Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca

Drug Studied: MEDI0382

Study Title: A study to learn how MEDI0382 affects the blood sugar levels and weight of participants who have type 2 diabetes

Thank you!

Thank you to the participants who took part in the clinical study for the study drug MEDI0382. All of the participants helped researchers learn more about using MEDI0382 to help people who have type 2 diabetes and are overweight or have obesity.

AstraZeneca sponsored this study and thinks it is important to share the results of the study with the participants and the public. An independent non-profit organization called CISCRP helped prepare this summary of the study results. We hope it helps the participants understand and feel proud of their 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 study started in August 2017 and ended in June 2019. It included 834 participants in Bulgaria, Canada, the Czech Republic, Germany, Mexico, Russia, Slovakia, and the United States.

The participants were in the study for a little less than 2 years. But, the entire study took about 2 years to finish.

When the study ended, the sponsor reviewed the data collected 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 people who have type 2 diabetes and are overweight or have obesity. Before a drug can be approved for patients to take, researchers need to do clinical studies to find out how it works and how safe it is.

In people who have type 2 diabetes, the body does not use insulin as well as it should. Insulin is a hormone made by the pancreas that controls the levels of sugar in the blood. If a person's blood sugar levels become too high, he or she can have medical problems. High blood sugar can also increase food cravings and decrease energy levels. This can lead to weight gain.

In this study, the researchers wanted to learn how MEDI0382 affects the blood sugar levels and weight in participants who have type 2 diabetes and are overweight or have obesity. They also wanted to find out if the participants had any medical problems during the study.

The participants in this study were already taking a drug called metformin to help control their blood sugar levels. Metformin works by decreasing the amount of blood sugar that the body creates and helps the body better respond to insulin. But metformin was not developed to control food cravings or energy levels. Also, metformin may not control the blood sugar levels or weight in some people who have diabetes.

The study drug, MEDI0382, is being developed to help people who have type 2 diabetes control their blood sugar levels. It was designed to help the body make insulin, control food cravings, and increase energy levels.

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

- Did MEDI0382 help lower the participants' blood sugar levels?
- Did MEDI0382 affect the participants' weight?
- 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 who had type 2 diabetes and were overweight or had obesity. All of the participants were already taking metformin. They were 19 to 82 years old when they joined.

What kind of study was this?

The main focus of this study was to compare the effects of MEDI0382 given with metformin to the effects of metformin given 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 caused by the study drug.

Though it was not the main focus of the study, the researchers also wanted to compare the effects of MEDI0382 given with metformin to the effects of a drug called liraglutide given with metformin. Liraglutide is a treatment for type 2 diabetes that works by helping the body make insulin. In previous clinical studies, some people who had type 2 diabetes who took liraglutide lost weight.

In this study, 612 participants got MEDI0382 through a needle under the skin, also called an injection. The MEDI0382 doses were measured in micrograms, also called µg.

There were also 110 participants who got liraglutide through an injection. The liraglutide doses were measured in milligrams, also called mg.

The other 112 participants in this study got the placebo as an injection.

All of the participants continued taking metformin by mouth throughout the study.

For the participants who got MEDI0382 or the placebo, this was a “double-blind” study. This means none of the participants, doctors, or other study staff knew what treatment each participant got.

For the participants who got liraglutide, this was an “open-label” study. This means the researchers and the participants knew what the participants were getting.

A computer program was used to randomly choose the study 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.

What happened during the study?

Before treatment, the participants visited their study site 2 times over the course of 4 weeks. During this time, the study doctors checked to make sure the participants could join the study.

The study doctors:

- did a physical examination
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG
- checked the participants' blood sugar levels
- asked the participants about their medical history, how they were feeling, and what medicines they were taking

During the first 2 weeks, the participants continued taking metformin and other medicines.

During the next 2 weeks, the participants continued taking metformin but stopped taking certain medicines. This was done so that the participants could continue managing their type 2 diabetes without affecting the study results.

During the study, the participants visited their study site about 16 times over the course of about 12 months. During the first 3 months of this time period, the participants visited their study site 6 times. At each visit, they got MEDI0382, liraglutide, or the placebo 1 time.

All of the participants who got MEDI0382 started at a dose of 100 µg. Once the researchers carefully studied the results, they increased the MEDI0382 dose for some of the participants. There were 3 different doses of MEDI0382:

- 100 participants got 100 µg of MEDI0382 each day
- 256 participants got 200 µg of MEDI0382 each day
- 256 participants got 300 µg of MEDI0382 each day

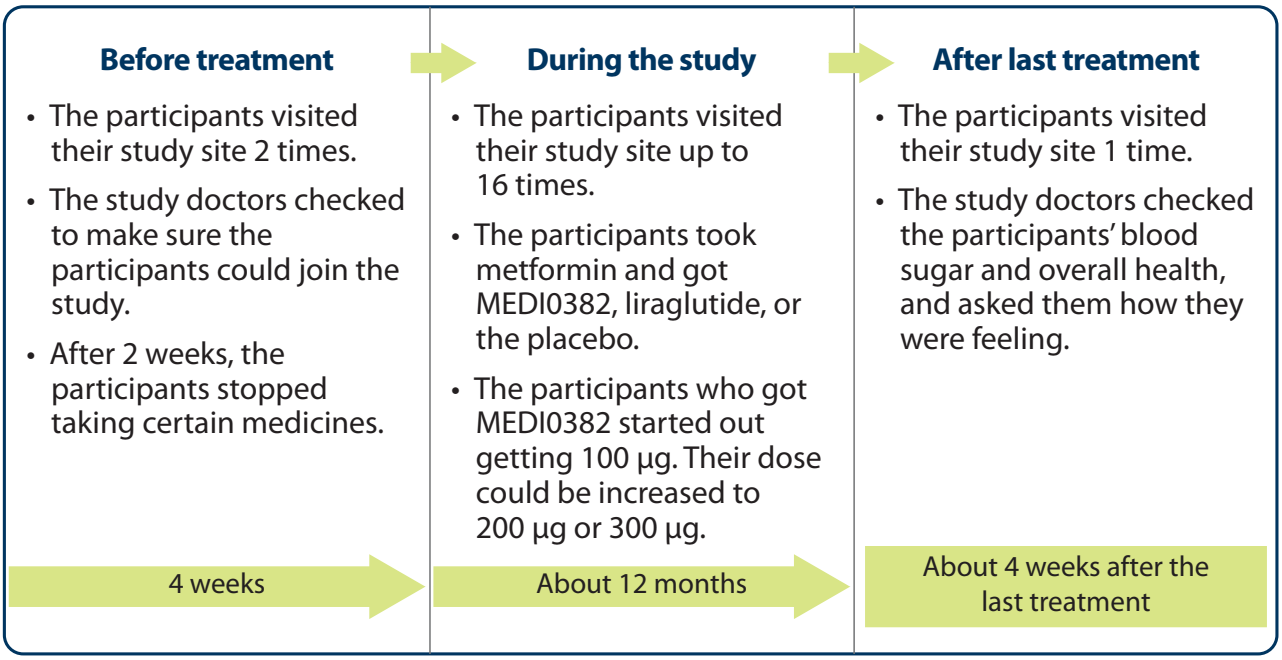
The other participants got either liraglutide or the placebo:

- 110 participants got 1.8 mg of liraglutide each day
- 112 participants got the placebo each day

After the first 3 months, the researchers carefully studied the results. They checked the participants' health and blood sugar levels to make sure they could continue the study. Then, for about 9 months, the participants who were getting MEDI0382 continued taking their same dose of MEDI0382. They visited their study site up to 10 times.

About 4 weeks after their last treatment, the participants visited their study site 1 time. At this visit, the study doctors checked the participants' blood sugar and overall health, and asked them how they were feeling.

The chart below shows how the study was done.



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 help lower the participants' blood sugar levels?

Yes. Overall, the researchers found that the participants who got MEDI0382 had a greater decrease in their blood sugar levels compared to the participants who got the placebo.

To answer this question, the researchers did a hemoglobin A1c test, also called an HbA1c test, of each participant's blood before treatment and throughout the study. The HbA1c test measures how much blood sugar is attached to a protein called hemoglobin, which is found in red blood cells. Since red blood cells live for about 3 months, the HbA1c test measures the average levels of sugar in the blood over the past 3 months.

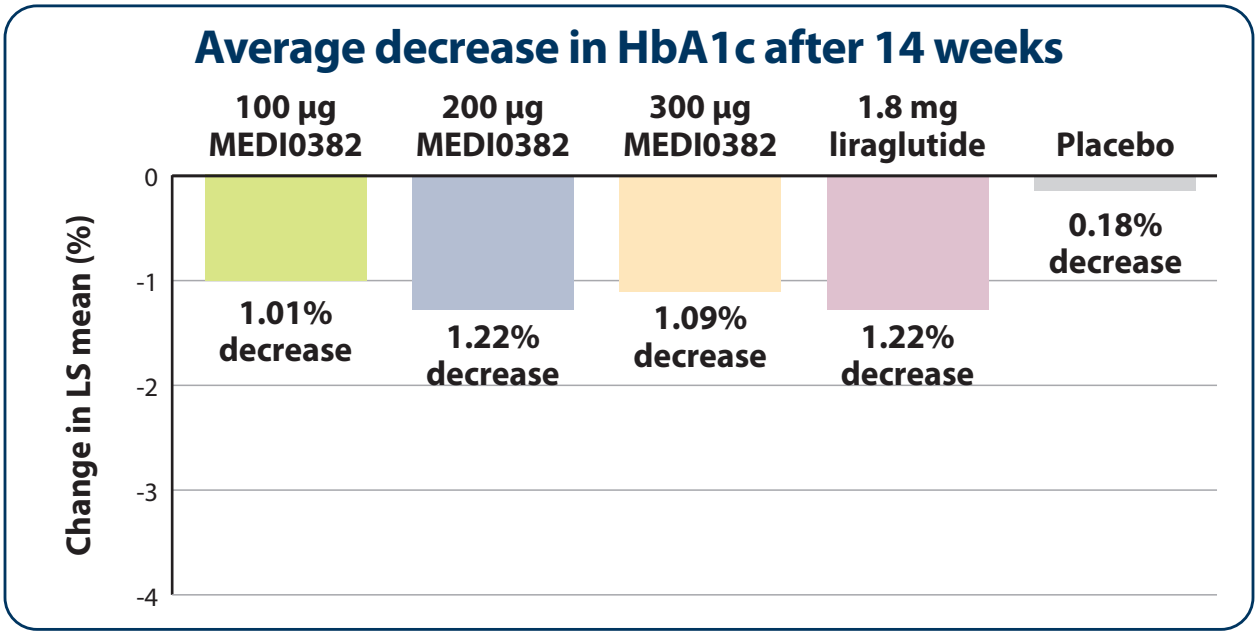
Researchers measure HbA1c by using a percentage. In this study, the researchers calculated the change in the participants' HbA1c after 14 weeks of treatment. This is also called the LS mean method. In this study, the LS mean method helped the researchers accurately measure the change in the participants' blood sugar levels and weight.

The researchers compared the results for the participants who got MEDI0382 to the results for the participants who got the placebo. The results for the participants who got liraglutide are also presented below, but those results were not the main focus of the study.

Overall, the researchers found that after 14 weeks of treatment:

- The participants who got 100 µg of MEDI0382 had an LS mean decrease in their blood sugar levels of 1.01%.
- The participants who got 200 µg of MEDI0382 had an LS mean decrease in their blood sugar levels of 1.22%.
- The participants who got 300 µg of MEDI0382 had an LS mean decrease in their blood sugar levels of 1.09%.
- The participants who got 1.8 mg of liraglutide had an LS mean decrease in their blood sugar levels of 1.22%.
- The participants who got the placebo had an LS mean decrease in their blood sugar levels of 0.18%.

The figure below shows these results.



Did MEDI0382 affect the participants' weight?

Yes. Overall, the researchers found that the participants who got MEDI0382 had a greater decrease in their weight compared to the participants who got the placebo.

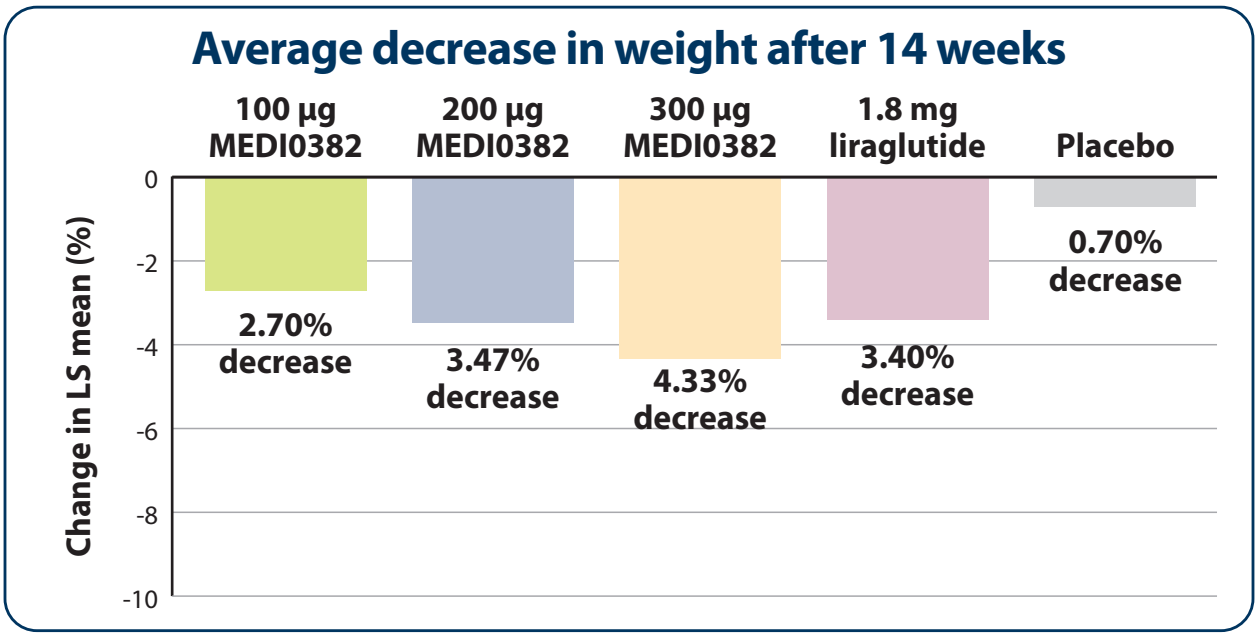
To answer this question, the researchers checked the participants' weight before treatment and throughout the study. Then, they used a percentage to calculate the LS mean change in weight after 14 weeks of treatment.

The researchers compared the results for the participants who got MEDI0382 to the results for the participants who got the placebo. The results for the participants who got liraglutide are also presented below, but those results were not the main focus of the study.

Overall, the researchers found that after 14 weeks of treatment:

- The participants who got 100 µg of MEDI0382 had an LS mean decrease in their weight of 2.70%.
- The participants who got 200 µg of MEDI0382 had an LS mean decrease in their weight of 3.47%.
- The participants who got 300 µg of MEDI0382 had an LS mean decrease in their weight of 4.33%.
- The participants who got 1.8 mg of liraglutide had an LS mean decrease in their weight of 3.40%.
- The participants who got the placebo had an LS mean decrease in their weight of 0.70%.

The figure below shows these results.



What medical problems did the 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 treatment. 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 treatment. A lot of research is needed to know whether a treatment causes an adverse reaction.

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.

How many participants had serious adverse reactions?

There were 0.4% of participants who had serious adverse reactions during the study that the study doctors thought were related to the study treatment. This was 3 out of 834 participants. One of the 3 participants had more than 1 serious adverse reaction.

The serious adverse reactions that happened during the study were:

- Pain in the upper stomach area. This happened in 1 participant who got 200 µg of MEDI0382, and in 1 participant who got the placebo.
- Gallstones. This happened in 1 participant who got 100 µg of MEDI0382, and in 1 participant who got 200 µg of MEDI0382.

None of the participants died due to serious adverse reactions during the study.

How many participants had adverse reactions?

There were 47.7% of participants who had adverse reactions during the study that the study doctors thought were related to the study treatment. This was 398 out of 834 participants.

The table below shows how many participants had adverse reactions during the study.

Adverse reactions during the study

	MEDI0382 100 µg (out of 100 participants)	MEDI0382 200 µg (out of 256 participants)	MEDI0382 300 µg (out of 256 participants)	Liraglutide 1.8 mg (out of 110 participants)	Placebo (out of 112 participants)
How many participants had adverse reactions during the study?	46.0% (46)	57.8% (148)	60.5% (155)	22.7% (25)	21.4% (24)
How many participants had serious adverse reactions during the study?	1.0% (1)	0.4% (1)	0.0% (0)	0.0% (0)	0.9% (1)
How many participants stopped treatment due to adverse reactions?	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	1.8% (2)

What adverse reactions did the participants have?

The most common adverse reaction during the study was nausea.

The table on the next page shows the adverse reactions that happened in at least 10 participants during the study. There were other adverse reactions that happened during the study, but those happened in fewer participants.

Most common adverse reactions during the study

	MEDI0382 100 µg (out of 100 participants)	MEDI0382 200 µg (out of 256 participants)	MEDI0382 300 µg (out of 256 participants)	Liraglutide 1.8 mg (out of 110 participants)	Placebo (out of 112 participants)
Nausea	23.0% (23)	30.9% (79)	38.7% (99)	14.5% (16)	8.9% (10)
Vomiting	9.0% (9)	18.0% (46)	14.5% (37)	0.9% (1)	3.6% (4)
Diarrhea	9.0% (9)	14.5% (37)	8.2% (21)	3.6% (4)	3.6% (4)
Indigestion	7.0% (7)	5.9% (15)	10.2% (26)	2.7% (3)	1.8% (2)
Headache	3.0% (3)	2.0% (5)	6.3% (16)	1.8% (2)	0.9% (1)
Burping	2.0% (2)	4.7% (12)	4.7% (12)	0.0% (0)	0.0% (0)
Decreased appetite	3.0% (3)	3.9% (10)	3.9% (10)	0.9% (1)	0.9% (1)
Dizziness	2.0% (2)	2.7% (7)	3.5% (9)	0.0% (0)	1.8% (2)
Redness at skin injection site	2.0% (2)	2.3% (6)	4.3% (11)	0.9% (1)	0.0% (0)
Passing gas	1.0% (1)	4.7% (12)	2.3% (6)	0.0% (0)	0.9% (1)
Itching at skin injection site	1.0% (1)	3.1% (8)	2.7% (7)	0.0% (0)	0.0% (0)
Constipation	0.0% (0)	2.7% (7)	3.1% (8)	0.9% (1)	0.0% (0)
Decrease in blood sugar	2.0% (2)	1.2% (3)	3.1% (8)	0.0% (0)	0.9% (1)
Feeling bloated	2.0% (2)	2.3% (6)	1.6% (4)	0.9% (1)	0.0% (0)
Stomach discomfort	0.0% (0)	1.2% (3)	2.0% (5)	0.9% (1)	0.0% (0)
Pain in upper stomach area	2.0% (2)	1.2% (3)	2.3% (6)	0.0% (0)	0.9% (1)
General discomfort	1.0% (1)	2.0% (5)	2.0% (5)	0.0% (0)	0.0% (0)
Skin sensitivity at injection site	1.0% (1)	1.6% (4)	2.3% (6)	0.0% (0)	0.0% (0)
Allergic reaction at skin injection site	2.0% (2)	0.8% (2)	2.0% (5)	0.9% (1)	0.0% (0)
Feeling tired	1.0% (1)	2.0% (5)	1.2% (3)	0.0% (0)	0.9% (1)

How has this study helped patients and researchers?

This study helped researchers learn how MEDI0382 affects the blood sugar levels and weight of people who have type 2 diabetes and are overweight or have obesity.

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 MEDI0382 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 **"NCT03235050"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2017-000626-35"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5670C00004"** into the search box, and click **"Find a Study"**.

Full study title: A Phase 2b, Randomised, Parallel, Double-Blind Placebo-Controlled and Open-Label Active Comparator Study to Evaluate the Efficacy and Safety of Cotadutide in the Treatment of Overweight and Obese Subjects with Type 2 Diabetes Mellitus

AstraZeneca Protocol Number: D5670C00004

AstraZeneca AB sponsored this study and has its headquarters in Södertälje, Sweden.

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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