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
Active, not recruiting	23 Countries	NCT04035005 2018-001511-73 2023-505980-36-00 WA40404

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A phase IIIb, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of ocrelizumab in adults with primary progressive multiple sclerosis

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 will consist of the following phases: screening, double-blind treatment, an optional post-double-progression ocrelizumab (PDP OCR) treatment, follow-up 1 (FU1), an optional open-label extension (OLE), and follow-up 2 (FU2).

Hoffmann-La Roche
Sponsor

Phase 3
Phase

NCT04035005 2018-001511-73 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.

Inclusion Criteria:

- EDSS score at screening and baseline >= 3.0 to 8.0, inclusive
- Disease duration from the onset of MS symptoms relative to randomization date:

Less than 20 years in participants with an EDSS score at screening 7.0 - 8.0 Less than 15 years in participants with an EDSS at screening 5.5 - 6.5 Less than 10 years in participants with an EDSS at screening <= 5.0

- Documented history or presence at screening of at least one of the following laboratory findings in a cerebrospinal fluid specimen: Elevated immunoglobulin G (IgG) index or one or more IgG oligoclonal bands detected by isoelectric focusing
- Screening and baseline 9-HPT completed in > 25 seconds (average of the two hands)
- Neurological stability for # 30 days prior to baseline
- Ability to complete the 9-HPT within 240 seconds with each hand at screening and baseline
- Neurological stability for >/= 30 days prior to baseline
- Participants previously treated with immunosuppressants, immunomodulators, or other immunomodulatory therapies must undergo an appropriate washout period according to the local label of the immunosuppressant/immunomodulatory drug used

- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use adequate contraceptive methods during the treatment period and for 6 or 12 months after the final dose of ocrelizumab. Adherence to local requirements, if more stringent, is required.
- For female participants without reproductive potential: Women may be enrolled if surgically sterile (i.e hysterectomy, complete bilateral oophorectomy) or post-menopausal unless the participant is receiving a hormonal therapy for her menopause or if surgically sterile

Exclusion Criteria:

- History of relapsing-remitting or secondary progressive MS at screening
- Confirmed serious opportunistic infection including: active bacterial, viral, fungal, mycobacterial infection or other infection, including tuberculosis or atypical mycobacterial disease
- Participants who have or have had confirmed or a high degree of suspicion of progressive multifocal leukoencephalopathy (PML)
- Known active malignancy or are being actively monitored for recurrence of malignancy
- Immunocompromised state
- Receipt of a live-attenuated vaccine within 6 weeks prior to randomization
- Inability to complete an MRI or contraindication to Gd administration.
- Participants requiring symptomatic treatment of MS and/or physiotherapy who are not on a stable regimen. Participants must not initiate symptomatic treatment of MS or physiotherapy within 4 weeks of randomization.
- Contraindications to mandatory premedications for infusion-related reactions, including:

uncontrolled psychosis for corticosteroids and closed-angle glaucoma for antihistamines

- Known presence of other neurologic disorders
- Pregnant or breastfeeding, or intending to become pregnant during the study and for 6 or 12 months after last infusion of the study drug
- Lack of peripheral venous access
- Significant, uncontrolled disease, such as cardiovascular, pulmonary, renal, hepatic, endocrine or gastrointestinal, or any other significant disease that may preclude participant from participating in the study
- Any concomitant disease that may require chronic treatment with systemic corticosteroids or immunosuppressants during the course of the study
- History of alcohol or other drug abuse
- History of primary or secondary immunodeficiency
- Treatment with any investigational agent within 24 weeks prior to screening (Visit 1) or 5 half-lives of the investigational drug (whichever is longer), or treatment with any experimental procedure for MS
- Previous treatment with B-cell targeting therapies
- Any previous treatment with bone marrow transplantation and hematopoietic stem cell transplantation
- Any previous history of transplantation or anti-rejection therapy
- Treatment with IV Ig or plasmapheresis within 12 weeks prior to randomization
- Systemic corticosteroid therapy within 4 weeks prior to screening
- Positive serum human chorionic gonadotropin (hCG) measured at screening or positive urine #-hCG at baseline
- Positive screening tests for hepatitis B
- Any additional exclusionary criterion as per ocrelizumab (Ocrevus®) local label, if more stringent than the above
- Lack of MRI activity at screening/baseline if more than 650 participants without MRI activity have already been enrolled, as defined by T1 Gd+ lesion(s) and/or new and/or enlarged T2 lesion(s) in the screening, to ensure that at least 350 participants with MRI activity will be randomized

Eligibility Criteria for OLE Phase:

- Completed the 144 weeks of double-blind treatment phase of the trial or are ongoing in the double blind treatment phase at the time of the primary analysis, and who, in the opinion of the investigator, may benefit from treatment with Ocrelizumab. Participants who withdrew from study treatment and received another DMT or commercial ocrelizumab will not be allowed to enter in the OLE phase.
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use adequate contraceptive methods during the treatment period and for 6 or 12 months after the final dose of ocrelizumab. Adherence to local requirements, if more stringent, is required.
- For female participants without reproductive potential: Women may be enrolled if surgically sterile (i.e. hysterectomy, complete bilateral oophorectomy) or post-menopausal unless the participant is receiving a hormonal therapy for her menopause or if surgically sterile