Clinical Trial Protocol
Iranian Registry of Clinical Trials

03 Aug 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 ≥ 2 prior to stroke, NIHSS ≥ 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

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Abdoreza Ghoreishi
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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 24with a total score of upper and lower limbs ≥ 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 Iatrogenic stroke Patients with severe mental disorders and dementia Significant lung disease (FEV1 ≤1.5 L, pO2 ≤70 on room air, pCO2 ≥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 ≥ 2 prior to stroke NIHSS ≥ 25 or ≤ 3 in admission Severe disturbance of consciousness: NIHSS category 1a for consciousness ≥ 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 2.0×ULN 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 Procplan 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
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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

Recruitment centers

1

Recruitment center
Name of recruitment center
Valiasr hospital
Full name of responsible person
Abdoreza Ghoreishi
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2

Recruitment center
Name of recruitment center
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Full name of responsible person
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3

Recruitment center
Name of recruitment center
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4

Recruitment center
Name of recruitment center
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5

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Name of recruitment center
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Sponsors / Funding sources

1

Sponsor
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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
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
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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
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

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Resident
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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