Clinical Study Results

MedImmune
A member of the AstraZeneca Group

Research sponsor: MedImmune, LLC

Drug studied: MEDI6012

Study title: A study to learn the effects of MEDI6012 in the body and how safe it is in people with cardiovascular disease caused by atherosclerosis

Thank you!

Thank you to the participants who took part in the clinical study for the study drug MEDI6012.

You and all of the participants helped researchers learn more about MEDI6012 to help people with cardiovascular disease caused by atherosclerosis.

MedImmune, LLC 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?

You were in the study for up to 18 weeks. But the entire study took almost 11 months to finish.

The study started in January 2017 and ended in November 2017. The study included 32 participants in the United States.

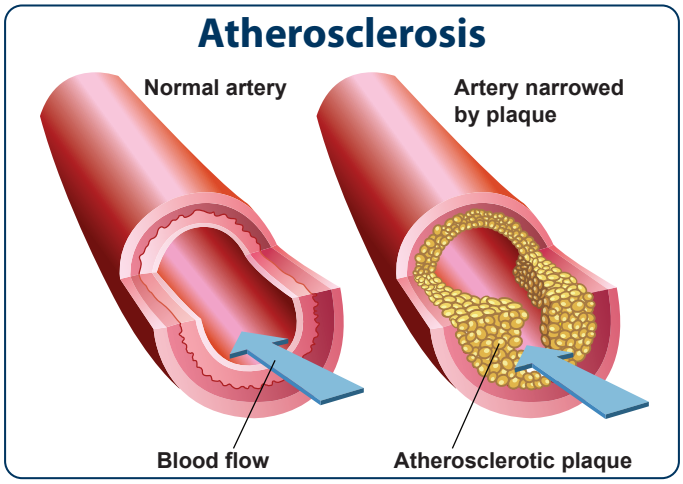
The sponsor reviewed the data collected when the study ended and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers are looking for a better way to treat people who have cardiovascular disease caused by atherosclerosis. Before a drug can be approved for patients 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 how MEDI6012 works in a small number of participants with cardiovascular disease caused by atherosclerosis. They also wanted to find out if the participants had any medical problems during the study.

Atherosclerosis is a condition in which deposits of cholesterol, fat, and other substances build up in the arteries and other blood vessels. These deposits, also called plaques, narrow the blood vessels and make it more difficult for blood to flow. This can lead to serious medical problems like a heart attack. People with cardiovascular disease caused by atherosclerosis have had medical problems with their heart or blood vessels because of these deposits.



Treatments for people with atherosclerosis include drugs that prevent blood clots from forming or reduce the total amount of cholesterol that gets made in the liver.

Cholesterol can be found in all of the body's cells. It plays an important part in making sure the body works properly. But there are good and bad types of cholesterol in the body. Bad cholesterol, also known as low-density lipoprotein cholesterol or LDL cholesterol, forms the plaques that clog arteries and other blood vessels. Good cholesterol, also known as high-density lipoprotein cholesterol or HDL cholesterol, actually helps remove bad cholesterol from the blood. Researchers think MEDI6012 might increase levels of good cholesterol and other substances that help reduce the build-up of bad cholesterol in blood vessels. This might reduce someone's chance of having a heart attack.

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

- How did MEDI6012 affect the amount of good cholesterol in the blood?
- 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 cardiovascular disease caused by atherosclerosis. The participants had a history of heart and blood vessel problems because of their atherosclerosis. Participants could join the study if their cardiovascular disease had been considered stable for at least 3 months. This means that during that time, participants had not experienced major medical problems caused by their cardiovascular disease such as a heart attack or stroke. The participants in this study were 61 to 76 years old. All of the participants were already taking a drug to lower their cholesterol.

What kind of study was this?

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

The participants got either MEDI6012 or a placebo. A placebo looks like a drug but does not have any medicine in it. Researchers use a placebo to help make sure any effects they see in the participants who take the study drug are actually caused by the study drug.

All the participants got MEDI6012 or a placebo through a needle placed in their vein. This is a process known as an intravenous infusion, also known as an IV.

A computer program was used to randomly choose whether the participants got MEDI6012 or a 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.

What happened during the study?

Before the study started, all the participants agreed to join. Then the doctors checked to make sure the participants were healthy enough to join the study. The doctors:

- did a physical examination
- took blood and urine samples
- checked their blood pressure, pulse, and temperature
- checked the heart health of the participants using an electrocardiogram, also known as an ECG
- asked the participants about their medical history, how they were feeling, and what medicines they were taking

During the study, the participants got MEDI6012 or a placebo in different ways.

Some of the participants got each treatment through a needle in their vein in a process that took about an hour to complete. This is called a 1-hour infusion. They got this treatment once a week for the first 3 weeks of the study. These participants got 1 of 3 doses of MEDI6012 or a placebo. The doses were measured in milligrams, also called mg:

- 40 mg of MEDI6012 or a placebo
- 120 mg of MEDI6012 or a placebo
- 300 mg of MEDI6012 or a placebo

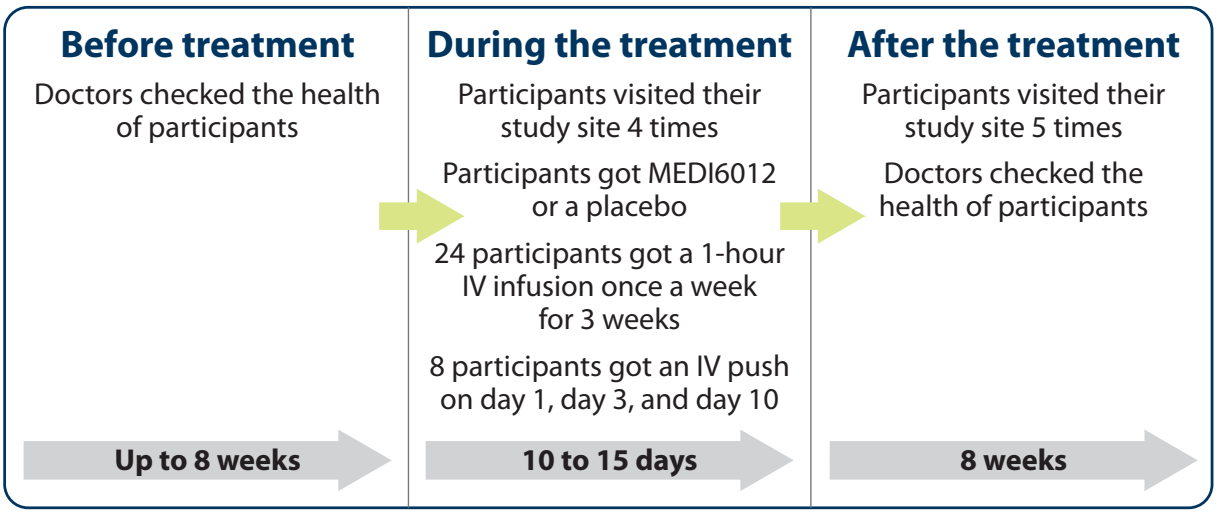
Other participants got their treatment through a needle in their vein more quickly in a process that only took about 1 to 3 minutes. This is called an "IV push". The researchers looked at the IV push to learn more about this treatment approach for future studies. These participants got different doses at different visits:

- 300 mg of MEDI6012 or a placebo at the first visit
- 150 mg of MEDI6012 or a placebo at the second visit 2 days after the first visit
- 100 mg of MEDI6012 or a placebo at the third visit 1 week after the second visit

The doctors asked the participants not to eat anything the night before their study visits. Throughout the study, the researchers continued checking the heart health of the participants and taking blood and urine samples.

After their last dose, the participants visited the study site 5 more times.

The figure 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.

How did MEDI6012 affect the amount of good cholesterol in the blood?

The researchers found that MEDI6012 increased the amount of good cholesterol in the participants' blood.

The researchers measured the amount of good cholesterol in the blood before treatment, during treatment, and for up to 8 weeks after treatment. They also measured the amount of other substances that play a role in removing bad cholesterol from the blood. To find out how MEDI6012 affected the amount of these substances in the blood, the researchers focused mainly on the amount in the blood during the 4 days after the last dose compared with the amount in the blood before treatment.

They found that the amounts of these substances increased in the participants who got MEDI6012 in a 1-hour IV infusion compared with the participants who got a placebo. The differences between the lowest dose of MEDI6012 and the placebo were too small in some cases for the researchers to know whether the 40 mg dose increased the amount of these substances in the blood compared to the placebo. The 40 mg dose was the lowest dose tested in this study.

The amounts of these substances also increased in the participants who got MEDI6012 in the IV push.

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 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.

The websites listed at the end of this summary may have more 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 the study. There was 1 serious medical problem during the study, but the study doctors did not think it was related to the study drug.

How many participants had adverse reactions?

During the study, adverse reactions happened in:

- 22.2% of participants who got MEDI6012 in a 1-hour IV infusion. This was 4 out of 18 participants. All of these adverse reactions happened in participants who got the 300-mg dose of MEDI6012.
- 16.7% of participants who got a placebo in a 1-hour IV infusion. This was 1 out of 6 participants.

None of the participants who got MEDI6012 or a placebo in an IV push had adverse reactions during the study.

None of the participants in any treatment group stopped taking MEDI6012 or a placebo because of adverse reactions they had during the study.

What adverse reactions did the participants have?

The most common adverse reaction was diarrhea. This was the only adverse reaction that occurred in more than 1 participant.

The table below shows the adverse reactions that happened in participants who got MEDI6012 or a placebo in this study. All of the adverse reactions with MEDI6012 happened in the participants who got the 300 mg dose of MEDI6012 in a 1-hour infusion.

Adverse reactions in this study						
Adverse reaction	**MEDI6012 40 mg 1 hour infusion (Out of 6 participants)**	**MEDI6012 120 mg 1 hour infusion (Out of 6 participants)**	**MEDI6012 300 mg 1 hour infusion (Out of 6 participants)**	**Placebo 1 hour infusion (Out of 6 participants)**	**MEDI6012 IV push (Out of 7 participants)**	**Placebo IV push (Out of 1 participant)**
Diarrhea	0% (0)	0% (0)	33.3% (2)	16.7%(1)	0% (0)	0% (0)
Redness at the needle site	0% (0)	0% (0)	16.7% (1)	0% (0)	0% (0)	0% (0)
A hard bump at the needle site	0% (0)	0% (0)	16.7% (1)	0% (0)	0% (0)	0% (0)
Pain at the needle site	0% (0)	0% (0)	16.7% (1)	0% (0)	0% (0)	0% (0)
Dizziness	0% (0)	0% (0)	16.7% (1)	0% (0)	0% (0)	0% (0)
Shortness of breath	0% (0)	0% (0)	16.7% (1)	0% (0)	0% (0)	0% (0)

Participants had other medical problems during the study, but the study doctors did not think these were related to the study drug.

How has this study helped participants and researchers?

This study helped researchers learn more about how MEDI6012 works in people with cardiovascular disease caused by atherosclerosis.

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 MEDI6012 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 also can be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT03004638"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5780C00005"** into the search box and click **"Find a Study"**.

Full study title: A Phase 2a Randomized, Blinded, Placebo-controlled Study to Evaluate the Safety, Pharmacokinetics and Pharmacodynamics of Multiple Ascending Doses of MEDI6012 in Subjects with Stable Atherosclerotic Cardiovascular Disease

MedImmune protocol number: D5780C00005

MedImmune, LLC, a wholly owned subsidiary of AstraZeneca PLC, sponsored this study and has its headquarters at 1 MedImmune Way in Gaithersburg, Maryland, 20878.

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 participants.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

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 patients for clinical studies, nor is it involved in conducting clinical studies.

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