ForPatients
by Roche

Multiple Sclerosis (MS) Primary Progressive Multiple Sclerosis (PPMS)

A clinical trial to compare the safety and effectiveness of ocrelizumab with placebo in people with primary progressive multiple sclerosis (PPMS)

A Study to Evaluate the Efficacy and Safety of Ocrelizumab in Adults With Primary Progressive Multiple Sclerosis

Trial Status	Trial Runs In	Trial Identifier
Recruiting	28 Countries	NCT04035005 2023-505980-36-00 WA40404

The source of the below information is the publicly available website ClinicalTrials.gov. It has been summarised and edited into simpler language.

Trial Summary:

This study will evaluate the efficacy and safety of ocrelizumab (Ocrevus®) compared with placebo in participants with primary progressive multiple sclerosis (PPMS), including participants later in their disease course. This study focuses on upper limit disability progression. This study will consist of the following phases: screening, double-blind treatment, follow-up 1 (FU1), an optional open-label extension (OLE), follow-up 2 (FU2), and B-cell monitoring (BCM).

Hoffmann-La Roche Sponsor	**Phase 3** Phase

NCT04035005 2023-505980-36-00 WA40404
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	>=18 Years & <= 65 Years	No

1. Why is this study needed?

Multiple sclerosis is a health condition in which the immune system attacks the protective covering of nerve fibres in the brain and spinal cord. This leads to communication problems between the brain and the rest of the body. MS is in an ‘active’ state when the immune system is attacking nerve fibres and causing symptoms. Symptoms include

unsteadiness, tiredness, weakness, blurred vision and tingling sensations. Primary progressive multiple sclerosis (PPMS) is a form of MS that is slow to start, and symptoms steadily worsen. At this time, there is no cure for MS.

This study is testing a medicine called ocrelizumab. Ocrelizumab is approved by health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) for treating PPMS. Studies show ocrelizumab may help people with PPMS to keep their ability to use their hands, arms and shoulders (known as ‘upper limb function’) for longer – but more information is needed.

This study aims to look at how well ocrelizumab works to stabilise or improve the signs and symptoms of PPMS compared with a drug that contains no active ingredients (placebo). It will also look at how safe and well ocrelizumab works to keep upper limb function versus placebo in people with PPMS.

2. Who can take part in the study?

People 18 to 65 years of age with PPMS can take part in the study if they have an EDSS score between 3.0 (mild – moderate disability with no problem walking) and 8.0 (restricted to a bed or chair with some use of arms) and can complete the 9-HPT in more than 25 seconds but within 4 minutes, with each hand.

People may not be able to take part in this study if they have or had certain treatments before, including ocrelizumab. Certain medical conditions such as active infections, another disease of the brain or spinal cord, heart, liver or lung problems, cancer or being unable to have an MRI scan will prevent participation too. People who are pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work?

People will be screened to check if they are able to participate in the study. The screening period will take place from 6 months before the start of treatment.

The study has two treatment phases. In the first phase, everyone who joins this study will join 1 of 2 groups randomly (like flipping a coin) and given either ocrelizumab or placebo as a drip into the vein (infusion) 6 times over about 2 and half years.

Participants will have an equal chance of being placed in either group.

The first phase is ‘placebo-controlled’ and double-blinded. Placebo-controlled means that participants are put in a group that will receive a medicine or a group that will receive ‘placebo’ (a medicine that contains no active ingredients but looks the same as the study medicine). Comparing results from the different groups helps researchers know if any changes seen result from the study medicine or occur by chance. Double blinded means

that neither the participants in the study nor the team running it will know which treatment is being given until the study is over. This is done to make sure that the results of the treatment are not affected by what people expected from the received treatment. However, the study doctor can find out which group the participant is in, if the participants' safety is at risk.

After this phase, participants who meet criteria and agree to continue treatment will join the second phase and will be given ocrelizumab as a drip into the vein (infusion) for at least another 4 doses. The second phase is ‘open-label’, which means everyone involved, including the participant and the study doctor, will know ocrelizumab has been given.

During this study, the study doctor will see participants twice during the first month of treatment then every 3 or 6 months They will see how well the treatment is working and any unwanted effects participants may have. Participants will have follow-up visit 6 months after completing the study treatment, during which the study doctor will check on the participant’s well being. Total time of participation in the study will be up to about 10 and a half years. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main results measured in the study to assess if the medicine has worked is the amount of time before upper limb function worsens by 20% measured using the 9-Hole Peg Test (9-HPT), or before physical ability worsens measured by an Expanded Disability Status Scale (EDSS) score

Other key results measured in the study include:

- Changes detected by brain scans (magnetic resonance imaging; MRI)
- The number and seriousness of unwanted effects
- How ocrelizumab gets to different parts of the body, and how the body changes and gets rid of it
- How ocrelizumab affects the immune system

5. Are there any risks or benefits in taking part in this study?

Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future.

It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. People interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo.

All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study drug Participants may have unwanted effects of the drug used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects.

Ocrelizumab Participants will be told about the known unwanted effects of ocrelizumab, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include infections, low levels of certain immune cells (called ‘B cells’) and of proteins that form part of body's natural defence against infection or other foreign substances (known as ‘antibodies’), and lower levels of protection from vaccination.

Ocrelizumab and placebo will be given as a drip into the vein (infusion). Known unwanted effects include itching, rash, throat pain, reddening of the skin, headache, fever, chills, feeling tired or weak, and feeling or being sick.

The study medicine(s) may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.