

Research Sponsor: AstraZeneca

Drug Studied: AZD8233

Study Purpose: This study was done to learn how well different doses of AZD8233 work in people with high levels of low-density lipoprotein cholesterol, also called LDL cholesterol

Protocol Number: D7990C00003

Thank you!

Thank you to the participants who took part in the clinical study for the study drug AZD8233. All of the participants helped researchers learn more about different doses of AZD8233 to help people with high levels of a type of cholesterol known as “low-density lipoprotein cholesterol”, also called LDL cholesterol or “bad” cholesterol.

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 high levels of LDL cholesterol. Before a drug can be approved for people to get, researchers do clinical studies to find out how it works and how safe it is.



What treatments did the participants get?

In this study, the participants either got 1 of 3 doses AZD8233, or a placebo. The participants got AZD8233 or the placebo through a needle under the skin, also known as a “subcutaneous injection”. 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:

- ▶ **How much did the different doses of AZD8233 reduce LDL cholesterol in the blood compared with the placebo?**

Overall, the researchers found that all 3 doses of AZD8233 reduced the levels of LDL cholesterol in the blood compared with the placebo.

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

There were 15.1% of participants who had medical problems that the study doctors thought might be related to the study drug during the study. The most common medical problem was pain around the area of the body where the injection was given.

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 high levels of a type of cholesterol known as “low-density lipoprotein cholesterol”, also called LDL cholesterol or “bad” cholesterol.

The participants in this study were 40 to 75 years old when they joined.

All of the participants had been diagnosed with high levels of LDL cholesterol and were taking LDL cholesterol-lowering drugs called “statins”. Participants were unable to take part if it was known that they had kidney, liver, or metabolism problems.

The study included 119 participants in Denmark, Slovakia, and the United States.



Why was the research needed?

Researchers are looking for a better way to treat high levels of LDL cholesterol. Before a drug can be approved for people to get, researchers do clinical studies to find out how it works and how safe it is.

LDL cholesterol is a fatty substance in the blood. High levels of LDL cholesterol can lead to clogged blood vessels, also known as “atherosclerosis”. This can cause disease in the heart or blood vessels, and increase the risk of stroke, heart attack, and other heart problems.

People with high levels of LDL cholesterol are usually given drugs called “statins”. But statin treatment does not lead to low enough levels of LDL cholesterol in many people.

Many factors can affect the levels of LDL cholesterol in the blood. One factor is a protein called “PCSK9” that can raise the levels of LDL cholesterol in the blood. A previous study in healthy volunteers showed that AZD8233 lowered the levels of PCSK9 and LDL cholesterol in blood.

In this study, the researchers wanted to find out if different doses of AZD8233 reduced LDL cholesterol in the blood compared with placebo. They also wanted to find out if the participants had any medical problems during the study.



What was the purpose of this study?

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

- ▶ How much did the different doses of AZD8233 reduce LDL cholesterol in the blood compared with placebo?
- ▶ What medical problems happened during this study?

The answers to these questions are important to know before other studies can be done to find out if AZD8233 helps improve the health of people with high levels of LDL cholesterol.



What treatments did the participants receive?




In this study, the participants either got 1 of 3 doses of AZD8233, or a placebo. They got their study treatment through a needle under the skin, also known as a subcutaneous injection. The dose of AZD8233 was measured in milligrams, also known as “mg”.

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.

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.

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 getting. Some studies are done this way because knowing what treatment the participants are getting can affect the results of the study. When the study ended, the research sponsor found out which treatment the participants got so they could create a report of the study results.

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

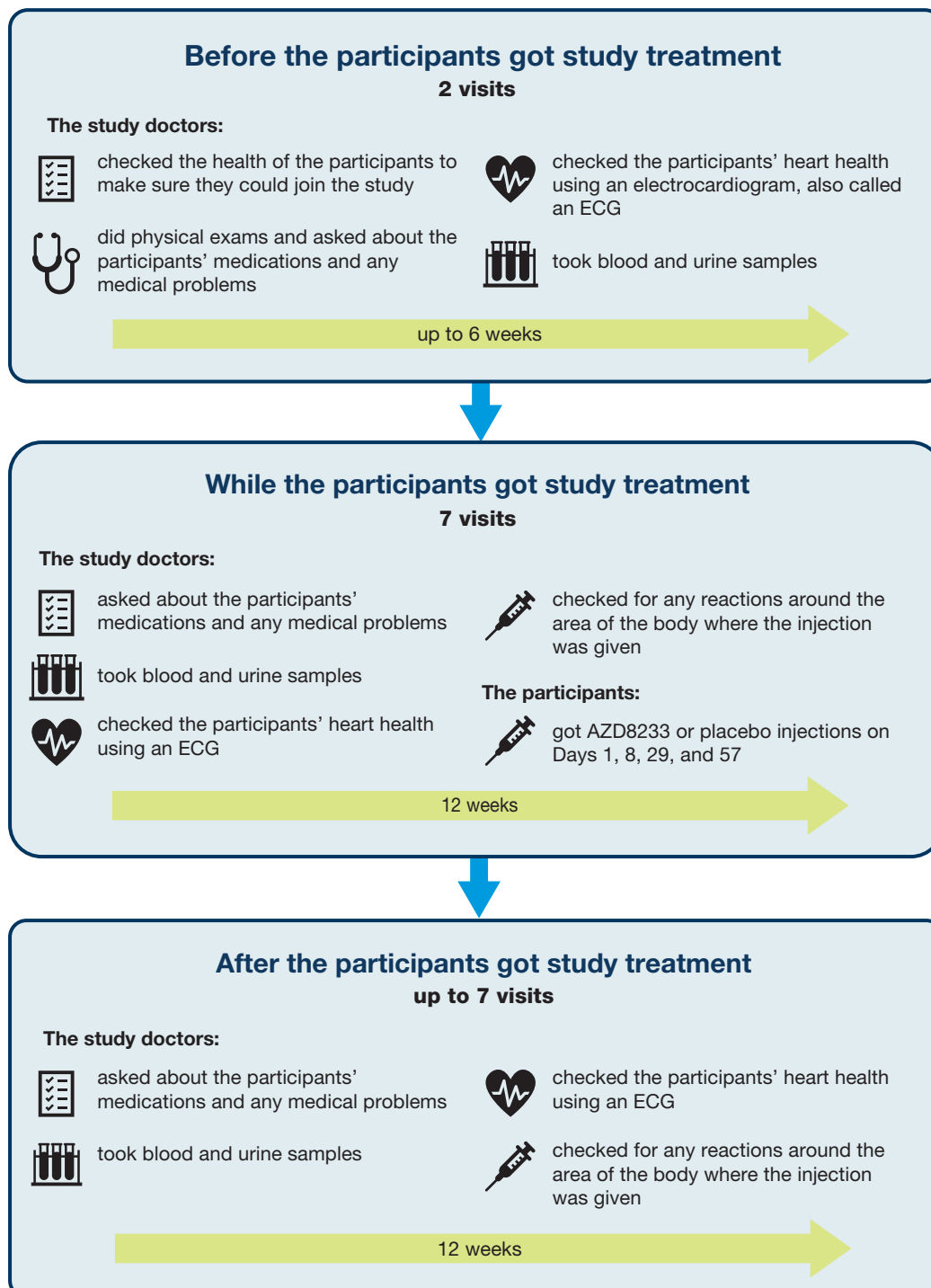
	AZD8233			Placebo
	29 participants	30 participants	30 participants	30 participants
	90 mg	50 mg	15 mg	Placebo
	One injection on days 1, 8, 29, and 57			



What happened during this study?

The participants were in the study for approximately 30 weeks. But the entire study took around 9 months to finish. The study started in October 2020 and ended in July 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.

How much did the different doses of AZD8233 reduce LDL cholesterol in the blood compared with placebo?

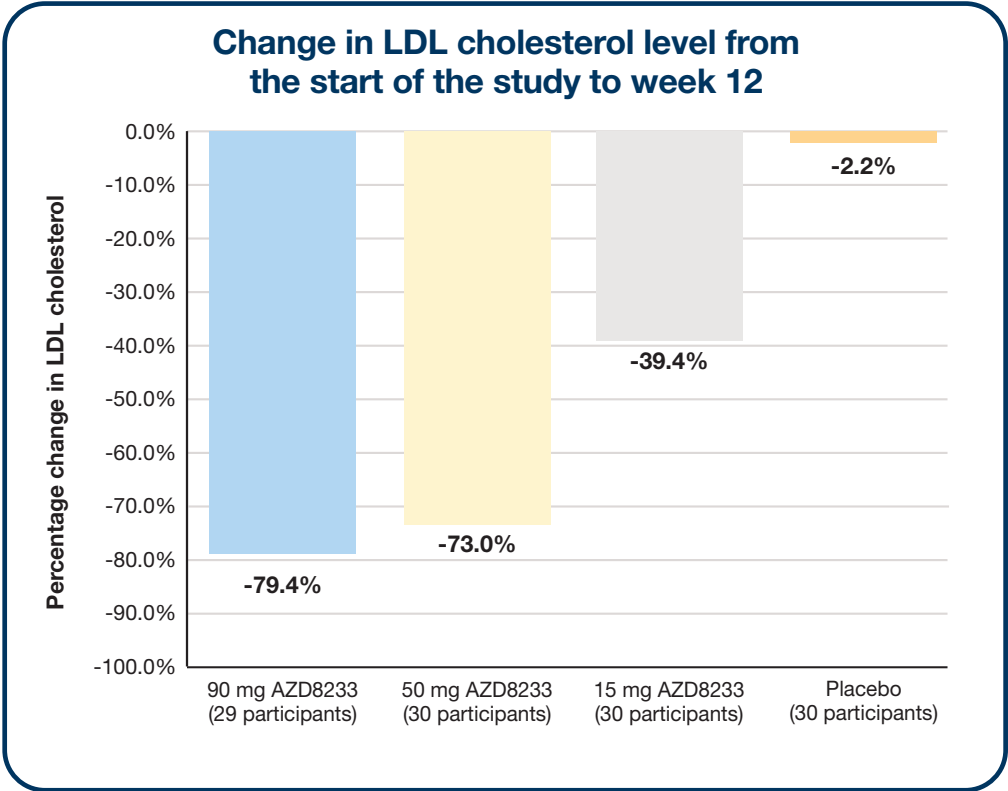
Overall, the researchers found that all 3 doses of AZD8233 reduced the levels of LDL cholesterol in the blood compared with placebo.

To answer this question, the researchers looked at all of the blood samples collected from each participant during the study. They compared the level of LDL cholesterol in the blood at the start of the study with the level in the blood after getting study treatment for 12 weeks.

Overall, the amounts that LDL cholesterol levels in the blood were **reduced** from the start of the study to Week 12 in the different groups were:

- ▶ **79.4%** for the participants getting **90 mg** AZD8233
- ▶ **73.0%** for the participants getting **50 mg** AZD8233
- ▶ **39.4%** for the participants getting **15 mg** AZD8233
- ▶ **2.2%** for the participants getting **placebo**

These results are shown in the graph below.





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 AZD8233.

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?

Overall, 15.1% of participants had adverse reactions. This was 18 out of 119 participants.

	90 mg AZD8233 (out of 29 participants)	50 mg AZD8233 (out of 30 participants)	15 mg AZD8233 (out of 30 participants)	Placebo (out of 30 participants)
How many participants had adverse reactions?	27.6% (8)	6.7% (2)	16.7% (5)	10.0% (3)
How many participants had serious adverse reactions?	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
How many participants stopped getting study treatment due to adverse reactions?	10.3% (3)	0.0% (0)	0.0% (0)	0.0% (0)

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 pain around the area of the body where the injection was given. The table below shows all of the adverse reactions that happened during the study.

Adverse reactions

Adverse reaction	90 mg AZD8233 (out of 29 participants)	50 mg AZD8233 (out of 30 participants)	15 mg AZD8233 (out of 30 participants)	Placebo (out of 30 participants)
Pain around the area of the body where the injection was given	6.9% (2)	3.3% (1)	3.3% (1)	0.0% (0)
Increased levels in the blood of a liver protein called transaminases, which may be a sign of liver dysfunction	6.9% (2)	0.0% (0)	0.0% (0)	0.0% (0)
Increased levels in the blood of a liver protein called ALT, which may be a sign of liver damage	3.4% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Increased levels of liver protein in the blood, which may be a sign of liver damage	3.4% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Increase in values of tests that check the functioning of the liver	3.4% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Pain in the abdomen	3.4% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Reaction around the area of the body where the injection was given	0.0% (0)	3.3% (1)	3.3% (1)	0.0% (0)
Headache	0.0% (0)	0.0% (0)	3.3% (1)	3.3% (1)
Low levels of red blood cells, which is also called anemia	0.0% (0)	0.0% (0)	3.3% (1)	3.3% (1)
Sudden collection of blood under the skin	0.0% (0)	0.0% (0)	3.3% (1)	0.0% (0)
Increased levels in the blood of a protein called creatine	0.0% (0)	0.0% (0)	3.3% (1)	0.0% (0)
Skin rash	0.0% (0)	0.0% (0)	0.0% (0)	3.3% (1)



How has this study helped patients and researchers?

This study helped researchers learn more about how different doses of AZD8233 work in people with high LDL cholesterol levels.

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 AZD8233 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 **"NCT04641299"** into the search box and click **"Search"**.
- ▶ www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"2020-000767-23"** in the search box and click **"Search"**.
- ▶ www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D7990C00003"** into the search box, and click **"Find a Study"**.

Full Study Title: A Randomized, Parallel, Double-blind, Placebo-controlled, Dose-ranging, Phase 2b Study to Evaluate the Efficacy, Safety and Tolerability of AZD8233 Treatment in Participants with Dyslipidemia

AstraZeneca Protocol Number: D7990C00003

National Clinical Trials Number: NCT04641299

EudraCT Number: 2020-000767-23

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.



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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