ForPatients
by Roche

Multiple Sclerosis (MS)

A study to evaluate the efficacy, safety and pharmacokinetics of a higher dose of ocrelizumab in adults with primary progressive multiple sclerosis (PPMS)

A Study to Evaluate the Efficacy, Safety and Pharmacokinetics (PK) of a Higher Dose of Ocrelizumab in Adults With Primary Progressive Multiple Sclerosis (PPMS)

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	22 Countries	NCT04548999 2020-000894-26 2023-506515-18-00 BN42083

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, Controlled Study to Evaluate the Efficacy, Safety and Pharmacokinetics of a Higher Dose of Ocrelizumab in Adults With Primary Progressive Multiple Sclerosis

Trial Summary:

This is a randomized, double blind, controlled, parallel group, multicenter study to evaluate efficacy, safety and pharmacokinetics of a higher dose of ocrelizumab per intravenous (IV) infusion every 24 weeks in participants with PPMS, in comparison to the approved 600 mg dose of ocrelizumab.

We are able to provide travel reimbursement or travel services for patients located in remote locations or in areas that do not have trial locations. For more information about the trial, please contact **mississauga.msprogram@roche.com**.

Hoffmann-La Roche	Phase 3
Sponsor	Phase

NCT04548999 2020-000894-26 2023-506515-18-00 BN42083
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers

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All	#18 Years & # 55 Years	No

1. Why is this study needed? Multiple sclerosis (MS) 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. Primary progressive multiple sclerosis (PPMS) is a form of MS that is slow to start. Then symptoms steadily worsen.

This study is testing a medicine called ocrelizumab. It is approved by health authorities (like the U.S. Food and Drug Administration and European Medicines Agency) for treating people with PPMS and relapsing MS. A relapse is the return of signs or symptoms of a disease after they have improved for a while.

This study aims to compare the effects of a higher-than-approved dose of ocrelizumab versus the approved dose of ocrelizumab in people with PPMS. The higher-than-approved dose may slow down worsening of MS even more than the approved dose.

2. Who can take part in the study? People of 18 to 55 years of age who have been diagnosed with PPMS can take part in the study. But only if they were diagnosed less than 10 or 15 years ago – depending on how they score on a disability scale.

People may not be able to take part in this study if they have certain infections. They also can't have had cancer within the last 10 years, have had certain treatments, or be unable to have a magnetic resonance imaging (MRI) scan. People who are pregnant, or currently breastfeeding cannot take part in the study.

3. How does this study work? Participants 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.

Everyone who joins this study will be placed into 1 of 2 groups randomly (like flipping a coin) and given either ocrelizumab at the approved dose OR at a higher dose, given as a drip into a vein. Participants will have a 2 in 3 chance of being placed in the higher dose group, and a 1 in 3 chance of being in the approved dose group. In both groups, the first dose of ocrelizumab will be given in 2 half-doses, 2 weeks apart. Then, the full dose will be given every 6 months.

The first part of this study is 'double-blinded'. This means that neither the participants in the study nor the team running it will know which treatment is being given until the double-blind period 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.

The study doctor will see participants every 3 months during the double-blind period. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have a follow-up visit 6 months after completing study treatment in the double-blind period, during which study doctor will check on the participant's wellbeing. The double-blind period will last until all participants have completed study treatment and had their follow-up visit.

After the double-blind period, participants may have the option of being given the higher dose of treatment at visits around every 5 and a half months in the 'open-label' period. 'Open-label' means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

Participants will have follow-up visits every 3 months for about a year after completing the study treatment, during which the study doctor will check on the participant's wellbeing. Because ocrelizumab can have a long-lasting effect on the level of B-cells (a type of white blood cell), participants may continue to be checked every 6 months until their B-cell levels are restored. Total time of participation in the study will be about 8 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 result measured in the study to assess if a higher-than-approved dose of ocrelizumab works better than the approved doses is:

- The amount of time between the start of treatment and a worsening of MS that lasts for 3 months

Worsening of MS can be measured in 1 or more ways. This includes changes in walking speed, hand control and the Expanded Disability Status Scale (EDSS) scores. The EDSS scores measure changes in a person's disability level over time.

Other key results measured in the study include:

- The amount of time between the start of treatment and a worsening of MS that lasts 3 months in participants who do not have a relapse before the worsening
- The amount of time between the start of treatment and a worsening of MS that lasts for 6 months
- The amount of time between the start of treatment and a worsening of walking speed, walking ability and mental ability that lasts 3 months
- How much the whole brain and a certain part of the brain change in size each year
- How much the amount of a sign of nerve damage in the blood changes at about 2 years compared with the start of the study
- 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 works in the body and the effects it has on the immune system

- The number of participants with different types of certain sections of DNA (known as genes)

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 medicine Participants may have unwanted effects of the medicine 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 of ocrelizumab include infections of the nose, throat, or sinuses that are usually caused by viruses (such as flu or common cold), reactions to drips into a vein and a decrease in specific proteins in the blood (immunoglobulin M) which help protect against infection.

Known unwanted effects from having a drip into a vein include itching, rash, throwing up, wanting to throw up, a feeling of coldness that makes the body shiver, low blood pressure, fever, reddening of the skin, pain or discomfort in the head, a rapid heart rate, breathing problems and throat irritation, pain or swelling.

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

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov

Trial-identifier: NCT04548999

Inclusion Criteria:

- Diagnosis of PPMS
- EDSS score at screening and baseline, from 3 to 6.5 inclusive

- Average T25FWT score over two trials at screening and over two trials at baseline respectively, up to 150 (inclusive) seconds
- Average 9HPT score over four trials (two trials with each hand) at screening and over four trials (two trials with each hand) at baseline respectively, up to 250 (inclusive) seconds
- Score of # to 2.0 on the Functional Systems (FS) scale for the pyramidal system that was due to lower extremity findings at screening and baseline
- Documented magnetic resonance imaging (MRI) of brain with abnormalities consistent with MS
- Participants requiring symptomatic treatment for MS and/or physiotherapy must be treated at a stable dose. No initiation of symptomatic treatment for MS or physiotherapy within 4 weeks of randomization
- Participants must be neurologically stable for at least 30 days prior to randomization and baseline
- Disease duration from the onset of MS symptoms; if EDSS score at screening is # 5, disease duration must be less than 10 years; If EDSS score at screening is > 5, disease duration must be less than 15 years
- Documented evidence of the presence of at least one cerebrospinal fluid-specific oligoclonal bands
- Females of childbearing potential: agreement to remain abstinent or use adequate contraceptive methods
- Female participants, without reproductive potential may be enrolled e.g. if post-menopausal or if surgically sterile

Exclusion Criteria:

- History of relapsing remitting or secondary progressive MS at screening
- Any known or suspected active infection at screening or baseline (except nailbed infections), or any major episode of infection requiring hospitalization or treatment with IV antimicrobials within 8 weeks or treatment with oral antimicrobials within 2 weeks, prior to and during screening
- History of confirmed or suspected progressive multifocal leukoencephalopathy
- History of cancer, including hematologic malignancy and solid tumors, within 10 years of screening
- Immunocompromised state
- Receipt of a live or live-attenuated vaccine within 6 weeks prior to randomization
- Inability to complete an MRI or contraindication to gadolinium administration
- Contraindications to mandatory pre-medications for infusion-related reaction (IRRs)
- Known presence of other neurologic disorders that could interfere with the diagnosis of MS or assessments of efficacy and/or safety during the study
- Any concomitant disease that may require chronic treatment with systemic corticosteroids or immunosuppressants during the course of the study
- Significant, uncontrolled disease that may preclude participant from participating in the study
- History of or currently active primary or secondary, non-drug-related, immunodeficiency
- Pregnant or breastfeeding or intending to become pregnant
- Lack of peripheral venous access
- History of alcohol or other drug abuse within 12 months prior to screening
- Treatment with any investigational agent or treatment with any experimental procedure for MS
- Previous use of anti-cluster of differentiation 20 (CD20s) (including ocrelizumab), unless the last infusion was more than 2 years before screening, B-cell count is normal, and the stop of the treatment was not motivated by safety reasons or lack of efficacy
- Any previous treatment with mitoxantrone, cladribine, atacicept, alemtuzumab, and daclizumab
- Previous treatment with fingolimod, siponimod, or ozanimod within 6 weeks of baseline
- Previous treatment with natalizumab within 4.5 months of baseline
- Previous treatment with interferons beta (1a or 1b), or glatiramer acetate within 2 weeks of baseline
- Previous treatment with any other immunomodulatory or immunosuppressive medication not already listed above without appropriate washout as described in the applicable local label. If the washout requirements are not described in the applicable local label, then the wash out period must be five times the half-life of the medication

- Any previous treatment with bone marrow transplantation and hematopoietic stem cell transplantation
- Any previous history of transplantation or anti-rejection therapy
- Treatment with IV immunoglobulin (Ig) or plasmapheresis within 12 weeks prior to randomization
- Systemic corticosteroid therapy within 4 weeks prior to screening
- Positive screening tests for active, latent, or inadequately treated hepatitis B
- Sensitivity or intolerance to any ingredient (including excipients) of ocrelizumab
- Any additional exclusionary criterion as per ocrelizumab local label, if more stringent than the above