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
26/03/2024

Date of registration in national regulatory agency
25/01/2018

Public title
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Acronym
Ensemble

Scientific title
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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 التصلّب المتعدّد المبكر. تعمل الاجسام المضادة الوحيدة النسيلة مثل جهاز مناعة المريض، وتتعلّق ببعض الخاليا بهدف الهجوم على الجراثيم وغيرها من الامراض في جسم المريض. يتعلّق اوكريليزوماب ببعض انواع كريات الدم البيضاء (الخاليا البائية) التي يعتقد انها تلعب دوراً في مرض التصلّب المتعدّد.
سوف تضمّ هذه الدراسة ما لا يقل عن 1,100 مريض.
سبق ان تم اعتماد اوكريليزوماب لعلاج التصلّب المتعدد في العديد من البلدان بما فيها الواليات المتحدة االميركية واوستراليا وكندا واالتحاد االوروبي وغيرها من الدول. غير ان هذا الدواء ما زال تجريبياً في بلدان اخرى، مّما يعني ان السلطات الصحية في هذه البلدان لم تقر استعمال اوكريليزوماب لعالج التصلّب 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 ≤ 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 UExclusions Related to Medications
• 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/dalfampridine (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. UExclusions Related to Laboratory Findings*
• 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 × 109PP/L)
• Absolute neutrophil count <1.0 × 103PP/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	Year of authorization	Month of authorization
Ocrelizumab	2018	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

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
American University of Beirut	Samia Khoury	Neuroscience	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	22/02/2021	Samia Khoury	sk88@aub.edu.lb	+961-1-350000 ext.: 5138

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