

Clinical Trial Protocol

Iranian Registry of Clinical Trials

06 Jul 2026

A randomized, double-blind , parallel groups, multi center, non-inferiority and phase III clinical trial to compare the Efficacy and Safety of Altelyse (bio-similar Alteplase) versus the brand Actilyse in Acute MI patients with ST elevation

Protocol summary

Study aim

To compare the Efficacy and Safety of Altelyse (bio-similar Alteplase) versus the brand Actilyse in Acute MI patients with ST elevation

Design

This is a randomized, double-blind , parallel groups, multi center, non-inferiority and phase III clinical trial study.

Settings and conduct

Study will be conducted in five hospitals in Tehran. They are Taleghani, Shohadaye-Tajrish, Loghman, Labafi-Nejad, and Fayazbakhsh hospitals.

Participants/Inclusion and exclusion criteria

Patients aged 18 years or older who have had an acute myocardial infarction with ST segment elevation and who either do not have access to Primary Percutaneous Cardiac Intervention (PPCI) or will take more than two hours to receive PPCI treatment, will be potentially eligible for this study. Patient should sign informed consent form and should not have any contraindication for thrombolytic therapy.

Intervention groups

There are two intervention groups in this study. All patients in both groups will receive usual treatments including Aspirin, ADP antagonist, and anti-coagulant therapies. In group 1 thrombolytic therapy patients will receive thrombolytic therapy using Altelyse (Alteplase made by Arena Hayat Danesh Co) and in group 2 patients will receive Actilyse (Alteplase made by boehringer-ingelheim). Thrombolytic therapy will be delivered by accelerated delivery including one bolus injection plus infusion over the next 1.5 hours.

Main outcome variables

Primary outcome in this study is ST resolution (STR) in 90 minutes. Secondary outcomes include complete or partial resolution of ST segment STR in 90 minutes, ST resolution in 180 minutes, all cause mortality in 30 days,

cardiovascular mortality in 30 days, all cause in-hospital mortality, Ventricular Ejection Fraction (EF), bleeding following thrombolytic treatment, allergic drug reaction, and Major Adverse Cardiac Events (MACE)

General information

Reason for update

clinical trial site update and patient recruitment update

Acronym

ARENA

IRCT registration information

IRCT registration number: **IRCT20190729044366N1**

Registration date: **2019-08-25, 1398/06/03**

Registration timing: **prospective**

Last update: **2021-10-03, 1400/07/11**

Update count: **2**

Registration date

2019-08-25, 1398/06/03

Registrant information

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Name of organization / entity

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2021-06-22, 1400/04/01

Expected recruitment end date

2022-07-21, 1401/04/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

A randomized, double-blind, parallel groups, multi-center, non-inferiority and phase III clinical trial to compare the Efficacy and Safety of Altelyse (bio-similar Alteplase) versus the brand Actilyse in Acute MI patients with ST elevation

Public title

Comparing the safety and efficacy of Altelyse with Actilyse in acute myocardial infarction

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Chest pain compatible with ischemic heart disease for more than 20 minutes Start of symptoms of Acute Myocardial Infarction (Peak of chest pain) 12 hours (Maximum) before thrombolytic treatment Signs of Acute Myocardial Infarction in Electrocardiogram: ST elevation of 0.1 milli-volt or more in two adjacent leads other than v2 and v3; ST elevation of 0.25 milli-volt or more in v2 and v3 leads in men younger than 40 years; ST elevation of 0.2 milli-volt or more in v2 and v3 leads in men older than 40 years; ST elevation of 0.15 milli-volt or more in v2 and v3 leads in women irrespective of their age. Lack of access to cath lab to do PPI, Primary Per-cutaneous Coronary Intervention or expecting a delay more than 2 hours between first medical contact and performance of first balloon dilatation excluding the time taken from first medical contact till the start of thrombolytic therapy. Signed informed consent Age of 18 years or more

Exclusion criteria:

Presence of left bundle block in electrocardiogram Presence of accompanying severe diseases such as renal failure (GFR<30); hepatic failure; Portal hypertension; Hepatitis; Thrombocytopenia; Known pancreatitis (information gathered from first clinical examination upon arrival because of chest pain Cardiogenic shock (Systolic pressure less than 90 mm Hg) Killip class III & IV Any history of intracranial bleeding or stroke with unknown origin irrespective of the time of occurrence Ischemic stroke Known central nervous system lesions, neoplasms (primary or metastatic), arteriovenous malformations Aortic dissection Active bleeding or known bleeding disorder (excluding menses) Major trauma to Head and Neck in the last 3 months Intracranial or spinal surgery in the last 2 months Other major trauma or surgery within the preceding month Gastrointestinal bleeding within the preceding month Sever uncontrolled hypertension (Resistant to emergency treatment) Non-compressible punctures in the past 24 hours (e.g. liver

biopsy, lumbar puncture) History of poorly controlled chronic hypertension Hypertension at the time of eligibility assessment: Systolic BP >180 mm Hg or diastolic BP > 110 mm Hg Transient ischemic attack in the preceding 6 months Dementia Pregnancy or within 1 week postpartum Internal bleeding within the last 2-4 weeks Active peptic ulcer Infectious endocarditis Cardiopulmonary resuscitation that has caused injury to the chest or lasted more than 10 minutes Patients who receive anticoagulant therapy such as warfarin Advanced liver disease Known intracranial lesions other than those listed as absolute contraindications for thrombolytic therapy Diabetic Hemorrhagic Retinopathy or other hemorrhagic ophthalmic conditions

Age

From 18 years old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data and Safety Monitoring Board

Sample size

Target sample size: 150

Randomization (investigator's opinion)

Randomized

Randomization description

We used block randomization stratified by hospitals using variable block size of 4 and 6. A separate chain of randomization sequence will be developed for each hospital. Excel software and rand() function will be used to create the random sequences. Concealment will be carried out and a random code will be assigned to every patient according to the randomization sequence. The codes will be put in sealed envelopes and the envelopes will be numbered incrementally from 1 according to the randomization sequence. For each eligible patient enrolled to the study an envelope will be opened according to the sequential number. Patients will receive the intervention assigned to them based on the code inside the envelope.

Blinding (investigator's opinion)

Double blinded

Blinding description

In this study we used secondary packaging of Actilyse and Alteplase to achieve blinding. The packages will be labelled using the concealment codes. Once the randomization is done, and the thrombolytic treatment package for the patient is known, a separate nurse not in the study team, will be given the responsibility to open the package and prepare the thrombolytic injection. It will then be given to the research team for use.

Placebo

Not used

Assignment

Parallel

Other design features

Acronym ARENA stands for Assessing Re-perfusion Efficacy in Nationally manufactured thrombolytic, Altelyse in AMI

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Shahid Beheshti University of Medical Science

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Province

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Postal code

-

Approval date

2019-07-21, 1398/04/30

Ethics committee reference number

IR.SBMU.REC.1398.025

Health conditions studied

1

Description of health condition studied

Acute Myocardial Infarction with ST elevation

ICD-10 code

I21.3

ICD-10 code description

ST elevation (STEMI) myocardial infarction of unspecified site

Primary outcomes

1

Description

Percentage of ST resolution (STR) at 90 minutes

Timepoint

90 minutes after start of thrombolytic therapy

Method of measurement

To estimate percentage of ST resolution at 90 minutes, we will measure the height of ST elevation at 20 milisecond after J point in those leads that have shown elevation of ST in a 12 lead standard ECG at time points 0 and 90. Sum of ST elevations in all 12 leads at 90 minutes will be deducted from the sum of ST elevations at time 0 to work out the total ST resolution (STR) at 90 minutes. We will then calculate the percentage of ST resolution by dividing total STR at 90 minutes to the sum of ST elevations at time 0. In a second measurement approach, percentage of patients who have had more than 50% resolution in their ECG lead with highest ST

elevation will be calculated.

Secondary outcomes

1

Description

Complete or partial resolution of ST segment (STR) in 90 minutes

Timepoint

90 Minutes after thrombolytic therapy

Method of measurement

Complete resolution is defined as 70% resolution in sum of ST elevations and partial resolution is defined as 30 to 70% resolution in sum of ST elevations. Method of calculation of STR is the same as the primary outcome.

2

Description

Percentage of ST resolution (STR) at 180 minutes

Timepoint

180 Minutes after thrombolytic therapy

Method of measurement

To estimate percentage of ST resolution at 180 minutes, we will measure the height of ST elevation at 20 milisecond after J point in those leads that have shown elevation of ST in a 12 lead standard ECG at time points 0 and 180. Sum of ST elevations in all 12 leads at 180 minutes will be deducted from the sum of ST elevations at time 0 to work out the total ST resolution (STR) at 180 minutes. We will then calculate the percentage of ST resolution by dividing total STR at 180 minutes to the sum of ST elevations at time 0.

3

Description

All cause mortality in 30 days

Timepoint

30 days after intervention

Method of measurement

All deaths irrespective of the cause of death in the first 30 days following thrombolytic therapy starting from the First Medical Contact (FMC) will be counted

4

Description

Cardiovascular mortality in 30 days

Timepoint

30 days after intervention

Method of measurement

All cardiovascular deaths in the first 30 days following thrombolytic therapy starting from the First Medical Contact (FMC) will be counted

5

Description

In-hospital mortality due to any cause

Timepoint

Up until discharge from hospital

Method of measurement

All deaths irrespective of their cause up until discharge from hospital will be counted

6

Description

Ventricular Ejection Fraction

Timepoint

2 to 5 days following thrombolytic therapy

Method of measurement

Echocardiography

7

Description

Bleeding

Timepoint

After thrombolytic therapy

Method of measurement

All episodes of major and minor bleeding following thrombolytic therapy will be recorded and categorized in three groups according to GUSTO 5 criteria. Severe or life threatening bleeding: Intracranial bleeding and any other bleeding that cause severe haemodynamic instability for the patient. Moderate bleeding: patient will need blood transfusion. Mild bleeding: all other bleeding

8

Description

Allergic drug reaction

Timepoint

After thrombolytic therapy

Method of measurement

Allergic skin reactions at the injection site and systemic reactions including anaphylactic shock, Angioedema, Urticaria, and drop in systolic blood pressure to 90 mmHg or lower, will be identified and recorded.

9

Description

MACE (Major Adverse Cardiac Events)

Timepoint

After thrombolytic therapy

Method of measurement

Any of the following adverse cardiac events will be counted: Death, Bleeding GUSTO type I and II, Cerebrovascular Accident (CVA)

Intervention groups

1

Description

Intervention group 1: This group will receive thrombolytic therapy using Altelyse (Alteplase made by Arena Hayat Danesh Co). People weighing more than 67kg will receive 15 mg bolus, 50 mg in the first 30 minutes and 35 mg within the next 60 minutes. People weighing 67kg or less will receive 15 mg bolus, 0.75 mg/kg in the first 30 minutes and 0.5 mg/kg within the next 60 minutes. All

patients in the intervention groups 1 and 2 will receive Aspirin, ADP receptor antagonists and Anticoagulant therapy. Aspirin therapy: All patients who are not on Aspirin will receive 300-325 mg Aspirin in the emergency room. ADP receptor antagonist therapy: People not on clopidogrel and 75 years old or less will receive 300 mg clopidogrel loading dose and then 75mg daily. People not on clopidogrel and older than 75 years will only receive the daily dose without the loading dose. Anticoagulant therapy: All patients will receive one bolus injection of Unfractionated heparin 60 unit per kg (maximum 4000 units) followed by 12u/kg (maximum 1000 units) per hour until PTT reaches to 1.5 to 2 times normal (50-70 seconds) and stays at that level. Beta blockers, Angiotensin Enzyme inhibitors (ACE/ARB receptor inhibitors/blockers) and Statins will be given according to the existing guidelines.

Category

Treatment - Drugs

2

Description

Intervention group 2: This group will receive thrombolytic therapy using Actilyse. People weighing more than 67kg will receive 15 mg bolus, 50 mg in the first 30 minutes and 35 mg within the next 60 minutes. People weighing 67kg or less will receive 15 mg bolus, 0.75 mg/kg in the first 30 minutes and 0.5 mg/kg within the next 60 minutes. All patients in the intervention groups 1 and 2 will receive Aspirin, ADP receptor antagonists and Anticoagulant therapy. Aspirin therapy: All patients who are not on Aspirin will receive 300-325 mg Aspirin in the emergency room. ADP receptor antagonist therapy: People not on clopidogrel and 75 years old or less will receive 300 mg clopidogrel loading dose and then 75mg daily. People not on clopidogrel and older than 75 years will only receive the daily dose without the loading dose. Anticoagulant therapy: All patients will receive one bolus injection of Unfractionated heparin 60 unit per kg (maximum 4000 units) followed by 12u/kg (maximum 1000 units) per hour until PTT reaches to 1.5 to 2 times normal (50-70 seconds) and stays at that level. Beta blockers, Angiotensin Enzyme inhibitors (ACE/ARB receptor inhibitors/blockers) and Statins will be given according to the existing guidelines.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

(Ayatollah) Taleghani Educational Hospital

Full name of responsible person

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2

Recruitment center

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4

Recruitment center

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5

Recruitment center

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Recruitment center

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7

Recruitment center

Name of recruitment center

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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

Arena Life Science Company

Proportion provided by this source

100

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**

Industry

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

Arena Life Science Co.

Full name of responsible person

Hoda Flah Shojaee

Position

Clinical Trial Manager

Latest degree

Master

Other areas of specialty/work

Medical Genetics

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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

Yes - There is 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

Not applicable

Title and more details about the data/document

These includes identified individual participant data on primary and secondary outcomes, study protocol, informed consent form and clinical study report

When the data will become available and for how long

Data will be available one year after study completion or publication of the main results whichever comes later

To whom data/document is available

Data will only be available to academic researchers at the universities

Under which criteria data/document could be used

Data will only be shared for the purpose of meta-analysis

From where data/document is obtainable

You can contact Ms Hoda Shojaei at Arenalifesciences Co

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

Medical Director of the Arenlifesciece co should make sure that the condition for sharing data is met and should approve it

Comments

none