Clinical Study Results

MedImmune
A member of the AstraZeneca Group

Research Sponsor: MedImmune Ltd., a wholly owned subsidiary of AstraZeneca

Drug Studied: MEDI0382, also known as cotadutide

Study Title: A study to learn about the safety of MEDI0382 in participants with type 2 diabetes who are overweight or obese

Thank you!

Thank you for taking part in the clinical study for the study drug MEDI0382, also called cotadutide. You and all of the participants helped researchers learn more about MEDI0382 to help people with type 2 diabetes mellitus, also called T2DM.

MedImmune Ltd., an AstraZeneca company, sponsored this study and thinks 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 doctor or staff at your study site.

What is happening with the study now?

The participants were in the study for about 4 months, but the entire study took about 5 months to finish. The study started in January 2019 and ended in May 2019.

This study included a total of 20 participants in Germany.

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

Why was the research needed?

Researchers are looking for a better way to treat T2DM in people who are overweight or obese. Before a drug can be approved for patients to take, researchers do clinical studies to find out how safe it is and to find out if 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 are also overweight, 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, MEDI0382, 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 MEDI0382 in a small number of participants with T2DM who were overweight or obese. They also wanted to find out if it causes any changes to their health.

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

- Did MEDI0382 affect the participants' overall health?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of men and women with T2DM who were overweight or obese. The participants in this study were 58 to 74 years old.

What kind of study was this?

This was a “double-blind” study. This means none of the participants, study doctors or other study staff knew what treatment each participant got.

In this study, MEDI0382 was compared with a placebo. A placebo looks like a drug but does not have any medicine in it. Researchers use a placebo to help make sure that any of the effects they see in the participants who get the study drug are actually related to the study drug.

A computer program was used to randomly choose the treatment each participant got. 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.

During the study, the participants got MEDI0382 or the placebo once a day through a needle under the skin, also called an injection. Some injections were given at the study site, and some were done by the participants at home. The doses of MEDI0382 were measured in micrograms, also known as µg.

There were 2 groups in this study. Each group got either the placebo or increasing doses of MEDI0382 for up to 8 weeks. The chart below shows the treatments in each group.

	Group 1 **(8 participants)**	**Group 2** **(12 participants)**
MEDI0382	**6 participants** • Starting dose of 20 µg injection once a day • Then, increasing doses up to 600 µg each day • The participants stayed on each dose for 7 days	**9 participants** • Starting dose of 20 µg injection once a day • Then, increasing doses up to 600 µg each day • The participants stayed on each dose for 7 days
Placebo	**2 participants** • An injection of the placebo once each day	**3 participants** • An injection of the placebo once each day

Group 1: At each MEDI0382 dose, the study doctors checked if any participants had any changes in their health. Then, the researchers decided whether or not to give the participants a higher dose of MEDI0382. The researchers stopped increasing the dose of MEDI0382 if the participants had health problems.

Group 2: The participants in Group 2 got the same increasing doses of MEDI0382 or the placebo as the participants in Group 1. But, the participants in Group 2 only got those doses of MEDI0382 that had not caused participants in Group 1 any health problems. Group 2 started the study at least 7 days after Group 1.

In both groups, the researchers found that the highest dose of 600 µg of MEDI0382 did not cause the participants any significant health problems. So, once the participants got 600 µg of MEDI0382 for 7 days, they continued to get this dose once a day for another 3 weeks. The participants getting the placebo continued getting the placebo for these 3 weeks.

In total, the participants got study treatment for up to 11 weeks during the study.

What happened during the study?

Before the participants got study treatment, they visited the study site about 2 times. At these visits, the study doctors checked the overall health of the participants to make sure that they could join the study. The study doctors:

- did a physical exam, measured the participants' weight, and checked vital signs
- took blood and urine samples
- asked about the participants' medical history
- checked the participants' heart health using an electrocardiogram, also called an ECG
- gave the participants a device called a glucometer to measure blood glucose levels by pricking their finger
- fitted a wearable sensor called a continuous glucose monitoring device, or a CGM device, to monitor the participants' blood glucose levels
- fitted a device to monitor the participants' blood pressure for 24 hours

While the participants got study treatment, they visited the study site up to 11 times. The study doctors checked the participants' health and did these same tests and measurements as mentioned above throughout the study.

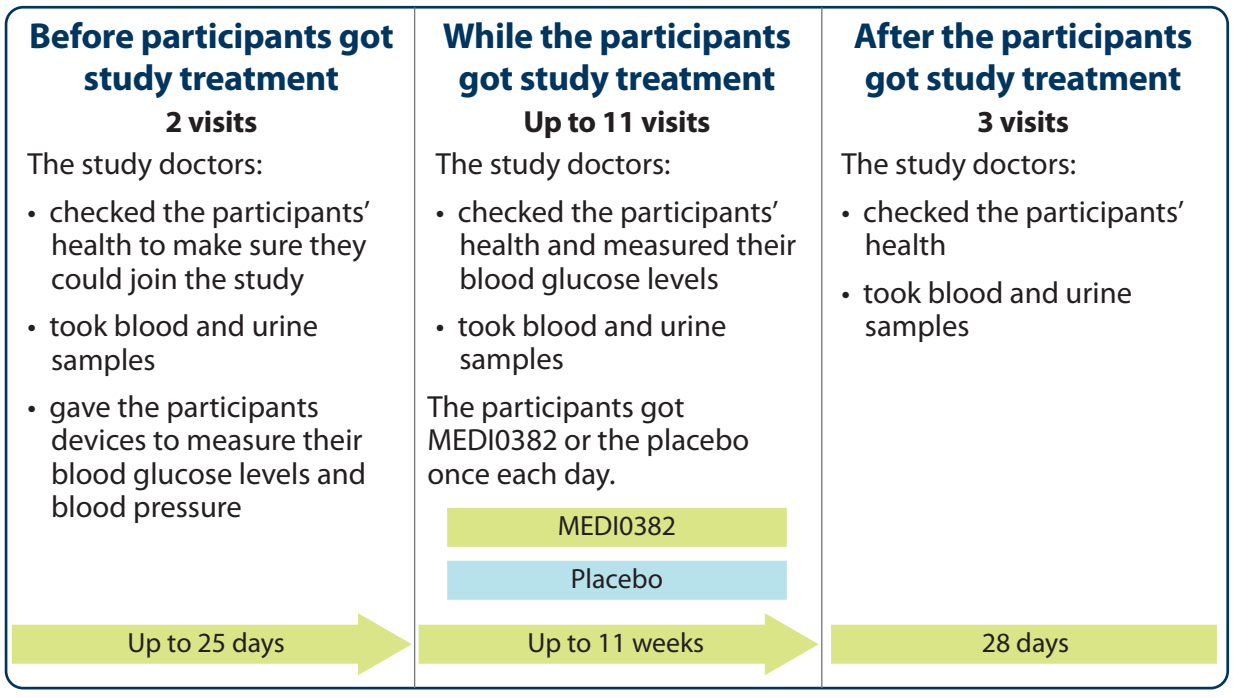
At some visits, the participants stayed at the study site for several days.

When the participants visited the study site, the study doctors or study staff gave them their injections and checked their glucose levels. When the participants were at home, they took their injections once a day and wore their CGM device the whole time. They also kept track of any medical problems in a diary.

After the participants finished getting study treatment, they visited their study site another 3 times. At some of these visits, the study doctors:

- did a physical exam, measured the participants' weight, and checked vital signs
- took blood and urine samples
- did an ECG
- asked about the participants' health and any medications they were taking

The chart below shows what happened during the study.



What were the results of the 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 the 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 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.

Did MEDI0382 affect the participants' overall health?

To answer this question, the researchers studied the results of the participants' tests and measurements before and after they took study treatment. Then they compared the results for the participants who took MEDI0382 and those who took the placebo.

Overall, the researchers found that there were no significant changes in the results of the blood and urine tests, physical exams, and ECG tests between participants who got MEDI0382 and those who got placebo.

But, the researchers found that the participants who got MEDI0382 had an increase in heart rate compared with those participants who got the placebo. At the end of the study, the participants who got MEDI0382 had their heart rate increase by an average of 14 beats per minute.

The 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.

An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant requires hospital care.

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

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 drug.

This section is a summary of all the adverse events, whether they might be related to the study drug or not. Later in this document, there will be a summary of the adverse events that the study doctors thought might be related to the study drug.

How many participants had adverse events?

In this study:

- 95% of participants had adverse events. This was 19 out of 20 participants.
- None of the participants had serious adverse events.
- 15% of participants stopped taking the study treatment because of adverse events. This was 3 out of 20 participants.

Most common adverse events

The most common adverse events in this study were constipation and injection site reactions.

The table on the next page shows the most common adverse events that happened in 2 or more participants during the study. There were other adverse events, but these happened in fewer participants.

Most common adverse events during the study

	Group 1		Group 2		
Adverse event	**MEDI0382 (out of 6 participants)**	**Placebo (out of 2 participants)**	**MEDI0382 (out of 9 participants)**	**Placebo (out of 3 participants)**	**Total (out of 20 participants)**
Constipation	66.7% (4)	0.0% (0)	22.2% (2)	33.3% (1)	35.0% (7)
Injection site reactions	50.0% (3)	0.0% (0)	44.4% (4)	0.0% (0)	35.0% (7)
Common cold	33.3% (2)	50.0% (1)	11.1% (1)	66.7% (2)	30.0% (6)
Bloated stomach	16.7% (1)	50.0% (1)	22.2% (2)	33.3% (1)	25.0% (5)
Diarrhea	33.3% (2)	0.0% (0)	33.3% (3)	0.0% (0)	25.0% (5)
Indigestion	0.0% (0)	0.0% (0)	44.4% (4)	33.3% (1)	25.0% (5)
Feeling of fullness	0.0% (0)	0.0% (0)	44.4% (4)	0.0% (0)	20.0% (4)
Loss of appetite	66.7% (4)	0.0% (0)	0.0% (0)	0.0% (0)	20.0% (4)
Skin redness at the injection site	33.3% (2)	0.0% (0)	22.2% (2)	0.0% (0)	20.0% (4)
Nausea	33.3% (2)	0.0% (0)	11.1% (1)	0.0% (0)	15.0% (3)
Feeling of spinning surroundings	16.7% (1)	0.0% (0)	11.1% (1)	0.0% (0)	10.0% (2)
Light-headedness or feeling of fainting	16.7% (1)	0.0% (0)	11.1% (1)	0.0% (0)	10.0% (2)
Stomach pain	0.0% (0)	0.0% (0)	22.2% (2)	0.0% (0)	10.0% (2)
Tiredness	0.0% (0)	0.0% (0)	22.2% (2)	0.0% (0)	10.0% (2)

What medical problems did participants have during the 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.

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

How many participants had serious adverse reactions?

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

How many participants had adverse reactions?

There were 85.0% of participants who had adverse reactions during the study. This was 17 out of 20 participants.

- 93.3% of participants who got MEDI0382 had adverse reactions during the study. This was 14 out of 15 participants.
- 60.0% of participants who got the placebo had adverse reactions during the study. This was 3 out of 5 participants.

There were 10.0% of participants who stopped taking the study treatment because of adverse reactions they had during the study. This was 2 out of 20 participants. Both of these participants got MEDI0382.

What adverse reactions did the participants have?

The most common adverse reactions were constipation and injection site reactions.

The table below shows the most common adverse reactions that happened in 2 or more participants during the study. There were other adverse reactions, but these happened in fewer participants. All of these adverse reactions are also listed in the adverse events section earlier in this summary.

Most common adverse reactions during the study

	Group 1		Group 2		
Adverse reaction	**MEDI0382 (out of 6 participants)**	**Placebo (out of 2 participants)**	**MEDI0382 (out of 9 participants)**	**Placebo (out of 3 participants)**	**Total (out of 20 participants)**
Constipation	66.7% (4)	0.0% (0)	22.2% (2)	33.3% (1)	35.0% (7)
Injection site reactions	50.0% (3)	0.0% (0)	44.4% (4)	0.0% (0)	35.0% (7)
Bloated stomach	16.7% (1)	50.0% (1)	22.2% (2)	33.3% (1)	25.0% (5)
Diarrhea	33.3% (2)	0.0% (0)	33.3% (3)	0.0% (0)	25.0% (5)
Feeling of fullness	0.0% (0)	0.0% (0)	44.4% (4)	0.0% (0)	20.0% (4)
Indigestion	0.0% (0)	0.0% (0)	44.4% (4)	0.0% (0)	20.0% (4)
Loss of appetite	66.7% (4)	0.0% (0)	0.0% (0)	0.0% (0)	20.0% (4)
Skin redness at the injection site	33.3% (2)	0.0% (0)	22.2%(2)	0.0% (0)	20.0% (4)
Nausea	33.3% (2)	0.0% (0)	11.1% (1)	0.0% (0)	15.0% (3)
Feeling of spinning surroundings	16.7% (1)	0.0% (0)	11.1% (1)	0.0% (0)	10.0% (2)
Stomach pain	0.0% (0)	0.0% (0)	22.2% (2)	0.0% (0)	10.0% (2)
Tiredness	0.0% (0)	0.0% (0)	22.2% (2)	0.0% (0)	10.0% (2)

How has this study helped patients and researchers?

This study helped researchers learn about the safety of different doses of MEDI0382 in participants with T2DM who were overweight or obese.

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 the study drugs are planned.

Where can I learn more about this 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.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT03745937"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5670C00030"** into the search box, and click **"Find a Study"**.

Full study title: A Phase 2a Randomized, Blinded, Placebo-controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of MEDI0382 in Overweight/Obese Subjects with Type 2 Diabetes Mellitus

National Clinical Trials number: NCT03745937

AstraZeneca Protocol Number: D5670C00030

MedImmune Limited, a wholly owned subsidiary of AstraZeneca, sponsored this study and has its headquarters in Cambridge, United Kingdom.

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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