



JIGSAW 117

Report of study results
for participants



THANK YOU

for taking part in the JIGSAW 117 (WA28117) 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 117 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.

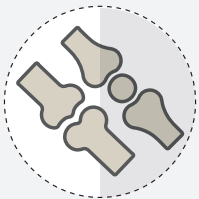
The information is based on results collected up to the end of the study in May 2016. Please note, the results shown in this report are a summary from all children in the JIGSAW 117 study and may not reflect all individual results.

What was the JIGSAW 117 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 swelling in five or more joints. This is known as **polyarticular-course juvenile idiopathic arthritis**, which is normally shortened to **pJIA** (or sometimes pcJIA).

pJIA, let's break it down...



Polyarticular
Affecting many 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 a needle 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 pJIA 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 by other treatments.

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 safe 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.

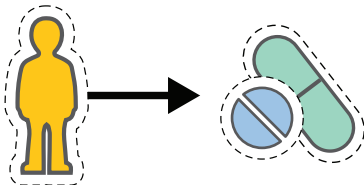
We also looked at whether your arthritis improved after you took the medicine.

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'.

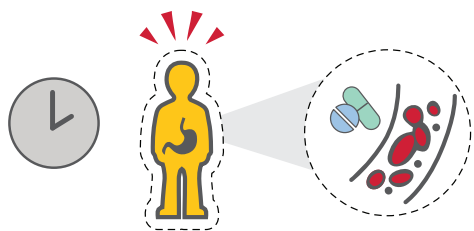
What are PK and PD?

Pharmacokinetics (PK)

Definition: what the body does to the medicine



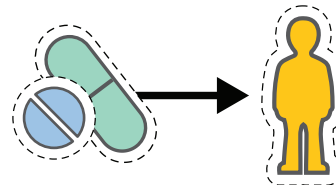
The types of things we look for: How long does it take the medicine to get to where it needs to be? How much medicine gets there? How long does it stay in the body?



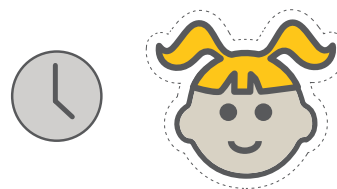
Example: When you take medicine for a headache, it takes a while for the medicine to start working. This is because your body needs to get the medicine from your stomach into your blood, so that your blood can take the medicine to where it hurts. After some time, the medicine stops working because your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

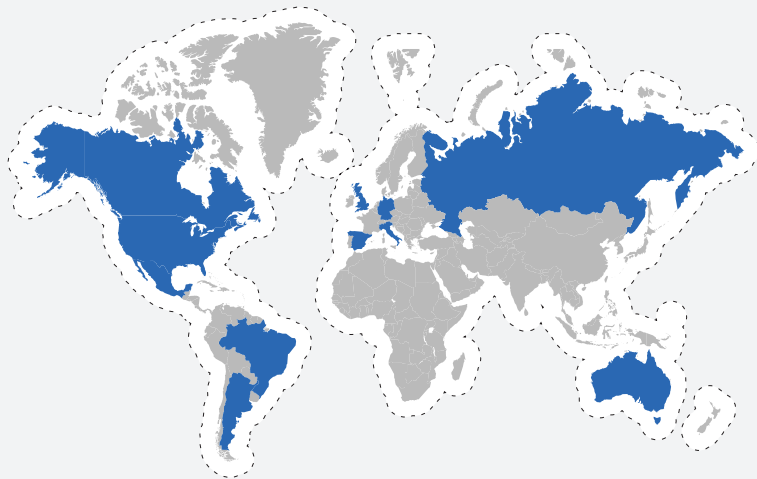


Example: When you take medicine for a headache, the medicine blocks how your body feels pain, which helps to get rid of the headache

How did we carry out the study?

How many children participated from each country?

USA	UK	Spain	Germany
11	9	7	6
Canada	Argentina	Brazil	Mexico
4	4	4	2
Italy	Russia	Australia	
2	2	1	



Who took part in the study?



52 children diagnosed with pJIA (between 1 and 17 years old)

31%



16 of the 52 children were boys

69%



36 of the 52 children were girls



Children who did not respond well to treatment with methotrexate (MTX)*

71%



37 children had never been treated with TCZ and had active pJIA

29%



15 children were being treated with intravenous TCZ and had well-controlled pJIA

* MTX is a common medicine used for the treatment of arthritis

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 117 into two groups and gave them a dosage of TCZ based on how much they weighed

Children weighing less than 30 kg



27 children



162 mg TCZ every 3 weeks

Children weighing at least 30 kg



25 children



162 mg TCZ every 2 weeks

How long was the study?



The study lasted about **1 year**



During that year, you visited the clinic about **15 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 and arthritis were 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

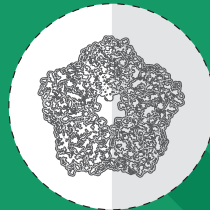


Lastly, your doctor regularly checked you for signs of arthritis, such as swollen and tender joints

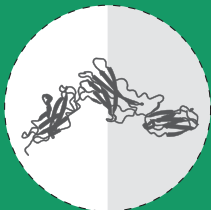
Which pharmacodynamic (PD) biomarkers did we look for?



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 pJIA in the two body weight groups. These were found to be:

Children weighing
less than 30 kg

A single
TCZ injection
every 3 weeks



Children weighing
at least 30 kg

A single
TCZ injection
every 2 weeks



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 felt better after taking the medicine for 1 year. The results showed that the **disease became inactive** in 70% of the children in the study.

This study confirmed that TCZ can help treat children with childhood arthritis at the dosages given by injection in JIGSAW 117.

Children weighing less than 30 kg

8/10 children had
inactive disease



Children weighing at least 30 kg

6/10 children had
inactive disease



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"

Were there any side effects?

Yes, there were some. Most children in the study had a small reaction when they were given the medicine by subcutaneous injection. None of these reactions were serious enough for anyone to leave the study.

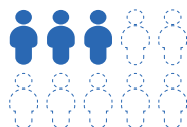
The side effects were like those seen when TCZ is given intravenously, or when other medicines are given by subcutaneous injection. We did not see any side effects in this study that we did not expect, so we do not have any new concerns about the safety of TCZ.

9/10



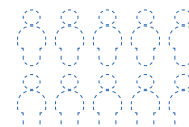
children had a side effect, but most of them were not serious. The most common side effects were infections

3/10



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

0/10



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 pJIA



Most children in the study felt that their arthritis got better after taking the medicine by subcutaneous injection for 1 year



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 117 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/NCT01904279>
- <https://www.clinicaltrialsregister.eu/ctr-search/trial/2012-003486-18/results>
- <https://forpatients.roche.com/en/trials/autoimmune-disorder/jia/a-study-of-subcutaneously--sc--administered-tocilizumab-80633.html>

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--sc--administered-tocilizumab-80633.html>
- Contact a representative at your local Roche office

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 questions about your own treatment:

- Speak to the doctor in charge of your treatment

Tocilizumab (TCZ) given by subcutaneous (SC) injection has been approved by many health authorities worldwide for the treatment of polyarticular juvenile idiopathic arthritis (pJIA) in children aged 2 years and older.

Glossary of key words

Arthritis

A swelling or tenderness of the joints (such as knuckles, knees, elbows, hips) that often causes pain.

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.

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.

Pharmacodynamics

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

Pharmacokinetics

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 changes in health that might be caused by taking a medicine.

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.

