# Clinical Study Results

**Research Sponsor:** AstraZeneca AB

**Drug Studied:** Ticagrelor

**Study Title:** A study to find out if ticagrelor prevents stroke or death in participants who are at increased risk of having a stroke

## *Thank you*

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

You and all of the participants helped researchers learn more about ticagrelor to help people at increased risk of having a stroke.

AstraZeneca AB 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

## Why was the research needed?

Researchers are looking for a better way to prevent strokes in people who are at increased risk of having a stroke. Before a drug can be approved for people to take, researchers do clinical studies to find out how it works and how safe it is.

## What treatments did the participants take?

The participants in this study took either ticagrelor or a placebo. A placebo looks like a drug but does not have any medicine in it. All of the participants also took an existing treatment for prevention of strokes called acetylsalicylic acid, also called ASA.

## What were the results of the study?

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

- **Did fewer participants who took ticagrelor have a stroke or die within 30 days of taking study treatment?**
  Yes. Overall, the researchers found that 5.4% of the participants who took ticagrelor and ASA had strokes or died within the 30 days of taking study treatment. They found that 6.5% of the participants who took the placebo and ASA had a stroke or died within the 30 days of taking study treatment.

- **What serious medical problems did the participants have during the study?**
  There were 1.5% of participants who had serious medical problems that the study doctors thought might be related to the study drug during the study. The most common serious medical problems were strokes caused by a blood clot and problems related to bleeding.

## Where can I learn more about this study?

You can find out more information about this study on the websites listed on the last page. When a full report of the study results is available, it can also be found on those websites.

## Who took part in the study?

The researchers asked for the help of men and women at increased risk of having a stroke. The participants in this study were 40 to 100 years old when they joined.

The study included 11,016 participants in 28 countries or regions: Argentina, Australia, Belgium, Brazil, Bulgaria, Canada, China, the Czech Republic, France, Germany, Hungary, Hong Kong, India, Italy, Mexico, Peru, Poland, Romania, Russia, Saudi Arabia, Slovakia, South Korea, Spain, Sweden, Taiwan, Thailand, Ukraine, and Vietnam.

## Why was the research needed?

Researchers are looking for a better way to prevent stroke in people at increased risk of having a stroke. Before a drug can be approved for people to take, researchers do clinical studies to find out how it works and how safe it is.

The participants in this study all had “acute cerebral ischemia”. This means that an area of their brain was damaged either from having a stroke or temporarily losing function from a “transient ischemic attack”, also called a TIA. Stroke and TIAs happen when there is a problem with the blood supply to the brain, such as a blood clot. This can cause sudden stroke symptoms, such as slurred speech and muscle weakness in the face, arms, and legs that can be long-lasting. A TIA happens when stroke-like symptoms disappear in minutes or hours. People who have recently had acute cerebral ischemia are at increased risk of having further strokes or TIAs.

People who may be at increased risk of having a stroke include those who:

- have had a recent stroke or TIA
- are older than 55 years old
- smoke
- have high blood pressure or high cholesterol
- have diabetes
- have other existing blood or heart problems

There are treatments for prevention of strokes, but these treatments may not always help people at increased risk of having a stroke. The study drug, ticagrelor, was designed to stop blood clots from forming. Researchers think this drug may help prevent strokes from happening in people at increased risk of having a stroke.

In this study, the researchers wanted to find out if ticagrelor works in a large number of participants who are at increased risk of having strokes. They also wanted to find out if the participants had any serious medical problems during the study.

## What was the purpose of this study?

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

- Did fewer participants who took ticagrelor have a stroke or die within 30 days of taking study treatment?
- What serious medical problems did the participants have during the study?

The answers to these questions are important to know to find out if ticagrelor helps improve the health of people who are at increased risk of having strokes.

## What treatments did the participants take?

The participants in this study took either ticagrelor 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 of the effects they see in the participants who take the drug are actually caused by the drug. All of the participants also took an existing treatment for strokes called acetylsalicylic acid in addition to ticagrelor or the placebo. Acetylsalicylic acid is also called ASA.

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

A computer program was used to randomly choose the treatment each participant took. 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 took ticagrelor and ASA or the placebo and ASA as tablets by mouth for 30 days. The doses were measured in milligrams, also called mg. The participants’ dose of ASA was either based on the participants’ normal dose if they were already taking ASA before the study, or based on what the study doctor recommended for each participant.

The chart below shows the treatments that were planned during the study.

| | Day 1 | Day 2 to 30 |
|---|---|---|
| **Ticagrelor and ASA (5,523 participants)** |  • 180 mg of ticagrelor as a tablet<br>• 300 to 325 mg of ASA as a tablet |  • 90 mg of ticagrelor as a tablet twice a day<br>• 75 to 100 mg of ASA as a tablet once a day |
| **Placebo and ASA (5,493 participants)** |  • A placebo tablet that looked like ticagrelor<br>• 300 to 325 mg of ASA as a tablet |  • A placebo tablet that looked like ticagrelor twice a day<br>• 75 to 100 mg of ASA as a tablet once a day |

## What happened during the study?

Each participant was in the study for 2 months. But, the entire study took almost 2 years to finish.

The study started in January 2018 and ended in December 2019.

The chart below shows what happened during the study.

## Day 1

**1 visit**

**The study doctors:**

- checked the health of the participants to make sure they could join the study
- did a physical exam and asked about the participants' medications and any medical problems
- did imaging of the participants' brain using e.g. computer tomography, also known as CT scans
- asked about the participants' smoking habits

**The participants:**

- answered questionnaires about their symptoms
- started taking ticagrelor and ASA or the placebo and ASA

## Days 2 - 30

**2 visits**

**The study doctors:**

- did a physical exam and asked about the participants' medications and any medical problems

**The participants:**

- answered questionnaires about their symptoms
- took ticagrelor or the placebo twice a day and took ASA once a day at home

## About 30 days after taking study treatment

**1 visit**

**The study doctors:**

- asked about the participants' medications and any medical problems

# 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 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.

## Did fewer participants who took ticagrelor have a stroke or die within 30 days of taking study treatment?

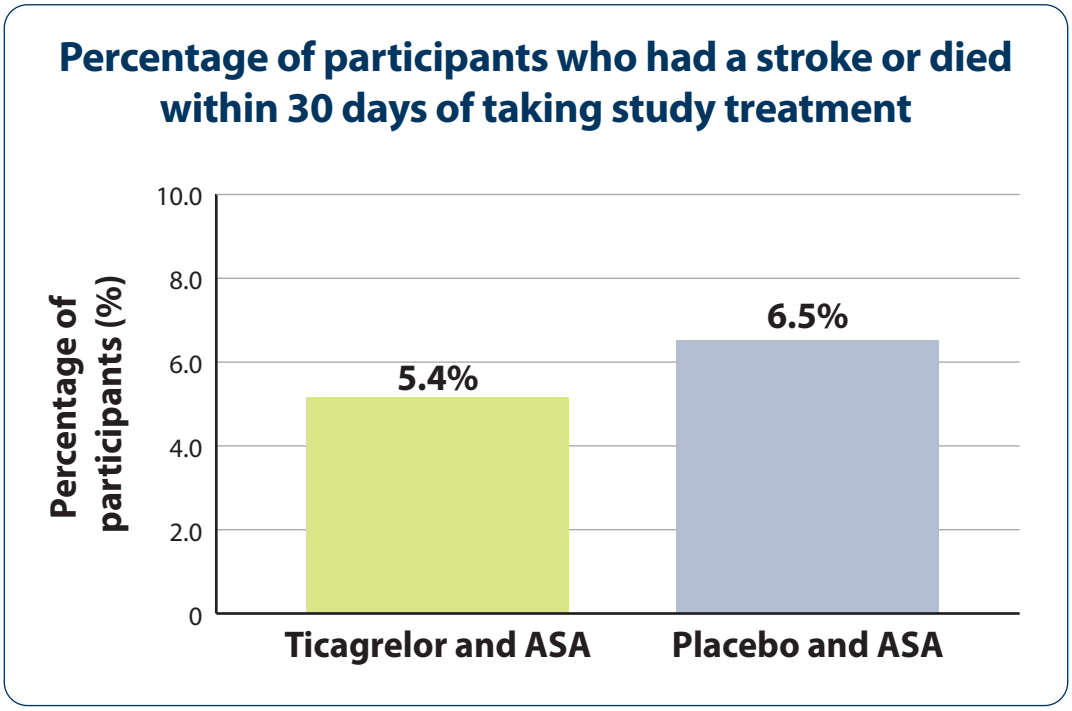
Yes. Overall, the researchers found that there were fewer participants who took ticagrelor who had strokes or died within 30 days of taking study treatment compared to the participants who took the placebo.

To answer this question, the researchers compared the number of participants who had a stroke or died within 30 days of taking either ticagrelor or the placebo.

Overall, the researchers found that within 30 days of taking study treatment:

- 5.4% of the participants who took ticagrelor and ASA had a stroke or died. This was 303 out of 5,523 participants.
- 6.5% of the participants who took the placebo and ASA had a stroke or died. This was 362 out of 5,493 participants.

The graph below shows these results.




## What serious medical problems happened during the study?

In clinical studies, researchers keep track of the medical problems that participants have that study doctors think 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.

In this study, the researchers wanted to learn if the participants taking ticagrelor had serious adverse reactions. They also wanted to learn if any participants stopped taking ticagrelor because of adverse reactions. This type of study did not require information on all adverse reactions to be collected.

This section is a summary of the serious adverse reactions that the study doctors thought might be related to ticagrelor.

These serious adverse reactions may or may not be caused by ticagrelor. When the participants had these serious adverse reactions, the study doctors did not know whether they were taking ticagrelor or the placebo.

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

**Did any serious adverse reactions happen during this study?**

| | Ticagrelor and ASA (out of 5,523 participants) | Placebo and ASA (out of 5,493 participants) |
|---|---|---|
| How many participants had serious adverse reactions? | 1.76% (97) | 1.29% (71) |
| How many participants stopped taking study treatment because of adverse reactions? | 4.27% (236) | 1.77% (97) |

There were 0.09% of participants who died because of serious adverse reactions that they had during the study. This was 10 out of 11,016 participants.

- 0.14% of participants who took ticagrelor died because of serious adverse reactions during the study. This was 8 out of 5,523 participants.
- 0.04% of participants who took the placebo died because of serious adverse reactions during the study. This was 2 out of 5,493 participants.

## What serious adverse reactions happened during this study?

The most common serious adverse reaction were strokes caused by a blood clot and problems related to bleeding.

The table below shows the most common serious adverse reactions that happened in more than 1 participant.

| Most common serious adverse reactions | | |
|---|---|---|
| **Serious adverse reaction** | **Ticagrelor and ASA (out of 5,523 participants)** | **Placebo and ASA (out of 5,493 participants)** |
| Stroke caused by a blood clot, also known as ischemic stroke | 0.34% (19) | 0.66% (36) |
| Stroke-related brain bleed, also known as hemorrhagic transformation stroke | 0.11% (6) | 0.07% (4) |
| Blood in the urine | 0.11% (6) | 0.0% (0) |
| Bleeding in the digestive tract | 0.09% (5) | 0.05% (3) |
| Stroke caused by a brain bleed, also known as hemorrhagic stroke | 0.09% (5) | 0.0% (0) |
| Bleeding in the upper digestive tract | 0.07% (4) | 0.0% (0) |
| Nosebleed | 0.07% (4) | 0.0% (0) |
| Bleeding from the anus | 0.05% (3) | 0.04% (2) |
| Breathlessness | 0.05% (3) | 0.04% (2) |
| Death of brain tissue from lack of blood flow, also known as cerebral infarction | 0.05% (3) | 0.0% (0) |
| Bleeding in the brain, also known as cerebral hemorrhage | 0.04% (2) | 0.04% (2) |
| Black bowel movements from old blood | 0.04% (2) | 0.0% (0) |
| Bleeding on the surface of the brain, also known as subarachnoid hemorrhage | 0.04% (2) | 0.0% (0) |
| Bleeding in the esophagus | 0.04% (2) | 0.0% (0) |
| Bleeding in the small intestine | 0.04% (2) | 0.0% (0) |
| Pneumonia | 0.02% (1) | 0.04% (2) |
| Allergic reaction | 0.02% (1) | 0.02% (1) |
| Transient ischemic attack, also known as TIA | 0.0% (0) | 0.05% (3) |
| Urinary tract infection | 0.0% (0) | 0.04% (2) |

## How has this study helped patients and researchers?

This study helped researchers learn more about ticagrelor in participants who are at increased risk of having a stroke.

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 ticagrelor in participants at increased risk of having a stroke 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 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 **"NCT03354429"** into the search box, and click **"Search"**.
- http://www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2016-004232-37"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5134C00003"** into the search box, and click **"Find a Study"**.

**Full Trial Title:** A Randomised, Double-Blind, Placebo-Controlled, International, Multicentre, Phase III Study to Investigate the Efficacy and Safety of Ticagrelor and ASA Compared with ASA in the Prevention of Stroke and Death in Patients with Acute Ischaemic Stroke or Transient Ischaemic Attack

**AstraZeneca AB Protocol Number:** D513400003

**National Clinical Trials number:** NCT03354429

**EudraCT number:** 2016-004232-37

**AstraZeneca AB** sponsored this study and has its headquarters at 151 85 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