

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

11 Jul 2026

### Evaluation of the effect of Levetiracetam on cognitive impairment in patients with relapsing- remitting multiple sclerosis (RRMS) based on minimal assessment of cognitive function in multiple sclerosis (MACFIMS)

#### Protocol summary

##### Study aim

Evaluation of the effect of Levetiracetam on cognitive impairment in patients with relapsing-remitting multiple sclerosis based on minimal assessment of cognitive function in multiple sclerosis

##### Design

Clinical trial with control group,with parallel groups,double-blind,randomized, phase 3 on 88 patients.For randomization by random block method

##### Settings and conduct

A double-blind clinical trial will be conducted at Sina Hospital MS Research Center.88 patients with relapsing-remitting MS were randomly divided into case and control groups and treated with levetiracetam or placebo for 16 weeks.The starting dose is 250 mg twice daily and the dose is Reaches 1000 mg twice a day.

##### Participants/Inclusion and exclusion criteria

Inclusion criteria: Patients with relapsing- remitting MS 18-60 years:Minimum education for cognitive tests:At least 2 years have passed since the disease - Receiving oral and injectable disease-modifying drugs(DMD):Expanded Disability Status Scale less 5.5  
Exclusion criteria: The type and dose of (DMD) have changed in the last six months:Corticosteroids received in the last thirty days:Attack in the last sixty days.

##### Intervention groups

Intervention group: 44 patients with relapsing-remitting MS(RRMS) are treated with levetiracetam for 16 weeks.The starting dose is 250 mg twice daily and 500 mg is added to the daily dose every week and the drug dose is 1000 mg twice daily.Control group: 44 (RRMS) patients are treated with placebo for 16 weeks.

##### Main outcome variables

Main Outcome:minimal assessment of cognitive function in multiple sclerosis (MACFIMS) ,

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20210707051810N2**

Registration date: **2021-10-05, 1400/07/13**

Registration timing: **registered\_while\_recruiting**

Last update: **2021-10-05, 1400/07/13**

Update count: **0**

##### Registration date

2021-10-05, 1400/07/13

##### Registrant information

##### Name

Maryam Sharif

##### Name of organization / entity

##### Country

Iran (Islamic Republic of)

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##### Email address

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##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2021-09-23, 1400/07/01

##### Expected recruitment end date

2022-09-22, 1401/06/31

##### Actual recruitment start date

empty

##### Actual recruitment end date

empty

##### Trial completion date

empty

**Scientific title**

Evaluation of the effect of Levetiracetam on cognitive impairment in patients with relapsing- remitting multiple sclerosis (RRMS) based on minimal assessment of cognitive function in multiple sclerosis (MACFIMS)

**Public title**

Evaluation of the effect of Levetiracetam on cognitive impairment in patients with MS

**Purpose**

Treatment

**Inclusion/Exclusion criteria****Inclusion criteria:**

Patients with relapsing-remitting multiplesclerosis age between 18 and 60 years Have a minimum education to perform cognitive tests RRMS (2017 Revisions of the "McDonald" Criteria ) At least 2 years have passed since the definitive diagnosis of the disease Receiving first-line injectable and oral disease modifying drugs (interferon beta, glatiramer acetate, triflunomide and dimethyl fumarate) Type and dose of DMD have not changed in the last six months Have not received corticosteroids in last 30 days Have not relapse in the last 60 days Expanded Disability Status Scale (EDSS) scores of 5.5 or less Voluntarily participated in the present study

**Exclusion criteria:**

History of drug or alcohol abuse in the last six months Pregnancy and lactation Having any acute or major mental disorder that is not under control (type of medication and amount of use in the last three months is constant) Having any seizure disorder History of any suicide attempt Chronic kidney disease (Estimated glomerular filtration rate less than 60 ml / min) Diabetes, hypothyroidism and anemia that is not under control Concomitant use of drugs that may affect cognitive function, such as antipsychotics, modafinil, methylphenidate, amphetamine and amphetamine-like compounds, tricyclic antidepressants and anticonvulsants other than gabapentin and pregabalin, benzodiazepines other than as sleeping pills Avar (if the dose and method of medication do not change in the last three months and during the study will not be prohibited).

**Age**

From **18 years** old to **60 years** old

**Gender**

Both

**Phase**

3

**Groups that have been masked**

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

**Sample size**

Target sample size: **88**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

Patients with relapsing-remitting MS will be divided into

two groups by quadruple block randomization. Random sequencing is performed by an epidemiologist using the online program at <https://www.sealedenvelope.com/> Hiding is also guaranteed using the block randomization method.

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

The study is a double-blind study and for this purpose, the participants, the main researcher, the health care personnel who are responsible for caring for the patient, do not know which participant received the main drug and which placebo. The end of the evaluation of the results between the two groups will be statistically analyzed. The main researcher is aware of the drug and the placebo of the cans, but remains blind as to which patient receives which drug code.

**Placebo**

Used

**Assignment**

Parallel

**Other design features****Secondary Ids**

empty

**Ethics committees****1****Ethics committee****Name of ethics committee**

Research Ethics Committee of Tehran University of Medical Sciences

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Tehran, Enghelab Square, 16 Azar St., University of Medical Sciences

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**Province**

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**Postal code**

1417614411

**Approval date**

2021-08-02, 1400/05/11

**Ethics committee reference number**

IR.TUMS.MEDICINE.REC.1400.515

**Health conditions studied****1****Description of health condition studied**

Relapsing-remitting multiple sclerosis

**ICD-10 code**

G35

**ICD-10 code description**

Multiple sclerosis

## Primary outcomes

### 1

#### **Description**

Minimal Assessment of Cognitive Function In Multiple Sclerosis (MACFIMS)

#### **Timepoint**

Beginning of study and end of week 16

#### **Method of measurement**

MACFIMS questionnaire

### 2

#### **Description**

California Verbal Learning Test (CVLT)

#### **Timepoint**

Beginning of study and end of week 16

#### **Method of measurement**

California Verbal Learning Test (CVLT)

### 3

#### **Description**

Brief Visuospatial Memory Test Revised (BVMT)

#### **Timepoint**

Beginning of study and end of week 16

#### **Method of measurement**

Brief Visuospatial Memory Test Revised (BVMT)

### 4

#### **Description**

Paced Auditory Serial Addition Test(PASAT)

#### **Timepoint**

Beginning of study and end of week 16

#### **Method of measurement**

Paced Auditory Serial Addition Test(PASAT)

### 5

#### **Description**

Symbol Digit Modalities Testing(SDMT)

#### **Timepoint**

Beginning of study and end of week 16

#### **Method of measurement**

Symbol Digit Modalities Testing(SDMT)

### 6

#### **Description**

Delis-Kaplan Executive Function System(D-KEFS)

#### **Timepoint**

Beginning of study and end of week 16

#### **Method of measurement**

Delis-Kaplan Executive Function System(D-KEFS)

### 7

#### **Description**

Controlled Oral Word Association Test(COWAT)

#### **Timepoint**

Beginning of study and end of week 16

## Method of measurement

Controlled Oral Word Association Test(VCOWAT)

### 8

#### **Description**

Judgment of Line Orientation(JLO)

#### **Timepoint**

Beginning of study and end of week 16

#### **Method of measurement**

Judgment of Line Orientation(JLO)

## Secondary outcomes

### 1

#### **Description**

Neuropsychiatry Complications of levetiracetam

#### **Timepoint**

The end of the fourth and sixteenth week

#### **Method of measurement**

Neuropsychiatry Inventory (NPI)

### 2

#### **Description**

Possible side effects of Levetiracetam

#### **Timepoint**

Every two weeks until the end of 16 weeks

#### **Method of measurement**

Case report form (CRF)

### 3

#### **Description**

White blood cells from blood cells and part of the immune system

#### **Timepoint**

Beginning of study and end of week 16

#### **Method of measurement**

Blood test

### 4

#### **Description**

Hemoglobin

#### **Timepoint**

Beginning of study and end of week 16

#### **Method of measurement**

Blood test

### 5

#### **Description**

Platelet

#### **Timepoint**

Beginning of study and end of week 16

#### **Method of measurement**

Blood test

### 6

#### **Description**

Alanine amino transferase ( ALT)

**Timepoint**

Beginning of study and end of week 16

**Method of measurement**

Blood test

7

**Description**

Aspartate amino transferase

**Timepoint**

Beginning of study and end of week 16

**Method of measurement**

Blood test

8

**Description**

Cratinine

**Timepoint**

Beginning of study and end of week 16

**Method of measurement**

Blood test

9

**Description**

Blood urea nitrogen (BUN)

**Timepoint**

Beginning of study and end of week 16

**Method of measurement**

Blood test

**Intervention groups**

1

**Description**

Intervention group: Patients in the case group are treated with Levetiracetam for 16 weeks from a reputable Abidi Pharmaceutical Factory. The initial dose is 250 mg (half a tablet) twice a day. 500 mg is added to the daily dose every week, and finally the dose of the drug reaches 1000 mg twice a day.

**Category**

Treatment - Drugs

2

**Description**

Control group: Patients in the control group are treated for 16 weeks with a placebo of Levetiracetam prepared by a Abidi Pharmaceutical Factory (Matching placebo). The initial dose of placebo is 250 mg (half a tablet) twice a day. 500 mg is added to the daily dose every week, and finally the dose of the drug reaches 1000 mg twice a day.

**Category**

Treatment - Drugs

**Recruitment centers**

1

**Recruitment center**

**Name of recruitment center**

Sina Hospital MS Research Center

**Full name of responsible person**

Hooshyar Honarmand

**Street address**

Sina Hospital, Imam Khomeini St, Hasan Abad Sq

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**Sponsors / Funding sources**

1

**Sponsor**

**Name of organization / entity**

Tehran University of Medical Sciences

**Full name of responsible person**

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**Grant name**

**Grant code / Reference number**

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

Yes

**Title of funding source**

Tehran University of Medical Sciences

**Proportion provided by this source**

100

**Public or private sector**

Public

**Domestic or foreign origin**

Domestic

**Category of foreign source of funding**

empty

**Country of origin**

**Type of organization providing the funding**

Academic

## Person responsible for general inquiries

### Contact

**Name of organization / entity**

Tehran University of Medical Sciences

**Full name of responsible person**

Hooshyar Honarmand

**Position**

Associate professor

**Latest degree**

Specialist

**Other areas of specialty/work**

Pharmacotherapy

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## Person responsible for scientific inquiries

### Contact

**Name of organization / entity**

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**Full name of responsible person**

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**Position**

Assistant Professor

**Latest degree**

Medical doctor

**Other areas of specialty/work**

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## Person responsible for updating data

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**Position**

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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**

No - There is not a plan to make this available

**Justification/reason for indecision/not sharing IPD**

According to the items mentioned in the informed consent, patients' information will not be disseminated.

**Study Protocol**

Yes - There is a plan to make this available

**Statistical Analysis Plan**

Yes - There is a plan to make this available

**Informed Consent Form**

Yes - There is a plan to make this available

**Clinical Study Report**

Yes - There is a plan to make this available

**Analytic Code**

No - There is not a plan to make this available

**Data Dictionary**

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

**Title and more details about the data/document**

Patient demographic data as well as variable outcome data will be shared after patients are unidentifiable.

**When the data will become available and for how long**

The data will be available after the study and is expected to be available on the Internet from March 2022.

**To whom data/document is available**

Medical activists

**Under which criteria data/document could be used**

The data will be available after obtaining the necessary permits from researchers.

**From where data/document is obtainable**

Tehran university of medical science

**What processes are involved for a request to access data/document**

A written request for data must be submitted by the individual.

**Comments**