Clinical Trial RESULTS

Roche

Research Sponsor: F. Hoffmann-La Roche Ltd.

Drug Studied: Tocilizumab (TCZ)

National Clinical Trial #: NCT01791153

EudraCT #: 2011-006022-25

Protocol #: WA28119

Results from Study Dates: July 2013 to April 2016

Full Title of Your Study: A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Tocilizumab in Subjects with Giant Cell Arteritis

Thank you!

As a clinical study participant, you belong to a large community of people around the world who advance the field of medicine. Your huge contribution and dedication to take part in a clinical study helps researchers answer important health questions.

Thank you for taking part in the global clinical study for the study drug tocilizumab. Researchers studied this treatment for use in patients with giant cell arteritis, or GCA. People with GCA are normally treated with medications called steroids, but these can cause unwanted side effects. You and the other patients helped researchers find out if adding tocilizumab to your steroid treatment helped you take less steroids while still controlling your GCA symptoms.

Your study is still ongoing. F. Hoffmann-La Roche, the sponsor of this study, thinks it is important for you to know the main results. The sponsor asked an independent non-profit organization called CISCRP and a medical writing organization called Synchrogenix to help prepare this summary for you. We hope it helps you understand the results and makes you feel proud of your important role in medical research. If you have questions about the results, please speak with your doctor, research nurse, or other team member at your study center.

What's happened since I joined the study?

Your study began in July 2013. This summary tells you the results up to April 2016. Study doctors are still collecting information, and some patients are still taking the study treatment.

Patients from 14 countries around the world were included in your study. A total of 250 patients at 76 study centers received at least 1 dose of a study drug. In the summer of 2016, Roche reviewed the data collected up to April 2016 and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers were looking for a different way to treat giant cell arteritis, or GCA. Patients with GCA develop swelling of the medium and large arteries that supply blood to the head and neck areas. This can result in symptoms like headache, tiredness, pain and stiffness in the shoulder and neck muscles, and jaw pain. More serious symptoms can include blindness and stroke.

GCA is normally treated with medications called steroids. Steroids can treat some patients with GCA. High doses of steroids taken for a long time usually help patients with GCA, but this can result in unwanted side effects like diabetes, high blood pressure, thinning of the bones, and weight gain. Because of these side effects, doctors try to slowly lower the dose of steroids as much as they can, but that can lead to a flare, or worsening, of GCA symptoms.

Tocilizumab, also called TCZ, is a drug that blocks a protein called IL-6R. IL-6R is a part of the immune system and plays an important role in causing GCA. This study was conducted to determine if TCZ may prevent GCA symptoms so patients do not have to take high doses of steroids for a long time. Researchers compared taking TCZ with a steroid to taking a placebo with a steroid. A placebo looks like a real drug but contains no real medicine.

In this study, researchers wanted to learn:

- Did fewer patients taking TCZ with a steroid have GCA symptoms come back compared to patients taking a placebo?
- Did patients taking TCZ take lower doses of a steroid over 52 weeks than patients taking a placebo?
- Did the quality of life improve more for patients taking TCZ and a steroid than for patients taking a placebo and a steroid?
- How did TCZ act in the body?
- What adverse events did patients have? An adverse event is a medical problem that may or may not be caused by the study drug.

This study included men and women who were at least 50 years old. All of them had GCA within 6 weeks of the first study visit and were taking a steroid.

What kind of study was this?

Your study had 2 parts:

- Part 1 was "double-blind". This means that none of the patients, study doctors, or study staff knew what treatment each patient took. Patients were randomly assigned to take either TCZ or a placebo along with a steroid for either 26 or 52 weeks. Patients had a 60% chance of taking TCZ and a steroid and a 40% chance of taking the placebo and a steroid.
- Part 2 was "open-label". This means that the patients, study doctors, and study staff knew what drugs patients were taking.

This summary includes the final results only for Part 1 of the study, because Part 2 is still ongoing.

What happened during the study?

Part 1 lasted 52 weeks. During this part of the study, you visited the study center every week for the first 4 weeks, then once every 4 weeks for scheduled visits.

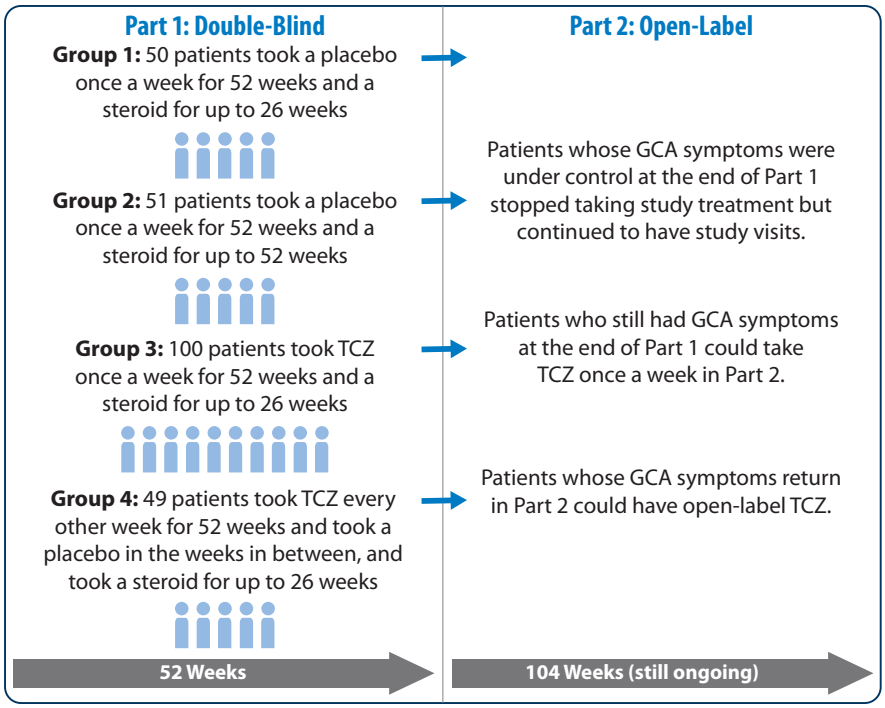
During Part 1, you took either TCZ or placebo and a steroid called prednisone. The TCZ and placebo were given through a syringe that was injected under your skin. You or your caregiver were trained on how to give these injections to yourself. The steroid was given by mouth as a tablet. Some patients took a steroid for the whole 52 weeks. Some patients took a steroid only for the first 26 weeks and then took a steroid placebo for the rest of Part 1. The dose of steroid you started taking when the study started was similar to what you were taking before the study started. If your GCA symptoms got worse at any time during the study, you could take a dose of steroid prescribed by your doctor to help with your symptoms.

You were randomly put in 1 of 4 treatment groups:

- Group 1: 50 patients took a placebo once a week for 52 weeks and took a steroid for up to 26 weeks.
- Group 2: 51 patients took a placebo once a week for 52 weeks and took a steroid for up to 52 weeks
- Group 3: 100 patients took TCZ once a week for 52 weeks and took a steroid for up to 26 weeks.
- Group 4: 49 patients took TCZ every other week for 52 weeks and took a placebo on the weeks in between, and took a steroid for up to 26 weeks.

Part 2 is still ongoing and will last for 104 weeks. All patients who finish Part 1 will enter into Part 2. During Part 2, patients whose GCA symptoms are under control at the end of Part 1 will stop taking TCZ but will continue to have study visits every 12 weeks. Patients who still have GCA symptoms at the end of Part 1 or whose GCA symptoms return during Part 2 can take TCZ once a week during Part 2. They will visit the study center every week for 4 weeks when they start TCZ, and then every 12 weeks thereafter.

The figure below shows what happened in your study.



During both parts of the study, study doctors checked your weight, heart rate, and blood pressure and also took blood samples. Study doctors also asked you how you were feeling and checked your GCA symptoms.

What were the study results?

This section is a summary of the main medical questions that were asked in this study and the results for Part 1. It is important to know that researchers look at the results of many studies to decide which medicines work best and are safest for patients.

Did fewer patients taking TCZ have GCA symptoms come back compared to patients taking a placebo?

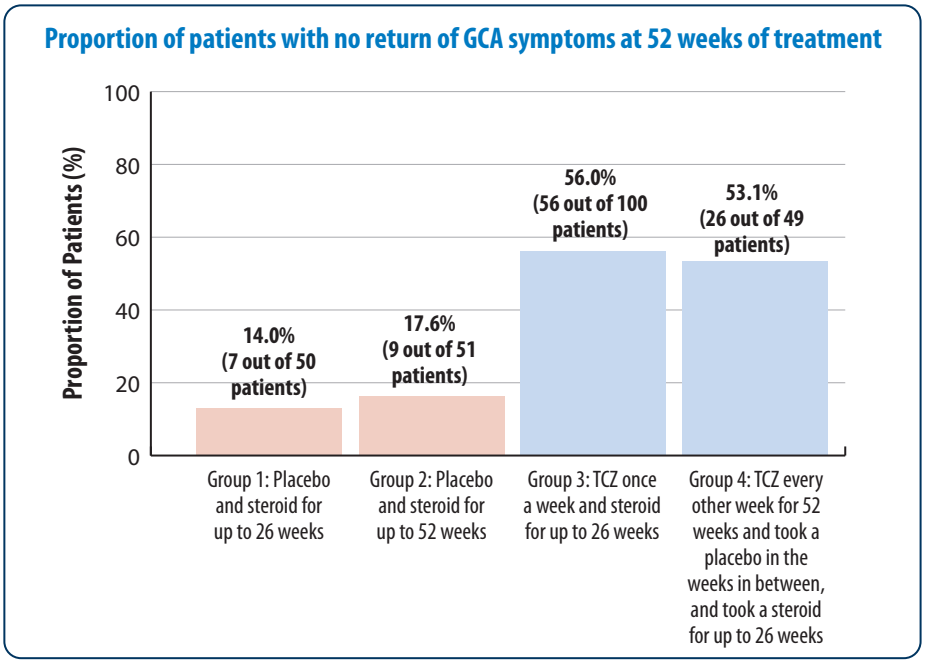
Yes, fewer patients who took TCZ with a steroid had GCA symptoms come back compared to patients who took the placebo with a steroid. Researchers look at the number of patients in each group who:

- had no GCA symptoms after 12 weeks of treatment
- had no return of GCA symptoms during the remaining 40 weeks of treatment in Part 1
- did not need to take additional steroids

This happened in the following number of patients in Part 1:

- 7 of 50 patients (14%) in Group 1. Group 1 took a placebo during Part 1 and took a steroid for up to 26 weeks.
- 9 of 51 patients (17.6%) in Group 2. Group 2 took a placebo during Part 1 and took a steroid for up to 52 weeks.
- 56 of 100 patients (56%) in Group 3. Group 3 took TCZ during Part 1 and took a steroid for up to 26 weeks.
- 26 of 49 patients (53.1%) in Group 4. Group 4 took TCZ and a placebo during Part 1 and took a steroid for up to 26 weeks.

The graph below shows how many patients had no return of GCA symptoms at 52 weeks of treatment.



Did patients taking TCZ take lower doses of steroid over 52 weeks than patients taking a placebo?

Researchers also measured the total steroid doses taken by patients in each group, including extra steroids taken if GCA symptoms got worse.

After 52 weeks, the median total steroid doses used by patients in Groups 3 and 4 were lower than the total doses used by patients in Groups 1 and 2:

- Group 1: median total dose of 3296 mg (50 patients). Group 1 took a placebo during Part 1 and took a steroid for up to 26 weeks.
- Group 2: median total dose of 3818 mg (51 patients). Group 2 took a placebo during Part 1 and took a steroid for up to 52 weeks.
- Group 3: median total dose of 1862 mg (100 patients). Group 3 took TCZ during Part 1 and took a steroid for up to 26 weeks.
- Group 4: median total dose of 1862 mg (49 patients). Group 4 took TCZ during Part 1 and took a placebo on the weeks in between. They also took a steroid for up to 26 weeks.

Patients also answered questions on surveys asking about their quality of life. Patients in both the placebo and TCZ groups reported improvement. Some surveys showed more improvement in patients who took TCZ and a steroid over those who took the placebo and a steroid.

What adverse events did patients have?

A lot of research is needed to know whether a drug causes a medical problem. So, when new drugs are being studied, study doctors keep track of all of the medical problems that patients have. These medical problems are called "adverse events", and may or may not be caused by the study drug. This section tells you about the adverse events that happened in your study.

How many patients had adverse events?

Most patients had at least 1 adverse event:

- Some adverse events were serious, and some were not.
- Some patients stopped taking the study drugs because of an adverse event.
- The percentage of patients in Group 3 and Group 4 who stopped taking the study drug because of an adverse event was about the same as patients in Group 1 who stopped taking the study drug because of an adverse event. Group 3 and Group 4 patients took TCZ and a steroid. Group 1 patients took a placebo and a steroid.
- No patients in Group 2 stopped taking the study drugs because of an adverse event. Group 2 patients took a placebo and a steroid.

The table below shows how many patients in each group had adverse events. It also shows how many stopped taking study drugs because of them.

Adverse events in this study

Adverse events in each group	Group 1: Placebo and steroid for up to 26 weeks (Out of 50 patients)	Group 2: Placebo and steroid for up to 52 weeks (Out of 51 patients)	Group 3: TCZ once a week and steroid for up to 26 weeks (Out of 100 patients)	Group 4: TCZ every other week and steroid for up to 26 weeks (Out of 49 patients)
Had at least 1 adverse event	48 (96.0%)	47 (92.2%)	98 (98.0%)	47 (95.9%)
Had at least 1 serious adverse event	11 (22.0%)	13 (25.5%)	15 (15.0%)	7 (14.3%)
Stopped taking study drugs because of an adverse event	6 (12.0%)	0 (0.0%)	11 (11.0%)	6 (12.2%)

How many patients had serious adverse events?

An adverse event is called "serious" when it is life-threatening, causes lasting problems, or the patient needs hospital care.

No patients died during Part 1 of your study.

In your study, 46 patients (18.4%) had at least 1 serious adverse event. More serious adverse events happened to patients in the placebo groups than to patients in the TCZ groups. Most types of serious adverse events only happened to 1 patient in a treatment group. The serious adverse events that happened to more than 1 patient in any group were:

- Two patients (3.9%) in Group 2 and 1 patient (1%) in Group 3 had a stomach virus.
- Two patients (3.9%) in Group 2 and 1 patient (1%) in Group 3 had shingles.
- Two patients (2%) in Group 3 had extremely high blood pressure (hypertensive crisis).

What were the most common adverse events?

The table below shows the most common adverse events that happened to at least 12% of patients in any group. There were other adverse events, but fewer patients had them.

Most common adverse events in this study

Adverse events in each group	Group 1: Placebo and steroid for up to 26 weeks (Out of 50 patients)	Group 2: Placebo and steroid for up to 52 weeks (Out of 51 patients)	Group 3: TCZ once a week and steroid for up to 26 weeks (Out of 100 patients)	Group 4: TCZ every other week and steroid for up to 26 weeks (Out of 49 patients)
Headache	16 (32.0%)	12 (23.5%)	27 (27.0%)	10 (20.4%)
Common cold	9 (18.0%)	13 (25.5%)	29 (29.0%)	12 (24.5%)
Peripheral edema (swelling in the limbs)	8 (16.0%)	6 (11.8%)	16 (16.0%)	12 (24.5%)
Joint pain	11 (22.0%)	8 (15.7%)	13 (13.0%)	8 (16.3%)
Dizziness	6 (12.0%)	8 (15.7%)	6 (6.0%)	10 (20.4%)
Back pain	7 (14.0%)	10 (19.6%)	14 (14.0%)	7 (14.3%)
Diarrhea	8 (16.0%)	5 (9.8%)	12 (12.0%)	3 (6.1%)
Alopecia (hair loss)	3 (6.0%)	5 (9.8%)	5 (5.0%)	7 (14.3%)
Upper respiratory tract infection	5 (10.0%)	7 (13.7%)	10 (10.0%)	6 (12.2%)
High blood pressure	4 (8.0%)	4 (7.8%)	12 (12.0%)	6 (12.2%)
Pain in the musculoskeletal system	5 (10.0%)	2 (3.9%)	12 (12.0%)	6 (12.2%)
Tiredness	8 (16.0%)	3 (5.9%)	8 (8.0%)	5 (10.2%)
Throat pain	5 (10.0%)	8 (15.7%)	7 (7.0%)	4 (8.2%)
Muscle spasms	6 (12.0%)	4 (7.8%)	4 (4.0%)	6 (12.2%)
Cough	7 (14.0%)	3 (5.9%)	6 (6.0%)	3 (6.1%)
Anxiety	6 (12.0%)	1 (2.0%)	3 (3.0%)	1 (2.0%)

Where can I learn more about this study?

This summary includes information and results only for Part 1 of the study. You can find more information about your study online at

- https://clinicaltrials.gov/ct2/show/results/NCT01791153
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2011-006022-25

If you have questions about the results in this summary, please speak with the doctor, research nurse, or other team member at your study center.

Researchers look at the results of many studies to decide which drugs work best and are safest for patients. It takes patients in many studies all around the world to advance medical science.

Address and telephone number for the sponsor of this study: F. Hoffmann-La Roche, the sponsor of this study, has its headquarters at Grenzacherstrasse 124 CH-4070 Basel, Switzerland.

The phone number for general information is +41-61-688-1111.

Thank you

It is said that the greatest gift is one that is given anonymously, given when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge. Thank you for the gift of your participation in clinical research.

THANK YOU for taking part in the GiACTA global clinical study for the drug tocilizumab.

This is a summary of the main medical question that was asked in this study and the results for Part 1. Part 2 is Open-Label[1] and still going on. It is important to know that researchers look at the results of many studies to decide which medicines work best and are safest for patients.

Drug Studied: Tocilizumab
National Clinical Trial #: NCT01791153
EudraCT #: 2011-006022-25

THE STUDY

Researchers are trying to find out if adding tocilizumab helped you to control your giant cell arteritis symptoms and take less steroids. Giant cell arteritis is also called GCA.

GLOSSARY

[1] **Open-Label** means that the patients, doctors, and study staff knew what drugs patients were taking.

[2] **Double-Blind** means that none of the patients, trial doctors, or staff knew what treatment each patient took.

[3] A **placebo** looks like a real drug but contains no real medicine.

Patients in Study

AGE 50+

GCA within 6 weeks of first study visit

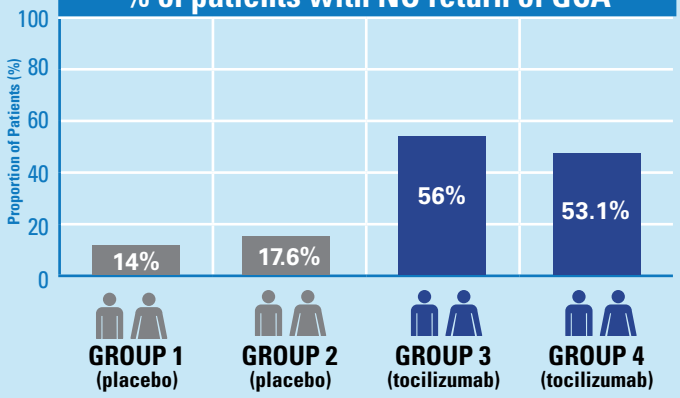
Taking Steroid

Part 1: Double-Blind[2] (52 weeks)

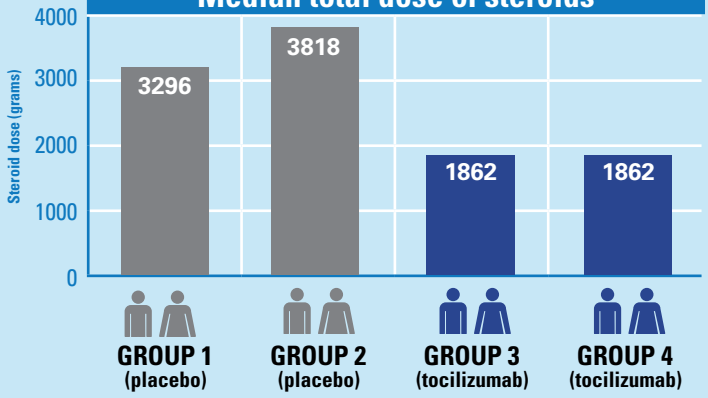
GROUP 1	50 patients	placebo[3] once a week for 52 weeks	+ steroid for up to 26 weeks
GROUP 2	51 patients	placebo once a week for 52 weeks	+ steroid for up to 52 weeks
GROUP 3	100 patients	tocilizumab once a week for 52 weeks	+ steroid for up to 26 weeks
GROUP 4	49 patients	tocilizumab + placebo in between every other week for 52 weeks	+ steroid for up to 26 weeks

STUDY RESULTS

% of patients with NO return of GCA



Median total dose of steroids



Most common adverse events[4]

- 46 patients (18.4%) had at least 1 serious adverse event
- More serious adverse events happened to patients in the placebo groups than to patients in the TCZ groups
- Most types of serious adverse events only happened to 1 patient in a treatment group
- The most common adverse events happened to at least 12% of patients in any group


headache


dizziness


joint pain

Adverse Events in this Study

	GROUP 1 (placebo)	GROUP 2 (placebo)	GROUP 3 (tocilizumab)	GROUP 4 (tocilizumab)
Had at least 1 adverse event	96.0%	92.2%	98.0%	95.9%
Had at least 1 serious adverse event	22.0%	25.5%	15.0%	14.3%
Stopped taking study drug because of an adverse event	12.0%	0.0%	11.0%	12.2%

[4] **Adverse events** are medical problems that patients have during a study. They may or may not be caused by the study drug.

Please review this page along with the **Clinical Trial Results Summary**. This page does not include all of the study results.