

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

07 Jul 2026

### Study of the efficacy and safety of rivastigmine as an adjuvant to antipsychotics in male patients with chronic schizophrenia: A randomized, double-blind, placebo-controlled trial

#### Protocol summary

##### Study aim

Assessment of the efficacy and safety of rivastigmine as an adjuvant to antipsychotics in patients with chronic schizophrenia

##### Design

A randomized, double-blind, placebo-controlled clinical trial, design of 30 patients with chronic schizophrenia (1:1 in each group) at 4 months

##### Settings and conduct

Care centers in Mazandran province

##### Participants/Inclusion and exclusion criteria

18-65 years old men with the diagnosis of schizophrenia based on DSM-5 criteria for at least two years and despite the anti-psychotic drug treatment, they are still symptomatic. They are treated with antipsychotics for at least one year and In the last month, the type and dosage of their antipsychotic drugs remain constant. If receiving medications such as mood stabilizer or anti depressants, their type and dosage will remain constant from one month before the start of the study and during the study.

##### Intervention groups

In the patient intervention group, in addition to prescription antipsychotic treatment, they receive the rivastigmine capsule at a dose of 1.5 mg twice daily for the first two weeks, then, if the patient tolerates, every two weeks the rheostigmine dose is 3. The dose is increased to 6 mg twice daily, and this dose is continued until the end of the study

##### Main outcome variables

To assess the severity of patients' psychotic symptoms from PANSS, CGI-S and CGI-I scales, to assess patients' cognitive status from BACS scale, to assess patients' depressive symptoms from CDSS scale and BARS, AIMS and SAS are used to evaluate motor effects at baseline and at the end of the first, second, third, and fourth months. The CGI-I is evaluated at the end of the first,

second, third, and fourth months.

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20120314009297N8**

Registration date: **2020-05-28, 1399/03/08**

Registration timing: **prospective**

Last update: **2020-05-28, 1399/03/08**

Update count: **0**

##### Registration date

2020-05-28, 1399/03/08

##### Registrant information

##### Name

narjes hendouei

##### Name of organization / entity

mazandaran university of medical science

##### Country

Iran (Islamic Republic of)

##### Phone

+98 911 327 0107

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##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2020-05-30, 1399/03/10

##### Expected recruitment end date

2021-05-31, 1400/03/10

##### Actual recruitment start date

empty

##### Actual recruitment end date

empty  
**Trial completion date**  
empty

**Scientific title**

Study of the efficacy and safety of rivastigmine as an adjuvant to antipsychotics in male patients with chronic schizophrenia: A randomized, double-blind, placebo-controlled trial

**Public title**

Evaluation of the effect of rivastigmine on male patients with chronic schizophrenia

**Purpose**

Treatment

**Inclusion/Exclusion criteria**

**Inclusion criteria:**

18-65 years old male patients. Patients with a diagnosis of schizophrenia based on DSM-5 criteria for at least two years who should still be symptomatic despite treatment with antipsychotic medications. Patients should be treated with antipsychotic medications for at least one year, and the type and dose of their antipsychotic medications should remain constant for the last three months. If they are taking medications such as mood stabilizers or antidepressants with their antipsychotic treatment regimen, their type and dose will remain the same for three months before the start of the study and during the study. If they are taking anticholinergic drugs (which include bipyridine or trihexylphenidyl) in combination with their antipsychotic treatment regimen for treatment or prevention the Movement side effects of antipsychotics, the type and dose of them remain stable for three months before the start of and during the study.

**Exclusion criteria:**

Going to the acute phase of the disease means a 20% increase in the overall score of PANSS (Scizospheria positive and negative evaluation criteria) Patients with acute suicidal behavior or a history of suicide last year, associated psychiatric disorders such as schizo-effective or other psychotic disorders, mental retardation or other cognitive impairment, bipolar disorder and depression, anxiety disorders such as current panic disorder or obsessive-compulsive disorder, Post-traumatic stress disorder, eating disorder History of substance abuse dependence (substance dependence criteria DSM-5) or abuse of substances in the three months prior to the start of the study or positive urine screening test for the substance at the beginning of the study Patients under ECT in the last six months People with thoughts or actions to harm themselves or others during the study or in the 6 months before the study People with mental retardation Patients with neurological disorders such as dementia, delirium, uncontrolled seizures, head trauma, seizure disorder (other than fever-related) and neurodegenerative diseases (such as Alzheimer's, Parkinson's, Stroke, and multiple sclerosis) People with underlying medical conditions are uncontrolled Patients with a history of NMS Patients treated with drugs that affect the patient's cognitive status are based on the criteria of Drugs on the Anticholinergic Burden (ACB) scale (17), such as drugs with anticholinergic properties

(except biperidin and trihexifenidyl), hypnotic antihistamines. , Antidepressants Patients with sensitivity to rivastigmine or other components of the drug or placebo Patients with rivastigmine in the last 6 months

**Age**

From **18 years** old to **65 years** old

**Gender**

Male

**Phase**

3

**Groups that have been masked**

- Participant
- Care provider
- Outcome assessor

**Sample size**

Target sample size: **60**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

Block randomization

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

rivastigmine and placebo capsules are completely similar in terms of color, size, smell and taste produced by a completely similar manufacturing and packagings. Patients were randomly tested in groups. Until the end of the study, no patient or study persons are aware of which drug the patient receives. And anybody other than those who are defective in the study is aware.

**Placebo**

Used

**Assignment**

Parallel

**Other design features**

**Secondary Ids**

empty

**Ethics committees**

**1**

**Ethics committee**

**Name of ethics committee**

Ethics committee of Mazandaran University of Medical Sciences

**Street address**

Moallem street, Moallem square, Vice chancellor for research

**City**

Sari

**Province**

Mazandaran

**Postal code**

33971-48157

**Approval date**

2020-05-04, 1399/02/15

**Ethics committee reference number**

IR.MAZUMS.REC.1399.163

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

chronic schizophrenia

**ICD-10 code**

F20.5

**ICD-10 code description**

Residual schizophrenia

**Primary outcomes****1****Description**

Score of general, positive and negative symptoms with Positive and Negative Symptom Scale (PANSS)

**Timepoint**

At baseline and the end of each month

**Method of measurement**

Positive and Negative Symptom Scale (PANSS)

**2****Description**

Score of change in severity of illness based on Clinical Global Impression - Improvement (CGI-I)

**Timepoint**

At the end of each month

**Method of measurement**

Clinical Global Impression -Improvement (CGI-I) score

**3****Description**

Score of severity of illness based on Clinical Global Impression of Severity (CGI-S)

**Timepoint**

En At baseline and at the end of each months

**Method of measurement**

Clinical Global Impression of Severity (CGI-S)

**4****Description**

Score of depression symptoms based on Calgary Depression Scale for Schizophrenia

**Timepoint**

At baseline and at the end of each months

**Method of measurement**

Calgary Depression Scale for Schizophrenia(CDSS)

**5****Description**

Score of improvement in cognitive symptoms based on Brief Assessment of Cognition in schizophrenia

**Timepoint**

At baseline and the end of the each months

**Method of measurement**

Brief Assessment of Cognition in schizophrenia(BACS)

**6****Description**

Score of SAS for extra pyramidal side effects

**Timepoint**

At baseline and the end of the each months

**Method of measurement**

Simpson-Angus Scale (SAS)

**7****Description**

Score of Barnes Akathisia Rating Scale (BARS)

**Timepoint**

At baseline and at the end of each months

**Method of measurement**

Barnes Akathisia Rating Scale (BARS)

**8****Description**

Score of Abnormal Involuntary Movement Scale (AIMS)

**Timepoint**

At baseline and at the end of each months

**Method of measurement**

Abnormal Involuntary Movement Scale (AIMS)

**Secondary outcomes**

empty

**Intervention groups****1****Description**

Intervention group: Previous prescription antipsychotic treatment + Rivastigmine in the first two weeks 1.5 mg twice a day, the second two weeks 3 mg twice a day, the third two weeks 4.5 mg twice a day, the fourth two weeks until the end of the study 6 mg twice a day if patients tolerate they do.

**Category**

Treatment - Drugs

**2****Description**

Control group: Previous prescription antipsychotic treatment + two placebo capsules that are similar to rivastigmine capsule in shape odor, taste, size and color in two divided dose.

**Category**

Placebo

**Recruitment centers**

## 1

### Recruitment center

**Name of recruitment center**

Psychiatric care centers in Mazandaran province

**Full name of responsible person**

Narjes Hendouei

**Street address**

Farvardin care center, Alivac, Farah Abad Blvd.

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nhendoei@mazums.ac.ir

## Sponsors / Funding sources

### 1

#### Sponsor

**Name of organization / entity**

Mazandaran University of Medical Sciences

**Full name of responsible person**

Ahmad Ali Enayati

**Street address**

Moallem street, Moallem square-Vice chancellor for research

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sari

**Province**

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**Phone**

+98 11 3326 1245

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tmaae@liv.ac.uk

**Grant name****Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

Mazandaran 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**

Mazandaran University of Medical Sciences

**Full name of responsible person**

Narjes Hendouei

**Position**

Assistant Professor

**Latest degree**

Specialist

**Other areas of specialty/work**

Clinical pharmacy

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## Person responsible for scientific inquiries

### Contact

**Name of organization / entity**

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## Person responsible for updating data

### Contact

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**Latest degree**

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**Other areas of specialty/work**

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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