AstraZeneca

Clinical Study Results

Research Sponsor: MedImmune, a wholly owned subsidiary of AstraZeneca

Drug Studied: Cotadutide

Study Purpose: This study was done to learn about the safety of cotadutide in participants with obesity and non-alcoholic fatty liver disease or non-alcoholic steatohepatitis

Protocol Number: D5671C00002

Thank you

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

You and all of the participants helped researchers learn more about cotadutide to help people with obesity and either:

- non-alcoholic fatty liver disease, also called NAFLD
- non-alcoholic steatohepatitis, also called NASH

MedImmune, a wholly owned subsidiary of AstraZeneca, sponsored this study and believes it is important to share the results of the study with you and the public. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you. We hope it helps you understand and feel proud of your important role in medical research.

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

Overview of this study

Why was the research needed?

Researchers are looking for a better way to treat people with obesity and NAFLD or NASH. 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.

What treatments did the participants take?

The participants in this study took cotadutide or a placebo. A placebo looks like a drug but does not have any medicine in it.

What were the results of this study?

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

- **What signs and symptoms did the participants have?**

  The most common symptom that the participants reported during this study was nausea.

- **What medical problems happened during this study?**

  Overall, there were 55.4% of participants who had medical problems that the study doctors thought might be related to the study drug during the study. This was 41 out of 74 participants. The most common medical problem was nausea.

More details about the results of this study are included later in this summary.

Where can I learn more about this study?

You can find more information about this study on the websites listed on the last page. When a full report of the study results is available, it also can be found on those websites.

Who took part in this study?

The researchers asked for the help of men and women with obesity and either:

- non-alcoholic fatty liver disease, also called NAFLD
- non-alcoholic steatohepatitis, also called NASH

The participants in this study were 21 to 79 years old when they joined. The participants in this study had:

- a body mass index, also called BMI, of more than 30 kilograms per meter squared.
- evidence of NAFLD or NASH from a magnetic resonance imaging scan, also called an MRI scan.

If the participants had diabetes, they had to meet certain criteria for how well their diabetes was controlled, and what medications they were taking.

The study included 74 participants in the United States and Puerto Rico.

Why was the research needed?

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

In this study, the researchers wanted to find out if cotadutide works in a small number of participants with obesity and NAFLD or NASH. They also wanted to find out if the participants had any medical problems during the study.

Some people with obesity can have inflammation and a build-up of fat in their liver. This is often linked to drinking alcohol. When it is not linked to drinking alcohol, it is called NAFLD. The build-up of liver fat can increase the risk of health problems such as liver disease and other diseases including heart attack and stroke. NASH is a type of NAFLD. Patients with NASH can have inflammation of the liver and liver damage, in addition to fat in their liver. Obesity can cause NAFLD and NASH. NAFLD and NASH can be more dangerous for people with obesity who already have an increased risk of liver disease and heart disease.

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. It is an established treatment for diabetes that improves control of blood sugar and fat levels in the body. Researchers think that cotadutide may help patients with obesity and NAFLD or NASH.

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

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 this 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 NAFLD or NASH.

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 if the participants took cotadutide or the placebo. 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 doses of cotadutide increased about every 2 weeks. The doses were measured in micrograms, also known as µg.

The chart below shows the treatments that the researchers planned to study.

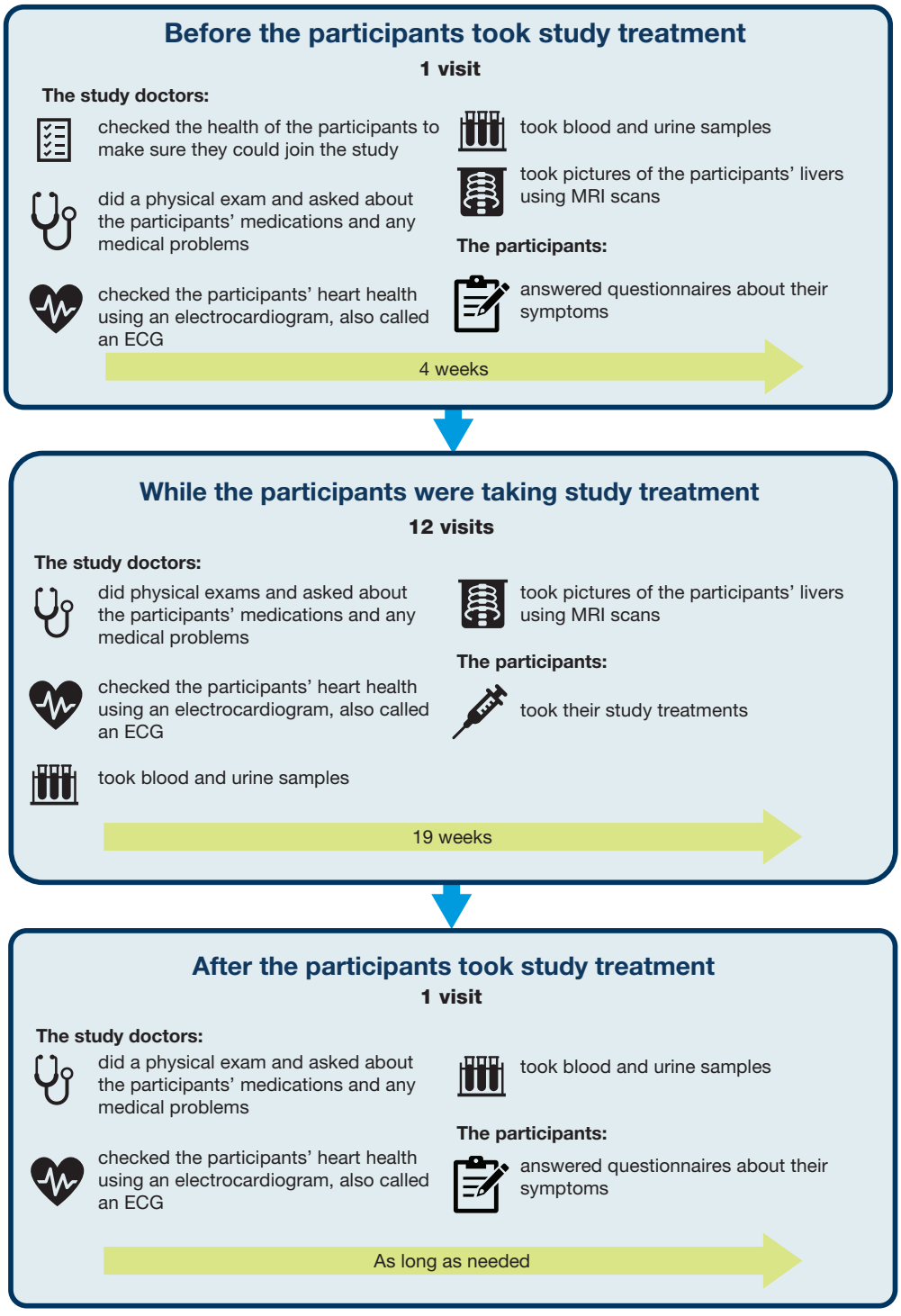
	50 participants	24 participants
	• starting at 50 µg of cotadutide and up to either 300 µg or 600 µg of cotadutide in each dose • injections under the skin	• placebo • injections under the skin
	1 injection every day for 19 weeks	

What happened during this study?

The participants were in the study for up to 6 months. But, the entire study took just over 19 months to finish.

The study started in September 2019 and ended in May 2021.

The chart below shows what happened during the study.



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. A full list of the questions that researchers wanted to answer can be found on the websites listed at the end of this summary. When 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 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.

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

To answer this question, the study doctors did tests and measurements throughout the study. The study doctors did physical exams and tested the participants' blood and urine samples to check their overall health. 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 treatment.

Later in this document, there will be a summary of the adverse events that the study doctors thought might be related to the study treatment. This section is a summary of all the adverse events, whether they might be related to the study treatment 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.

In the table below, the results for all the participants who took cotadutide are grouped together, and the results for all the participants who took the placebo are grouped together.

	Cotadutide (out of 50 participants)	**Placebo (out of 24 participants)**
How many participants had adverse events?	84.0% (42)	37.5% (9)
How many participants had serious adverse events?	4.0% (2)	4.2% (1)
How many participants stopped taking study treatment due to adverse events?	12.0% (6)	4.2% (1)

There were 4.1% of participants who had serious adverse events. This was 3 out of 74 participants.

The serious adverse events were:

- Appendicitis, which is an inflammation of the appendix
- Diverticulitis, which is a disease affecting the gut
- Fainting

There were 68.9% of participants who had adverse events. This was 51 out of 74 participants.

The most common adverse events were:

- Nausea
- Vomiting
- Reduced appetite
- Diarrhea
- Headache
- A reaction at the site of the injection
- Urinary tract infection
- Bloating of the abdomen

There were 8.1% of participants who stopped getting study treatment due to adverse events. This was 6 out of 74 participants.

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 drug. 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 drug. A lot of research is needed to know whether a drug 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?

	Cotadutide (out of 50 participants)	**Placebo (out of 24 participants)**
How many participants had adverse reactions?	66.0% (33)	33.3% (8)
How many participants had serious adverse reactions?	0.0% (0)	0.0% (0)
How many participants stopped taking study treatment due to adverse reactions?	12.0% (6)	4.2% (1)

What serious adverse reactions happened during this study?

None of the participants had a serious adverse reaction.

What adverse reactions happened during this study?

The most common adverse reaction was nausea.

The table below shows the adverse reactions that happened in 10.0% or more of participants during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions

Adverse reaction	Cotadutide (out of 50 participants)	Placebo (out of 24 participants)
Nausea	60.0% (30)	8.3% (2)
Vomiting	26.0% (13)	0.0% (0)
Reduced appetite	20.0% (10)	4.2% (1)
Diarrhea	12.0% (6)	4.2% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of cotadutide in participants with obesity and NAFLD or NASH.

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 one 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. When a full report of the study results is available, it can also be found here.

- www.clinicaltrials.gov Once you are on the website, type **"NCT04019561"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D5671C00002"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase 2, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Pharmacodynamic Effects of MEDI0382 in Obese Subjects With Non-alcoholic Fatty Liver Disease (NAFLD)/ Non-alcoholic Steatohepatitis (NASH)

MedImmune Protocol Number: D5671C00002

National Clinical Trials Number: NCT04019561

MedImmune sponsored this study and has its headquarters in Gaithersburg, MD, USA

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

Thank you

Clinical study participants 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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