A study called ENSEMBLE to look at whether the medicine, ocrelizumab, was able to reduce disease activity and was safe in people with newly diagnosed relapsing-remitting multiple sclerosis who took ocrelizumab as their first multiple sclerosis treatment

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 (September 2023). More information may now be known.

The study started in March 2017 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

Thank you to the people who took part in this study

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

Key information about this study

- This study was done to find out how well the medicine ocrelizumab (that is approved for use in people with MS) reduces disease activity over a period of 4 years in people with newly diagnosed (diagnosis within the last 3 years) relapsing-remitting multiple sclerosis (RRMS), who had not yet started any treatment for MS.
- In MS, a person's immune system attacks the protective coating around the nerves; ocrelizumab is a protein that helps to prevent these attacks.
- The study also looked at how safe ocrelizumab is in these people.
- This study report included 678 people with RRMS in 29 countries.
- The main finding was that most study participants had no evidence of disease activity (which means that people had no relapses, no increase in overall disability and that their MRI images did not show any signs of disease that is currently causing symptoms or worsening disease) for at least 4 years of taking ocrelizumab.
- Around 85% of people (573 out of 678 people) taking ocrelizumab had no serious side effects, which are negative reactions experienced by people in the study.

1. General information about this study

Why was this study done?

In this study, researchers looked at how people with newly diagnosed RRMS, who had not started on any other treatments, responded to treatment with ocrelizumab as their first MS treatment.

What was the medicine being studied?

'Ocrelizumab' is a medicine to treat MS (pronounced 'oh-kre-liz-ooh-mab').

- Ocrelizumab is a protein that attaches to specific types of cells (B cells) in your immune system and destroys them. This prevents your 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). All the people in this study had the form of MS called RRMS.

What did researchers want to find out?

The main questions that researchers wanted to answer included:

1. How many people in the study had no MS disease activity after taking ocrelizumab for 4 years?
2. What were the effects on disability progression and on the number of relapses, and the level of brain damage seen in people in the study who took ocrelizumab for 4 years?
3. What changes in terms of symptoms, physical and psychological impact, and impact on work, did participants report while taking ocrelizumab? (see section 4 “What were the results of the study?”)
4. How safe is ocrelizumab when taken for 4 years? (see section 5 “What were the side effects?”)

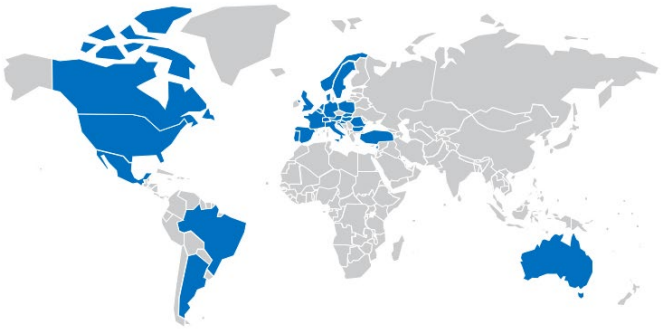
What kind of study was this?

This was an ‘open-label’, ‘single-arm’ study. This means that both the people taking part in the study and the study doctors knew the study medicine that people were taking.

When and where did the study take place?

The study started in March 2017 and finished in April 2023. This summary was written after the study had ended.

The study took place at 186 study centres across 29 countries around the world. The following map shows the countries where this study took place.



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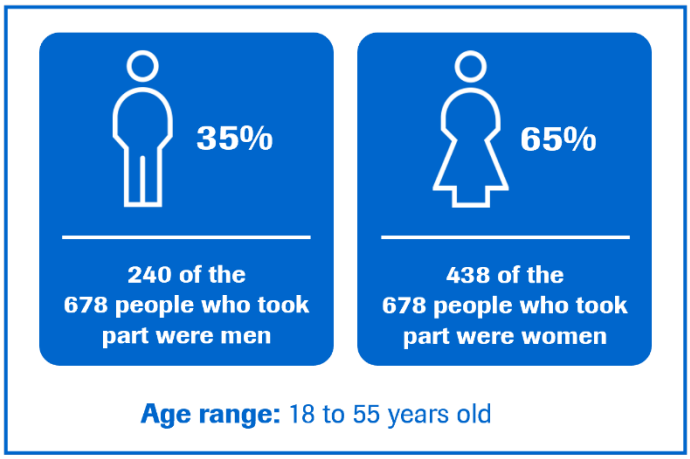
- Lebanon
- Mexico
- Netherlands
- Norway
- Poland
- Portugal
- Romania
- Slovakia
- Slovenia
- Spain
- Sweden
- Switzerland
- Turkey
- United Kingdom
- United States of America

2. Who took part in this study?

In this study report, 678 people with RRMS were included.

People who took part in the study were between 18 and 55 years of age. 240 of the 678 people (35%) were male and 438 of the 678 people (65%) were female. There were a greater number of females who enrolled in the study than males as RRMS is more common in females than in males.



People could take part in the study if:

- They had newly diagnosed RRMS.
- They had not taken any previous treatment for their RRMS.
- They had experienced one or more relapses, or one or more signs of disease activity related to MS on an MRI scan.

3. What happened during the study?

All people who took part in the study received ocrelizumab via a drip in a vein (called infusion), every 6 months for 4 years.

At the start of the study (called baseline), after 8 weeks, 6 months, 1 year, 2 years, 3 years and 4 years of the study, participants had an MRI scan. This allowed researchers to see if there was any new scarring in the brain or if any scarring that was already present in the brain had gotten worse, a sign of MS disease activity.

In addition, MS disease progression was evaluated by using clinical assessments of disability build-up, like the Expanded Disability Status Scale (EDSS) that is used to assess physical disability.

Brain function was also assessed at the start of the study, followed by checks every year thereafter for 4 years, using the assessment tool called 'Brief International Cognitive Assessment for MS' (BICAMS).

It was also important for researchers to gather information directly reported by study participants and that's why the study participants were asked to answer the following questionnaires:

- Work Productivity and Activity Impairment (WPAI) questionnaire, that allows researchers to measure the effect of MS on people's ability to work.
- SymptoMScreen, a tool that provides people with MS with a way to describe how bad their symptoms are.
- Multiple Sclerosis Impact Scale (MSIS)-29, a questionnaire made up of physical and emotion-related questions that gives a score related to the study participant's wellbeing.

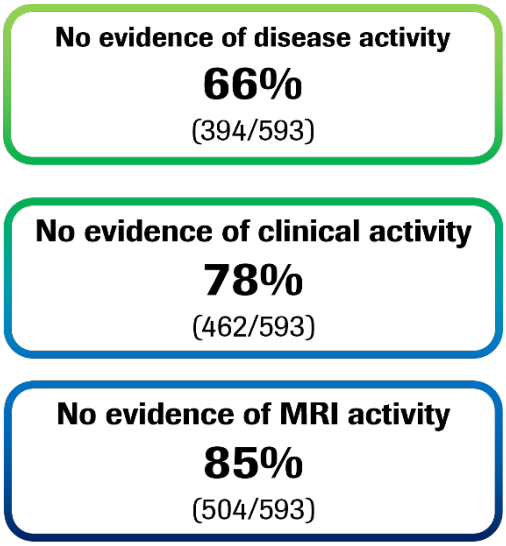
4. What were the results of the study?

Question 1: How many people in the study had no MS disease activity after taking ocrelizumab for 4 years?

Researchers looked at the number of study participants who had no MS disease activity, which means:

- They had no clinical activity (which includes relapses and increase in disability), **and** no MRI activity (as per MRI scans).

A high number of people – over 66% – had no evidence of any disease activity during the 4 years of ocrelizumab treatment. 91% of people did not experience relapses, while 82% did not have signs of confirmed disability progression. The vast majority of study participants – 85% – did not have evidence of MRI activity and 78% of participants had no evidence of clinical activity.



Question 2: What do other disability progression assessments show?

The majority of people (82%) in this study remained stable or improved on a disability assessment tool called EDSS and only 18% of people experienced disability worsening during the study.

Question 3: What changes in terms of symptoms, physical and psychological impact, and impact on work, did participants report while taking ocrelizumab?

- WPAI questionnaires showed that people missed less work than before due to their MS and showed overall less negative impact on their ability to work than before treatment with ocrelizumab.
- Using SymptoMScreen, people reported a lower burden of MS symptoms on daily activities at the end of 4 years.
- MSIS-29 questionnaires showed that overall, study participants experienced an improvement in both physical and psychological impacts of their MS over 4 years of ocrelizumab treatment.

Question 4: How safe is ocrelizumab when taken for 4 years?

Other information that researchers collected was on the side effects that people experienced during 4 years of ocrelizumab treatment (see section 5). Overall, ocrelizumab was found to be safe for use over the period of 4 years in this study.

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, for example) that happen during the study. They may or may not be caused by the study treatment (for example, an injury occurred during a car accident will still be included in a summary of all side effects in the study).

- Not all the people in this study had all the side effects.
- Side effects may be mild to very serious and can differ from person to person.
- 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, or needs hospital care, or causes lasting problems.

During this study, 16% of people had at least one serious side effect.

The most common serious side effects are shown in the following table – these are the four most common serious side effects across the people in this study receiving ocrelizumab. 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 taking ocrelizumab** (678 people total)
Infection	7% (47 out of 678)
Injuries	2% (13 out of 678)
Side effects related to the brain and nervous system	2% (10 out of 678)
Side effects occurring upon infusion	Less than 1% (3 out of 678)

There were 6 out of 678 people (1%) who died during the 4-year study period. Four of these deaths were related to COVID-19. The other two deaths were a result of lung infection and a problem with the recovery of the immune system.

Most common side effects

During this study, around 95 out of every 100 people (95%) had a side effect that was not considered serious.

The five most common 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.

Most common side effects reported in this study	**People taking ocrelizumab** (678 people total)
Side effects occurring upon infusion	52% (351 out of 678)
Common cold	29% (198 out of 678)
Headache	27% (185 out of 678)
Urinary tract infection (an infection that affects the kidney, bladder or the urinary tubes)	16% (106 out of 678)
Upper respiratory tract infection (an infection of the nose, nasal cavities or throat)	14% (97 out of 678)

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 study of 678 people with RRMS. These results helped researchers learn more about the effect of ocrelizumab as the first treatment on disease activity in people newly diagnosed with RRMS.

After receiving ocrelizumab for a period of 4 years, most people showed no MS disease activity. Serious side effects during this study occurred in a small number of people over the 4-year period. No new safety signals were observed when people were treated with ocrelizumab in this study compared with other studies that tested the drug. Overall, long-term use of ocrelizumab (4 years) for the treatment of MS was shown to be effective and safe.

One limitation of the study was that this was an open-label, single-arm study, which means that all people knew which drug they were taking and there is no other drug to compare the effects of ocrelizumab with. This means that researchers do not know how the effects of ocrelizumab would compare if some participants were taking a different MS therapy or no MS medicine at all in the same study.

No single study can tell us everything about the risks and benefits of a 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://classic.clinicaltrials.gov/ct2/show/NCT03085810
- https://forpatients.roche.com/en/trials/autoimmune-disorder/multiple-sclerosis/study-to-evaluate-the-effectiveness-and-safety-of-ocrelizumab-in.html

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-evaluate-the-effectiveness-and-safety-of-ocrelizumab-in.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: “Study to Evaluate the Effectiveness and Safety of Ocrelizumab in Participants with Early Stage Relapsing-Remitting Multiple Sclerosis (RRMS)”.

The study is known as ‘ENSEMBLE’.

- The protocol number for this study is: MA30143.
- The ClinicalTrials.gov identifier for this study is: NCT03085810.
- The EudraCT number for this study is: 2016-002937-31.