% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of cotadutide in Japanese participants with obesity and T2DM.

Researchers look at the results of many studies to decide which treatments work best and are safest. This summary shows only the main results from this 1 study. Other studies may provide new information or different results.

Further clinical studies with cotadutide are planned.

Where can I learn more about this study?

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

- www.clinicaltrials.gov Once you are on the website, type **"NCT04208620"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D5671C00003"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase 1 Randomized, Blinded, Placebo-controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of Cotadutide in Japanese Obese Subjects with Type 2 Diabetes Mellitus

AstraZeneca Protocol Number: D5671C00003

National Clinical Trials number: NCT04208620

AstraZeneca, K.K. sponsored this study and has its headquarters at Osaka, Japan.

The phone number for the AstraZeneca Information Center is +1-877-240-9479.

Thank you

Clinical study participants and their families belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting participants for clinical studies, nor is it involved in conducting clinical studies.

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