Summary of Clinical Trial Results

A study to look at how ocrelizumab impacted three known biomarkers of 'multiple sclerosis' — a disease that affects the way the brain signals to nerves in the body

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document) – written for:

- members of the public and
- people who took part in the study.

This summary is based on information known at the time of writing.
The study started in April 2016 and finished in April 2023. This summary was written after the study had ended.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

Contents of the summary

Glossary

- Multiple sclerosis / MS = a disease that affects the way the brain signals to nerves in the body.
- Biomarker = a biological molecule found in blood, body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease.

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about a disease that affects the way the brain signals to nerves in the body (multiple sclerosis or MS) and the medicine studied – 'ocrelizumab'.

1. General information about this study

Why was this study done?

Multiple sclerosis is a disease that affects the way the brain signals to nerves in the body. There are three types of multiple sclerosis. You can think of these different types as a way for physicians to describe how the symptoms present and progress over time instead of being three different conditions. In many people the disease continues to progress. The cause of multiple sclerosis is not known. However, it is known that in most people with multiple sclerosis, the immune system and 2 types of white blood cells (called 'B cells' and 'T cells') by mistake attack certain parts of the brain and spinal cord and cause damage to nerves. There is a need to get medical treatments that work for multiple sclerosis. The findings of biomarkers for multiple sclerosis are very important and will help us understand the changes in the disease, how the disease progresses, and how a medical treatment works.

'Ocrelizumab' is a medicine that attaches to certain types of white blood cells (called 'B cells') that are thought to play a role in multiple sclerosis and removes them from the body.

This study was done to find out what effects, good or bad, ocrelizumab had on people with multiple sclerosis. This study also looked at the way ocrelizumab changed certain biomarkers related to multiple sclerosis in the body.

What was the medicine being studied?

A medicine called 'ocrelizumab' was the focus of this study.

'Ocrelizumab' is an approved medicine given to people with multiple sclerosis.

- You say this as 'oh kruh li zuh mab'.
- Ocrelizumab is thought to work by helping to remove and kill specific cells of the immune system, called 'B cells', known to play a role in multiple sclerosis and that contribute to nerve damage.
- Ocrelizumab helps to reduce disease activity and helps to slow the progression of disease.
- In this study ocrelizumab was given as a drip (infusion) into a vein.

What did researchers want to find out?

- Researchers did this study to see how well ocrelizumab worked at different times during the study (see section 4 "What were the results of the study?").
- They also wanted to find out how safe the medicine was – by checking how many people had side effects and how serious those side effects were, while people were taking the medicine during this study (see section 5 "What were the side effects?").

This was an open label study:

- In the long-term phase of this study, some of the people who had taken part in the main study for up to 1 year continued taking ocrelizumab on a long-term basis for up to 5 years, after the main study had finished.
- Researchers wanted to gather long-term information on ocrelizumab:
    - How safe ocrelizumab was in the long-term
    - How well ocrelizumab continued to work over longer time periods.

The main question that researchers wanted to answer was:

1. How ocrelizumab worked in people with multiple sclerosis by looking at biomarkers at different times?

What kind of study was this?

This study was a 'Phase 3' study. This means that ocrelizumab had been tested in a number of people with multiple sclerosis before the medicine was approved.

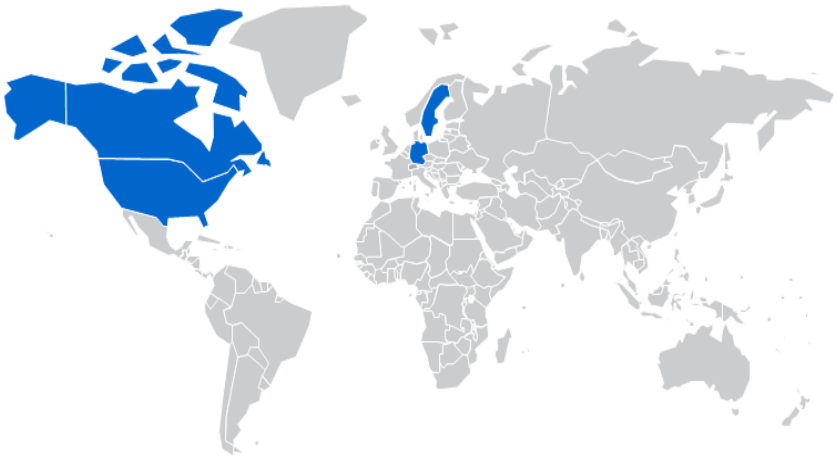
This was an 'open label' study. This means that both the people taking part in the study and the study doctors knew the study medicine people were taking.

When and where did the study take place?

The study started in April 2016 and finished in April 2023. This summary was written after the study had ended.

The study took place at 17 study centres – across 4 countries in Europe and North America. The countries were: Canada, Germany, Sweden, and United States.

- Canada
- Germany
- Sweden
- United States



2. Who took part in this study?

In this study, 131 people with multiple sclerosis took part in one of two groups.

Group A: People with 'relapsing multiple sclerosis'.
People who took part in this group of the study were between 20 and 56 years of age.
32 of the 100 people (32%) were male and 68 of the 100 people (68%) were female.

Group B: People with 'primary progressive multiple sclerosis'.
People who took part in this group of the study were between 24 and 55 years of age.
16 of the 32 people (50%) were male and 16 of the 32 people (50%) were female.

People could take part in the study if:

- They had a type of multiple sclerosis – called 'relapsing multiple sclerosis'
- They had a type of multiple sclerosis – called 'primary progressive multiple sclerosis'
- They had a disability score between 0 to 5 points or 3 to 6 points at the beginning of the study (based on the 'Expanded Disability Status Scale' or EDSS, a way of measuring disability)
- They had a disease duration less than 10 or 15 years from the first appearance of the symptoms of multiple sclerosis in relapsing multiple sclerosis
- They had a disease duration less than 10 years from the first appearance of the symptoms of multiple sclerosis in primary progressive multiple sclerosis.

People could not take part in the study if:

- They had a type of multiple sclerosis – called 'secondary progressive multiple sclerosis'– without flare-ups called 'relapses' for at least 1 year
- They had secondary progressive multiple sclerosis without relapses
- They had certain lung problems, viral infections, or cancer
- They had other neurologic disorders.

3. What happened during the study?

During the study, all people got the same treatment.

There were 2 parts to this study:

- **The main treatment study. This lasted up to 1 year**
  - **Group A** – drip (infusion) into a vein at Weeks 1, 3, 24, and 48. Weeks 1 and 3 were the first treatment, split into two doses. Biomarkers samples were collected at these different times.
    - The first dose was given as two drips of 300 mg on Day 1 and Day 15. Following doses were given as one drip of 600 mg every 6 months.

    In a subgroup of Group A, the treatment was delayed for 12 weeks to allow for biomarker samples to be collected before the beginning of treatment. The first dose was given as two drips of 300 mg on Day 1 and Day 15. Following doses were given every 6 months as one drip of 600 mg.
  - **Group B –** drip (infusion) into a vein (split into two treatments) every 24 weeks. Biomarkers samples were collected at these different times.
    - The treatment was given as two drips of 300 mg separated by 14 days.

- **The Long-term treatment phase. This lasted up to 5 years**

This means people from Group A or Group B opted to continue in the study to look at long-term changes in biomarkers.

  - **Group A and B** – continued to receive drip (infusion) into a vein every 24 weeks with the long-term treatment phase beginning at Week 72.

The treatment was given as one drip of 600mg in people in Group A and Group B.

People in the study took the treatments for up to 5 years. When the study finished, the people who took part were asked to go back to their study centre for more visits – to check their overall health. Look below to see more information about what happened in the study.

4. What were the results of the study?

Question 1: How ocrelizumab worked in people with multiple sclerosis by looking at biomarkers at different times?

Researchers looked at how well ocrelizumab treatment worked by studying levels of a known biomarker in multiple sclerosis – a protein called the 'neurofilament light chain' (NfL) – that is released when nerves are damaged. Researchers also looked at how well ocrelizumab treatment worked by studying levels of two other biomarkers – special types of white blood cells ('B cells' and 'T cells'). These biomarkers - NfL, B cells, and T cells – were measured in the fluid surrounding the brain and spinal cord. These biomarkers were looked at in different groups at different times during the study.

Group A: People with 'relapsing multiple sclerosis'

- In the main treatment study, people had lower NfL levels after their first, second, and third drips of ocrelizumab. This showed that ocrelizumab was helpful in reducing damage to nerves. In the long-term treatment phase, people who were given ocrelizumab continued to have less nerve damage. This was shown by lower NfL levels.
- In the main treatment study, levels of certain types of B cells and T cells that play a role in brain inflammation were lowered while people were given ocrelizumab treatment. In the long-term treatment phase, the levels of those types of B cells and T cells remained lowered.

Group B: People with 'primary progressive multiple sclerosis'

- People had lower NfL, B cell, and T cell levels similar to Group A in the main treatment study.
- Because very few people in this group had biomarker levels measured during the long-term treatment phase (most likely because of the COVID-19 pandemic), there was not enough information available for researchers to make any conclusions about how ocrelizumab was working during the long-term treatment phase.

This section only shows the key results from this study. You can find information about all other results on the websites at the end of this summary (see section 8).

5. What were the side effects?

Side effects are medical problems (such as feeling dizzy) that happen during the study.

- The side effects described in this summary are those the study doctor believes were related to the treatments in the study.
- Not all of the people in this study had all of the side effects.
- Side effects may be mild to very severe and can be different from person to person.
- It is important to be aware that the side effects reported here are from this single study. Therefore, the side effects shown here may be different from those seen in other studies, or those that appear on the medicine leaflet.
- Serious and common side effects are listed in the following sections.

Serious side effects

A side effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.

Group A: People with 'relapsing multiple sclerosis'
During this study, 16 in every 100 people (16%) had at least one serious side effect.

Group B: People with 'primary progressive multiple sclerosis'
During this study, 9 in every 31 people (29%) had at least one serious side effect.

The most common serious side effect across both groups is shown in the table below.

Serious side effects reported in this study	**Group A: People with relapsing multiple sclerosis taking ocrelizumab** (100 people total)	**Group B: People with primary progressive multiple sclerosis taking ocrelizumab** (31 people total)
Infections	8% (8 out of 100)	13% (4 out of 31)

Most common side effects

Group A: People with 'relapsing multiple sclerosis'
During this study, around 96 out of every 100 people (96%) had a side effect that was not considered serious.

Group B: People with 'primary progressive multiple sclerosis'
During this study, around 31 out of every 31 people (100%) had a side effect that was not considered serious.

The most common side effects are shown in the following table – these are the 3 most common side effects across both groups. Some people had more than one side effect – this means that they are included in more than one row in the table.

Most common side effects reported in this study	**Group A: People with relapsing multiple sclerosis taking ocrelizumab** (100 people total)	**Group B: People with primary progressive multiple sclerosis taking ocrelizumab** (31 people total)
Infusion related reaction	51% (51 out of 100)	39% (12 out of 31)
Infection of the upper respiratory tract (nose, sinuses, throat, wind pipe, and voice box)	35% (35 out of 100)	42% (13 out of 31)
Urinary tract infection or 'UTI', infection that affects the kidney, bladder or the tubes in which people pass water from the body	21% (21 out of 100)	39% (12 out of 31)

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see section 8.

6. How has this study helped research?

The information presented here is from a single study of 131 people with a disease that affects the way the brain signals to nerves in the body (multiple sclerosis or MS). These results helped researchers learn more about multiple sclerosis and ocrelizumab.

The study of multiple sclerosis biomarkers helped researchers understand disease activity and how the disease progressed, and how medical treatment worked.

The main results of the study have shown that:

- In people with 'relapsing multiple sclerosis' (Group A) and in people with 'primary progressive multiple sclerosis' (Group B), people who took ocrelizumab had less damage to the cells in the brain as early as 12 weeks after taking the medicine, which continued over 52 weeks.
- In people with 'relapsing multiple sclerosis' (Group A), some people who took ocrelizumab had less damage to the cells in the brain for up to 5 years.
- In people with 'primary progressive multiple sclerosis' (Group B), the number of people taking ocrelizumab for up to 5 years who contributed biomarker samples was smaller, and no conclusions could be made on how well the treatment worked on damage to the cells in the brain.
- The side effects reported in people were known to be related to ocrelizumab, and there were no new side effects reported during the study.
- The most important limitation of the study: because of COVID-19 pandemic and its restrictions, a number of people did not go to all study visits or, if they did go, they did not want to have their biomarker levels looked at.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

Studies with ocrelizumab in multiple sclerosis are still happening.

At the time of writing this summary, there are studies ongoing that are looking at biomarkers in people with multiple sclerosis, including the studies called 'CHIMES', 'ENSEMBLE' and 'CONSONANCE'.

8. Where can I find more information?

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

- https://clinicaltrials.gov/ct2/show/results/NCT02688985
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-004616-37/DE
- https://forpatients.roche.com/en/trials/autoimmune-disorder/multiple-sclerosis/study-to-explore-the-mechanism-of-action-of-ocrelizumab-and-b-ce.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: “Emerging Cerebrospinal Fluid Biomarkers of Disease Activity and Progression in Multiple Sclerosis”. The authors of the scientific paper are: A. H. Cross, J. M. Gelfand, S. Thebault, J. L. Bennett, H. C. von Büdingen and others. The paper is published in the journal ‘JAMA Neurology’, volume number 81, on pages 373-383.

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/autoimmune-disorder/multiple-sclerosis/study-to-explore-the-mechanism-of-action-of-ocrelizumab-and-b-ce.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.

Who organised and paid for this study?

This study was organised and paid for by Genentech, Inc., a member of the Roche Group, who have their headquarters in South San Francisco, California, USA.

Full title of the study and other identifying information

The full title of this study is: “An Open-Label, Multicenter, Biomarker Study to Explore the Mechanism of Action of Ocrelizumab and B-Cell Biology in Patients With Relapsing Multiple Sclerosis or Primary Progressive Multiple Sclerosis”

The study is known as ‘OBOE’.

- The protocol number for this study is: ML29966.
- The ClinicalTrials.gov identifier for this study is: NCT02688985.
- The EudraCT number for this study is: 2015-004616-37.