AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: Ticagrelor

Study Purpose: A study to learn if ticagrelor works and about the safety of ticagrelor in children with sickle cell disease

Protocol Number: D5136C00009

Thank you

Thank you to the participants who took part in the clinical study for the study drug ticagrelor, and to their parents or caregivers.

All of the participants helped researchers learn more about ticagrelor to help children and teenagers with sickle cell disease, also called SCD or sickle cell anaemia.

AstraZeneca sponsored this study and believes it is important to share the results of the study.

An independent non-profit organisation called CISCRP helped prepare this summary of the study results. We hope it helps the participants and their parents or caregivers understand and feel proud of their important role in medical research.

If you or the child in your care 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 sickle cell disease in children and teenagers. In this summary, sickle cell disease will be referred to as SCD. Before a drug can be approved for people to take, researchers do clinical studies to find out if 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.

What were the results of the study?

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

> **Did ticagrelor lower the number of pain crises that the participants had during the study?**

"Pain crises" are a common symptom of SCD that happen when blood vessels become blocked. Overall, the researchers found that there were no important differences between the group of participants who took ticagrelor and the group who took the placebo.

> **Did the participants feel that ticagrelor helped their symptoms and quality of life?**

Overall, the researchers found that the participants who took ticagrelor and those who took the placebo did not feel that the study treatment helped their symptoms and quality of life.

> **What medical problems did the participants have during the study?**

There were 4.2% of participants who had medical problems that the study doctors thought might be related to the study drug during the study. This was 8 out of 192 participants. The most common medical problems were headache and dizziness. 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 can also be found on those websites.

Who took part in the study?

The researchers asked for the help of male and female children and teenagers with SCD. The participants in this study were 3 to 17 years old when they joined. All of the participants had at least 2 "pain crises" in the year before they joined the study. Pain crises are a common symptom of SCD that happen when blood vessels become blocked.

The study included 193 participants in 16 countries. These were Belgium, Brazil, Egypt, Ghana, Greece, India, Italy, Kenya, Lebanon, South Africa, Spain, Tanzania, Turkey, Uganda, the United Kingdom, and the United States.

Why was the research needed?

Researchers are looking for a better way to treat SCD in children and teenagers. 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.

In this study, the researchers wanted to find out if ticagrelor works in a large number of participants with SCD. They also wanted to find out if the participants had any medical problems during the study.

SCD is a disease that you are born with where red blood cells that are normally round become crescent or "sickle" shaped. Sickle cells do not flow easily through blood vessels. They can cause blockages in the blood vessels by clumping together with other cells and forming blood clots. This stops the blood from taking oxygen to some parts of the body, which can cause damage.

In people with SCD, blocked blood vessels can become very painful, particularly in the chest. These pain events are known as "vaso-occlusive crises" or pain crises, and can cause fever, breathing difficulties, and infections.

There are treatments to lower the number of pain crises in people with SCD, but they may cause medical problems for some people. The study drug, ticagrelor, was designed to stop blood clots from forming. Researchers thought it might also help improve blood flow in people with SCD.

In this study, the researchers wanted to find out if ticagrelor lowered the number of pain crises in children and teenagers with SCD.

What was the purpose of this study?

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

- Did ticagrelor lower the number of pain crises that the participants had during the study?
- Did the participants feel that ticagrelor helped their symptoms and quality of life?
- What medical problems did the participants have during the study?

The answers to these questions are important to help know if ticagrelor can be given to improve the health of children and teenagers with SCD.

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 a result of taking the drug.

This was a "double-blind" study. This means none of the participants, their parents or caregivers, researchers, study doctors, or other study staff knew what treatment each participant was taking. Some studies of this type 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 or the placebo as tablets by mouth twice a day. The doses were measured in milligrams, also called mg. The dose each participant took depended on their body weight.

The chart below shows the treatments that were planned during the study and the number of participants who took each treatment.

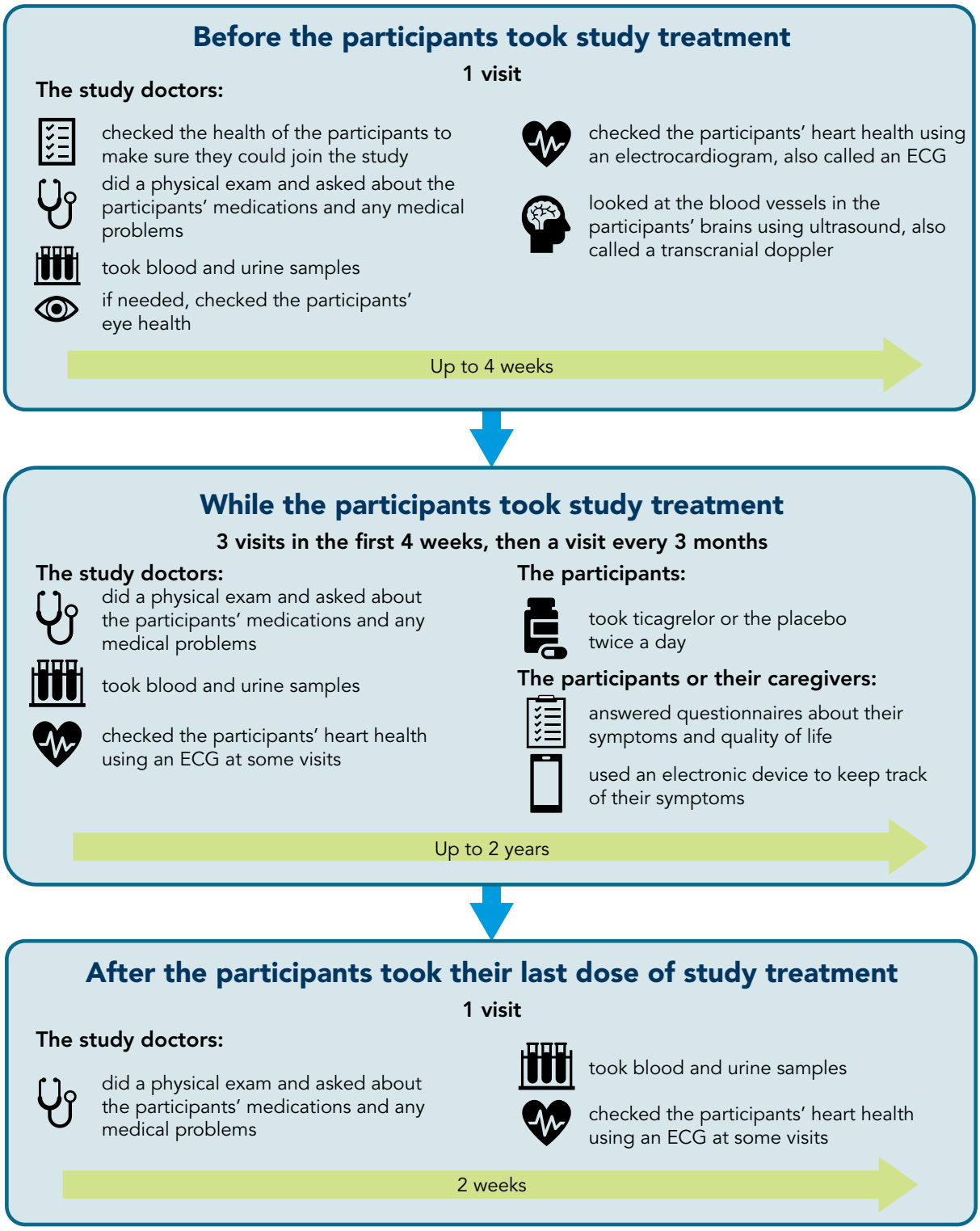
	Ticagrelor	Placebo
	• 101 participants	• 92 participants
	• 15 mg to 45 mg of ticagrelor based on body weight	• Placebo
	• 1 to 3 tablets twice a day	• 1 to 3 tablets twice a day

What happened during the study?

Each participant was planned to be in the study for up to 2 years. But, the study sponsor stopped the study early because the researchers did not think ticagrelor was helping the participants.

The study started in September 2018 and ended in August 2020.

The chart below shows what happened during the study.



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. 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 ticagrelor lower the number of pain crises that the participants had during the study?

No. Overall, the researchers found that there were no important differences between the group of participants who took ticagrelor and the group who took the placebo.

To answer this question, the researchers counted the number of pain crises each participant had per year during the study and calculated the average.

Overall, the researchers found that the average number of pain crises per year was:

- 2.74 pain crises for the participants who took ticagrelor
- 2.60 pain crises for the participants who took placebo

This difference was so small that the researchers did not consider it to be important.

Did the participants feel that ticagrelor helped their symptoms and quality of life?

Overall, the researchers found that the participants who took ticagrelor and those who took the placebo did not feel that the study treatment helped their symptoms and quality of life.

To answer this question, the study doctors asked the participants if their study treatment helped their symptoms and quality of life. The participants or their caregivers answered 2 different questionnaires. These were called:

- The Paediatric Quality of Life Sickle Cell Disease Module
- The Paediatric Quality of Life Multidimensional Fatigue Scale

The participants or their caregivers also answered surveys that asked about:

- how strong the participants' pain was during their pain crises
- how many days of school or work they missed because of SCD
- how easy the ticagrelor or placebo tablets were to take

The researchers then scored the participants' responses to each of the questionnaires and surveys. They compared the scores between the participants who took ticagrelor and those who took the placebo.

Overall, the researchers found that the scores were similar between the two groups. The participants who took ticagrelor and those who took the placebo did not feel that the study treatment helped their symptoms and quality of life.

What medical problems happened 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. 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.

The results below are for 192 out of 193 participants who took at least 1 dose of study treatment and reported if they had any medical problems.

Did any adverse reactions happen during this study?		
	Ticagrelor (out of 100 participants)	**Placebo (out of 92 participants)**
How many participants had adverse reactions?	6.0% (6)	2.2% (2)
How many participants had serious adverse reactions?	1.0% (1)	0.0% (0)
How many participants stopped taking study treatment due to adverse reactions?	1.0% (1)	0.0% (0)

The study sponsor stopped this study early because the researchers did not think ticagrelor was helping the participants.

What serious adverse reactions happened during this study?

There was 1 participant out of 100 who took ticagrelor who had a serious adverse reaction during the study and who died owing to a serious adverse reaction. This was 1.0% of participants. The serious adverse reaction was a sudden unexplained death.

None of the other participants who took ticagrelor had serious adverse reactions during the study or died owing to serious adverse reactions.

None of the participants who took the placebo had serious adverse reactions or died owing to serious adverse reactions.

What adverse reactions happened during this study?

The most common adverse reactions were headache and dizziness.

The table below shows the adverse reactions that happened during the study. Some participants may have had more than 1 adverse reaction.

Adverse reactions		
Adverse reaction	**Ticagrelor (out of 100 participants)**	**Placebo (out of 92 participants)**
Headache	2.0% (2)	0.0% (0)
Dizziness	1.0% (1)	1.1% (1)
Infection in the upper airways	1.0% (1)	0.0% (0)
Bleeding gums	1.0% (1)	0.0% (0)
Pain in the upper belly	1.0% (1)	0.0% (0)
Sore throat	1.0% (1)	0.0% (0)
Sudden unexplained death	1.0% (1)	0.0% (0)
Vomiting	0.0% (0)	1.1% (1)
Nosebleed	0.0% (0)	1.1% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about ticagrelor for children and teenagers with SCD.

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 children and teenagers with SCD 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 **"NCT03615924"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2017-002421-38"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5136C00009"** into the search box, and click **"Find a Study"**.
- **Full Study Title:** A Randomized, Double-Blind, Parallel-Group, Multicentre, Phase III Study to Evaluate the Effect of Ticagrelor versus Placebo in Reducing the Rate of Vaso-Occlusive Crises in Paediatric Patients with Sickle Cell Disease (HESTIA3)

AstraZeneca AB Protocol Number: D5136C00009

National Clinical Trials Number: NCT03615924

EudraCT Number: 2017-002421-38

AstraZeneca AB sponsored this study and has its headquarters in Cambridge, UK.

The phone number for the AstraZeneca Information Centre is +1-877-240-9479.

Thank you

Clinical study participants and their families 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 organisation 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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Version 1.0_2021_03_01