



JIGSAW 118

Report of study results
for participants



THANK YOU

for taking part in the JIGSAW 118 (WA28118) 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 has been written to help you understand a little more about the JIGSAW 118 study and what we learned from the results.

Since some of the words used to describe the results can be difficult to understand, we have included a few definitions in the glossary at the end of this report to explain them more clearly.

The information is based on results collected up to the end of the study in June 2017. Please note, the results shown in this report are a summary from all children in the JIGSAW 118 study and may not tell us everything about the risks and benefits of a medicine.

What was the JIGSAW 118 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**, which is normally shortened to **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 with daily increases in body temperature, skin rash, and painful, stiff joints. Children who have more severe sJIA may have damage to their joints, trouble moving normally, or in the most serious cases, it can cause complications that may lead to death.

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 disability

About the study medicine: tocilizumab (TCZ)

TCZ is a medicine that is already used to treat some types of arthritis in adults and children. Before this study, TCZ could only be given to children through a tube connected to a vein (intravenously)—this has to be done at the hospital and takes about 1 hour.

In this study we wanted to find out if TCZ could be given to children as an injection just below the skin (subcutaneously), so that it would be easier to take at home. We also wanted to find out what the best dosage would be to treat sJIA when it is given by subcutaneous injection.

Some of the children who took part in this study were already being treated with intravenous TCZ, and their arthritis was under control. The rest of the children who took part had never been treated with TCZ, and their arthritis was poorly controlled.

What did we know before this study?

We knew



The **subcutaneous injection** dosage for **adults**



The **intravenous** dosage for **children**

We needed to find out



The **subcutaneous injection** dosage for **children**

What is the ‘best dosage’ and why is it important?

When taking any medicine, your doctor will tell you how much to take and how often to take it—this is called **the dosage**

Studies like JIGSAW are important because they inform doctors about how the medicine works in the body and the dosages that are most suitable and effective

Your doctor will decide on the best dosage for you based on a number of things, such as:

- How healthy you are now
- What illnesses you have had in the past
- What medicines you are taking now or used to take
- How much you weigh
- How you respond to the medicine

What did we test?

In this study we looked at the **pharmacokinetics (PK)** and **pharmacodynamics (PD)** of TCZ.

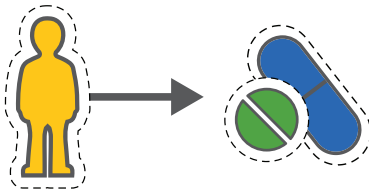
We also looked at whether your arthritis improved after you took the medicine.

Safety was important to us as well. So, we recorded any changes in your health after you took the medicine. These changes are known as 'side effects'.

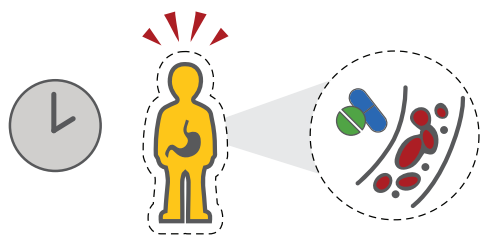
What are PK and PD?

Pharmacokinetics (PK)

Definition: what the body does to the medicine



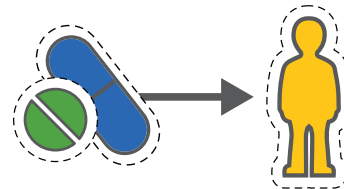
The types of things we look for: How long does it take the medicine to get to where it needs to be? How much medicine gets there? How long does it stay in the body?



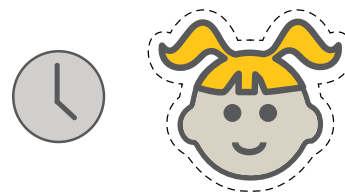
Example: When you take medicine for a headache, it takes a while for the medicine to start working. This is because your body needs to get the medicine from your stomach into your blood, so that your blood can take the medicine to where it hurts. After some time, the medicine stops working because your body has used it up

Pharmacodynamics (PD)

Definition: what the medicine does to the body



The types of things we look for: How does the body react after receiving the medicine?

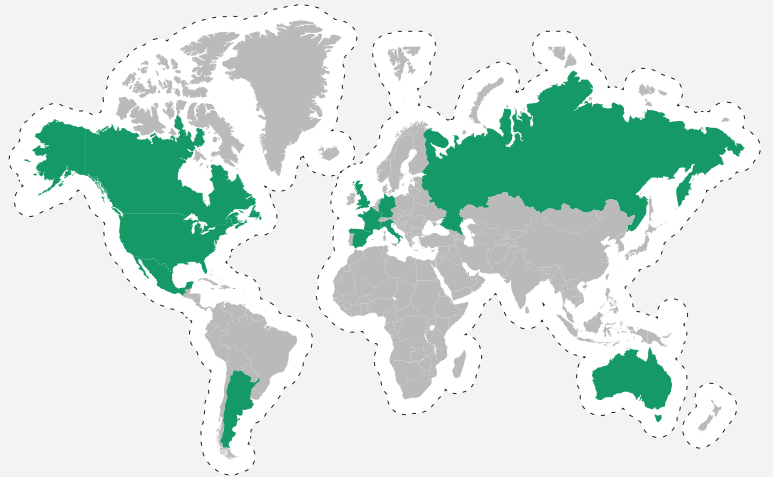


Example: When you take medicine for a headache, the medicine blocks how your body feels pain, which helps to get rid of the headache

How did we carry out the study?

How many children participated from each country?

USA	Germany	Spain	Canada
11	10	10	5
Argentina	Mexico	UK	France
3	3	2	2
Russia	Australia	Italy	
2	2	1	



Who took part in the study?



51 children diagnosed with sJIA (between 1 and 17 years old)

43%



22 of the 51 children were boys

57%



29 of the 51 children were girls



Children who did not respond well to non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids

51%



26 children had never been treated with TCZ and had poorly controlled sJIA

49%



25 children were being treated with intravenous TCZ and had well-controlled sJIA

How did we divide you into study groups?

Everyone who took part in the study was put into one of two groups. This was based on your body weight—whether you weighed **less than 30 kg** or **more than 30 kg**.

Why did we do this?

The dosage of medicines is sometimes changed depending on a person's body weight, to make sure that everyone has the same amount of medicine in their blood and gets the same effect.

- We know from previous studies with TCZ that children who weigh **less than 30 kg** usually need less TCZ than those who weigh **more than 30 kg**
- We therefore split the children who took part in JIGSAW 118 into two groups and gave them a dosage of TCZ based on how much they weighed
- **Note:** based on the expected levels of TCZ in the blood, children who weighed **less than 30 kg** were given the medicine every 10 days at the start of the study. The early results showed that some children in this group may have had higher levels of TCZ in their blood than in the other group, so the dosage was changed to every 2 weeks. This change helped to find the best dosage

Children weighing less than 30 kg



25 children

162 mg TCZ
every **10 days** or
every **2 weeks**

Children weighing at least 30 kg



26 children

162 mg TCZ
every **1 week**

How long was the study?



The study lasted
about **1 year**



During that year, you
visited the clinic up to
24 times

What types of tests did we do?

We took a blood sample at each clinic visit to allow us to regularly measure the amount of TCZ in your blood (PK), and how your body was responding to the medicine (PD).

We also measured specific substances in your blood known as **biomarkers** to understand more about how the medicine was working in your body (PD).



Another way to help us measure whether your arthritis was getting better was by asking you to fill out a survey called the *Childhood Health Assessment Questionnaire (CHAQ-DI)*. The answers helped us to understand how you were feeling and if it was hard for you to do daily activities



We also calculated your *Juvenile Arthritis Disease Activity Score (JADAS-71)* by using the results we collected during the study

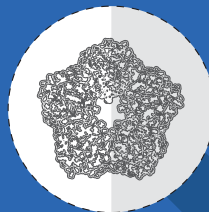


Lastly, your doctor regularly checked you for signs of arthritis, such as swelling and tenderness

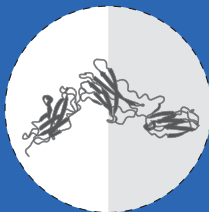
Which pharmacodynamic (PD) biomarkers did we look for?



IL-6
interleukin-6



CRP
C-reactive protein



sIL-6R
soluble interleukin-6
receptor



ESR
erythrocyte
sedimentation rate

What did we learn?

Did we find the best dosage for subcutaneous injection of TCZ?

Yes, we did. Using the PK and PD tests, we found out the best dosages of injected TCZ for children with sJIA in the two body weight groups. These were found to be:

Children weighing less than 30 kg

A single
TCZ injection
every 2 weeks



Children weighing at least 30 kg

A single
TCZ injection
every 1 week



Did arthritis get better after treatment?

Based on the two test scores we used (*CHAQ-DI* and *JADAS-71*), and the results of the biomarker tests that we measured, most children had inactive disease and over half were in clinical remission after taking the medicine for 1 year.

Some children did not see a change in their arthritis by the end of the study. This is because medicines do not always work the same way for everyone. Further research may help us to understand the reasons for this.

This study confirmed that TCZ can help treat children with sJIA at the dosages given by injection in JIGSAW 118.

By the end of the study

8/10 children had
inactive disease



By the end of the study

6/10 children were in
clinical remission



What does 'inactive disease' mean?

If the signs and symptoms of your arthritis (such as joint pain or swelling) disappear, then your doctor may tell you that your "disease is inactive"

What does 'clinical remission' mean?

If you have inactive disease for at least 6 months in a row, then your doctor may tell you that "your sJIA is in clinical remission". In some people the disease may come back after a while, but for other people it might never come back

Were there any side effects?

Yes, there were some. Nearly all of the children in the study had a side effect when they were given the medicine by injection, but most of them were not serious. Two children (out of 51) had a side effect that led to them stopping taking part in the study. Two children (out of 51) died during the study due to rare complications following serious infections.

Overall, the side effects were like those seen when TCZ is given intravenously to children with sJIA, apart from reactions at the injection site, which were similar to when other medicines are given by subcutaneous injection to children with sJIA.

Safety summary



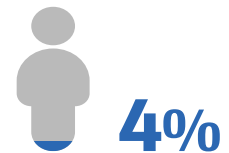
of children had a side effect, but most of them were not serious. The most common side effects were infections



of children had a reaction where the needle was injected (for example: pain, swelling, bruising, redness or itchiness)



of children had a side effect that was considered to be serious



of children stopped taking part in the study because of the side effects they experienced

In summary

What were the key results?



We found the best dosage for subcutaneous injection of TCZ for children with sJIA



After 1 year of treatment with subcutaneous TCZ, most children had inactive disease and over half were in clinical remission



The side effects were similar to those seen for intravenous TCZ or when other medicines are given by subcutaneous injection

THANK YOU

As a participant of the JIGSAW 118 study, you are part of a very important group of people around the world who are helping to advance medical research to treat arthritis in children.

We are so grateful that you and your family took part in this study. Thank you for generously 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/NCT01904292>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2012-003490-26/results>
- <https://forpatients.roche.com/en/trials/autoimmune-disorder/jia/a-study-of-subcutaneously-administered-tocilizumab-in-p-36947.html>

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

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

If you have any further questions after reading this report:

- Visit the ForPatients platform and fill out the contact form:
<https://forpatients.roche.com/en/trials/autoimmune-disorder/jia/a-study-of-subcutaneously-administered-tocilizumab-in-p-36947.html>
- Contact a representative at your local Roche office

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.

Biomarker

A specific substance in the body that can be used to measure the presence and progress of a condition. In this study, we measured pharmacodynamic (PD) biomarkers for childhood arthritis.

Clinical remission

When a disease (like arthritis) is inactive for at least 6 months in a row then the doctor may say that the disease is in clinical remission. In some people the disease may come back after a while, but for other people it might never come back.

Dosage

How much and how often a medicine is taken, as prescribed by the doctor.

Idiopathic

The exact cause is unknown.

Inactive disease

When the signs or symptoms of a disease (like arthritis) disappear, then the doctor may say that the disease is inactive.

Intravenous

When a medicine is given directly into a vein. This can either be through an injection or infusion, and is usually done at the hospital.

Juvenile

Occurring in children.

kg

This is a short way of writing kilograms, which is a unit of weight.

mg

This is a short way of writing milligrams, which is a unit of weight.

NSAIDs (non-steroidal anti-inflammatory drugs)

Medicines that are used to lower pain and swelling.

Pharmacodynamics (PD)

What the medicine does to the body. In other words, how the body reacts after receiving the medicine.

Pharmacokinetics (PK)

What the body does to the medicine. In other words, how long does it take the medicine to get to where it needs to be? How much medicine gets there? How long does the medicine stay in the body?

Side effects

Any symptoms someone experiences after taking a medicine, like a headache or a cough. These are recorded and reviewed during a study to monitor the safety of participants.

Subcutaneous injection

When a medicine is given by needle into the layer of fat just below the skin. In this study TCZ was given as a subcutaneous injection.

Systemic

Affecting the whole body.

