



# AN OPEN-LABEL, SINGLE-ARM STUDY TO EVALUATE THE EFFECTIVENESS AND SAFETY OF OCRELIZUMAB IN PATIENTS WITH EARLY STAGE RELAPSING REMITTING MULTIPLE SCLEROSIS

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## Main Information

**Primary registry identifying number**

LBCTR2020033434

**Protocol number**

MA30143

**MOH registration number**

**Study registered at the country of origin**

Yes

**Study registered at the country of origin: Specify**

**Type of registration**

Retrospective

**Type of registration: Justify**

Study started before establishment of LBCTR

**Date of registration in national regulatory agency**

25/01/2018

**Primary sponsor**

F. HOFFMANN-LA ROCHE LTD

**Primary sponsor: Country of origin**

Switzerland

**Date of registration in primary registry**

03/09/2020

**Date of registration in national regulatory agency**

25/01/2018

**Public title**

AN OPEN-LABEL, SINGLE-ARM STUDY TO EVALUATE THE EFFECTIVENESS AND SAFETY OF OCRELIZUMAB IN PATIENTS WITH EARLY STAGE RELAPSING REMITTING MULTIPLE SCLEROSIS

**Acronym**

Ensemble

**Scientific title**

AN OPEN-LABEL, SINGLE-ARM STUDY TO EVALUATE THE EFFECTIVENESS AND SAFETY OF OCRELIZUMAB IN PATIENTS WITH EARLY STAGE RELAPSING REMITTING MULTIPLE SCLEROSIS

**Acronym**

Ensemble

**Brief summary of the study: English**



This study is a prospective, multicenter, open-label, single-arm effectiveness and safety study in patients with early stage RRMS. The first dose of ocrelizumab will be administered as an initial dose of two 300-mg infusions (600 mg total) in 250 mL 0.9% sodium chloride each separated by 14 days (i.e., Days 1 and 15) followed by one 600-mg infusion in 500 mL 0.9% sodium chloride every 24 weeks for the remainder of the study duration.

The study will consist of the following periods:

- Screening period: Up to 4 weeks
- Treatment period: Open-label treatment period of 192 weeks (i.e. 24 weeks after the last dose of ocrelizumab, which will be administered at Week 168)
- A follow-up period of at least 48 weeks, which is independent treatment (DMT) administered as explained below. Follow-up Period: Patients who discontinue treatment early will be followed up for at least 48 weeks after the last infusion of study drug. Patients who complete the 192 weeks Treatment Period and, in agreement with their treating neurologist, decide not to continue in a separate long term extension (LTE) study, will be followed up for at least 48 weeks after the end of the Treatment Period (i.e. 192 weeks + 48 weeks).

Patients whose B-cells have not been repleted after 48 weeks of Follow-up Period will continue with visits every 24 weeks, and telephone contacts every 8 weeks, until B-cell repletion (Continued B-cell monitoring). If the patients are receiving other B-cell targeted therapies, then the Follow-up Period is only 48 weeks regardless of their B-cell count.

A structured telephone interview will be conducted by site personnel every 8 weeks between the study visits (starting after the site visit at 8 weeks) during the treatment period and follow-up to identify and collect information on any changes in the patient's health status that warrant an unscheduled visit (including new or worsening neurological symptoms) and possible events or infections.

#### Brief summary of the study: Arabic

ان الهدف من هذه الدراسة هو معرفة ما اذا كان اوكريليزوماب (دواء الدراسة) سيوقف تفاقم اشارات واعراض التصلب المتعدد المعكبر. تعمل الاجسام المضادة الوحيدة النسيلة مثل جهاز مناعة المريض، وتتعلق ببعض الخلايا بهدف الهجوم على الجراثيم وغيرها من الامراض في جسم المريض. يتعلق اوكريليزوماب ببعض انواع كريات الدم البيضاء (الخلايا البائية) التي يعتقد انها تلعب دوراً في مرض التصلب المتعدد . مريض 1,100 سوف تصم هذه الدراسة ما لا يقل عن سيق ان تم اعتماد اوكريليزوماب لعلاج التصلب المتعدد في العديد من البلدان بما فيها الولايات المتحدة الميركية واوستراليا وكندا والاتحاد الوروبي وغيرها من الدول. غير ان هذا الدواء ما زال تجريبياً في بلدان اخرى، مما يعني ان السلطات الصحية في هذه البلدان لم تقر استعمال اوكريليزوماب لعلاج التصلب المتعدد.

#### Health conditions/problem studied: Specify

This study will evaluate the effectiveness and safety of ocrelizumab in early stage relapsing-remitting multiple sclerosis (RRMS) patients.

#### Interventions: Specify

Ocrelizumab (Ocrevus) - recombinant humanized anti-human monoclonal antibody

#### Key inclusion and exclusion criteria: Inclusion criteria

Patients must meet the following criteria for study entry:

- Signed informed consent form
- Able to comply with the study protocol, in the investigator's judgment
- Age 18 – 55 years, inclusive
- Have a definite diagnosis of RRMS, as per the revised McDonald 2010 criteria (Polman et al. 2011)
- Have a length of disease duration, from first documented clinical attack consistent with MS disease of  $\leq 3$  years
- Within the last 12 months:

One or more clinically reported relapse(s)

OR

One or more signs of MRI activity

- EDSS of 0.0 to 3.5 inclusive, at screening
- For women of childbearing potential: agreement to use an acceptable birth control method during the treatment period and for at least 6 months after the last dose of study drug.

A woman is considered to be of childbearing potential if she is postmenarcheal, has not reached a postmenopausal state ( 12 continuous months of amenorrhea with no identified cause other than menopause), and has not undergone surgical sterilization (removal of ovaries and/or uterus).

The following are acceptable contraceptive methods: progestogen-only oral hormonal contraception, where inhibition of ovulation is not the primary mode of action, male or female condom with or without spermicide, and cap, diaphragm, or sponge with spermicide. A combination of male condom with cap, diaphragm, or sponge with spermicide (double-barrier methods) is considered acceptable.

**Key inclusion and exclusion criteria: Gender**

Both

**Key inclusion and exclusion criteria: Specify gender****Key inclusion and exclusion criteria: Age minimum**

18

**Key inclusion and exclusion criteria: Age maximum**

55

**Key inclusion and exclusion criteria: Exclusion criteria**

Patients who meet any of the following criteria will be excluded from study entry:

- Secondary progressive multiple sclerosis progressive relapsing MS
- Inability to complete an MRI (contraindications for MRI include but are not restricted to pacemaker, cochlear implants, presence of foreign substances in the eye, intracranial vascular clips, surgery within 6 weeks of entry into the study, coronary stent implanted within 8 weeks prior to the time of the intended MRI, claustrophobia, weight > 140 kg, etc.)
- Known presence of other neurological disorders, including but not limited to, the following:
  - History of ischemic cerebrovascular disorders (e.g., stroke, transient ischemic attack) or ischemia of the spinal cord
  - History or known presence of CNS or spinal cord tumor (e.g., meningioma, glioma)
  - History or known presence of potential metabolic causes of myelopathy (e.g., untreated vitamin B12 deficiency)
  - History or known presence of infectious causes of myelopathy (e.g., syphilis, Lyme disease, human T-lymphotropic virus 1 [HTLV-1], herpes zoster myelopathy)
  - History of genetically inherited progressive CNS degenerative disorder (e.g., hereditary paraparesis; MELAS [mitochondrial myopathy, encephalopathy, lactic acidosis, stroke] syndrome)
  - Neuromyelitis optica
  - History or known presence of systemic autoimmune disorders potentially causing progressive neurologic disease (e.g., lupus, anti-phospholipid antibody syndrome, Sjogren's syndrome, Behçet's disease, sarcoidosis)
  - History of severe, clinically significant brain or spinal cord trauma (e.g., cerebral contusion, spinal cord compression)

**UExclusions Related to General Health**

- Pregnancy or lactation
- Any concomitant disease that may require chronic treatment with systemic corticosteroids or immunosuppressants during the course of the study
- History or currently active primary or secondary immunodeficiency
- Lack of peripheral venous access
- History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies
- Significant or uncontrolled somatic disease or any other significant disease that may preclude patient from participating in the study
- Congestive heart failure (New York Heart Association [NYHA] III or IV functional severity)
- Known active bacterial, viral, fungal, mycobacterial infection or other infection, (excluding fungal infection of nail beds) or any major episode of infection requiring hospitalization or treatment with intravenous (IV) antibiotics within 4 weeks prior to screening or oral antibiotics 2 weeks prior to screening.

Note: Active infections should be treated and effectively controlled before possible inclusion in the study

- History of major opportunistic infections (i.e. cryptococcosis, Pneumocystis pneumonia, progressive multifocal leukoencephalopathy [PML])
- History or known presence of recurrent or chronic infection (e.g., human immunodeficiency virus [HIV], syphilis, tuberculosis [TB])
- History of malignancy, including solid tumors and hematological malignancies, except basal cell carcinoma, in situ squamous cell carcinoma of the skin, and in situ carcinoma of the cervix of the uterus that have been previously completely excised with documented, clear margins.
- History of alcohol or drug abuse within 24 weeks prior to baseline
- History or laboratory evidence of coagulation disorders
- Received any prior approved DMT with a label for MS, for example, interferons, glatiramer acetate, natalizumab, alemtuzumab, daclizumab, fingolimod, teiflunomide and dimethylfumarate.
- Receipt of a live vaccine or attenuated live vaccine within 6 weeks prior to the baseline visit. In rare cases when patient requires vaccination with a live vaccine, the screening period may be extended but cannot exceed 8 weeks.
- Treatment with any investigational agent within 24 weeks of screening (Visit 1) or five half-lives of the investigational drug (whichever is longer) or treatment with any experimental procedures for MS (e.g., treatment for chronic cerebrospinal venous insufficiency).
- Contraindications to or intolerance of oral or IV corticosteroids, including methylprednisolone administered IV, according to the country label, including:
  - a) Psychosis not yet controlled by a treatment;
  - b) Hypersensitivity to any of the constituents.
- Previous treatment with B-cell targeted therapies (i.e., rituximab, ocrelizumab, atacicept, belimumab, or ofatumumab).
- Systemic corticosteroid therapy within 4 weeks prior to screening.
- Any previous treatment with immunosuppressants/ immunomodulators/ antineoplastic therapies (cyclophosphamide, azathioprine, mycophenolate mofetil, cyclosporine, methotrexate, cladribine, mitoxantrone, laquinimod, total body irradiation, or bone marrow transplantation).
- Treatment with IV immunoglobulins (Ig) within 12 weeks prior to baseline.
- Treatment with investigational DMT
- History of recurrent aspiration pneumonia requiring antibiotic therapy
- Treatment with fampridine/dalfamipridine (Fampyra®)/Ampyra® unless on stable dose for ≥ 30 days prior to screening. Wherever possible, patients should remain on stable doses throughout the 96-week treatment period.
- Positive serum β human chorionic gonadotropin (hCG) measured at screening
- Positive screening tests for hepatitis B (hepatitis B surface antigen [HBsAg] positive, or positive hepatitis B core antibody [total HBcAb] confirmed by a positive viral DNA polymerase chain reaction [PCR])
- Lymphocyte count below lower limit of normal (LLN)
- CD4 count < 250/μL.
- Aspartate aminotransferase (AST)/ serum glutamic oxaloacetic transaminase (SGOT) or alanine aminotransferase (ALT) /serum glutamic pyruvic transaminase (SGPT) ≥ 3.0 × the upper limit of normal (ULN)



- Serum creatinine >1.4 mg/dL (> 124 µmol/L) for women or > 1.6 mg/dL (> 141µmol/L) for men
- Hemoglobin < 8.5 g/dL (< 5.15 mmol/L)
- Platelet count <100,000/µL (<100 × 10<sup>9</sup>PP/L)
- Absolute neutrophil count <1.0 × 10<sup>3</sup>PP/µL

**Type of study**

Interventional

**Type of intervention**

Pharmaceutical

**Type of intervention: Specify type**

N/A

**Trial scope**

Other

**Trial scope: Specify scope****Study design: Allocation**

N/A: Single arm study

**Study design: Masking**

Open (masking not used)

**Study design: Control**

Uncontrolled

**Study phase**

3

**Study design: Purpose**

Treatment

**Study design: Specify purpose**

N/A

**Study design: Assignment**

Single

**Study design: Specify assignment**

N/A

**IMP has market authorization**

Yes, Lebanon and Worldwide

**IMP has market authorization: Specify**

United States of America, Albania, Australia, Israel, Kosovo, Kuwait, Panama, Paraguay, Russian Federation, Ukraine, United Arab Emirates, and Canada

**Name of IMP**

Ocrelizumab

**Year of authorization**

2018

**Month of authorization**

10

**Type of IMP**

Immunological

**Pharmaceutical class**

Ocrelizumab is a recombinant humanized anti-human monoclonal antibody that selectively targets and eliminates CD20-expressing B cells.

**Therapeutic indication**

Relapsing remitting multiple sclerosis

**Therapeutic benefit**

The majority of the clinical trials of DMTs in MS target patients who are already progressed, for example the mean duration of disease is around six years for many clinical trials (Wiendl and Meuth. 2015). There is, however, evidence suggesting that early intervention might be effective in reducing the rate of relapses in patients with RRMS and in slowing the course of MS progression (Noyes and Weinstock-Guttman. 2013).

A follow-up of the phase 3 clinical trial (n = 160) of IFNβ-1a vs. placebo in early RRMS patients described above, patients randomized to IFNβ-1a (n=79) were significantly less likely to progress to an EDSS score of 4.0 or greater (44.3% vs 65.4%; P=.007) or 5.0 or greater (34.2% vs 54.3%; P=.01) than patients randomized to placebo (n=81) at the 8-year follow-up assessment (Rudick et al. 2010). Other long-term studies have also demonstrated a positive impact of early therapy in patients with RRMS. In a long-term follow-up of the pivotal PRISMS study (n=560), patients originally randomized to both the 22-µg and 44-µg doses of IFNβ-1a had sustained reductions in relapses and less disease progression compared with patients originally randomized to placebo. Although all patients received IFNβ-1a treatment by year 3 of the pivotal study (patients originally randomized to placebo were switched to either the 22- or 44-µg dose), the increased disability observed in patients for whom treatment was delayed was sustained (Kappos et al. 2006), suggesting that delaying treatment for as little as 2 years may result in irreversible consequences.



**Study model**

N/A

**Study model: Explain model**

N/A

**Study model: Specify model**

N/A

**Time perspective**

N/A

**Time perspective: Explain time perspective**

N/A

**Time perspective: Specify perspective**

N/A

**Target follow-up duration**

**Target follow-up duration: Unit**

**Number of groups/cohorts**

**Biospecimen retention**

None retained

**Biospecimen description**

NA

**Target sample size**

10

**Actual enrollment target size**

6

**Date of first enrollment: Type**

Actual

**Date of first enrollment: Date**

08/03/2018

**Date of study closure: Type**

Actual

**Date of study closure: Date**

16/01/2024

**Recruitment status**

Complete

**Recruitment status: Specify**

**Date of completion**

21/01/2019

**IPD sharing statement plan**

Yes

**IPD sharing statement description**



During this study, health and personal information about subjects will be collected. This section describes the protection, use, and sharing of information, which consists of the following:

- Information in the medical record, which is held by Sites.
- Information that is collected or produced during this study ("study data"), which is held by sites, Roche, Roche affiliates, and Roche's representatives.

Subject privacy is very important, and Roche uses many safeguards to protect privacy, in accordance with applicable data privacy laws and laws related to the conduct of clinical trials. Subject study data and samples will be labelled with a patient identification (ID) number that is unique and not related to or derived from information that identifies subject (such as name, picture, or any other personally identifying information). Roche, Roche affiliates, and Roche's representatives will only have access to study data and samples labelled with a patient ID number, except as described below. Subjects medical record, which includes personal information that can identify subjects, will not be accessed for the purposes of this study, except as described below:

Information (which includes information in medical record that can identify subjects) may need to be reviewed to make sure the study is being done properly or to check the quality of the information. This information will be kept private. The following people and groups of people may and/or copy this information:

- Study monitors of Roche and/or CRO, a company hired by Roche to perform certain study activities
- The Institutional Review Board or Ethics Committee
- Regulatory authorities

Roche, Roche affiliates, and Roche's collaborators and licensees (people and companies who partner with Roche) may use study data labelled with patient ID number for research purposes or to advance science and public health.

Study data may be submitted to government or other health research databases or shared with researchers, government agencies, companies, or other groups that are not participating in this study. These data may be combined with or linked to other data and used for research purposes, to advance science and public health, or for analysis, development, and commercialization of products to treat and diagnose disease. These data will not include information that identifies subjects, and extra steps will be taken to safeguard privacy.

Subject information will not be given to insurance company or employer, unless required by law. If the results from this study are published in a medical journal or presented at a scientific meeting, subjects will not be identified.

Information from this study will be retained by Sites for 15 years after the end of the study. In addition, Roche will retain the study data for up to 25 years after the end of the study.

**Additional data URL**

**Admin comments**

**Trial status**

Approved

## Secondary Identifying Numbers

No Numbers



## Sources of Monetary or Material Support

No Sources

## Secondary Sponsors

No Sponsors

## Contact for Public/Scientific Queries

No Contacts

## Centers/Hospitals Involved in the Study

No Centers/Hospitals

## Ethics Review

No Reviews

## Countries of Recruitment

No Countries

## Health Conditions or Problems Studied

No Problems Studied



## Interventions

No Interventions

## Primary Outcomes

No Outcomes

## Key Secondary Outcomes

No Outcomes





## Trial Results

**Summary results**

**Study results globally**

**Date of posting of results summaries**

**Date of first journal publication of results**

**Results URL link**

**Baseline characteristics**

**Participant flow**

**Adverse events**

**Outcome measures**

**URL to protocol files**