AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: AZD4076

Study Purpose: This study was done to learn how AZD4076 works and about its safety in participants with type 2 diabetes who have non-alcoholic fatty liver disease.

Protocol Number: D5590C00002

Thank you!

Thank you for taking part in the clinical study for the study drug AZD4076.

AstraZeneca 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.

This study happened in 3 groups. This summary shows the results from Group 3. The results from Groups 1 and 2 are in different summaries.

Who took part in this study?

The researchers asked for the help of men and women with type 2 diabetes and non-alcoholic fatty liver disease, also called NAFLD. The participants in this study were 41 to 67 years old when they joined.

The study included 14 participants in the United States.

Why was the research needed?

Researchers are looking for a different way to treat NAFLD in people with type 2 diabetes, also called T2DM. Before a drug can be approved for people to get, researchers do clinical studies to find out how safe it is and how it works.

In people with T2DM, the body does not make enough insulin. Insulin is a hormone that controls the level of blood sugar, which is also called glucose. T2DM causes blood glucose levels to rise higher than normal, which can cause medical problems.

Some people with T2DM can have inflammation and a build-up of fat in their liver that is not linked to drinking alcohol. This is NAFLD. The build-up of liver fat can increase the risk of health problems such as liver disease, but also other diseases including heart attack and stroke. This is even more dangerous for people with T2DM who already have an increased risk of liver disease and cardiovascular disease.

The study drug, AZD4076, was designed to make the body more sensitive to insulin and to reduce fat in the liver. In this study, the researchers wanted to find out more about the safety of AZD4076 in participants with T2DM and NAFLD. They also wanted to find out if AZD4076 changed the amount of blood sugar and liver fat in the participants.

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?
- Did AZD4076 affect the liver fat or the blood sugar of the participants?
- 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 AZD4076 helps improve the health of people with T2DM and NAFLD.

What treatments did the participants get?

In this study, the participants got either AZD4076 or a placebo as an injection through a needle under the skin of the belly. 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 get the drug are actually caused by the drug.

This was a "single-blind" study. This means the researchers, study doctors, and other study staff knew what the participants were getting but the participants did not.

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.

The participants who got AZD4076 in this study got more frequent doses during the first 10 days of treatment compared to doses after. This is called a "loading dose". The doses of AZD4076 were measured in milligrams, also known as mg. The participants in Group 2 got a higher loading dose than the participants in Group 1.

After the loading doses, the study doctors gave the participants a less frequent dose of AZD4076 once a week for the rest of the study. This is called a "maintenance dose".

It was planned to include another group of participants who would get a higher dose of AZD4076 after the loading doses. But, the sponsor decided to end the study early. So, there were only 3 treatment groups.

The chart below shows the treatments the researchers studied.

	Group 1 AZD4076	**Group 2 AZD4076**	**Group 3 Placebo**
	• 6 participants	• 2 participants	• 6 participants
	• 5 loading doses of 20 mg AZD4076 were given every other day • After this, 5 doses of 20 mg AZD4076 were given once a week	• 5 loading doses of 100 mg AZD4076 were given every other day • After this, up to 3 doses of 50 mg AZD4076 were given once a week	• Placebo was given for the same number of injections as for AZD4076
	• Injection under the skin of the belly for up to 6 weeks		

What happened during this study?

The study started in July 2016 and study treatment was stopped in February 2017. The researchers stopped the study early because some study participants had an increase in a liver protein called ALT. The researchers stopped the study to prevent any future increases in ALT in the study participants.

Study participants were monitored up until October 2019. This was done to make sure the study treatment was no longer in the participants' blood.

Before the participants got study treatment, they visited their study site 1 time on 1 day. This part of the study lasted for 6 weeks. At this visit, the study doctors checked the health of the participants to make sure they 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
- took pictures of each participant's liver using magnetic resonance imaging, also called MRI. This was done to measure the amount of fat in the liver
- checked how much sugar was in the participants' blood and measured how well insulin was working in the body using a method called "clamp"

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

While the participants got study treatment, as loading doses followed by maintenance doses, researchers planned that they would visit their study site 8 times. This part of the study was planned to last about 8 weeks.

- The study participants got the study drug for 6 of the 8 weeks.
- There were 3 visits when the participants stayed overnight at the study site.
- There were 3 visits when the participants visited the study site for the day.

After the participants got study treatment, researchers planned that they would visit their study site 4 times. This part of the study lasted about 16 weeks. Some of the participants had more follow up visits. At these visits, the study doctors checked the health of the participants.

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 more information about the study results.

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. They also did ECGs to check the participants' heart health. Overall, the researchers found that some study participants had an increase in a liver protein called ALT. The researchers decided to stop the study to prevent any future increases in ALT in the study participants.

After the study treatment was stopped, all of the participants were monitored until their increased ALT levels had gone back to normal and there was no AZD4076 in the participants' blood.

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 participants who got AZD4076 are grouped together.

	AZD4076 (out of 8 participants)	**Placebo** (out of 6 participants)
How many participants had adverse events?	87.5% (7)	83.3% (5)
How many participants had serious adverse events?	12.5% (1)	0.0% (0)
How many participants stopped getting study treatment due to adverse events?	12.5% (1)	0.0% (0)

The only serious adverse event that happened was chest discomfort.

The most common adverse events were diarrhea, flu-like symptoms, and increased levels of a liver protein called ALT. The participant who had increased levels of ALT stopped getting study treatment.

The researchers also wanted to learn if the participants had a reaction when they received the injection of the study treatment. Other studies with AZD4076 showed that the participants in those studies had a reaction where they were injected.

The researchers found that in this study:

- 25.0% of the participants who got AZD4076 had a reaction where they were injected. This was 2 out of 8 participants.
- 16.7% of the participants who got the placebo had a reaction where they were injected. This was 1 out of 6 participants.

Did AZD4076 affect the liver fat or the blood sugar of the participants?

To answer this question, the study doctors recorded the results of the participants' tests and measurements that were done throughout the study. They measured the amount of fat in the participants' liver using MRI. They also measured the amount of sugar in the participants' blood.

Overall, they found that there were small changes in the results of these tests and measurements during the study. But, the researchers did not consider these to be meaningful.

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 the study drug.

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?

In the table below, the results for all participants who got AZD4076 are grouped together.

Adverse Reactions		
Adverse reaction	**AZD4076** (out of 8 participants)	**Placebo** (out of 6 participants)
Increased level of a liver protein called ALT	37.5% (3)	0.0% (0)
Diarrhea	12.5% (1)	16.7% (1)
Redness at the site of the injection	12.5% (1)	16.7% (1)
Increased level of a liver protein called AST	12.5% (1)	0.0% (0)
Increased liver activity	12.5% (1)	0.0% (0)
Headache	12.5% (1)	0.0% (0)
Uncontrollable eye movements	12.5% (1)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn more about how AZD4076 works and about its safety in participants with T2DM and non-alcoholic fatty liver disease.

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 AZD4076 are not 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 **"NCT02826525"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5590C00002"** into the search box, and click **"Find a Study"**.

Full Study Title: A randomized, single-blind, placebo-controlled study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of AZD4076 following multiple ascending dose administration to Type 2 Diabetes subjects with Non-Alcoholic Fatty Liver Disease.

AstraZeneca Protocol Number: D5590C00002

National Clinical Trials number: NCT02826525

AstraZeneca sponsored this study and has its headquarters at 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.

CISCRP | One Liberty Square, Suite 1100 • Boston, MA 02109 | 1-877-MED-HERO | www.ciscrp.org

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