AN OPEN-LABEL, SINGLE-ARM 4-YEAR STUDY TO EVALUATE EFFECTIVENESS AND SAFETY OF OCRELIZUMAB TREATMENT IN PATIENTS WITH PROGRESSIVE MULTIPLE SCLEROSIS

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Main Information

Primary registry identifying number
LBCTR2020030186

Protocol number
MN39159

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
16/07/2018

Primary sponsor
F. HOFFMANN-LA ROCHE LTD

Primary sponsor: Country of origin
Switzerland

Date of registration in primary registry
23/12/2020

Date of registration in national regulatory agency
16/07/2018

Public title
AN OPEN-LABEL, SINGLE-ARM 4-YEAR STUDY TO EVALUATE EFFECTIVENESS AND SAFETY OF OCRELIZUMAB TREATMENT IN PATIENTS WITH PROGRESSIVE MULTIPLE SCLEROSIS

Acronym
CONSONANCE

Scientific title
AN OPEN-LABEL, SINGLE-ARM 4-YEAR STUDY TO EVALUATE EFFECTIVENESS AND SAFETY OF OCRELIZUMAB TREATMENT IN PATIENTS WITH PROGRESSIVE MULTIPLE SCLEROSIS

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Brief summary of the study: English

The purpose of this study is to see if ocrelizumab (study drug) will halt the worsening of the signs and symptoms of the progressive form of MS. Ocrelizumab is a type of drug called a monoclonal antibody. Monoclonal antibodies act like the body's immune system and attach to certain cells in order to attack germs and other illnesses in the subject's body. Ocrelizumab attaches to certain types of white blood cells (B cells) that are thought to play a role in MS.
About 600 people will take part in this study.
As of November 2017, ocrelizumab has been approved for the treatment of MS in the United States of America, Albania, Australia, Israel, Kosovo, Kuwait, Panama, Paraguay, Russian Federation, Ukraine, United Arab Emirates, and Canada (only for relapsing form of MS), however it is an experimental drug in other countries as of today, which means the health authorities in those countries have not approved ocrelizumab for the treatment of MS.

Brief summary of the study: Arabic

الغرض من هذه الدراسة هو معرفة ما إذا كان عقار أوكرليزوماب (عقار الدراسة) سيحول دون تدهور علامات وأعراض مرض التصلُّب المتعدد من النوع المترقي. ويُعد عقار أوكرليزوماب نوعًا من العقاقير يُسمى جسمًا مضادًّا أحادي النسيلة. الأجسام المضادة أحادية النسيلة تقوم بالتصرف كجهاز مناعي وترتبط بخلايا معينة من أجل مهاجمة الجراثيم والأمراض الأخرى في جسم المريض. عقار أوكرليزوماب يرتبط بأنواع معينة من خلايا الدَّم البيضاء (B cells) التي يعتقد أن لها دورًا في مرض التصلُّب المتعدد.
سيُشارك في هذه الدراسة حوالي 600 مريض.
تمت الموافقة على عقار أوكرليزوماب لعلاج مرض التصلُّب المتعدد في الولايات المتحدة الأمريكية، الاتحاد الاوروبي ألبانيا، أستراليا،كوبا و السلفادور وجمهورية الدومينيكان إسرائيل، كوسوفو، الكويت، نيوزيلاندا وجورجيا, ، باراجواي، قطر الاتحاد الروسي، السعوديه و سويسرا وأوكرانيا، الإمارات العربية المتحدة، وكندا (لعلاج مرض التصلُّب المتعدد من النوع الانتكاسي "الارتدادي" فقط) ولكنه لا يزال عقارًا تجريبيًّا في دول أخرى اعتبارًا من هذا اليوم، مما يعني أنَّ السلطات الصحية في هذه الدول لم تعتمد عقار أوكرليزوماب لعلاج مرض التصلُّب المتعدد. اعتبارًا من 31 يناير 2018

Health conditions/problem studied: Specify

Progressive Multiple Sclerosis

Interventions: Specify

The investigational medicinal product (IMP) for this study is Ocrelizumab IV (OCREVUS).

Key inclusion and exclusion criteria: Inclusion 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□65 years, inclusive at screening.
-Have a definite diagnosis of PMS (as per the revised McDonald 2010 criteria for PPMS* or Lublin et al. 2014 criteria for PMS*).
EDSS ≤6.5 at screening.
-Have a length of disease duration since PMS disease symptom onset ≤10 years if baseline EDSS ≤5.0 and ≤15 years if baseline EDSS >5.0.
-Have documented evidence of disability progression independent of relapse activity at any point over the 2 years prior to the screening visit. In case relapse(s) have occurred in the last 2 years, disability progression will have to be considered as independent of relapse activity as per treating physician's judgment.
-Fulfill at least one of the 21 criteria assessing the evidence of disability progression independent of relapse activity in the last 2 years using the pre-baseline disability progression rating system checklist (Appendix 3Appendix 3Appendix 3Appendix 3).
-Have experience of having used a smartphone and connecting a smartphone to Wi-Fi network providers.
-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.
*For both, PPMS patients according to revised McDonald 2010 criteria and RMS patients meeting criteria for PMS disease course as per Lublin et al. 2014, it will be documented whether or not they fulfill each of the three following McDonald Criteria:
1. Evidence for Dissemination in space (DIS) in the brain based on ≥1 T2 lesions in at least one area characteristic for MS (periventricular, juxtacortical, or infratentorial).
2. Evidence for DIS in the spinal cord based on ≥2 T2 lesions in the cord.
3. Positive findings in a cerebrospinal fluid (CSF) specimen (isoelectric focusing evidence of oligoclonal bands and/or elevated immunoglobulin (Ig) G index) [If a recent CSF sample or results from a previous CSF test from each patient is not available, this data will be considered missing information].

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

65

Key inclusion and exclusion criteria: Exclusion criteria

Exclusion Criteria:
Patients who meet any of the following criteria will be excluded from study entry:
-Relapsing-remitting multiple sclerosis (RRMS) at screening.
-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.).
-Gadolinium (Gd) intolerance
-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).
Exclusions 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.
-Hypersensitivity to ocrelizumab or to any of its excipients.
-Significant or uncontrolled somatic disease or any other significant disease that may preclude patient from participating in the study.
-Active infections must be treated and resolved before possible inclusion in the study.
-Patients in a severely immunocompromised state until the condition resolves
-Patients with known active malignancies or being actively monitored for recurrence of malignancy
-Patients who have or have had confirmed progressive multifocal leukoencephalopathy (PML)

Exclusions Related to Medications:
-All vaccines should be given at least 6 weeks before the first infusion of ocrelizumab. Live/live attenuated vaccines should be avoided during treatment and safety follow-up period until B cells are peripherally repleted.
-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) within 24 weeks of screening (Visit 1).
-Previous treatment with B-cell targeted therapies (i.e., rituximab, ocrelizumab, atacicept, tabalumab, belimumab, ofatumumab, or obinutizumab).
-Any previous treatment with alemtuzumab (Campath/Mabcampath/Lemtrada), total body irradiation, or bone marrow transplantation.
-Previous treatment with natalizumab, daclizumab or fingolimod in the last 8 weeks.
-Previous treatment with natalizumab where PML has not been excluded according to specific algorithm in Appendix 10
-Patients previously treated with teriflunomide, unless an accelerated elimination procedure is implemented until its completion before screening visit
Accelerated elimination procedure after stopping treatment with teriflunomide:
-- cholestyramine 8g is administered 3 times daily for a period of 11 days, or cholestyramine 4g three times a day can be used, if cholestyramine 8g three times a day is not well tolerated,
-- alternatively, 50g of activated powdered charcoal is administered every 12 hours for a period of 11 days
As per Aubagio SmPC: Following the accelerated elimination procedures, verification by 2 separate tests at an interval of at least 14 days and a waiting period of one-and-a-half months between the first occurrence of a plasma concentration below 0.02 mg/l and fertilisation is required.
-Previous treatment with azathioprine, cyclophosphamide, mycophenolate mofetil or methotrexate in the last 12 weeks.
-Previous treatment with mitoxantrone, cyclosporine or cladribine in the last 96 weeks.
-Contraindications to or intolerance of oral or intravenous (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.
-Treatment with fampridine/dalfampridine (Fampyra®)/Ampyra®) or other symptomatic MS treatment unless on stable dose for ≥30 days prior to screening. Wherever possible, patients should remain on stable doses throughout the treatment period.

Exclusions 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]) or hepatitis C (HepCAb).

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

recombinant humanized monoclonal antibody

Therapeutic indication

Relapsing and Primary Progressive forms of Multiple Sclerosis (MS)

Therapeutic benefit

Ocrelizumab has demonstrated a significant reduction in clinical disability outcomes as well as a reduction of MRI disease burden measures compared with placebo in PPMS patients.

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

Samples with DNA**

Biospecimen description

Serum and Plasma samples

Target sample size

Actual enrollment target size

10

6

Date of first enrollment: Type

Actual

Date of first enrollment: Date

29/05/2019

Date of study closure: Type

Actual

Date of study closure: Date

28/03/2024

Recruitment status

Recruiting

Recruitment status: Specify

Date of completion

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

Full name of issuing authority	Secondary identifying number
NA	NA

Sources of Monetary or Material Support

Name
F. HOFFMANN-LA ROCHE LTD

Secondary Sponsors

Name
NA

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Bassem Yamout	American University of Beirut, Medical Center	Lebanon	+961 01/350000	yamoutba@gmail.com	Nehme and Therese Tohme Multiple Sclerosis Center - American University of Beirut Medical Center
Scientific	Nagi Riaci	Lebanese American University - Rizk Hospital	Lebanon	+9613229324	najiriachi@hotmail.com	Lebanese American University - Rizk Hospital

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Nehme and Therese Tohme Multiple Sclerosis Center - American University of Beirut Medical Center	Dr. Bassem Yamout	Neurologist	Approved
Lebanese American University, Rizk Hospital	Dr. Nagi Riachi	Neurologist	Approved
Lebanese American University	Dr Rechdi Ahdab	Neurologist	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	17/01/2019	Dr. Deborah Mukherji	irb@aub.edu.lb	+9611350000 ext. 5445
Lebanese American University- University Medical Center Rizk Hospital	16/07/2018	Dr. Costantine Daher	irb@lau.edu.lb	+9611786456

Countries of Recruitment

Name
Lebanon
Bosnia and Herzegovina
Brazil
Canada
Colombia
Costa Rica
Czech Republic
Denmark
Egypt
France
Guatemala
Hungary
Ireland
Italy
Mexico
Morocco
Netherlands
Panama
Poland
Russian Federation
Spain
United Arab Emirates
United States of America

Health Conditions or Problems Studied

Condition	Code	Keyword
Multiple Sclerosis	Multiple sclerosis (G35)	MS

Interventions

Intervention	Description	Keyword
Ocrelizumab	The investigational medicinal product (IMP) for this study is Ocrelizumab IV (OCREVUS). recombinant humanized monoclonal antibody.	Ocrevus

Primary Outcomes

Name	Time Points	Measure
To evaluate the effectiveness of ocrelizumab treatment in patients with PMS disease course.	Proportion of patients with no evidence of progression (NEP)	Defined as no progression sustained for at least 24 weeks on all of the following three components (CDP#; ≥20% increase in T25FWT; ≥20% increase in 9HPT) from baseline to Week 96, Week 96 to Week 192 and baseline to Week 192
To evaluate the effectiveness of ocrelizumab treatment in patients with PMS disease course.	Proportion of patients with no evidence of progression and no active disease (NEPAD)	Defined as no progression sustained for at least 24 weeks on all of the three components of NEP (CDP, T25FWT, 9HPT), no protocol-defined relapse, no enlarging or new T2 lesion, and no T1 gadolinium (Gd+)- enhancing lesion from baseline to Week 96, Week 96 to Week 192 and baseline to Week 192

Key Secondary Outcomes

Name	Time Points	Measure
To evaluate the effectiveness of ocrelizumab treatment in patients with PMS disease course	Change from baseline in cognitive function	as measured by the symbol digit modalities test (SDMT) [as part of the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery]
To evaluate the effectiveness of ocrelizumab treatment in patients with PMS disease course	Mean change from baseline in the EDSS score over the course of the study	NA
To evaluate the effectiveness of ocrelizumab treatment in patients with PMS disease course	Time to onset of first CDP sustained for at least 24 and 48 weeks	NA
To evaluate the effectiveness of ocrelizumab treatment in patients with PMS disease course	Time to onset of first ≥20% increase in T25FWT sustained for at least 24 weeks	NA
To evaluate the effectiveness of ocrelizumab treatment in patients with PMS disease course	Time to onset of first ≥20% increase in 9HPT sustained for at least 24 weeks	NA
To evaluate the effectiveness of ocrelizumab treatment in patients with PMS disease course	Proportion of patients with NEP	defined above from Week 24 to Week 96, Week 24 to Week 192 and Week 48 to Week 192
To evaluate the effectiveness of ocrelizumab treatment in patients with PMS disease course	Proportion of patients with NEPAD	defined above from Week 24 to Week 96, Week 24 to Week 192 and Week 48 to Week 192
To evaluate the effectiveness of ocrelizumab treatment in PMS patients using a range of patient- relevant measures	Change from baseline in the following patient-reported outcomes (PROs): – Multiple Sclerosis Impact Scale (MSIS-29) – Multiple Sclerosis Walking scale (MSWS-12) – ABILHAND-56 Questionnaire – Fatigue scale for Motor and cognitive function (FSMC) – SymptoMScreen – 88-item Multiple Sclerosis Spasticity Scale (MSSS-88) – Numerical Pain Rating Scale (NPRS) – Patient Global Impression of Severity (PGIS) for upper limb, lower limb and cognitive functions • Change from baseline in the number of falls and near-falls	NA
To evaluate the effectiveness of ocrelizumab treatment in PMS patients using advanced imaging outcomes	Change in the following MRI volumetric measures: • Whole brain volume • Cerebral white matter volume • Cortical grey matter volume • Thalamic and hippocampal volumes • Cerebellar volume (whole, grey matter, white matter) • Cervical cord cross-sectional area • Cervical cord grey matter area • Cervical cord white matter area	NA

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