ARTHUR

Report of study results for participants

Genentech

Roche

THANK YOU

for taking part in the ARTHUR (WA28029) study!

Thanks to you, we now know more about how the study medicine works in children with juvenile idiopathic arthritis.

About this report:

This report will help you understand more about the ARTHUR study and what we learned from the results.

Some of the words used to describe the results of the study can be difficult to understand. We have included definitions in the glossary at the end of this report to explain these words.

This report shows results collected during the study from June 2013 to October 2019. These results may not tell us everything about the risks and benefits of the study medicine.

What was the ARTHUR study about?

The aim of the study was to learn more about the medicine **tocilizumab (TCZ)** when it is used to treat a type of childhood arthritis known as **juvenile idiopathic arthritis (JIA)**.

Everyone who took part in the study had a rare type of JIA known as **systemic juvenile idiopathic arthritis**. In this report we shorten this and say **sJIA**. This is a serious condition where swelling occurs in the joints, but also affects the whole body. The most common symptoms of sJIA are fever, skin rash, and painful, stiff joints. Children who have more severe sJIA may have damage to their joints or trouble moving normally.

Let's break it down...

Systemic
The whole body is affected, not just the joints

Juvenile
Occurs in children

Idiopathic
We don't know what causes it

Arthritis
Swelling or tenderness of the joints (such as knuckles, wrists, knees, hips) that often causes pain and trouble moving

About the study medicine: tocilizumab (TCZ)

TCZ is a medicine that is already used to treat some types of arthritis in adults and children. For children with sJIA, TCZ can be given **every 2 weeks**. TCZ can be given through a tube connected to a vein (an infusion) or a needle just under the skin (an injection).

When taking TCZ, children may have abnormal blood test results. We call these **laboratory abnormalities**. These changes to your blood might happen even though your arthritis is well-controlled. If your blood test shows that you have a laboratory abnormality, your doctor will ask you to stop taking TCZ until your blood test is normal again.

If you stop taking TCZ, the signs and symptoms of your arthritis may get worse—this is called a **flare**. It is important for doctors to keep children safe and their arthritis well-controlled. This means limiting both laboratory abnormalities and flares in children taking TCZ.

In this study, we wanted to find out if children whose arthritis was well-controlled with TCZ, but had a laboratory abnormality, **could be given TCZ less often** *(instead of stopping TCZ)*.

What does 'well-controlled sJIA' mean?

When the signs and symptoms of arthritis (such as joint pain or swelling) are reduced, and there are no flares or fever.

What are laboratory abnormalities?

Your body reacts to the medicines you take. Doctors measure certain things in your blood to make sure your body is reacting safely to medicine. If the following things change in your blood while you are taking TCZ, doctors will say you have a laboratory abnormality:

Platelet
A low level of 'platelets'—the part of blood that helps it to clot. This is a warning sign of a higher risk of bleeding

White blood cell
A low level of white blood cells. This is a warning sign of a higher risk of infections

Liver enzyme
A high level of proteins in your liver. This is a warning sign of possible liver damage

What did we test?

In this study we looked at whether giving TCZ as an infusion **every 3 weeks** or **every 4 weeks** (instead of **every 2 weeks**) continued to control children's arthritis.

Safety was also important to us. So, we recorded any unwanted changes in children's health while they were in the study. These changes are known as **side effects**. Side effects may or may not be caused by taking a medicine.

TCZ infusion every 3 weeks

TCZ infusion every 4 weeks

How did we carry out the study?

There were two parts to the study: Part 1 and Part 2 **(the main study)**.

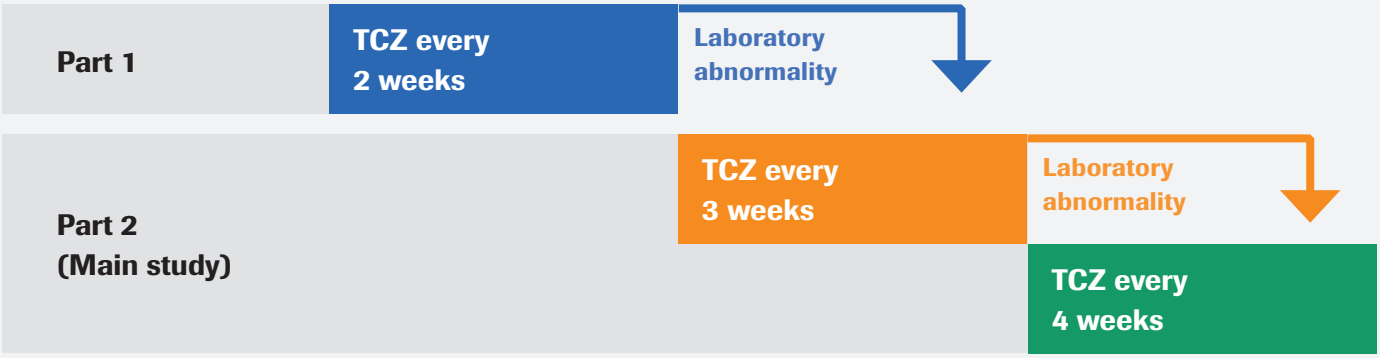
What happened during Part 1?

The purpose of Part 1 was to help us **find children who could take part in Part 2 (the main study)**.
In Part 1, 19 children were given TCZ **every 2 weeks** for up to 24 weeks. They could move to the main study if:

- ✓ They had a laboratory abnormality and
- ✓ Their arthritis was well-controlled

What happened during Part 2 (the main study)?

All children in the main study were given TCZ **every 3 weeks** for up to 1 year. If a child had a laboratory abnormality during this time, they were switched to receiving TCZ **every 4 weeks**.



Who took part in the main study?

22 children diagnosed with sJIA (between 2 and 17 years old)

6 children came from Part 1 of the study

16 children came directly into the main study

64%

14 of the 22 children were girls

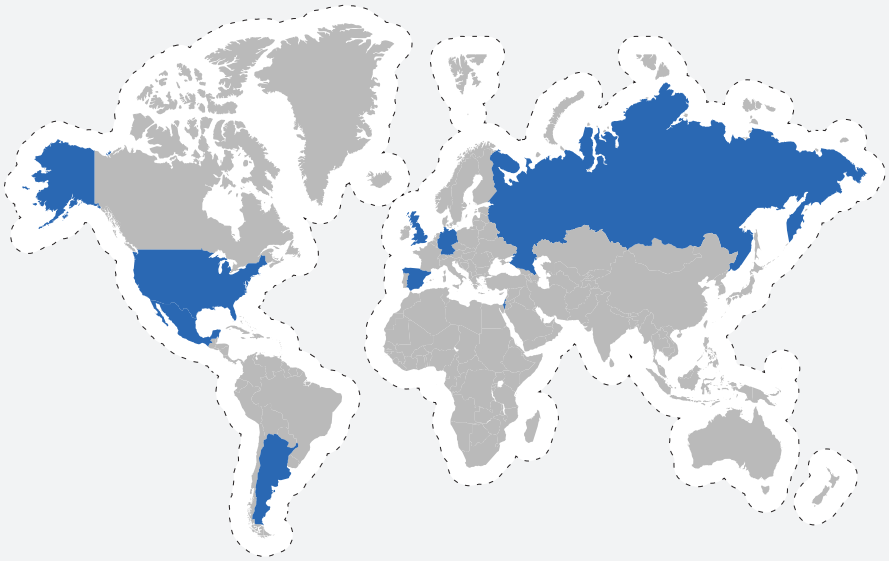
36%

8 of the 22 children were boys

All children had a laboratory abnormality while receiving TCZ **every 2 weeks** and their sJIA was well-controlled

How many children participated from each country?

Germany	Russia
4	**4**
Spain	USA
4	**3**
Argentina	Israel
2	**2**
Mexico	UK
2	**1**



What types of tests did we do?

We took a blood sample at each clinic visit to check for laboratory abnormalities. We also measured the amount of TCZ in children's blood. We did this to make sure the right amount of TCZ was in their bodies to get the right effect.

Doctors paid close attention to the signs of arthritis in children who took part in the main study. They did this by:

- Noting down any sJIA flares
- Measuring the children's temperature to detect fever caused by sJIA
- Calculating the children's *Juvenile Arthritis Disease Activity Score (JADAS-71)*, which is a score that helps us to know if sJIA is staying well-controlled

We also asked children in the main study and their parents or caregivers to complete 3 surveys. We did this to help us measure whether their arthritis was staying well-controlled.

- The *Childhood Health Assessment Questionnaire (CHAQ-DI)*. The answers helped us to understand if it was hard for the children to do daily activities
- The *Parents/patient's global assessment of overall well-being*. The answers helped us to understand how the children were feeling
- Finally, we asked the children to score the level of pain they were feeling

How long was the main study?

The study lasted about **1 year**

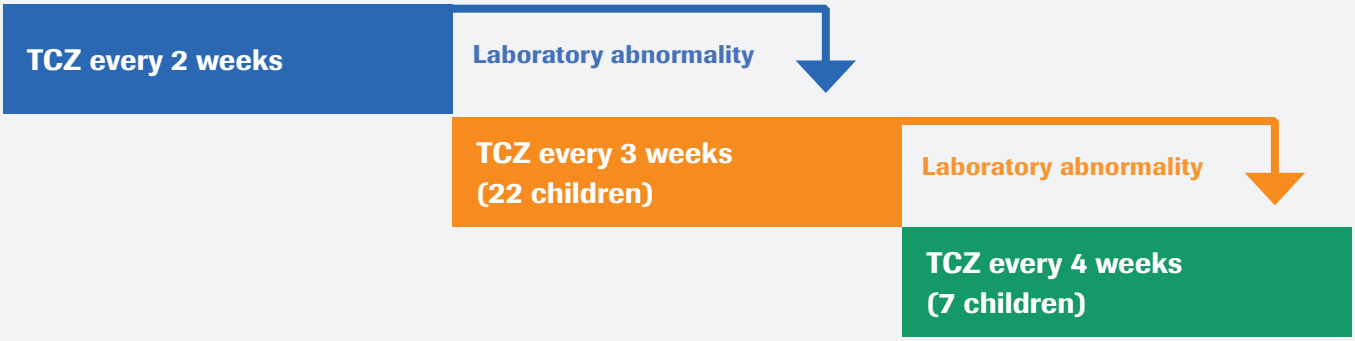
During that year, children who took part visited the clinic up to **27 times**

What did we learn?

Did children have laboratory abnormalities when they received TCZ less often?

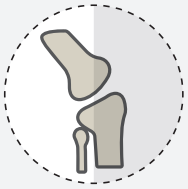
Yes, about half of the children did. The other half did not.

- **12/22** children in the main study had a laboratory abnormality when receiving TCZ less often
- **7** of these children switched to receiving TCZ **every 4 weeks**



Did receiving TCZ less often keep children's arthritis well-controlled?

In most children it did.



sJIA continued to be well-controlled in most children in the main study.

- **5/22 children** experienced an sJIA flare:
  - **4 children** were receiving TCZ **every 3 weeks**
  - **1 child** was receiving TCZ **every 4 weeks**

None of the children had a fever because of their sJIA

JADAS-71 scores stayed low for most children during the main study. This told us most children's sJIA continued to be well-controlled

Answers to the 3 surveys completed by children and their parents or caregivers also told us that sJIA continued to be well-controlled

Did the amount of TCZ in children's bodies change?

Yes, it did.

- When we gave TCZ less often, the amount of TCZ in children's bodies went down. This was expected
- Because sJIA stayed well-controlled for most children, we know TCZ continued to have the right effect

Were there any side effects?

Yes, there were some side effects.

Most children had a side effect, but the majority were not serious. The most common side effects were infections. Infections are illnesses caused by organisms living in your body that are not usually there.

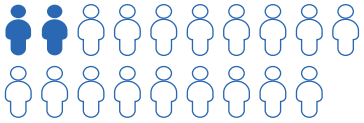
Overall, the side effects were like those seen in other sJIA studies with TCZ.

Part 1 safety summary

16/19 (84%)

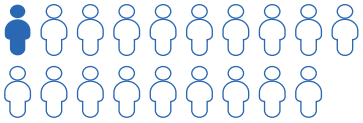
children had a side effect during the *24 weeks*, but most of them were not serious

2/19 (11%)



children stopped taking TCZ because of the side effects they experienced

1/19 (5%)



children had a side effect that was serious. One child had a serious complication of sJIA called macrophage activation syndrome (MAS). During MAS, the immune system (that normally protects the body) overreacts, and it can be dangerous

Part 2 safety summary

21/22 (95%)

children had a side effect during the *52 weeks*, but most of them were not serious

1/22 (5%)

children stopped taking TCZ because of the side effects they experienced

2/22 (9%)

children had a side effect that was serious. One child had pneumonia, an infection in the lungs. Another child had hypertransaminasaemia, a problem with how the liver works

What were the key results?

Most children continued to have well-controlled sJIA while receiving TCZ less often. Some children did have sJIA flares

The side effects were like those seen in other sJIA studies where children were given TCZ

About half of the children had a laboratory abnormality while receiving TCZ **every 3** or **every 4 weeks**

THANK YOU

You are part of a very important group of people around the world who are helping advance sJIA research.

We are so grateful that you and your family took part in the ARTHUR study. Thank you for giving your time to attend the clinic visits and to complete all the tests.

Where can I find more information?

You can find more information about this study on the websites listed below:

- https://clinicaltrials.gov/ct2/show/NCT01734382
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2012-000444-10/results
- https://forpatients.roche.com

If you have any further questions after reading this report:

- Visit the ForPatients platform and fill out the contact form: https://forpatients.roche.com
- Contact a representative at the Roche office in your region

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study clinic

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment

Glossary of key words

Arthritis

A swelling or tenderness of the joints (such as knuckles, knees, elbows, hips) that often causes pain. For children with sJIA, this can also cause fever and skin rash.

Idiopathic

The exact cause is unknown.

Juvenile

Occurring in children.

Laboratory abnormality

A change in blood causing an abnormal blood test result.

Side effects

Unwanted changes in health that may or may not be caused by taking a medicine.

sJIA flare

When the signs and symptoms of sJIA get worse.

Systemic

Affecting the whole body.

Well-controlled sJIA

When the signs and symptoms of arthritis (such as joint pain or swelling) are reduced, and there are no flares or fever.