Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca AB

Drug Studied: Anifrolumab

Study Title: A study to learn what happens to anifrolumab and how injections of anifrolumab act in the body of participants with systemic lupus erythematosus

Thank you!

Thank you to the participants who took part in the clinical study for the study drug anifrolumab, also called MEDI-546. All of the participants helped researchers learn about using anifrolumab to help people with systemic lupus erythematosus, also called lupus or SLE.

AstraZeneca AB sponsored this study and thinks it is important to share the results of the study with the participants and the public. An independent non-profit organization called CISCRP helped prepare this summary of the study results. We hope it helps the participants understand and feel proud of their 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?

The participants were in the study for up to 15 months. But, the entire study took a little less than 2 years to finish. The study started in February 2017 and ended in December 2018.

The study included 36 participants in Hungary, South Korea, Poland, and the United States.

When the study ended, the sponsor reviewed the data collected 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 lupus and to give the study drug. Before a drug can be approved for patients to take, researchers do clinical studies to find out how safe it is and if it works.

In this study, the researchers wanted to find out how anifrolumab works in the body of a small number of participants with lupus. They also wanted to find out if the participants had any medical problems that occurred during the study.

Lupus is an immune system disease. This means that the body's natural defense system attacks healthy tissues. This causes inflammation in the joints, and in the skin and in other organs.

Researchers think that specific proteins in the body called "type 1 interferons" are involved in the inflammation that causes lupus. Interferons are also called IFN and are made by the immune system. In people with immune system diseases like lupus, the body can make too much IFN. There is also high activity of IFN genes in their blood. Anifrolumab is an antibody that works by stopping the type 1 IFN from sending signals through the body. Researchers think that this could reduce inflammation in patients with lupus and reduce disease symptoms.

In this study, the researchers wanted to learn more about how different doses of anifrolumab act in the blood.

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

- What was the highest amount of anifrolumab in the participants' blood after they got the first dose?
- What was the amount of anifrolumab in the participants' blood before the dose at week 12?
- Did the participants have less activity of IFN genes in their blood at week 12 of getting anifrolumab?
- What medical problems did the participants have that occurred during the study?

To answer the questions in this study, the researchers asked for the help of men and women diagnosed with lupus. The participants in this study were aged between 24 and 65. They had high activity of IFN genes in their blood and were already getting treatment for their lupus.

What kind of study was this?

This was a “double-blind” study. This means none of the participants, doctors or other study staff knew what treatment each participant received. Some studies are done this way because knowing what treatment the participants are getting can affect the results of the study. When the study ended, the sponsor found out which treatment the participants received so they could create a report of the study results.

The participants in this study were given either anifrolumab 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 get the study drug are actually caused by the study drug.

Anifrolumab and the placebo were each given through a needle under the skin, also called an injection. Doses of anifrolumab were measured in milligrams, also known as mg.

A computer program was used to randomly choose the treatment each participant was given. 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.

There were 4 groups in this study. The table below shows the different groups:

Group number	Study treatment	Number of injections per dose
Group 1 (14 participants)	150 mg of anifrolumab	1
Group 2 (13 participants)	300 mg of anifrolumab	2
Group 3 (5 participants)	Placebo to match 150 mg anifrolumab	1
Group 4 (4 participants)	Placebo to match 300 mg anifrolumab	2

What happened during the study?

Before the participants were given their first dose of study drug, the doctors checked their overall health to make sure that they could join the study.

The doctors:

- did a physical exam
- took blood and urine samples
- did a chest x-ray
- did a blood test to make sure the participants did not have tuberculosis
- checked the participants' lupus symptoms
- reviewed participants' lupus and other medications

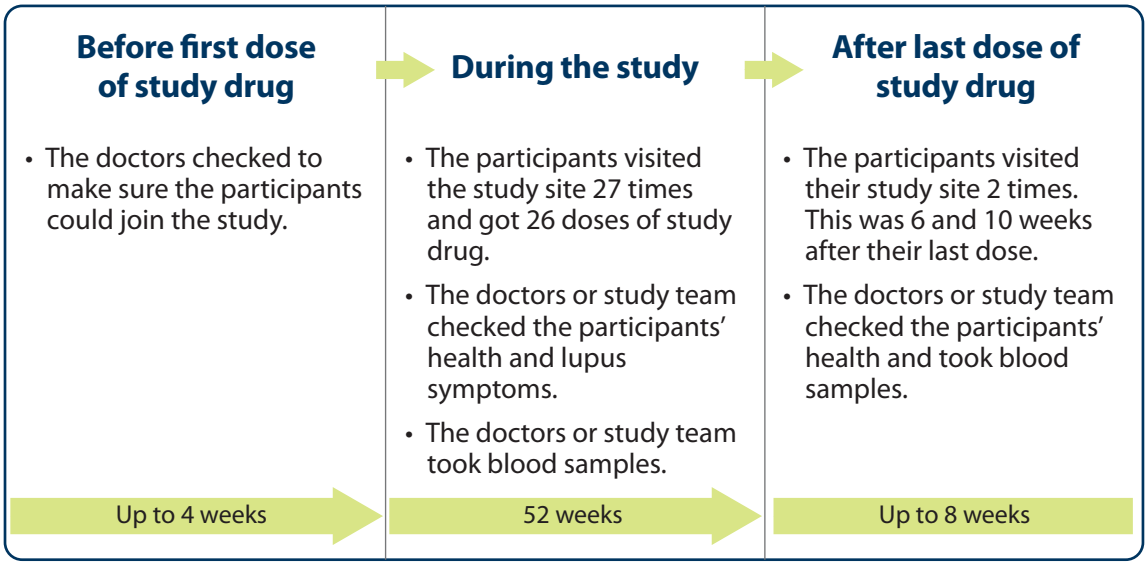
During the study, the participants visited their study site every 2 weeks, for a total of 27 visits. At each visit, the doctors or study team:

- did a physical exam and checked the participants' overall health
- checked the participants' lupus symptoms

At some visits, the doctors or study team took blood samples.

At each visit except the final visit, the doctors or study team gave the participants their dose of study drug.

After the participants were given their last dose of study drug, they visited their study site 2 times: during the 6th week, and during the 10th week after their last dose. At these visits, the doctors or study team checked the participants' overall health and took a blood sample.



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 individual results 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. 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.

What was the highest amount of anifrolumab in the participants' blood after receiving the first dose?

To answer this question, the researchers took blood samples from the participants right after they received their first dose of anifrolumab. The researchers measured the amount of anifrolumab in the blood in Groups 1 and 2. This was measured in micrograms per milliliter, also called µg/mL.

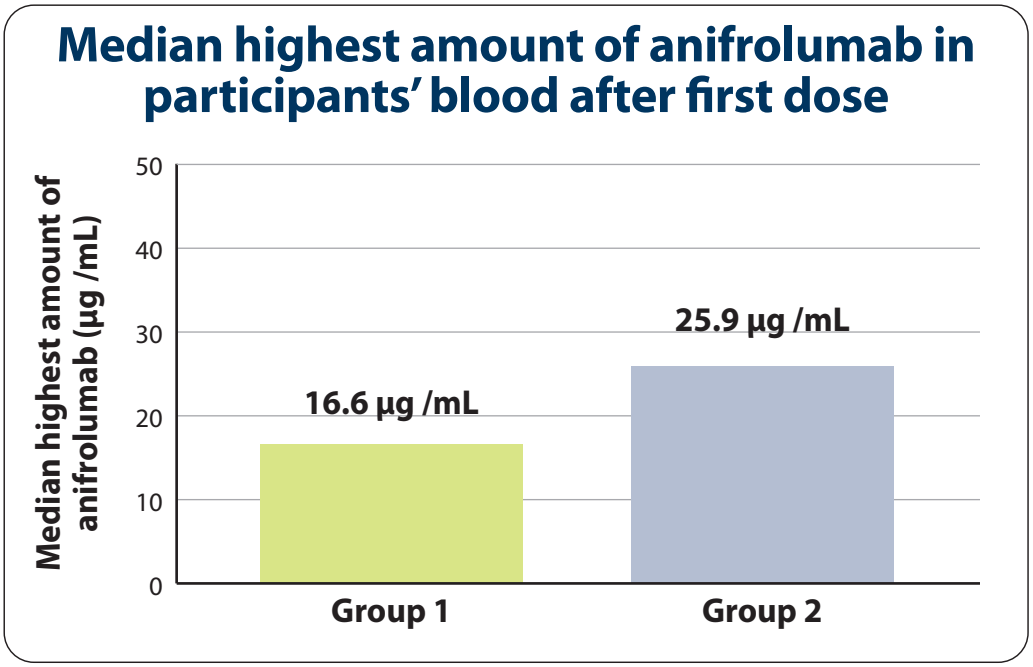
The researchers looked at the highest amounts of anifrolumab in the participants' blood using the median. The median is the middle number in a set of numbers. It is between the highest and lowest numbers. So, researchers collected all the values for the highest amount of anifrolumab and used the middle one of these.

They found that after the first dose, the median highest amount of anifrolumab was higher in the participants who received 300 mg of anifrolumab than in the participants who received 150 mg of anfrolumab.

After the first dose, the median highest amount of anifrolumab in the blood of participants who got anifrolumab was:

- 16.6 µg/mL in Group 1
- 25.9 µg/mL in Group 2

These measurements were not done for Groups 3 and 4, since the participants in these groups did not get anifrolumab.



What was the amount of anifrolumab in the participants' blood before the dose at week 12?

The researchers wanted to know how much anifrolumab stayed in the participants' blood after getting several doses. To answer this question, the researchers took blood samples from the participants just before they received their dose of anifrolumab at week 12 of the study. They measured the amount of anifrolumab in the blood in Groups 1 and 2. This was measured in micrograms per milliliter, also called µg/mL.

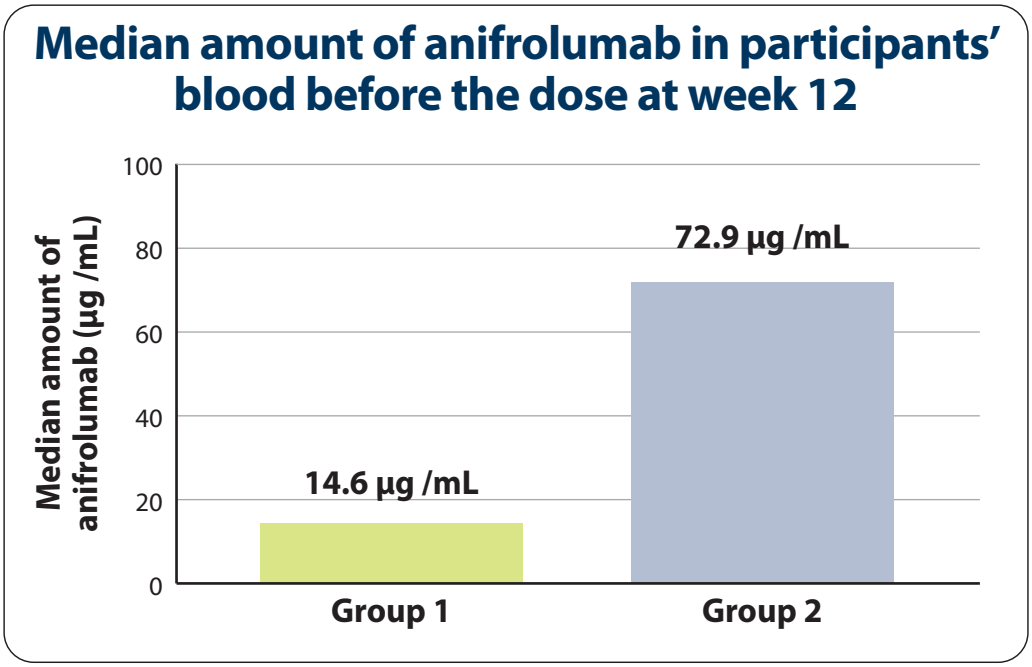
The researchers looked at these measurements using the median.

They found that at week 12, the median amount of anifrolumab was higher in the participants who had been getting 300 mg of anifrolumab than in the participants who had been getting 150 mg of anfrolumab.

The median amount of anifrolumab in the participants' blood before getting the dose at week 12 was:

- 14.6 µg/mL in Group 1
- 72.9 µg/mL in Group 2

These measurements were not done for Groups 3 and 4, since the participants in these groups did not receive anifrolumab. The graph below shows the median amount of anifrolumab in the participants' blood before the dose at week 12 for groups 1 and 2.



Did participants have less activity of IFN genes in their blood at week 12 of getting anifrolumab?

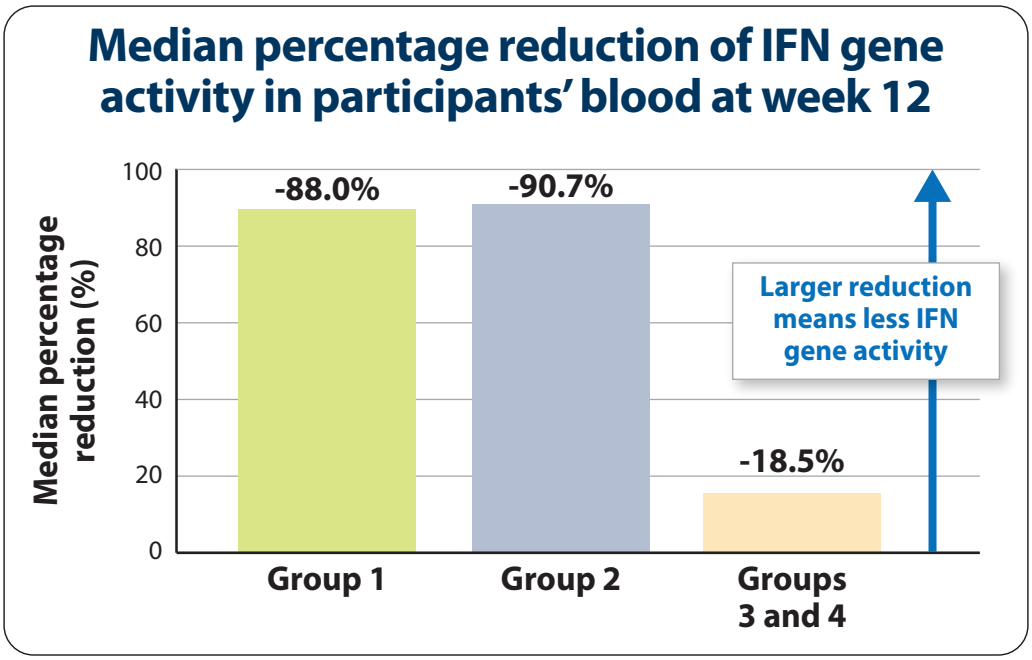
Yes. To answer this question, the researchers took blood samples from the participants in each treatment group before they got their dose of anifrolumab or placebo at week 12. The participants in the study had high activity of IFN genes when they started treatment. The researchers measured the activity of IFN genes in the blood and calculated the percentage that it reduced after treatment. They looked at these percentages using the median.

The researchers found that there was less IFN gene activity, when measured as a median, in the participants who got anifrolumab compared to those who got the placebo. They looked at the results for Groups 3 and 4 together, since the participants in both of these groups got the placebo.

The researchers found that after 12 weeks of treatment, the median percentage reduction of IFN gene activity was:

- 88.0% in Group 1
- 90.7% in Group 2
- 18.5% in Groups 3 and 4 combined

The chart below shows these results.



What medical problems did participants have that occurred during the study?

This section is a summary of the medical problems the participants had, which occurred during the study and 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.

In the results below, Group 1 participants were given 150 mg anifrolumab and Group 2 participants were given 300 mg anifrolumab. Results from Group 3 and 4 are combined. This is because the participants in both of these groups got the placebo.

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 other information about adverse reactions or other medical problems that happened during this study.

How many participants had serious adverse reactions?

There were 5.6% of participants who had serious adverse reactions that occurred during the study. This was 2 out of 36 participants. All the participants who had serious adverse reactions were in Group 1. Some participants had more than 1 serious adverse reaction. The serious adverse reactions were:

- ear infection
- shingles infection, which is caused by the herpes zoster virus
- mouth ulcers

There were 2.8% of participants who stopped taking anifrolumab because of adverse reactions that occurred during the study. This was 1 out of 36 participants.

None of the participants died due to serious adverse reactions that occurred during the study.

How many participants had adverse reactions?

There were 41.7% of participants who had adverse reactions that occurred during the study. This was 15 out of 36 participants.

- 57.1% of participants in Group 1 had adverse reactions that occurred during the study. This was 8 out of 14 participants.
- 30.8% of participants in Group 2 had adverse reactions that occurred during the study. This was 4 out of 13 participants.
- 33.3% of participants in Groups 3 and 4 combined had adverse reactions that occurred during the study. This was 3 out of 9 participants.

What adverse reactions did the participants have?

The most common adverse reaction that occurred across the groups during the study was shingles infection, which is caused by the herpes zoster virus.

The table below shows the most common adverse reactions that happened in more than 10% of participants who got anifrolumab. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during the study

	Group 1 (150 mg anifrolumab) Total 14 participants	Group 2 (300 mg anifrolumab) Total 13 participants	Groups 3 and 4 (Placebo) Total 9 participants
Shingles infection, which is caused by the herpes zoster virus	21.4% (3)	0.0% (0)	11.1% (1)
Infection of the airways	7.1% (1)	15.4% (2)	0.0% (0)
Headache	14.3% (2)	0.0% (0)	0.0% (0)

How has this study helped researchers and how will it help patients in the future?

This study helped researchers learn about how anifrolumab injections act in the blood of people with lupus and it may help patients with lupus in the future.

Researchers look at the total 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 study drug are ongoing.

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 **"NCT02962960"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"2016-003246-93"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D3461C00008"** into the search box, and click **"Find a Study"**.

Full study title: A Multicenter, Randomized, Double-Blind, Placebo-controlled, Phase 2 Study Characterizing the Pharmacokinetics, Pharmacodynamics, and Safety of Anifrolumab Following Subcutaneous Administration in Adult Systemic Lupus Erythematosus Subjects with Type 1 Interferon test High Result and Active Skin Manifestations

National Clinical Trials number: NCT02962960

AstraZeneca Protocol Number: D3461C00008

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

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