Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 2026

A Phase III, randomized, two-armed, double-blind, parallel,active-controlled, clinical trial to evaluate equivalency of the efficacy and safety of Ocrelizumab (CinnaGen, Iran) in comparison to reference product, Ocrevus® (Roche, Switzerland) in patients with relapsing multiple sclerosis

Protocol summary

Study aim

The aim of this study is to evaluate the efficacy and safety of Ocrelizumab (CinnaGen) in comparison to reference product, Ocrevus® (Roche) in patients with relapsing multiple sclerosis

Design

A phase III, Active-controlled, Parallel, double-blind, randomized clinical trial

Settings and conduct

This is a multicenter, double-blinded study.

Participants/Inclusion and exclusion criteria

Patients with MS between 18 and 55 years of age who have EDSS between 0-5.5 and have had at least two attacks in the last 2 years or an attack in one year and Neurological stability for ≥ 30 days prior to enrolling in study. Patients of reproductive potential must use reliable means of contraception. Ability to provide written, informed consent and to be compliant with the schedule of protocol assessments. Patients with a primary progressive MS. Disease duration of more than 10 years in patients with an EDSS ≤ 2.0 at screening. Inability to complete an MRI, and presence of other neurological disorders that mimic symptoms of MS, pregnancy, and lactation, other diseases that require treatment with corticosteroids or immunosuppressants. The presence of immunodeficiency (primary or secondary), lack of peripheral venous access, history of anaphylactic reaction to monoclonal antibodies, Significant or uncontrolled somatic disease or any other significant disease, presence of active infections or need for admission and receiving antibiotics, History or known presence of recurrent or chronic infection, history of PML, history of malignancy, alcohol and drug abuse, history or laboratory evidence of coagulation disorders, receiving a live vaccine, participating in other experimental trials, receiving other drugs or the laboratory evidences that are excluded according to the protocol.

Intervention groups

Ocrelizumab (CinnaGen, Iran) 600 mg every 24 weeks

Main outcome variables

Annualized Relapse Rate (ARR) by 48 weeks

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20150303021315N13**
Registration date: **2019-06-10, 1398/03/20**
Registration timing: **prospective**

Last update: **2020-06-28, 1399/04/08**
Update count: **2**

Registration date

2019-06-10, 1398/03/20

Registrant information

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date
2019-06-22, 1398/04/01
Expected recruitment end date
2022-06-22, 1401/04/01
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
A Phase III, randomized, two-armed, double-blind, parallel,active-controlled, clinical trial to evaluate equivalency of the efficacy and safety of Ocrelizumab (CinnaGen, Iran) in comparison to reference product, Ocrevus® (Roche, Switzerland) in patients with relapsing multiple sclerosis

Public title
Evaluating the efficacy and safety of Ocrelizumab (CinnaGen, Iran) in comparison to Ocrevus® (Roche, Switzerland) in patients with relapsing multiple sclerosis
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Ability to provide written, informed consent and to be compliant with the schedule of protocol assessments. Ages 18-55 years at screening, inclusive. Diagnosis of MS, in accordance with the revised McDonald criteria (2010). At least two relapses having occurred within the past 2 years or one relapse within the past 12 months prior to screening. Neurological stability for ≥ 30 days prior to both screening and baseline. EDSS, at screening, from 0 to 5.5 inclusive. Patients of reproductive potential must use reliable means of contraception.
Exclusion criteria:
Diagnosis of primary progressive or relapsing progressive MS. Disease duration of more than 10 years in patients with an EDSS ≤ 2.0 at screening. Inability to complete an MRI (contraindications for MRI include but are not restricted to claustrophobia, weight ≥ 140 kg, 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, etc). Known presence of other neurological disorders which may mimic MS including but not limited to: neuromeylitis optica, untreated vitamin B12 deficiency, neurosarcoidosis and cerebrovascular disorders. 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 (NYHA III or IV functional severity). Known active bacterial, viral, fungal, mycobacterial infection or other infection, excluding fungal infection of nail beds. Infection requiring hospitalization or treatment with I.V. antibiotics within 4 weeks prior to baseline visit or oral antibiotics within 2 weeks prior to baseline visit. History or known presence of recurrent or chronic infection (e.g., hepatitis B or C, HIV, syphilis, tuberculosis). History of progressive multifocal leukoencephalopathy (PML). 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. Receipt of a live vaccine within 6 weeks prior to baseline. 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 or five half-lives of the investigational drug. Contraindications to or intolerance of oral or i.v. corticosteroids. Treatment with dalfamipridine unless on stable dose for ≥ 30 days prior to screening. Patients should remain on stable doses throughout the 48 weeks' treatment period. 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 anti-CD4, cladribine, mitoxantrone, daclizumab, teriflunomide, laquinimod, total body irradiation or bone marrow transplantation. Treatment with cyclophosphamide, azathioprine, mycophenolate mofetil (MMF), cyclosporine, methotrexate or natalizumab within 24 months prior to screening. Patients previously treated with natalizumab will be eligible for this study only if duration of treatment with natalizumab was < 1 year. Treatment with fingolimod or dimethyl fumarate (DMF) within 4 weeks prior to screening. Only patients with T lymphocyte count ≥ LLN will be eligible for this study. Treatment with I.V. immunoglobulin within 12 weeks prior to baseline. Positive serum β hCG measured at screening. Positive screening tests for hepatitis B CD4 count < 300/µL. AST/SGOT or ALT/SGPT ≥ 2.0 Upper Limit of Normal (ULN). Platelet count <100,000/µL (<100 x 109/L). Levels of serum IgG <%18 of LLN Levels of serum IgM <%8 of LLN Total neutrophil count <1500/µL.
Age
From **18 years** old to **55 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

- Data analyser

Sample size
Target sample size: **170**
Randomization (investigator's opinion)
Randomized
Randomization description
Eligible patients will be assigned to treatment with the use of a dynamic randomization algorithm that will be designed to achieve overall balance between groups. Randomization will be stratified according to The Expanded Disability Status Scale (EDSS) (≤ 4 vs > 4). After randomization procedure, a code will be allocated to each patient that will be used as patient identifier throughout the study. The assigned code will be denoted by 4 initials (corresponding to the first two letters of first name, first two letters of surname) and 3 numbers (center code). Moreover, the described code is followed by study unique identification code consisting of first three letters of the generic name of the investigational product, i.e. OCR and four numbers (corresponding to the randomization number), e.g. ABCD001OCR-001.
Blinding (investigator's opinion)
Double blinded
Blinding description
Both Ocrelizumab products used in the study will be entirely indistinguishable for patients and health care providers since they are identical in shape, size, label, and color. The container of the drugs will be labeled using identical Labels so they will be impossible to differentiation. Patients groups and their drugs will not be disclosed to investigators. After that, the patient signed Informed consent and considered to be eligible base on the inclusion and exclusion criteria; he or she will be allocated to one of each group. The investigator will not be informed of randomization, and all the drug codes will be placed in an opaque pocket inside each sites trial Master file. Data analyzers will not be informed of the patients' group
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
The Ethics Committee of Tehran University of Medical Sciences
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Approval date
2019-05-24, 1398/03/03
Ethics committee reference number
IR.TUMS.VCR.REC.1398.164

2

Ethics committee
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Approval date
2019-07-21, 1398/04/30
Ethics committee reference number
IR.SBMU.REC.1398.024

Health conditions studied

1

Description of health condition studied
Relapsing Multiple Sclerosis (RMS)
ICD-10 code
G35
ICD-10 code description
Multiple sclerosis (of):NOSbrain stemcorddisseminatedgeneralized

Primary outcomes

1

Description
Evaluate Annualized Relapse Rate
Timepoint
at weeks 0, 2, 12, 24, 48
Method of measurement
Physical examination and record the symptoms

Secondary outcomes

1

Description
The time to onset of sustained disability progression
Timepoint
at weeks 0, 2, 12, 24, 48, 72 and 96
Method of measurement
Neurological examination

2

Description
The time to onset of sustained disability progression
Timepoint
at weeks 0, 2, 12, 24, 48, 72 and 96
Method of measurement
Neurological examination

3

Description
The proportion of relapse-free patients
Timepoint
by 96 weeks
Method of measurement
Statistical analysis

4

Description
The total number of new Gadolinium (Gd)-enhancing lesions as detected
Timepoint
week 24, 48 & 96
Method of measurement
by brain MRI

5

Description
The total number of new, and/or enlarging T2 hyperintense lesions
Timepoint
week 24, 48 & 96
Method of measurement
by brain MRI

6

Description
The change in total T2 lesion volume
Timepoint
from baseline to week 96
Method of measurement
by brain MRI

7

Description
Evaluate Advarese Events
Timepoint
Every 12 weeks during the 96-week
Method of measurement
Clinical monitoring

8

Description
Evaluate injection site reactions
Timepoint
Every 24 weeks during the 96-week
Method of measurement
Clinical monitoring

9

Description
Evaluate the immunogenicity of the Ocrelizumab
Timepoint
week 24, 48 & 96
Method of measurement
ELISA

Intervention groups

1

Description
Intervention group: Ocrelizumab (CinnaGen, Iran) 600 mg (given as dual infusions of ocrelizumab 300 mg on Days 1 and 15 of the first 24-week treatment cycle and as single infusions of 600 mg on Day 1 for each 24-week treatment cycle, thereafter) every 24 weeks, intravenously at weeks 0, 2, 24, 48 and 72
Category
Treatment - Drugs

2

Description
Intervention group: Ocrelizumab (Roche, Switzerland) 600 mg (given as dual infusions of ocrelizumab 300 mg on Days 1 and 15 of the first 24-week treatment cycle and as single infusions of 600 mg on Day 1 for each 24-week treatment cycle, thereafter) every 24 weeks, intravenously at weeks 0, 2, 24, 48 and 72.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
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Sponsors / Funding sources

1

Sponsor
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Email
cinnagen@cinnagen.com
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
CinnaGen company
Proportion provided by this source
100
Public or private sector
Private
Domestic or foreign origin
Domestic

Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Industry

Person responsible for general inquiries

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Undecided - It is not yet known if there will be a plan to make this available
Study Protocol
Undecided - It is not yet known if there will be a plan to make this available
Statistical Analysis Plan
Not applicable
Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available
Clinical Study Report
Undecided - It is not yet known if there will be a plan to make this available
Analytic Code
Undecided - It is not yet known if there will be a plan to make this available
Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available