AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Anifrolumab

Study Purpose: This study was done to learn how anifrolumab works in participants with active proliferative lupus nephritis

Protocol Number: D3461C00007

Thank you!

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

You and all of the participants helped researchers learn more about anifrolumab to help people with active proliferative lupus nephritis.

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 of this study

Why was the research needed?

Researchers are looking for a better way to treat active proliferative lupus nephritis. Before a drug can be approved for people to get, researchers do clinical studies to find out how it works and how safe it is.

What treatment did the participants get?

The participants in this study got either a low or high dose of anifrolumab, or a placebo. A placebo looks like a drug but does not have any medicine in it. They also got standard of care treatment. Standard of care is the treatment the medical community thinks is appropriate and widely accepted for a condition.

What were the results of this study?

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

- **Did anifrolumab plus standard of care decrease inflammation in the kidneys compared to a placebo plus standard of care?**

  To answer this question, the researchers measured the levels of proteins in the urine as a measure of kidney inflammation. Overall, for both the anifrolumab and the placebo group, there was a decrease in inflammation in the kidneys after 52 weeks. The researchers did not find a difference between how much anifrolumab and the placebo decreased inflammation in the kidneys.

- **What medical problems happened during this study?**

  There were 36.6% of participants who had medical problems that the study doctors thought might be related to either anifrolumab or the placebo during the study. This was 53 out of 145 participants. The most common medical problem was herpes zoster infection, also called shingles.

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 also can be found on these websites.

Who took part in this study?

The researchers asked for the help of men and women with active proliferative lupus nephritis.

The participants in this study were 18 to 67 years old when they joined.

The study included 147 participants in Argentina, Australia, Belgium, France, Germany, Hungary, Italy, Mexico, Peru, Poland, Russia, Serbia, South Korea, Spain, Taiwan, and the United States.

Why was the research needed?

Researchers are looking for a better way to treat active proliferative lupus nephritis. Before a drug can be approved for people to get, 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 anifrolumab works in participants with active proliferative lupus nephritis. They also wanted to find out if the participants had any medical problems during the study.

Normally, the body's immune defense system only attacks infections or cancer cells. But in people with lupus, the body's immune defense system wrongly attacks the body's own healthy tissues. This can cause inflammation in the joints, skin, kidneys, and other organs. When there is inflammation of the kidneys in someone with lupus, it is known as "lupus nephritis". Doctors can tell the type of lupus nephritis a person has by taking a small piece of the kidney with a small surgical procedure called a biopsy. Doctors can then look at this small piece of the kidney, under a microscope to see if it has a certain pattern called "active proliferative lupus nephritis" and needs a certain type of treatment.

Researchers think that specific proteins in the body called "type 1 interferons" are involved in the inflammation that causes lupus and lupus nephritis. Interferons are also called IFN and are made by the immune system. In people with lupus and other diseases of the immune system, also called autoimmune diseases, the body can make too much IFN.

Anifrolumab is a drug that works by stopping the type 1 IFN from sending signals through the body. Researchers think that this could decrease inflammation and disease symptoms in people with lupus and lupus nephritis.

In this study, the researchers wanted to find out if anifrolumab works in participants with active proliferative lupus nephritis.

What was the purpose of this study?

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

- Did anifrolumab plus standard of care decrease inflammation in the kidneys compared to a placebo plus standard of care?
- What medical problems did the participants have during the study?

The answers to these questions are important to know before other studies can be done to find out if anifrolumab helps improve the health of people with active proliferative lupus nephritis.

What treatments did the participants get?

In this study, all of the participants got either a low or high dose of anifrolumab plus standard of care or a placebo plus standard of care.

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 drug are actually caused by the drug.

"Standard of care" means the treatment that the medical community thinks is appropriate and widely accepted for a condition.

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 getting. 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 research sponsor found out which treatment the participants got so they could create a report of the study results.

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

Each treatment was given slowly through a needle into a vein. This is known as an IV infusion.

The chart below shows the treatments the participants got in Year 1.

	Anifrolumab plus standard of care	Placebo plus standard of care
	• 98 participants	• 49 participants
	• Anifrolumab as an IV infusion • Standard of care	• Placebo as an IV infusion • Standard of care
	• Low dose of anifrolumab once every 4 weeks for 52 weeks Or • High dose of anifrolumab once every 4 weeks for 12 weeks, then low dose of anifrolumab once every 4 weeks for 40 weeks	• Placebo once every 4 weeks for 52 weeks

What happened during this study?

The participants were in the study for up to 116 weeks. But the entire study took about 5 years to finish.

The study started in November 2015 and ended in January 2021.

The chart below shows what happened during the study.

Before the participants got study treatment

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
- took blood and urine samples
- took x-ray scans of the participants' chests
- checked the participants' heart health using an electrocardiogram, also called an ECG
- if necessary, used surgery to take a sample of the kidney, also known as a biopsy
- checked how well the participants were able to do their usual daily activities

4 weeks

While the participants got study treatment

at least 13 visits

The study doctors:

- did a physical exam and asked about the participants' medications and any medical problems
- took blood and urine samples
- checked how well the participants were able to do their usual daily activities

The participants:

- got IV infusions of their study drug once every 4 weeks for 52 weeks
- could receive the same study drug for another 52 weeks if they had a response to their study drug
- took standard of care treatment as tablets by mouth every day

104 weeks

After the participants got study treatment

2 visits

The study doctors:

- did a physical exam and asked about the participants' medications and any medical problems
- took blood and urine samples
- checked how well the participants were able to do their usual daily activities

8 weeks

What were the results of this 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 list of 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 anifrolumab plus standard of care decrease inflammation in the kidneys compared to a placebo plus standard of care?

No. To answer this question, the researchers measured the levels of protein in the urine over a 24-hour period.

Sometimes when the kidneys are inflamed or damaged, proteins that normally stay in the kidneys can get into the urine. A high level of proteins leaking into the urine can show ongoing kidney inflammation or permanent kidney damage. A low level of proteins in the urine means that there is little kidney inflammation or damage.

The researchers measured the levels of protein in the participants' urine at the start of the study and after 52 weeks. They then calculated the change in the levels of protein leakage into the urine at 52 weeks of treatment as compared to leakage before treatment for both the anifrolumab and placebo groups. The low and high dose group of anifrolumab were grouped and calculated together.

Overall, for both the anifrolumab and the placebo groups, the researchers found a decrease in inflammation in the kidneys after 52 weeks. The researchers did not find a difference between how much anifrolumab and the placebo decreased inflammation in the kidneys.

What medical problems happened during this 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 anifrolumab.

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.

It was planned that 98 participants would get anifrolumab plus standard of care. But, there were 2 participants who did not get anifrolumab plus standard of care. So, the results below include only 96 of the 98 participants for that group.

Did any adverse reactions happen during this study?

	Anifrolumab plus standard of care (out of 96 participants)	**Placebo plus standard of care (out of 49 participants)**
How many participants had adverse reactions?	38.5% (37)	32.7% (16)
How many participants had serious adverse reactions?	11.5% (11)	10.2% (5)
How many participants stopped getting study treatment due to adverse reactions?	7.3% (7)	4.1% (2)

What serious adverse reactions happened during this study?

The most common serious adverse reaction was herpes zoster, also called shingles, which is an infection caused by the same virus as chickenpox and leads to a painful, blistering rash in 1 part of the body. The table below shows the serious adverse reactions that happened during the study.

Serious adverse reactions

Serious adverse reaction	Anifrolumab plus standard of care (out of 96 participants)	Placebo plus standard of care (out of 49 participants)
Shingles	4.2% (4)	0.0% (0)
Cancer in the lining of the womb	1.0% (1)	0.0% (0)
Diarrhea and vomiting caused by a viral infection	1.0% (1)	0.0% (0)
Feeling generally unwell	1.0% (1)	0.0% (0)
Flu infection	1.0% (1)	0.0% (0)
Infection in the groin, caused by a bacteria	1.0% (1)	0.0% (0)
Inflammation in the lungs	1.0% (1)	0.0% (0)
Reaction related to the infusion	1.0% (1)	0.0% (0)
A viral infection called cytomegalovirus	1.0% (1)	2.0% (1)
Infection caused by breathing in spores or fungus, which has spread to other parts of the body	0.0% (0)	2.0% (1)
Infection in the lungs	0.0% (0)	2.0% (1)
Inflammation of the membranes that surround the brain and spinal cord	0.0% (0)	2.0% (1)
Infection of the outer ear, caused by a bacteria	0.0% (0)	2.0% (1)

What adverse reactions happened during this study?

The most common adverse reaction was shingles.

The table below shows the adverse reactions that happened in more than 1 participant during the study. There were other adverse reactions but these happened in only 1 participant.

Most common adverse reactions

Adverse reaction	Anifrolumab plus standard of care (out of 96 participants)	Placebo plus standard of care (out of 49 participants)
Shingles	11.5% (11)	4.1% (2)
Infection of the parts of the body that carry urine	6.3% (6)	0.0% (0)
Nose and throat infection	5.2% (5)	0.0% (0)
Inflammation of the airways in the lungs	6.3% (6)	4.1% (2)
Inflammation of the nose and throat	4.2% (4)	4.1% (2)
Herpes in the mouth	3.1% (3)	2.0% (1)
Herpes simplex, a viral infection of the mouth or the genitals	2.1% (2)	2.0% (1)
Infection of the middle ear	2.1% (2)	2.0% (1)
Infusion-related reaction	1.0% (1)	4.1% (2)
Allergic reactions	2.1% (2)	0.0% (0)
Diarrhea	1.0% (1)	2.0% (1)
Infection of the lungs	1.0% (1)	2.0% (1)
Reddening of the skin	1.0% (1)	2.0% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about how anifrolumab works in participants with active proliferative lupus nephritis.

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 anifrolumab are planned.

Where can I learn more about this study?

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

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02547922"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search",** then type **"2015-001442-29"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D3461C00007"** into the search box, and click **"Find a Study"**.

Full Study Title: A Multicentre, Randomised, Double-blind, Placebo-controlled, Phase 2 Study Evaluating the Efficacy and Safety of Anifrolumab in Adult Subjects with Active Proliferative Lupus Nephritis

AstraZeneca AB Protocol Number: D3461C00007

National Clinical Trials Number: NCT02547922

EudraCT Number: 2015-001442-29

AstraZeneca AB sponsored this study and has its headquarters in Söderltälje, 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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Version 1.0 2021_10_27