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 sudy.

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 nformed 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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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 mili-volt or more in two adjacent leads other than v2 and v3; ST elevation of 0.25 mili-volt or more in v2 and v3 leads in men younger than 40 years; ST elevation of 0.2 mili-volt or more in v2 and v3 leads in men older than 40 years; ST elevation of 0.15 mili-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 between first medical contact and performance of first balloon dilatation excluding the time takes 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; Thrombocytopaenia; Known pancreatitis (information gathered from first clinical examination upon arrival because of cheat 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 envelops and the envelops will be numbered incrementally from 1 according to the randomization sequence. For each eligible patient enrolled to the study an envelop will be opened according to the sequential number. Patients will receive the intervention assigned to them based on the code inside the envelop.
Blinding (investigator's opinion)
Double blinded
Blinding description
In this study we used secondary packaging of Actilyse and Altlelyse 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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-
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
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4

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7

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1

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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

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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