

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

10 Jun 2026

### The Study of the Efficacy of Edaravone in Combination with Thrombolysis in Acute Ischemic Stroke Patients: A randomized controlled clinical trial

#### Protocol summary

##### Study aim

To evaluate the efficacy of intravenous Edaravone in combination with thrombolysis in Acute Ischemic Stroke outcome.

##### Design

A randomized, placebo-controlled, triple blinded, Phase 3 clinical trial with sample volume of 244, using randomized block design methods.

##### Settings and conduct

This study will be done multi-centric. The blinding process will be carried out using codes. All patients will undergo CT scan and MRI of the brain, electrocardiogram, blood investigation, organ function tests and daily neurological evaluation during the hospital stay.

##### Participants/Inclusion and exclusion criteria

Inclusion criteria: 18 to 75 years old patients with acute ischemic stroke included receiving r-TPA and NIHSS between 4 and 24 and receiving Edaravone within 1 to 24 hour of admission. Exclusion criteria: ICH, iatrogenic stroke, vasculitis, arterial dissection, unable to control blood pressure, severe mental disorders and dementia, significant lung disease, psychiatric illness requiring medication, prior consumption of therapeutic neuroprotective agents, malignant tumors or receiving concurrent anti-tumor treatment, severe systemic disease or life expectancy less than 90 days, pregnant or lactating women, history of hypersensitivity to Edaravone or any of the inactive ingredients, MRS  $\geq 2$  prior to stroke, NIHSS  $\geq 25$  in admission, severe disturbance of consciousness, history of AIS within 3 months, severe heart, renal or liver disease, infections requiring antibiotic administration, transient ischemic attack

##### Intervention groups

Patients with acute ischemic attack referring to university hospital and receiving thrombolysis therapy will be evaluated consecutively.

##### Main outcome variables

-Admission, after 24 hours and discharge NIHSS -In hospital Mortality and Survival at 3 months after stroke - Admission and 3 months after stroke MRS

#### General information

##### Reason for update

##### Acronym

E.T.I.S

##### IRCT registration information

IRCT registration number: **IRCT20210530051440N1**

Registration date: **2021-06-27, 1400/04/06**

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

Last update: **2021-06-27, 1400/04/06**

Update count: **0**

##### Registration date

2021-06-27, 1400/04/06

##### Registrant information

##### Name

Abdoreza Ghoreishi

##### Name of organization / entity

##### Country

Iran (Islamic Republic of)

##### Phone

+98 24 3302 3863

##### Email address

ghoreishi@zums.ac.ir

##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2021-06-22, 1400/04/01

##### Expected recruitment end date

2021-11-22, 1400/09/01

##### Actual recruitment start date

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

The Study of the Efficacy of Edaravone in Combination with Thrombolysis in Acute Ischemic Stroke Patients: A randomized controlled clinical trial

**Public title**

Efficacy of Edaravone with Thrombolysis in Acute Ischemic Stroke

**Purpose**

Treatment

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

Diagnosis AIS as acute onset of neurological symptoms, confirming by neuroimaging examination of the head - computed tomography (CT) or magnetic resonance imaging (MRI) Patients included receiving r-TPA Age 18-75 years NIHSS between 4 and 24 with a total score of upper and lower limbs  $\geq 2$  on motor deficits Patients receiving Edaravone within 1 to 24 hour of admission

**Exclusion criteria:**

Cranial CT scan finds intracranial bleeding disorders Vasculitis Arterial dissection, Despite initial controlling of blood pressure (BP); systolic BP still greater than or equal to 220 mmHg, or diastolic BP greater than or equal to 120 mmHg Ischemic stroke Patients with severe mental disorders and dementia Significant lung disease (FEV1  $\leq 1.5$  L, pO<sub>2</sub>  $\leq 70$  on room air, pCO<sub>2</sub>  $\geq 45$ ) Psychiatric illness requiring medication Prior consumption of therapeutic neuroprotective agents, including commercially available Edaravone, Nimodipine, Ganglioside, Citicoline or Piracetam Patients with malignant tumors or receiving concurrent antitumor treatment Patients with severe systemic disease or life expectancy less than 90 days Pregnant or lactating women History of hypersensitivity to Edaravone or any of the inactive ingredients, including sulfite hypersensitivity MRS  $\geq 2$  prior to stroke NIHSS  $\geq 25$  or  $\leq 3$  in admission Severe disturbance of consciousness: NIHSS category 1a for consciousness  $\geq 2$  History of AIS within 3 months Severe heart disease (Ejection Fraction less than 30%) Baseline Creatinine clearance less than 30 ml/min, creatinine 150 mol/L or previously known severe renal diseases ALT or AST is greater than 2.0xULN or previously known liver diseases, such as acute hepatitis, chronic active hepatitis or liver cirrhosis Infections requiring antibiotic administration Manifesting considerable improvement in neurologic signs and symptoms indicating transient ischemic attack

**Age**

From **18 years** old to **75 years** old

**Gender**

Both

**Phase**

3

**Groups that have been masked**

- Participant
- Care provider

- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

**Sample size**

Target sample size: **244**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

Patients will be allocated randomly into 2 groups by randomized block design methods with block size equal to four, using S.A.S. and Proclan software according to random numbers.

**Blinding (investigator's opinion)**

Triple blinded

**Blinding description**

Blinding process will be done for 3 groups: those who choose patients for the study, those who measure the parameters and follow up the patients and those who supervise the study process. The company supplying Edaravone, with assign codes for drug and placebo vials which cannot be separated by centers. All executors and colleagues will be kept blind till end of the study and decoding process will be carried out only by a statistics analyst, at the end of study.

**Placebo**

Used

**Assignment**

Parallel

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

empty

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

Ethics committee of Zanjan University of Medical Sciences

**Street address**

Neurology department of Valiasr hospital, Valiasr Sqr., Zanjan

**City**

Zanjan

**Province**

Zanjan

**Postal code**

4515777978

**Approval date**

2021-05-16, 1400/02/26

**Ethics committee reference number**

IR.ZUMS.REC.1400.054

**Health conditions studied**

## 1

### **Description of health condition studied**

Acute Ischemic Stroke

### **ICD-10 code**

I63.9

### **ICD-10 code description**

Cerebral infarction, unspecified

## **Primary outcomes**

### 1

#### **Description**

National Institutes of Health Stroke Scale (NIHSS) score

#### **Timepoint**

At Admission, 24 hours later and at discharge

#### **Method of measurement**

Physical Examination

### 2

#### **Description**

Modified Rankin Scale (MRS) score

#### **Timepoint**

(Pre-stroke) At admission and 3 months after discharge

#### **Method of measurement**

Questionnaire

### 3

#### **Description**

Mortality

#### **Timepoint**

In-hospital and during 3 months after discharge

#### **Method of measurement**

Medical records and follow up information

## **Secondary outcomes**

### 1

#### **Description**

Symptomatic Intracranial Hemorrhage

#### **Timepoint**

During hospitalization

#### **Method of measurement**

Physical Examination and Imaging

### 2

#### **Description**

Acute Hepatic Failure

#### **Timepoint**

During hospitalization

#### **Method of measurement**

Paraclinic assessment

### 3

#### **Description**

Acute Renal Failure

#### **Timepoint**

During hospitalization

#### **Method of measurement**

Paraclinic assessment

### 4

#### **Description**

Mechanical ventilation rate

#### **Timepoint**

Within 2 days of hospitalization

#### **Method of measurement**

Clinical assessment

### 5

#### **Description**

Infarction Volume

#### **Timepoint**

On third day MRI (Magnetic Resonance Imaging)

#### **Method of measurement**

Paraclinic assessment

### 6

#### **Description**

Brain midline shift

#### **Timepoint**

On third day MRI (Magnetic Resonance Imaging)

#### **Method of measurement**

Paraclinic assessment

### 7

#### **Description**

Alberta stroke program early CT score (ASPECTS)

#### **Timepoint**

At admission and at discharge

#### **Method of measurement**

Paraclinic assessment

## **Intervention groups**

### 1

#### **Description**

Intervention group: Case group consists of patients receiving Alteplase within 4.5 hours of onset of manifestations and dose of 0.6 to 0.9 mg/kg in combination with Edaravone within 1 to 24 hours of admission (after receiving Creatinine result) and dose of 60 mg every 12 hours (40 ml of drug in 160 ml of saline infusion in 1 hour), continued for five days.

#### **Category**

Treatment - Drugs

### 2

#### **Description**

Control group: Control group consists of patients receiving Alteplase within 4.5 hours of onset of manifestations and dose of 0.6 to 0.9 mg/kg in with 40ml of placebo in 160 ml of saline, every 12 hours for five days.

**Category**

Placebo

3719964797

**Phone**

+98 25 3612 2000

**Email**

sharifipour.e@gmail.com

**Recruitment centers****1****Recruitment center****Name of recruitment center**

Valiasr hospital

**Full name of responsible person**

Abdoreza Ghoreishi

**Street address**

Neurology department of Valiasr hospital, Valiasr Sqr., Zanzan

**City**

Zanzan

**Province**

Zanzan

**Postal code**

4515777978

**Phone**

+98 24 3377 0801

**Email**

Ghoreishi@zums.ac.ir

**2****Recruitment center****Name of recruitment center**

Namazi hospital

**Full name of responsible person**

Afshin Borhan Haghighi

**Street address**

Neurology department of Namazi hospital, Namazi Sqr., Zand Ave., Shiraz

**City**

Shiraz

**Province**

Fars

**Postal code**

1331171936

**Phone**

+98 71 3647 4332

**Email**

neuro.ab@gmail.com

**3****Recruitment center****Name of recruitment center**

Shahid Beheshti hospital

**Full name of responsible person**

Ehsan Sharifipour

**Street address**

Neurology department of Shahid Beheshti hospital, Shahid Beheshti Ave., Qom

**City**

Qom

**Province**

Ghous

**Postal code****4****Recruitment center****Name of recruitment center**

Emam Reza hospital

**Full name of responsible person**

Elyar Sadegi Hokm Abadi

**Street address**

Neurology department of Emam Reza hospital, Golgasht Ave., Tabriz

**City**

Tabriz

**Province**

East Azarbaijan

**Postal code**

5166614756

**Phone**

+98 41 3335 2073

**Email**

aeass@yahoo.com

**5****Recruitment center****Name of recruitment center**

Emam Hosein hospital

**Full name of responsible person**

Farhad Assar Zadegan

**Street address**

Neurology department of Emam Hosein hospital, Shahid Madani Ave., Tehran

**City**

Tehran

**Province**

Tehran

**Postal code**

1617763141

**Phone**

+98 21 0007 3430

**Email**

Assarfarhad@gmail.com

**Sponsors / Funding sources****1****Sponsor****Name of organization / entity**

Zanzan University of Medical Sciences

**Full name of responsible person**

Alireza Shoghli

**Street address**

Zanzan University of Medical Sciences, Gavazang Blvd., Zanzan

**City**

Zanzan

**Province**

Zanjan

**Postal code**

4513956184

**Phone**

+98 24 0033 0180

**Email**

Research@zums.ac.ir

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

Yes

**Title of funding source**

Zanjan University of Medical Sciences

**Proportion provided by this source**

10

**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

**2****Sponsor****Name of organization / entity**

Zistdaru Danesh company

**Full name of responsible person**

Ilka Hooshmand

**Street address**

No. 33, Ebne Yamin Ave., Sohrevardi Blvd., Tehran

**City**

Tehran

**Province**

Tehran

**Postal code**

1555633114

**Phone**

+98 21 4231 8000

**Email**

ilka@zistdaru.ir

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

Yes

**Title of funding source**

Zistdaru Danesh company

**Proportion provided by this source**

90

**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**

Other

**Person responsible for general inquiries****Contact****Name of organization / entity**

Zanjan University of Medical Sciences

**Full name of responsible person**

Shahin Nateghi

**Position**

Resident

**Latest degree**

Medical doctor

**Other areas of specialty/work**

Neurology

**Street address**

Neurology department of Valiasr hospital, Valiasr Sqr., Zanjan

**City**

Zanjan

**Province**

Zanjan

**Postal code**

4515777978

**Phone**

+98 24 3377 0801

**Email**

Shahin.nateghi@gmail.com

**Person responsible for scientific inquiries****Contact****Name of organization / entity**

Zanjan University of Medical Sciences

**Full name of responsible person**

Abdoreza ghoreishi

**Position**

Associate professor

**Latest degree**

Specialist

**Other areas of specialty/work**

Neurology

**Street address**

Neurology department of Valiasr hospital, Valiasr Sqr., Zanjan

**City**

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**Province**

Zanjan

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4515777978

**Phone**

+98 24 3377 0801

**Email**

Ghoreishi@zums.ac.ir

**Person responsible for updating data****Contact****Name of organization / entity**

Zanjan University of Medical Sciences

**Full name of responsible person**

Shahin Nateghi

**Position**

Resident

**Latest degree**

Medical doctor

**Other areas of specialty/work**

Neurology

**Street address**

Neurology department of Valiasr hospital, Valiasr  
Sqr., Zanzan

**City**

Zanzan

**Province**

Zanzan

**Postal code**

4515777978

**Phone**

+98 24 3377 0801

**Email**

Shahin.nateghi@gmail.com

**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