# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

07 Nov 2026

## Efficacy and safety of peginterferon beta-1a (CinnaGen) versus CinnoVex® (CinnaGen) in reducing the annualized relapse rate (ARR) in participants with relapsing-remitting multiple sclerosis: A phase III, randomized, parallel, non-inferiority study.

## Protocol summary

**Study aim**
Pegylated interferon beta-1a (CinnaGen) is non-inferior to CinnoVex® (CinnaGen) for treatment of relapsing-remitting Multiple Sclerosis.

**Design**
Phase III, randomized, parallel-group, and non-inferiority. The patient randomization process will be centrally conducted by simple randomization method (complete algorithm) in PASS software for a total of 168 patients (with a 1: 1 allocation ratio). After the randomization procedure, a code will be allocated to each patient that will be used as patient identifier throughout the study.

**Settings and conduct**
The trial will be performed by principle and co-investigators in Tehran (Sina, Imam Hossein, and Amiralam hospitals), Isfahan (Kashani hospital), Mashhad (Ghaem hospital), Sari (Buali hospital), Tabriz (Imam Reza hospital) and Rasht (Ghaem hospital), Hamedan (Sina).

**Participants/Inclusion and exclusion criteria**
Inclusion Criteria: Age 18-50 years, RRMS diagnosis, EDSS 0–5, At least one relapse within the past 12 months, Signed Informed Consent. Exclusion Criteria: Other types of MS, Surgery or treatment with other agents to treat MS symptoms or underlying disease as specified in the protocol, Abnormal screening lab tests, History of any medical condition that would preclude participation in the trial, MS relapse within 30 days prior to randomization and/or not stabilized from a previous relapse prior to randomization, Pregnancy and lactation, Unwillingness or inability to comply with the requirements of the protocol, The decision of the Investigator and Others specified in the protocol.

**Intervention groups**
Group I: Pegylated interferon beta-1a (CinnaGen), Physioject™ autoinjector, 125mcg, subcutaneous, every 2 weeks for 96 weeks. Group II: CinnoVex® (CinnaGen), prefilled syringe, 30mcg, intramuscular, once a week for 96 weeks.

**Main outcome variables**
The annualized relapse rate in a 96 weeks study period

## General information

**Reason for update**
AMENDMENT *Change in Randomization *Changes in study schedule from month to week

**Acronym**

**IRCT registration information**
IRCT registration number: **IRCT201612306135N8**
Registration date: **2017-01-14, 1395/10/25**
Registration timing: **prospective**

Last update: **2020-11-25, 1399/09/05**
Update count: **3**

**Registration date**
2017-01-14, 1395/10/25

**Registrant information**

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**Recruitment status**
**Recruitment complete**

**Funding source**

CinnaGen Pharmaceutical Company

**Expected recruitment start date**
2018-03-15, 1396/12/24
**Expected recruitment end date**
2019-09-22, 1398/06/31
**Actual recruitment start date**
empty
**Actual recruitment end date**
empty
**Trial completion date**
empty

**Scientific title**
Efficacy and safety of peginterferon beta-1a (CinnaGen) versus CinnoVex® (CinnaGen) in reducing the annualized relapse rate (ARR) in participants with relapsing-remitting multiple sclerosis: A phase III, randomized, parallel, non-inferiority study.

**Public title**
Efficacy and safety of peginterferon beta-1a (CinnaGen) in relapsing-remitting multiple sclerosis patients.
**Purpose**
Treatment
**Inclusion/Exclusion criteria**
**Inclusion criteria:**
Age 18-50 years Relapsing-remitting multiple sclerosis (RRMS) (McDonald criteria 2010) Expanded Disability Status Scale (EDSS) is 0–5 At least one relapse having occurred within the past 12 months Subjects have refused alternative treatments and other available therapies Ability to understand the purpose and risks of the study and provide signed and dated an informed consent Negative pregnancy test for childbearing women
**Exclusion criteria:**
Primary progressive, secondary progressive, or progressive- relapsing MS Female subjects considering becoming pregnant while in the study or currently breastfeeding Subjects for whom MRI was contraindicated, i.e., who had pacemakers or were allergic to gadolinium,... Unwillingness or inability to comply with the requirements of the protocol Pre-specified laboratory abnormalities History of any clinically significant that would preclude participation in a clinical trial History of malignant disease (with the exception of squamous cell carcinomas of the skin that are cured) History of seizure disorder or unexplained blackouts OR history of a seizure within 3 months prior to Baseline History of suicidal ideation or an episode of severe depression within 3 months prior to Baseline Alanine transaminase/serum glutamate pyruvate transaminase (ALT/SGPT) greater than 2 times the upper limit of normal Aspartate transaminase/serum glutamic oxaloacetic transaminase (AST/SGOT) greater than 2 times the upper limit of normal Bilirubin greater than 1.5 times the upper limit of normal Total white blood cell count (WBC) <4000 /mm3 Absolute Neutrophil Count (ANC) of < 1500 /mm3 Platelet count <120,000 c/mm3 Hemoglobin <10 g/dL in female subjects; <11 g/dL in male subjects Serum creatinine upper limit of normal lab value An MS relapse that has occurred within the 30 days prior to randomization or the subject has not stabilized from a previous relapse prior Elective surgery performed from 2 weeks prior or scheduled through the end of the study Any prior treatment with Total Lymphoid Irradiation, Cladribine, T-cell Vaccine, Natalizumab, Rituximab, BIIB017, Fingolimod, Dimethyl fumarate, and Teriflunomide Prior treatment within 1 with Cyclophosphamide– Mitoxantrone Prior treatment within 6 months with Cyclosporine, Plasma exchange, Intravenous immunoglobulin (IVIG), Azathioprine, Methotrexate Any prior treatment within 6 months with interferon Prior treatment within 30 days prior with Systemic Corticosteroids Prior treatment with Glatiramer Acetate within 4 weeks prior to randomization Treatment with another investigational drug within the 6 months prior to randomization Other reasons, that in the opinion of the investigator, made the subject unsuitable for enrolment
**Age**
From **18 years** old to **50 years** old
**Gender**
Both

**Phase**
3
**Groups that have been masked**
*No information*
**Sample size**
Target sample size: **168**
**Randomization (investigator's opinion)**
Randomized
**Randomization description**
The patient randomization process will be centrally conducted by simple randomization method (complete algorithm) in PASS software for a total of 168 patients (with a 1: 1 allocation ratio). After the randomization procedure, a code will be allocated to each patient that will be used as patient identifier throughout the study. The code will consist of four numbers (corresponding to the randomization number), 4 initials (corresponding to the first two letters of first name, first two letters of surname), and 3 numbers (center code), e.g. ABCD001PE3-0001. Randomization numbers will be determined sequentially.
**Blinding (investigator's opinion)**
Not blinded
**Blinding description**
**Placebo**
Not used
**Assignment**
Parallel
**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**
**Name of ethics committee**
Tehran University of Medical Sciences

**Street address**
TUMS Ethic Committee, 6th floor, Central Building, Ghods st, Keshavarz Blvd., Tehran, Iran
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1417653761
**Approval date**
2016-11-05, 1395/08/15
**Ethics committee reference number**
IR.TUMS.REC.1395.2868

**2**

**Ethics committee**
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Tabriz University of Medical Sciences
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**Approval date**
2016-10-17, 1395/07/26
**Ethics committee reference number**
IR.TBZMED.REC.1395.759

## Health conditions studied

**1**

**Description of health condition studied**
Multiple sclerosis
**ICD-10 code**
G35
**ICD-10 code description**
Multiple sclerosis

## Primary outcomes

**1**

**Description**
Annual relapse rate
**Timepoint**
Ralapse rate counts during 96 weeks/ every 4 weeks visits
**Method of measurement**
A relapse is defined as an episode of neurological symptoms that happens at least 30 days after any previous episode began, lasts at least 24 h and is not attributable to another cause and occurs in the absence of an infection or fever.

## Secondary outcomes

**1**

**Description**
Number of new or newly enlarging hyperintense lesions on T2-weighted images (relative to baseline MRI)
**Timepoint**
Baseline, 24th, 48th, 96th week
**Method of measurement**
MRI evaluation

**2**

**Description**
Proportion of patients with 12 weeks of sustained disability progression
**Timepoint**
During 96 weeks of study follow up
**Method of measurement**
Clinical evaluation

**3**

**Description**
Gadolinium-enhancing lesions, New active lesions (T2), Volume of new or newly enlarging T2 hyperintense, gadolinium-enhancing, and T1 hypointense lesions, brain atrophy
**Timepoint**
24th, 48th, 96th week
**Method of measurement**
MRI evaluation

**4**

**Description**
Any - Adverse events (AEs), Adverse drug reactions (ADR) including: o Flu-like symptoms, injection site reaction (redness, pain, itching, necrosis), o Rising AST, ALT or ALP 2.5 times more than normal value,or Hyperbilirubinemia: 1.5 Times more than Upper normal limit, Leukopenia (WBC <3000), Thrombocytopenia (Platelet count < 100,000),..
**Timepoint**
During 96 weeks of study follow up
**Method of measurement**
Clinical and laboratory evaluation

## Intervention groups

**1**

**Description**
Intervention group 1: Pegylated interferon beta-1a (CinnaGen) autoinjector (Physioject™) for patients with dose of 125micrograms, subcutaneous (S/C) injection every 2weeks for 96 weeks
**Category**
Treatment - Drugs

**2**

**Description**
Intervention group 2: CinnoVex® (CinnaGen) 30 mcg, prefilled syringe, injected intramuscularly once a week for 96 weeks

**Category**
Treatment - Drugs

## Recruitment centers

**1**

**Recruitment center**

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**Name of recruitment center**
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**9**

**Recruitment center**

**Name of recruitment center**
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## Sponsors / Funding sources

**1**

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http://www.cinnagen.com

**Grant name**

**Grant code / Reference number**

**Is the source of funding the same sponsor organization/entity?**
Yes

**Title of funding source**
CinnaGen Pharmaceutical 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**
Persons

## Person responsible for general inquiries

**Contact**

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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**
Undecided - It is not yet known if there will be a plan to make this available
**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