Clinical Trial RESULTS

AstraZeneca

Research Sponsor: AstraZeneca AB

Drug Studied: Ticagrelor

National Clinical Trial #: NCT02482298

Eudra Clinical Trial #: 2014-005420-10

Protocol #: D5136C00008

Study Date: July 2015 to November 2016

Short Study Title: A study to learn if ticagrelor reduces the number of days with pain in adult patients with sickle cell disease

Thank you!

As a clinical study participant, you belong to a large community of participants around the world. You help researchers answer important health questions and discover new medical treatments.

Thank you for taking part in the clinical study for the drug ticagrelor. This drug is being developed to treat patients with a blood disease called sickle cell disease. You and all the other participants helped researchers learn if ticagrelor helps reduce the number of days with pain in patients with sickle cell disease.

AstraZeneca AB, the sponsor of this study, thanks you for your help and thinks it is important for you to know the results of the study. An independent non-profit organization called CISCRP prepared this summary of the study results for you with the help of a medical writing organization. We hope it helps you understand and feel proud of your important role in medical research. If you have questions about the results, please speak with the doctor or staff at your study site.

What's happened since my study ended?

Your study started in July 2015 and ended in November 2016. The study included 87 participants at 18 study sites in Egypt, Italy, Kenya, Lebanon, Turkey, the United Kingdom, and the United States. The table on the next page shows the number of participants in each country.

Number of participants in each country in this study	
Country	**Number of participants**
European Union	
Italy	1
United Kingdom	6
Non-European Union	
Egypt	21
Kenya	33
Lebanon	7
Turkey	13
United States	6

Why was the research needed?

Researchers in this study wanted to find a new way of treating sickle cell disease. This disease causes pain when red blood cells get stuck in small blood vessels in your body. Normally, red blood cells are flexible and round and can move through your blood vessels easily to deliver oxygen to organs in your body. But if you have sickle cell disease, your red blood cells are curved and stiff. These abnormal red blood cells are called "sickle cells". When they get stuck, they slow down or block the flow of blood. This causes pain and can damage your organs and tissues.

The study drug, ticagrelor, is being tested for the treatment of sickle cell disease. Researchers wanted to learn if taking ticagrelor could ease the pain in people with sickle cell disease. Another type of blood cell, called a "platelet", can get stuck along with sickle cells. Ticagrelor may make this happen less. In this study, researchers want to know if two different doses of ticagrelor could reduce the number of days with pain in participants with sickle cell disease more than a placebo. A placebo looks like the study drug but contains no real medicine. Researchers use placebos to compare the results for participants who take study drugs with the results for participants who take no medicine at all.

In your study, researchers wanted to know:

- Did participants who took ticagrelor have fewer days with pain than participants who took the placebo?
- Did participants who took ticagrelor have milder pain than participants who took the placebo?
- Did participants who took ticagrelor use pain-relieving medicine less often than participants who took the placebo?
- What medical problems did participants have after taking ticagrelor?

In your study, participants were 18 to 30 years old. Out of the 87 participants, 47 (54.0%) were women and 40 (46.0%) were men. For more information about which participants could join this study, please refer to the website listed on the last page of this summary.

What kind of study was this?

Your study was a "double-blind" study. This means that none of the participants, researchers, doctors, or staff knew what treatment each participant took until after the study ended. Some studies are done this way because knowing what treatment each participant is taking can affect the results of the study. This way, the results are looked at fairly.

You and the other participants took either ticagrelor or the placebo. The treatment that each participant took was decided by chance, like rolling dice. Participants had an equal chance of taking either 10 milligrams ticagrelor or 45 milligrams ticagrelor or the placebo.

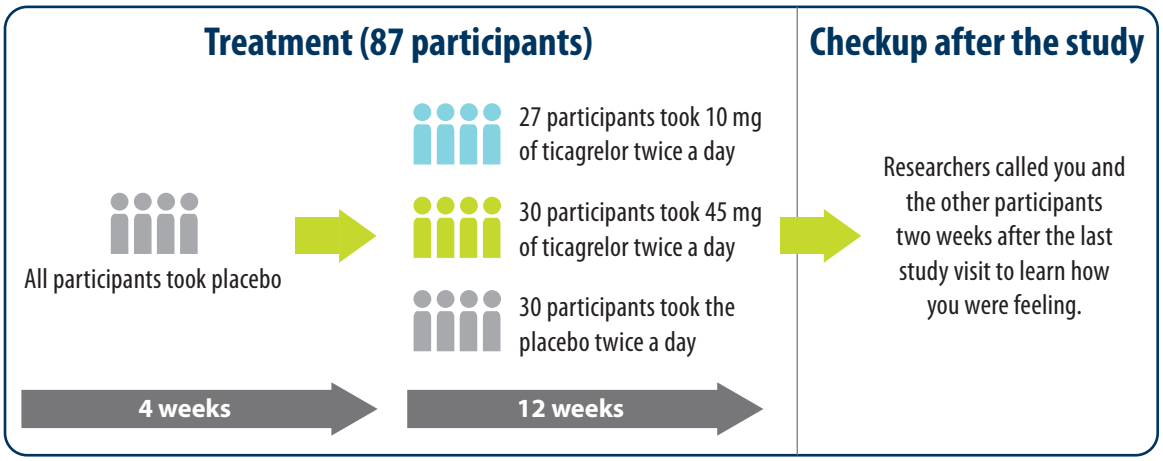
What happened during the study?

To see if you could join the study, the doctors did a full physical exam, took blood and urine samples, and checked your heart health. During this time, the doctors also gave you a diary to write down the times when you had pain. They checked these diaries during the study.

Treatment lasted 16 weeks. Once you entered the study, you took placebo for the first four weeks. If you had pain for at least four days during these four weeks, you were then randomly assigned to take either ticagrelor or continue the placebo for 12 weeks. Each participant took study tablets twice a day, no matter what the dose or medicine was.

Two weeks after your last study visit, the doctors called you to ask how you were feeling and if you took any new medicines.

The figure below shows how the study was done.



What were the study results?

Did participants who took ticagrelor have fewer days with pain than participants who took the placebo?

No. The researchers counted the average number of days when participants had pain after 12 weeks of treatment and compared it to before treatment. Overall, the researchers found that participants in all three treatment groups had fewer days with pain on average after treatment. But the difference among the treatment groups was too small to know if one treatment was better than the other treatments.

Participants who took 10 mg of ticagrelor reported pain on about

- 43% of the days before treatment
- 32% of the days after treatment

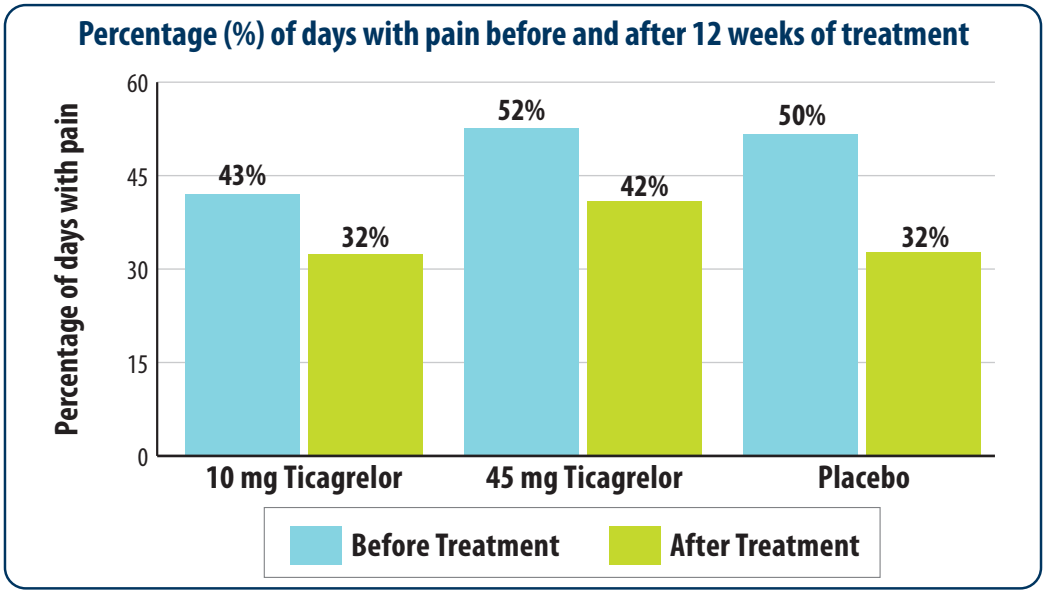
Participants who took 45 mg of ticagrelor reported pain on about

- 52% of the days before treatment
- 42% of the days after treatment

Participants who took the placebo reported pain on about

- 50% of the days before treatment
- 32% of the days after treatment

The chart below shows the average percentage of days participants reported pain before and after 12 weeks of treatment.



Did participants who took ticagrelor have milder pain than participants who took the placebo?

No. Researchers measured how strong the pain was, on average, after treatment and compared it to before treatment. Overall, they found that participants in all three treatment groups had milder pain, on average, after treatment compared to before treatment. But the difference among the treatment groups was too small to know if one treatment was better than the other treatments.

Did participants who took ticagrelor use pain-relieving medicine less often than participants who took the placebo?

No. Researchers measured how many days, on average, did participants use pain-relieving medicine after treatment and compared it to before treatment. They found that participants in all three treatment groups used pain-relieving medicine on fewer days, on average, after treatment than before treatment. But the difference among the treatment groups was too small to know if one treatment was better than the other treatments.

What medical problems did participants have?

A lot of research is needed to know whether a drug causes a medical problem. So, when new drugs are being studied, researchers keep track of all medical problems that participants have during the study. These medical problems are called "adverse events". They may or may not be caused by the study drug.

Out of the 87 participants in the study, researchers had information about medical problems from 86 participants. The missing information was because one participant was assigned to take 10 mg of ticagrelor but did not have at least four days of pain during the first four weeks when everyone took the placebo.

How many participants had medical problems in the study?

About the same number of participants in each treatment group had medical problems in the study. One participant in the 45 mg ticagrelor group and one participant in the placebo group stopped taking the study drug because of medical problems. The table below shows how many participants in each treatment group had medical problems.

	10 mg of Ticagrelor (Out of 26 participants)	45 mg of Ticagrelor (Out of 30 participants)	Placebo (Out of 30 participants)
How many participants had medical problems?	19 (73.1%)	21 (70.0%)	20 (66.7%)
How many participants had serious medical problems?	6 (23.1%)	5 (16.7%)	6 (20.0%)
How many participants stopped taking the study drug because of medical problems?	0 (0.0%)	1 (3.3%)	1 (3.3%)

How many participants had serious medical problems?

A medical problem is considered serious when it causes death, is life-threatening, causes lasting problems, causes birth defects, needs hospital care, or is considered an important medical event. In this study, participants had serious medical problems that either needed hospital care or was considered important by a participant's doctor. No participants died in this study.

The number of participants who had serious medical problems in this study was about the same in each treatment group. The table below shows the serious medical problems that happened to more than one participant in the study. All the other serious medical problems happened to single participants. Doctors did not think any of the serious medical problems were related to the study drug.

Serious medical problem	10 mg of Ticagrelor (Out of 26 participants)	45 mg of Ticagrelor (Out of 30 participants)	Placebo (Out of 30 participants)
Sickle cell anemia with crisis (sickle cell disease-related attack)	5 (19.2%)	3 (10.0%)	3 (10.0%)
Stomach flu	0 (0.0%)	1 (3.3%)	2 (6.7%)
Acute chest syndrome (sickle cell disease-related lung condition)	1 (3.8%)	1 (3.3%)	0 (0.0%)

What were the most common medical problems in the study?

Headache was the most common medical problem in this study. The table below shows the most common medical problems that happened to at least four participants in any treatment group.

Common medical problem	10 mg of Ticagrelor (Out of 26 participants)	45 mg of Ticagrelor (Out of 30 participants)	Placebo (Out of 30 participants)
Headache	11 (42.3%)	8 (26.7%)	8 (26.7%)
Joint pain	6 (23.1%)	9 (30.0%)	6 (20.0%)
Sickle cell anemia with crisis (sickle cell disease-related attack)	5 (19.2%)	5 (16.7%)	3 (10.0%)
Belly pain	5 (19.2%)	3 (10.0%)	3 (10.0%)
Back pain	4 (15.4%)	4 (13.3%)	8 (26.7%)
Pain in arms, hands, legs, or feet	4 (15.4%)	9 (30.0%)	5 (16.7%)

Where can I learn more about the study?

If you have questions about the results, please speak with the doctor or staff at your study site. You can find more information about your study online at www.clinicaltrials.gov/show/results/NCT02482298.

Official study title: A randomised, double-blind, double-dummy, parallel-group, multicenter, phase IIb study to evaluate the effect of ticagrelor 10 mg and 45 mg bid versus placebo in reducing the number of days with pain in young adults with sickle cell disease

The central AstraZeneca Information Center is in the United States, and the phone number is +1-877-240-9479.

The results presented here are for a single study. Other studies may provide new information or different results. You should not make changes to your therapy based on the results of a single study without first consulting your healthcare professional.

Thank you

It is said that the greatest gift is one which is given anonymously, giving when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge and benefits public health.

Thank you for the gift of your participation in clinical research.

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 participants for clinical trials, nor is it involved in conducting clinical trials.

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