Summary of Clinical Trial Results

A study to find the best dose of ocrelizumab to be given as an injection under the skin in people with multiple sclerosis

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 (November 2024). More information may now be known.

The study started in August 2019 and is predicted to end by June 2025. This summary includes the results that were collected and analysed in November 2023. At the time of writing this summary, the study is still ongoing – study doctors are still collecting information.

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

- MS = A disease that affects the way the brain signals to nerves in the body – called 'multiple sclerosis' or 'MS'

Thank you to the people who took part in this study

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

Key information about this study

- This study was done to find the best dose of the medicine ocrelizumab to be used as an injection under the skin (subcutaneous injection), twice a year, in people with relapsing MS (RMS) or primary progressive MS (PPMS).
- In this study, people were given different doses of ocrelizumab as a subcutaneous injection in the abdomen by a healthcare provider, to try and find the dose that had a similar effect to the approved 600-mg dose of ocrelizumab given as a drip (infusion) into a vein (intravenous infusion).
- This study included 134 people from 20 study centres across the USA.
- So far, the study has shown that a dose of 920 mg ocrelizumab given subcutaneously is most similar to the 600 mg dose of ocrelizumab given intravenously.
- People who received ocrelizumab subcutaneously in this study had similar side effects to people who have received ocrelizumab intravenously in other studies. However, injection reactions specifically occurred in those who received ocrelizumab subcutaneously.
- During this study, 11 out of 118 people (9.3%) given 920 mg ocrelizumab as a subcutaneous injection had at least one serious side effect.
- At the time of writing this summary, the study is still ongoing. It is currently predicted to end by approximately June 2025.

1. General information about this study

Why was this study done?

MS is a disease in which a person's immune system attacks parts of the person's own nerve cells in the brain and spinal cord causing problems in communication between the brain and the rest of the body. Eventually, MS can cause the nerves to become more damaged and die. There are several different medicines that are used to treat MS, but not all of them work for all people. Finding treatments that work well, and can be safely switched to, is therefore very important.

Ocrelizumab is given as a drip into the vein (intravenous [IV] infusion) every 6 months over 2 to 3.5 hours. This can be challenging for some people with MS if they cannot receive a drip infusion or if there are limited IV facilities available nearby. Experience with other medicines has shown that subcutaneous injection, which is an injection just under the skin, may be more convenient for patients.

In this study, researchers wanted to find the best dose of ocrelizumab to be given as an injection under the skin twice a year to treat people with RMS and PPMS.

What was the medicine being studied?

'Ocrelizumab' (pronounced 'oh-kre-liz-oo-mab') is a medicine given to people with MS.

- Ocrelizumab is a monoclonal antibody, which is a protein that attaches to specific types of cells (B cells) in your immune system and destroys them. This prevents the immune system from attacking the protective myelin coating around the nerve cells, reducing the chance of having a relapse and slowing down disease worsening (called progression). A relapse, in the case of MS, is a period of at least 24 hours during which new symptoms are experienced or old symptoms become worse.

This study looked at two ways of receiving ocrelizumab:

- **Intravenous infusion of ocrelizumab** – a drip (infusion) into a vein.
- **Subcutaneous injection of ocrelizumab** – an injection just under the skin.

Both methods work the same way, but the time it takes to administer them is different. An ocrelizumab IV infusion takes about 2 to 3.5 hours to put into your body, while a subcutaneous injection only takes about 10 minutes. There's also a difference in how much liquid is used. For an IV infusion, the medicine is mixed into an IV saline bag with either 250 mL or 500 mL of liquid, which is slowly dripped into your vein. For a subcutaneous injection, the medicine comes already prepared in a liquid form and is injected under your skin in a volume of 23 mL.

What did researchers want to find out?

- Researchers did this study to find the best dose of ocrelizumab to be given as a subcutaneous injection to treat people with MS.
- To do this, the 'pharmacokinetics' (PK) of ocrelizumab given subcutaneously were looked at in this study. This means that information was collected about how the medicine is taken up by the body. Researchers also looked at how the body broke the medicine down (see section 4 "What were the results of the study?").
- Researchers also wanted to find out how safe ocrelizumab was, when given as a subcutaneous injection – by checking how many people had side effects and seeing how serious they were (see section 5 "What were the side effects?").

The main questions that researchers wanted to answer were:

1. What is the best dose of ocrelizumab that can be given to people with MS as an injection under the skin?
2. How safe is ocrelizumab when given as an injection under the skin? (see section 5 "What were the side effects?")

What kind of study is this?

This study is a 'Phase 1b' study, which means that this is the first study in which ocrelizumab was given to humans as an injection under the skin.

This is an 'open-label' study. This means that both the people taking part in the study and the study doctors know what the study medicine is.

When and where is the study taking place?

The study started in August 2019 and is predicted to end by June 2025. This summary includes the results up until November 2023. At the time of writing this summary, the study is still ongoing – study doctors are still collecting information.

The study is taking place at 20 study centres across the USA.

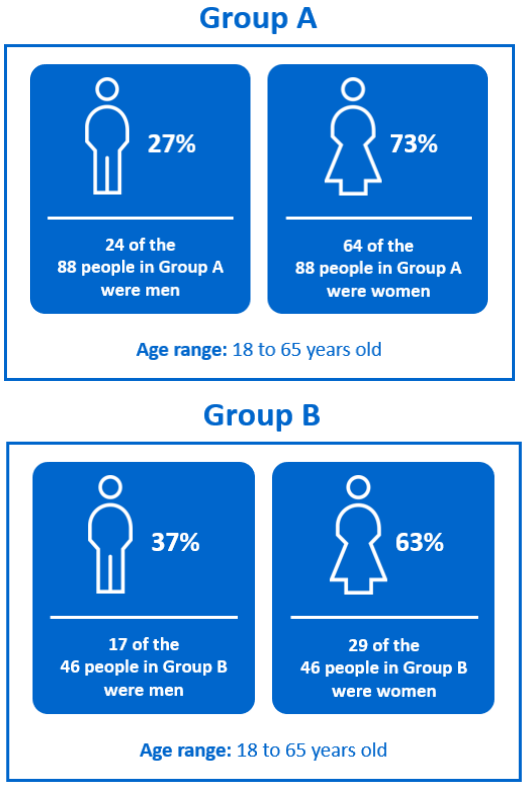
2. Who took part in this study?

In this study, 134 people with MS are taking part and have already received treatment in the study.

People who are taking part in the study were between 18 and 65 years of age at the time the study started. Overall, 41 of the 134 people (30.6%) in the study are men and 93 of the 134 people (69.4%) are women.

This study included people who had already had at least two 600-mg doses of ocrelizumab given intravenously (Group A), and people who had never taken ocrelizumab before (Group B).

More information on the people who took part is given below:



People could take part in the study if they:

- Were between the ages of 18 and 65 years – the average age of people in Group A was 45.7 years and the average age of people in Group B was 39.7 years.
- Had a diagnosis of RMS or PPMS.
- Had an Expanded Disability Status Scale (EDSS) score of 0.0–6.5 at screening; this scale measures physical disability in MS on a scale from 0 to 10, with a higher score meaning a higher level of disability.
- Had no relapses for 30 days before the screening visit; a relapse is a period of at least 24 hours during which new symptoms are experienced or old symptoms become worse.

People could not take part in the study if they had:

- MS for more than 15 years with an EDSS score less than 2.0 at screening.
- A history of severe allergic or anaphylactic reaction to similar medicines.

3. What happened during the study?

This study is still ongoing, so some people are still being treated with the study medicine. When the treatment finishes, the people who took part will be asked to go back to their study centre for one more visit – to check their overall health. Look below to see more information about what has happened in the study so far – and what the next steps are.

Dose escalation

The first stage of the study was aimed at finding the best dose of subcutaneous ocrelizumab. This was done via a 'dose-escalation' stage, in which different groups of people were initially given different doses of subcutaneous ocrelizumab and were closely monitored for any side effects. The first group of patients received a low dose of 40 mg. Once this dose was found to be safe and handled well by the people in that group, a subsequent group of people were given a dose of 200 mg. This process was repeated, such that additional groups of patients received 600 mg, and finally, 1,200 mg of subcutaneous ocrelizumab. During this stage, each patient received only one injection of the specific dose assigned to their group.

The treatment groups for the escalation stage were:

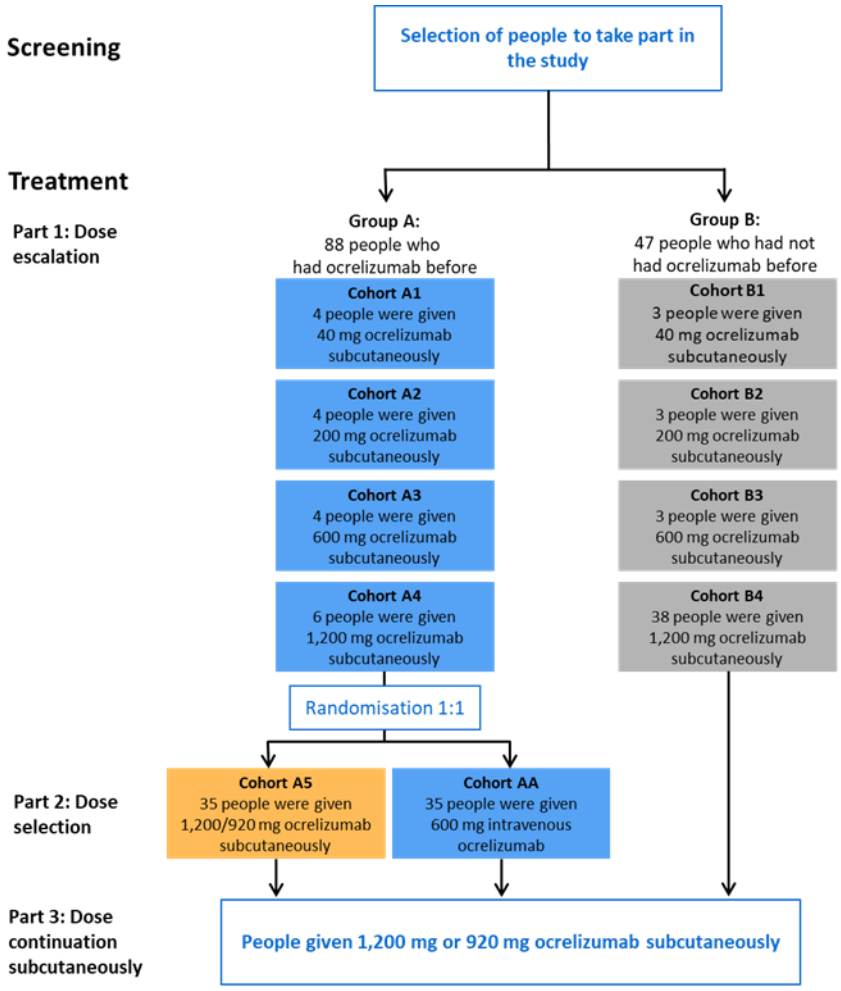
- **Group A –** people who had already been given at least two 600-mg doses of ocrelizumab intravenously before the screening tests done at the start of the study.
- **Group B –** people who had never received ocrelizumab (either intravenously or subcutaneously).

People in Group A were the first to receive treatment with a subcutaneous injection of ocrelizumab at each of the dose levels (Cohort A1, 40 mg; Cohort A2, 200 mg; Cohort A3, 600 mg; Cohort A4, 1,200 mg). Once a given dose was seen to be safe and handled well by people in Group A, the same doses were tested in people in Group B (Cohort B1, 40 mg; Cohort B2, 200 mg; Cohort B3, 600 mg; Cohort B4, 1,200 mg).

Dose selection

After the dose-escalation stage of the study, more people were enrolled in Group A. These people were selected by chance to get either one injection of the 1,200-mg dose of subcutaneous ocrelizumab tested in the dose-escalation phase of the study, or one 600-mg dose of intravenous ocrelizumab. The treatments were selected at random – by a computer. The treatment groups were:

- **Cohort A5** – one dose of 1,200 mg ocrelizumab given subcutaneously.
- **Cohort AA –** one dose of 600 mg ocrelizumab given intravenously.



Researchers thought that a dose of 1,200 mg ocrelizumab given under the skin would have similar effects as a dose of 600 mg ocrelizumab given intravenously. After looking at the PK data from the people who had received 1,200 mg, researchers concluded that a lower dose of 920 mg subcutaneous ocrelizumab was more likely to be similar to 600 mg intravenous ocrelizumab in terms of its PK. To make sure this was correct, the researchers changed the dose that new patients entering Cohort A5 could receive, from 1,200 mg to 920 mg.

The last six people randomized into Cohort A5 received a dose of 920 mg. The twenty-nine people randomized before received a dose of 1,200 mg.

Dose continuation

After dose selection, people could continue to receive ocrelizumab as a subcutaneous injection during a 'dose-continuation' stage, which lasts up to the end of 2024, resulting in about four 4 years of treatment. Similar to what was described above for Cohort A5, people entering the dose-continuation stage received a dose of 1,200 mg. After the researchers changed the dose in Cohort A5 from 1,200 mg to 920 mg, all people in the continuation stage switched to the 920-mg dose for the remainder of their treatment in the study.

4. What were the results of the study?

Question 1: What is the best dose of ocrelizumab that can be given to people with MS as an injection under the skin?

Researchers looked at various doses of ocrelizumab given as an injection just under the skin. A dose of 920 mg subcutaneous ocrelizumab was found to be the most similar to the 600-mg intravenous dose in terms of how the medicine is taken up by the body and how the body breaks it down.

Question 2: How safe is ocrelizumab when given as an injection under the skin?

Other information that researchers collected was on the side effects that people experienced during ocrelizumab treatment (see section 5). Overall, when ocrelizumab was given as a subcutaneous injection, it was found to be well handled across all doses tested in the study and most of the side effects were similar to those seen when ocrelizumab is given intravenously.

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.

- They are described in this summary because the study doctor may have considered the side effects to be related to the treatments in the study.
- Not all of the people in this study had all of the side effects.
- Side effects can vary in severity 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

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

During this study, 11 out of 118 people (9.3%) who were given one or more doses of 920 mg ocrelizumab subcutaneously had at least one serious side effect.

The serious side effects are shown in the following table. Some people had more than one side effect – this means that they are included in more than one row in the table.

Serious side effects reported in this study	**People who were given 920 mg ocrelizumab subcutaneously** (118 people total)
Lung infection (pneumonia)	3.4% (4 out of 118)
COVID-19	1.7% (2 out of 118)
COVID-19 pneumonia	Less than 1% (1 out of 118)
Skin infection (pilonidal disease)	Less than 1% (1 out of 118)
Heart attack (acute myocardial infarction)	Less than 1% (1 out of 118)
Drug overdose (intentional overdose)	Less than 1% (1 out of 118)
Muscular weakness	Less than 1% (1 out of 118)
Papillary thyroid cancer	Less than 1% (1 out of 118)
Symptoms like a relapse, which occur for a short while (MS pseudo relapse)	Less than 1% (1 out of 118)
Kidney stones (nephrolithiasis)	Less than 1% (1 out of 118)
Blood clot in the lung (pulmonary embolism)	Less than 1% (1 out of 118)

One person who had received 1,200 mg ocrelizumab subcutaneously died due to COVID-19 pneumonia.

During the study, two people who had received the 920-mg dose of subcutaneous ocrelizumab decided not to continue treatment because of side effects.

Most common side effects

During this study, 105 out of 118 people (89.0%) had one or more side effects. Eleven out of 118 people (9.3%) had serious side effects (described above).

The most common side effects (occurring in more than 50% of people who were receiving 920 mg ocrelizumab subcutaneously) were local injection reactions. Local injection reactions are side effects to the actual injection and can occur around the point where the needle goes into the skin. Symptoms include pain, itching, swelling, and redness around the site of the injection (erythema).

Local injection reactions occurred in 65 out of 118 people (55.1%) who were receiving 920 mg subcutaneous ocrelizumab. These side effects were not considered serious. The most common symptoms of these reactions are shown in the table below:

Most common side effect and symptoms	**People who were given 920 mg ocrelizumab subcutaneously** (118 people total)
Local injection reaction	55.1% (65 out of 118)
Pain	36.4% (43 out of 118)
Erythema	26.3% (31 out of 118)
Swelling	26.3% (31 out of 118)

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 134 people with MS. These results helped researchers find the best dose of ocrelizumab to be given as an injection under the skin in people with MS. Ocrelizumab given in this way may offer an additional treatment option for patients with RMS and PPMS.

The side effects seen with ocrelizumab given subcutaneously were similar to those seen when it is given intravenously, except that injection reactions occurred.

Limitations of the study include the fact that information has not yet been collected over many years, and that brain scans were not done on people. In addition, the people in the study were all quite similar (for example, most of the people in the study were white and had RMS).

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 are still happening, and further studies are planned.

8. Where can I find more information?

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

- https://clinicaltrials.gov/study/NCT03972306
- https://forpatients.roche.com/en/trials/autoimmune-disorder/multiple-sclerosis/a-study-to-investigate-the-pharmacokinetics--safety--an-81373.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: "Subcutaneous ocrelizumab in multiple sclerosis: Results of the Pphase 1b OCARINA I study". The authors of the scientific paper are: Scott D Newsome, Lawrence Goldstick, Derrick S Robertson, James D Bowen, Robert T Naismith and others. The paper is published in the journal '*Annals of Clinical and Translational Neurology*' 2024 Oct 26. doi: 10.1002/acn3.52229.

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/a-study-to-investigate-the-pharmacokinetics--safety--an-81373.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 F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: "A Study to Investigate the Pharmacokinetics, Safety and Tolerability of Subcutaneous Ocrelizumab Administration in Participants with Multiple Sclerosis".

The study is known as 'OCARINA I'.

- The protocol number for this study is: CN41144.
- The ClinicalTrials.gov identifier for this study is: NCT03972306.