

Clinical Trial Protocol

Iranian Registry of Clinical Trials

10 Jun 2026

Aspirin plus Rivaroxaban Efficacy and Safety in Embolic Stroke of Undetermined Source: A Randomized, Placebo Controlled, Outcome Assessor Blind, Clinical Trial

Protocol summary

Study aim

Efficacy and safety of rivaroxaban plus aspirin in reduce stroke recurrence in a patient with Embolic Stroke of Undetermined Source

Design

This is a randomized, parallel, placebo-controlled study on recent (7-60 days) ischemic stroke of undetermined source.

Settings and conduct

Present study will be conducted in Buali hospitals in Sari. After meeting inclusion and exclusion criteria patients will be randomized to Rivaroxaban 2.5 mg BID plus ASA 80 mg daily or ASA 80 mg plus placebo (1:1 ratio) and have visit every three months until 1 year. All adverse events, serious adverse events, outcome events will be recorded.

Participants/Inclusion and exclusion criteria

Adult patients with recent stroke and ESUS with one potential embolic risk but not high risk for bleeding events

Intervention groups

Patients in intervention group take ASA (enteric coated tablet) 80 mg once daily plus Rivaroxaban (film coated tablet) 2.5 mg BID and patients in control group take ASA (enteric coated tablet) 80 mg once daily plus tab Placebo BID

Main outcome variables

The primary outcome is the rate and time of stroke or systemic embolism and major bleeding events according to the criteria of the International Society of Thrombosis and Hemostasis.

General information

Reason for update

the study design changed to " outcome assessor blind" because of placebo size difference

Acronym

IRCT registration information

IRCT registration number: **IRCT20200112046094N1**
Registration date: **2020-08-14, 1399/05/24**
Registration timing: **prospective**

Last update: **2021-07-26, 1400/05/04**

Update count: **1**

Registration date

2020-08-14, 1399/05/24

Registrant information

Name

Athena Sharifi-Razavi

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

+98 11 3334 3014

Email address

athena.sharifi@yahoo.com

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-08-22, 1399/06/01

Expected recruitment end date

2022-03-20, 1400/12/29

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Aspirin plus Rivaroxaban Efficacy and Safety in Embolic

Stroke of Undetermined Source: A Randomized, Placebo Controlled, Outcome Assessor Blind, Clinical Trial

Public title

Rivaroxaban in Embolic Stroke of Undetermined Source(ESUS)

Purpose

Prevention

Inclusion/Exclusion criteria**Inclusion criteria:**

Signing the informed consent Recent ischemic stroke, with criteria of ESUS defined as: Stroke detected by CT or MRI that is not lacunar, Absence of extracranial or intracranial atherosclerosis causing $\geq 50\%$ luminal stenosis in arteries supplying the area of ischemia, No major-risk cardioembolic source of embolism, No other specific cause of stroke identified only one risk factor of potential embolic source including: PTFV1 in standard ECG ≥ 0.05 mm.s or ≥ 0.005 mv.s, LVH in standard ECG (Sokolow index ≥ 35 mm), Moderate or severe MR, AR or AS in echocardiography, LVH in echocardiography, left atrium hypertrophy in echocardiography, PFO not candidate for closure

Exclusion criteria:

History of hypersensitivity to the investigational medicinal product Indication for anticoagulation Indication for dual antiplatelet therapy Contraindication to investigational medications History of intracranial, intraocular, spinal, retroperitoneal or atraumatic intra-articular bleeding Gastrointestinal bleeding or major surgery within 3 months Planned or likely revascularization (any angioplasty or vascular surgery) within the next 3 months HAS-BLED score > 3 Severe non-cardiovascular comorbidity with life expectancy < 3 months Severe renal failure, defined as Glomerular Filtration Rate (GFR) < 15 ml/min, Dialysis, transplant, Cr > 2.26 mg/dL Severe hepatic insufficiency, Cirrhosis or Bilirubin $> 2x$ Normal or AST/ALT/AP $> 3x$ Normal Modified Rankin Scale of ≥ 4 Inability to swallow medications Hemorrhagic transformation of infarction

Age

From **18 years** old

Gender

Both

Phase

3

Groups that have been masked

- Outcome assessor
- Data analyser

Sample size

Target sample size: **40**

Randomization (investigator's opinion)

Randomized

Randomization description

Patients are randomized in a 1:1 fashion to intervention or comparator group. A list of random numbers generated then by using a block randomization method with 4 block size, anonymized patient list encoded. The codes are written on an envelope and the group type (intervention or comparison) is placed on paper inside the envelope. These envelopes are stacked in order. At

the time of enrollment of each patient who met the inclusion and exclusion criteria, the upper envelope is removed, and based on the code inside it, it is determined which group it belongs to.

Blinding (investigator's opinion)

Single blinded

Blinding description

Patient list concealed by statistics. Neurologist give drugs or placebo according to randomized code, neurology resident who assess patients outcome so is blind.

Placebo

Used

Assignment

Parallel

Other design features**Secondary Ids****1****Registry name**

clinicaltrial.gov

Secondary trial Id

NCT04273516

Registration date

2020-02-18, 1398/11/29

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

Ethics committee of Mazandaran University of Medical Sciences

Street address

Bou-Ali Sina Hospital, Pasdaran Blvd, Sari

City

Sari

Province

Mazandaran

Postal code

4815838477

Approval date

2020-07-08, 1399/04/18

Ethics committee reference number

IR.MAZUMS.REC.1399.454

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

Ischemic Stroke

ICD-10 code

I63

ICD-10 code description

Cerebral infarction

Primary outcomes

1

Description

Rate of stroke or systemic embolism recur

Timepoint

12 months after drug administration

Method of measurement

recording in case report form

2

Description

Major bleeding events

Timepoint

12 month after drug administration

Method of measurement

recording in case report form based on International Society on Thrombosis and Haemostasis bleeding scale

Secondary outcomes

1

Description

all-cause mortality rate

Timepoint

at the end of 1 year

Method of measurement

recording in case report form

2

Description

non-major bleeding

Timepoint

at the end of 1 year

Method of measurement

recording in case report form

3

Description

fatal bleeding

Timepoint

at the end of 1 year

Method of measurement

record in case study form

Intervention groups

1

Description

Intervention group: ASA (enteric coated tablet) 80 mg once daily plus Rivaroxaban (film coated tablet)2.5 mg BID for 1 year

Category

Treatment - Drugs

2

Description

Control group: ASA (enteric-coated tablet) 80 mg once daily plus placebo BID for 1 year. Placebo will be made in mazandarn university pharmacy school , similar to rivaroxaban.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Bou-Ali Sina Hospital

Full name of responsible person

Athena Sharifi-Razvi

Street address

Pasdaran Blvd,Sari

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Mazandaran University of Medical Sciences

Full name of responsible person

Athena Sharifi-Razavi

Street address

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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

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

Fatemeh Ramezanzpour

Position

Neurology Resident

Latest degree

Specialist

Other areas of specialty/work

Neurology

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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

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Latest degree

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

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

Yes - There is a plan to make this available

Study Protocol

Yes - There is 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

Yes - There is 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

Title and more details about the data/document

all unrecognizable data would be sharing

When the data will become available and for how long

6 month after result publication

To whom data/document is available

Data will be available for researchers and scientific persons.

Under which criteria data/document could be used

If there is a similar published or documented proposal

From where data/document is obtainable

via email address athena.sharifi@yahoo.com

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

after request and review the proposal .It takes about 1 month.

Comments