ForPatients
by Roche

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

Study to Explore the Mechanism of Action of Ocrelizumab and B-Cell Biology in Participants With Relapsing Multiple Sclerosis (RMS) or Primary Progressive Multiple Sclerosis (PPMS)

Trial Status	Trial Runs In	Trial Identifier
Completed	4 Countries	NCT02688985 2015-004616-37 ML29966

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:

An Open-Label, Multicenter, Biomarker Study to Explore the Mechanism of Action of Ocrelizumab and B-Cell Biology in Patients With Relapsing Multiple Sclerosis or Primary Progressive Multiple Sclerosis

Trial Summary:

This is an open-label, multicenter, biomarker study designed to be hypothesis-generating in order to better understand the mechanism of action of ocrelizumab and B-cell biology in RMS or PPMS. The study will be conducted in two cohorts i.e. RMS cohort (4 arm group) and PPMS cohort (one arm group). RMS cohort: Ocrelizumab will be administered as two intravenous (IV) infusions of 300 milligrams (mg) on Days 1 and 15. Subsequent doses will be given as single 600-mg infusions at Weeks 24 and 48. Participants will be randomized in 1:1:1 ratio to receive lumbar puncture (LP) post-treatment at Week 12, 24, or 52 following the first dose of ocrelizumab in three arm groups. A fourth RMS arm with delayed treatment start (Arm 4 [control group]) will not be a part of the randomization and will be recruited separately, wherein treatment with ocrelizumab will be delayed for 12 weeks from pre-treatment baseline. PPMS cohort: Ocrelizumab 600 mg will be administered as two 300-mg IV infusions separated by 14 days at a scheduled interval of every 24 weeks. Participants will receive a LP at the start of the study before dosing with ocrelizumab and second LP at Week 52 following the first dose of ocrelizumab. A long-term extension will be conducted for participants that complete the study and continue to receive ocrelizumab. Treatment with ocrelizumab in the entire study will continue for approximately 4.5 years after the first infusion.

Genentech, Inc.	Phase 3
Sponsor	Phase

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Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	**# 18 Years & # 55 Years**	**No**

Inclusion Criteria:

General Inclusion Criteria:

- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods that result in a failure rate of <1 percent (%) per year during the treatment period and for at least 24 weeks after the last dose of study treatment or until their B-cells have repleted, whichever is longer

Inclusion Criteria Specific to RMS Participants:

- Diagnosis of RMS in accordance with the 2010 revised McDonald criteria
- Expanded Disability Status Scale (EDSS) score of 0 to 5.5 points, inclusive, at Screening
- Disease duration from the onset of multiple sclerosis symptoms less than (<) 15 years in participants with an EDSS score greater than (>) 5.0 at Screening
- Either treatment-naive or receiving treatment with disease-modifying therapies, including prior use of interferon (IFN)-beta-1a (Avonex®, Rebif®), IFN-beta-1b (Betaseron®/Betaferon), or glatiramer acetate (Copaxone®).
- At least one clinically documented relapse in the past year and/or at least one T1-weighted Gadolinium (Gd)-enhancing lesion in the past year and/or at least one new T2 lesion in the past year at the time of enrollment

Inclusion Criteria Specific to RMS Cohort Arm 4 Participants:

- Must meet inclusion criteria for the RMS cohort
- Separate signed Informed Consent Form for the RMS Delayed Time to Start Control Arm (Arm 4)
- Must be willing to remain on the same dose and regimen of current standard of care, or no treatment if treatment-naïve, for 12 weeks after study enrollment The treating and/or study physician must agree that the participant is eligible to remain on the same dose and regimen of their current standard of care at Screening, or to receive no treatment if the participant is treatment-naïve, for 12 weeks after study enrollment

Inclusion Criteria Specific to PPMS Participants:

- Diagnosis of PPMS in accordance with the 2010 revised McDonald criteria
- EDSS score of 3.0 - 6.5 points, inclusive, at Screening
- Disease duration from the onset of multiple sclerosis symptoms <10 years in participants with an EDSS at Screening less than or equal to (</=) 5.0
- Documented history of either elevated immunoglobulin G (IgG) Index or one or more IgG oligoclonal bands (OCBs) detected by isoelectric focusing

Exclusion Criteria:

- Diagnosis of secondary progressive multiple sclerosis without relapses for at least 1 year
- History or known presence of recurrent or chronic infection (e.g., human immunodeficiency virus [HIV], syphilis, tuberculosis)
- History of recurrent aspiration pneumonia requiring antibiotic therapy
- History of cancer, including solid tumors and hematological malignancies (except basal cell, in situ squamous cell carcinomas of the skin, and in situ carcinoma of the cervix of the uterus that have been excised and resolved with documented clean margins on pathology)
- History of or currently active primary or secondary immunodeficiency
- History of coagulation disorders
- History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies
- History of alcohol or other drug abuse within 24 weeks prior to enrollment
- Known presence or history of other neurologic disorders Significant, uncontrolled disease, such as cardiovascular (including cardiac arrhythmia), pulmonary (including chronic obstructive pulmonary disease), renal, hepatic, endocrine, gastrointestinal, or any other significant disease
- Congestive heart failure (according to New York Heart Association III or IV functional severity)
- Known active bacterial, viral, fungal, mycobacterial infection, or any major episode of infection requiring hospitalization or treatment with IV antibiotics
- Any concomitant disease that may require chronic treatment with systemic corticosteroids or immunosuppressants during the course of the study
- Contraindications or intolerance to oral or IV corticosteroids, including IV methylprednisolone, according to the country label
- Contraindication for LP
- Previous treatment with B cell-targeted therapies (such as rituximab, ocrelizumab, atacicept, belimumab, or ofatumumab)
- Previous treatment with natalizumab/Tysabri®, alemtuzumab, anti-CD4 agents, cladribine, teriflunomide, cyclophosphamide, mitoxantrone, azathioprine, mycophenolate mofetil, cyclosporine, methotrexate, total body irradiation, or bone marrow transplantation
- Treatment with fingolimod/Gilenya®, dimethyl fumarate/Tecfidera®, or similar treatment within 6 months prior to enrollment
- Receipt of a live vaccine within 6 weeks prior to enrollment
- Systemic corticosteroid therapy within 4 weeks prior to Baseline
- Previous or concurrent treatment with any investigational agent or treatment with any experimental procedure for multiple sclerosis (such as treatment for chronic cerebrospinal venous insufficiency)
- Certain laboratory abnormalities or findings at Screening
- Inability to complete an MRI
- Lack of peripheral venous access
- Pregnant or lactating, or intending to become pregnant during the study

Exclusion Criteria Specific to RMS Participants:

- Diagnosis of PPMS or secondary progressive multiple sclerosis without relapses