Clinical Trial Protocol
Iranian Registry of Clinical Trials

22 Nov 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 undermine 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 (entric coated tablet) 80 mg once daily plus Rivaroxaban (film coated tablet)2.5 mg BID and patients in control group take ASA (entric 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)

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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 ≥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) <15ml/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 (entric 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
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Mazandaran University of Medical Sciences
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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 Ramezanpour
Position
Neurology Resident
Latest degree
Specialist
Other areas of specialty/work
Neurology
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Person responsible for updating data

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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 pblication
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 adders 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