Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Epoetin alfa

Study Title: A study to learn how much of different forms of epoetin alfa are in the blood of healthy participants over time

Thank you!

Thank you to the participants who took part in the clinical trial to study different forms of epoetin alfa. AstraZeneca AB sponsored this study and thinks it is important to share the results. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you.

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?

The study started in June 2018 and ended in November 2018. The sponsor reviewed the data collected when the study ended and created a report of the results. This is a summary of that report.

The study included 53 participants in Germany.

Why was the research needed?

Researchers are looking for ways to treat anemia in people with chronic kidney disease. Before a drug can be approved for patients to take, researchers do clinical studies to find out how safe it is and how it works.

Anemia develops when there are not enough red blood cells in the blood to carry oxygen throughout the body. People with anemia can feel tired or weak because their cells are not getting enough oxygen. Anemia often occurs in people with chronic kidney disease. This is because the kidney is not making enough of a protein called erythropoietin, which helps make red blood cells.

Epoetin alfa is a drug similar to erythropoietin that helps the body make more red blood cells. There are different forms of epoetin alfa available in Europe and in the United States to treat anemia.

In this study, the researchers wanted to find out if similar amounts of the different forms of epoetin alfa were in the blood of healthy participants over time.

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

- Was the amount of the US and European forms of epoetin alfa in the blood similar over time?
- Was the amount of two different batches of the US form of epoetin alfa in the blood similar over time?
- What medical problems did the participants have during the study?

The answers to these questions are important to know to understand if the different forms of epoetin alfa that are available in different countries work in the same way.

The researchers asked for the help of healthy men with normal amounts of red blood cells. Everyone in the study was 23 to 50 years old when they joined.

What kind of study was this?

This was an “open-label” study. This means the researchers and the participant knew what the participant was getting.

All of the participants in this study got an injection of epoetin alfa through a needle into their blood. There were 4 different forms of epoetin alfa:

- Form A, also known as Binocrit, available in Europe
- Form B, also known as Eprex, available in Europe
- Form C, also known as Epogen batch 1, available in the US
- Form D, also known as Epogen batch 2, available in the US

The participants got 1 injection of each of the forms, but in a different order. A computer program was used to randomly choose the order that each participant got the treatments. 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 taking epoetin alfa, the doctors checked the overall health of the participants to make sure that they could join the study. This included:

- blood and urine tests
- physical examinations, blood pressure, and pulse rate measurements
- heart health tests using an electrocardiogram, also called an ECG

There were 4 parts to this study. Each part lasted 4 weeks. Each participant took a different form of epoetin alfa during each part.

In each part, the participants visited their study center and stayed overnight. Each participant got an injection of epoetin alfa, had blood tests, and had their blood pressure and pulse rate measured. They visited their study center 24 hours before the injection and stayed until 48 hours after the injection.

The participants visited their study center 7 more times for blood tests. They did not need to stay overnight for these blood tests.

Participants took part in all 4 parts of the study, but in a different order. In total, the participants stayed at the study center 4 times, and visited the study center 28 times for blood tests. A total of 53 participants took part in the study and got at least 1 injection. Some participants left the study before they got all 4 forms of epoetin alfa. A total of 47 participants completed the study and 6 participants left the study early.

After all 4 parts, the participants visited their study center 1 more time. The doctors asked how they were feeling and took blood samples.

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.

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 change.

The websites listed at the end of this summary may have a full report of the study results.

Was the amount of the US and European forms of epoetin alfa in the blood similar over time?

Yes. Although there was a small difference between the European and US forms, the difference was so small that researchers considered them to be the same.

To answer this question, the doctors measured the amount of epoetin alfa in the blood at different times during the 48 hours after each injection. They then calculated the average amount of each form of epoetin alfa in the blood.

Once the researchers found the averages, they calculated the ratio as a percentage. In this study, the researchers compared the following forms of epoetin alfa:

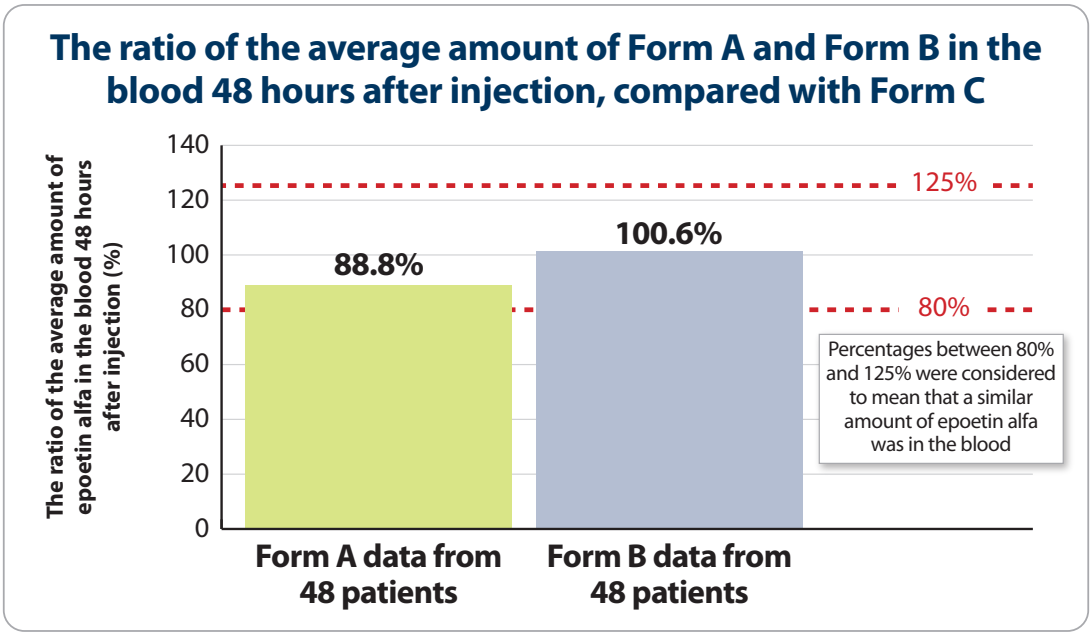
- The European forms (Form A and Form B) to the first US form (Form C)
- The European forms (Form A and Form B) to the second US form (Form D)

When comparing the different forms, percentages between 80% and 125% were considered to mean that a similar amount of epoetin alfa was in the blood over time. A percentage higher than 100% meant that there was more of the US form than the European form. A percentage lower than 100% meant that there was more of the European form than the US form.

When comparing Forms A and B to Form C, the researchers found that the ratio of the other forms of epoetin alfa in the participants' blood was:

- 88.8% for Form A
- 100.6% for Form B

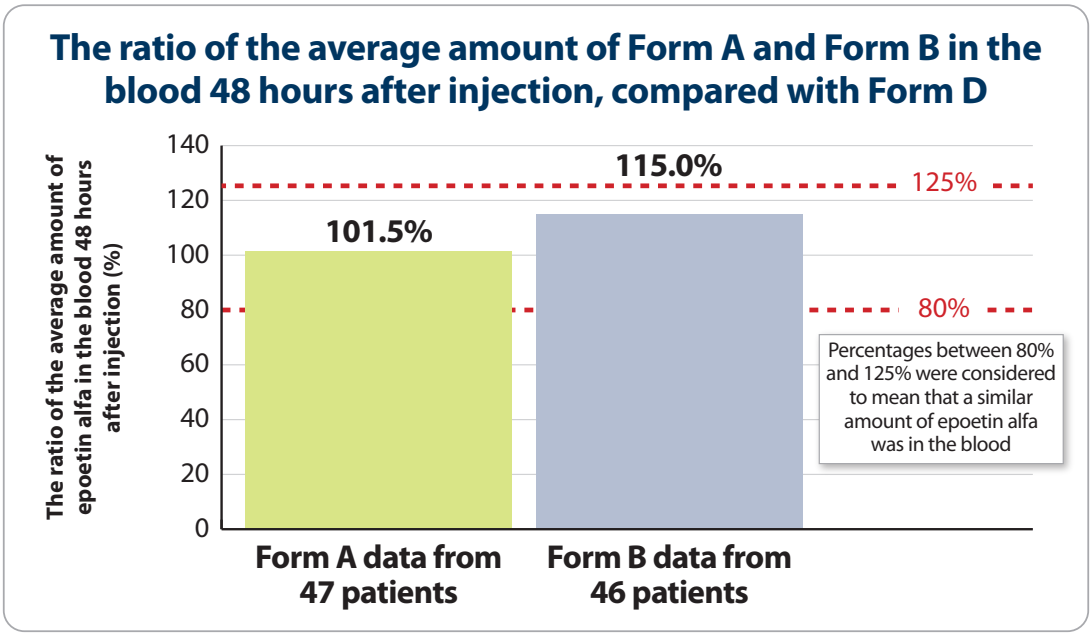
The chart below shows these results.



When comparing Forms A and B to Form D, the researchers found that the average amount of epoetin alfa in the participants' blood was:

- 101.5% for Form A
- 115.0% for Form B

The chart below shows these results.



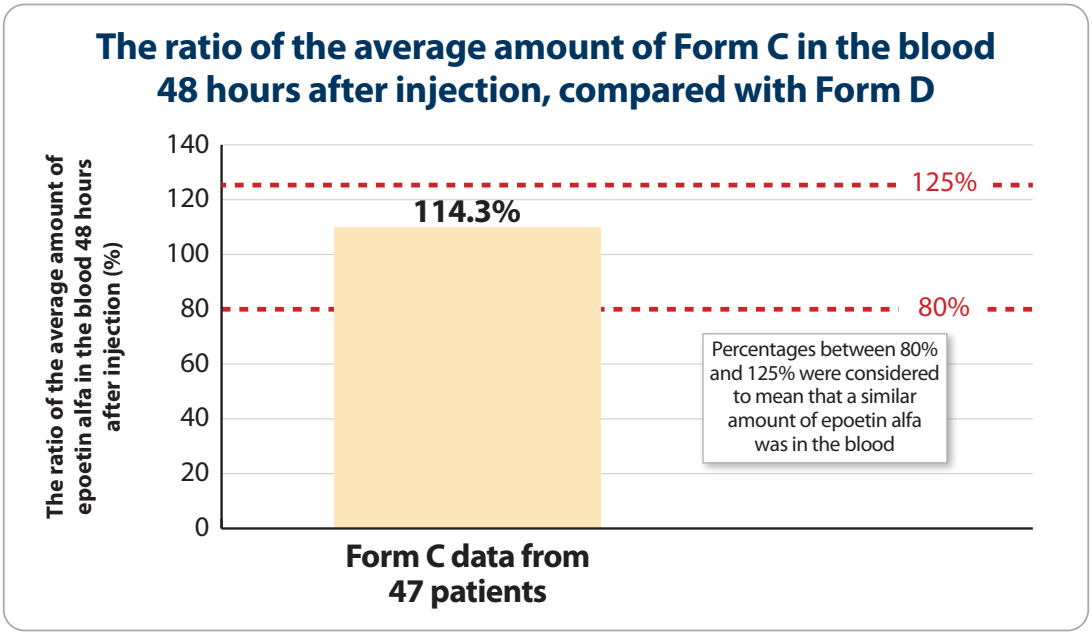
Was the amount of the two US forms of epoetin alfa in the blood similar over time?

Yes. Although there was a small difference in between the two US forms, the difference was so small that researchers considered them to be the same.

The researchers used the same method to compare the two US forms as they used to compare the European and US forms of epoetin alfa.

When comparing Form C to Form D, the researchers found that the average amount of epoetin alfa in the participants' blood was 114.3% for Form C.

The chart below shows these results.



What medical problems did 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 drugs. 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 drugs. 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 other 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 this study.

How many participants had adverse reactions?

- There were 45.3% of participants who had adverse reactions during the study. This was 24 out of 53 participants.

The amount of participants who had adverse reactions when they took the different forms of epoetin alfa were:

- 21.5% of participants when they got Form A during the study. This was 11 out of the 51 participants who got Form A.
- 13.7% of participants when they got Form B during the study. This was 7 out of the 51 participants who got Form B.
- 16.0% of participants when they got Form C during the study. This was 8 out of the 50 participants who got Form C.
- 25.5% of participants when they got Form D during the study. This was 12 out of the 47 participants who got Form D.

There were 5.9% of participants who stopped taking Form A because of adverse reactions they had during the study. This was 3 out of the 51 participants who received Form A.

What adverse reactions did the participants have?

The most common adverse reaction was headaches.

The table below shows the most common adverse reactions that happened in more than 1 participant during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during the study

	Form A (out of 51 participants)	Form B (out of 51 participants)	Form C (out of 50 participants)	Form D (out of 47 participants)
Headache	7.8% (4)	2.0% (1)	6.0% (3)	8.5% (4)
Dizziness	2.0% (1)	2.0% (1)	4.0% (2)	2.0% (1)
Diarrhea	2.0% (1)	2.0% (1)	0.0% (0)	2.0% (1)
Tiredness	0.0% (0)	2.0% (1)	2.0% (1)	0.0% (0)
Lacking energy	0.0% (0)	0.0% (0)	2.0% (1)	2.0% (1)
Muscle pain	0.0% (0)	0.0% (0)	4.0% (2)	0.0% (0)
Nausea	0.0% (0)	2.0% (1)	2.0% (1)	2.0% (1)
Small red bruises	2.0% (1)	0.0% (0)	0.0% (0)	2.0% (1)
Red, bumpy rash	2.0% (1)	2.0% (1)	0.0% (0)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn if the different forms of epoetin alfa that are available in different countries are similar.

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 epoetin alfa are not currently planned by AstraZeneca.

Where can I learn more about this study?

More information about this study is available on the website listed below.

- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5740C00003"** into the search box, and click **"Find a Study"**.

Full Trial Title: An Open-label, Randomized, Cross-over, Single-center Study to Compare Single-dose Pharmacokinetic and Pharmacodynamic Characteristics of US-marketed (Epogen®) and Two European-marketed Epoetin Alfas (Eprex® and Binocrit®) in Healthy Subjects

AstraZeneca Protocol Number: D5740C00003

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 participants.

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.

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