Clinical Trial Protocol
Iranian Registry of Clinical Trials

16 Sep 2026

Effect of Empagliflozin on diastolic function and renal dynamics and biochemical parameters in people with heart failure with preserved ejection fraction

Protocol summary

Study aim
Comparison of change of ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (E') (E/E' ratio)' assessed by Echocardiography before and after Empagliflozin adding vs placebo [Time Frame: Week 0_12_26]

Design
Two arm with parallel design of 200 patients (100 in each arm) phase three randomized trial with double blinded and placebo controlled

Settings and conduct
In 2 Iranian tertiary heart and endocrine centers in Tehran, we will enroll heart failure preserved ejection fraction patients in a triple – blind, randomized controlled trial comparing Empagliflozin effect on diastolic function and renal dynamics and biochemical parameters vs standard practice in diabetic and non-diabetic patients.

Participants/Inclusion and exclusion criteria
Patients with heart failure preserved ejection fraction would be enrolled (100 diabetic patients & 100 non diabetic patients in each arm).If there is a history of renal failure or decompensated heart failure or the presence of contraindication for Empagliflozin taking , they will be excluded.

Intervention groups
Therapeutic intervention (Empagliflozin or Placebo) in patients with Heart Failure preserved Ejection Fraction

Main outcome variables
The ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (E') (E/E' ratio)' changes assessed by echocardiography

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20190122042450N2**
Registration date: **2019-05-20, 1398/02/30**
Registration timing: **prospective**

Last update: **2019-05-20, 1398/02/30**
Update count: **0**

Registration date
2019-05-20, 1398/02/30

Registrant information

Name
Mohammad Ebrahim Khamseh

Name of organization / entity

Country
Iran (Islamic Republic of)

Phone
+98 21 8894 5246

Email address
khamseh.m@iums.ac.ir

Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2019-06-21, 1398/03/31

Expected recruitment end date
2020-02-20, 1398/12/01

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
Effect of Empagliflozin on diastolic function and renal dynamics and biochemical parameters in people with heart failure with preserved ejection fraction

Public title

Effect of Empagliflozin in heart failure preserved ejection fraction

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Heart Failure Preserved Ejection Fraction : HF symptom NYHA Class 2 or 3 and Ejection Fraction≥50 by Echocardiography and BNP (B type Natriuretic Peptide) >100 pg/mL within 2 month prior to enrollment The ability to walk more than 50 meters No significant changes in diuretic dosage (doubling dose or new prescription) within 1 week prior to enrollment

Exclusion criteria:

Poor echocardiography finding History of cancer within 3 years prior to enrollment Uncontrolled hypothyroidism (TSH>4.5) or Hyperthyroidism (TSH<0.4) Sever hepatic failure (Liver enzyme >3 ULN) History of taking Pioglitazone within 8 weeks prior to enrollment Myocardial infraction, unstable angina, percutaneous coronary intervention, or coronary bypass surgery within 60 days prior to enrollment Decompensated heart failure within 4 weeks prior to enrollment An estimated glomerular filtration rate (eGFR) of at least 30 ml per minute per 1.73 m2 body- surface area, according to CKD-EPI formula. Pregnancy and/or lactation History of alcohol and other substance abuse Active or recent (within 2 weeks prior to enrollment) genitourinary infection Don't have compliance to taking medicine History of including in another study within 3 month prior to enrollment Start Angiotensin-Converting Enzyme (ACE) inhibitors, Hydralazine, long-acting nitrates, beta blockers & Angiotensin Receptor Blockers (ARBs) within 1 month prior to enrollment History of allergy with Empagliflozin History of taking Empagliflozin within 12 week prior to enrollment Active gross hematuria History of heart or kidney transplant HF because of restrictive cardiomyopathy, active myocarditis, ,Constrictive Pericarditis, Sever valvular heart stenosis & hypertrophic cardiomyopathy Uncontrolled Systolic Blood Pressure ≥ 180 mmHg in two outpatient visit Symptomatic hypotension or SBP < 100 mmHg In type 2 diabetes patients who have been treated with at least one blood glucose lowering agent (oral, non-insulin) with any dosage change, within 12 weeks prior to enrollment In type 2 diabetes patients daily dose of insulin would be changed exceed 10% of the base dose within 3 months before screening 7.5% > HbA1c >9.5% within 3 months before screening in type 2 diabetes patients

Age

From **40 years** old to **80 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: **200**

Randomization (investigator's opinion)

Randomized

Randomization description

4 block randomization: Each lables has one letter A or B. Randomization sequence will be created using www.sealedenvelope.com using random block sizes of 4 based on treatment group A or B for 200 patients.

Blinding (investigator's opinion)

Triple blinded

Blinding description

In this trial we use Empagliflozin and placebo with same package ,color and shape with different cod combination number (based on table of random numbers) and letters A & B. After enrollment , one code is assigned to each patient , which will be recognized by this code until the end of this study. Participants, Principle Investigator,Cardiologist, , laboratory technician, outcome assessor & data analyser, all of them are blind because they don't know this cod is Empagliflozin or placebo.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Iran University of Medical Sciences

Street address

Iran University of Medical Sciences, Shahid Hemmat Highway, Tehran

City

Tehran

Province

Tehran

Postal code

1449614535

Approval date

2019-02-24, 1397/12/05

Ethics committee reference number

IR.IUMS.REC.1398.015

Health conditions studied

1

Description of health condition studied

Heart Failure preserved Ejection Fraction

ICD-10 code

I50.1

ICD-10 code description

Left ventricular failure

Primary outcomes

1

Description

The ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (E') (E/E' ratio)'Changes

Timepoint

Week 0_ 12_ 26

Method of measurement

Echocardiography

Secondary outcomes

1

Description

Hospilization due to heart failure

Timepoint

Time Frame: Randomization through each subject's last visit, up to a maximum of 26 weeks per subject

Method of measurement

Question

2

Description

Mortality due to heart failure

Timepoint

Randomization through each subject's last visit, up to a maximum of 26 weeks per subject

Method of measurement

Evaluate during follow up

3

Description

Change mean blood pressure in setting position

Timepoint

0_12_26 Week

Method of measurement

Question

4

Description

 Change mean peak VO2 ("V" for volume, "O2" for oxygen) (mL/kg/min)

Timepoint

0_12_26 Week

Method of measurement

cardiopulmonary exercise test

5

Description

Myocardial oxygen consumption

Timepoint

0_12_26 Week

Method of measurement

SBP* HR

6

Description

six minutes' walking distance

Timepoint

0_12_26 Week

Method of measurement

six minutes' walking test

7

Description

Mortality due to renal failure

Timepoint

Time Frame: Randomization through each subject's last visit, up to a maximum of 26 weeks per subject

Method of measurement

evaluate during follow up

8

Description

Hospitalization due to renal failure

Timepoint

Randomization through each subject's last visit, up to a maximum of 26 weeks per subject

Method of measurement

Question

9

Description

Assessment of renal function over time

Timepoint

0_12_26 Weeks

Method of measurement

Glomerular Filtration Rate (GFR) equation with CKD-EPI

10

Description

Renal replacement therapy

Timepoint

Randomization through each subject's last visit, up to a maximum of 26 weeks per subject

Method of measurement

Question

11

Description

Progression of albuminuria

Timepoint

0_12_26 Week

Method of measurement

urinary albumin to creatinine ratio

12

Description
All-cause Mortality
Timepoint
Randomization through each subject's last visit, up to a maximum of 26 weeks per subject
Method of measurement
Evaluate during follow up

13

Description
Total Hospitalizations (Including Repeat Hospitalizations) for the Management of Heart Failure
Timepoint
Randomization through each subject's last visit, up to a maximum of 26 weeks per subject
Method of measurement
Question

14

Description
Duration of admission
Timepoint
Randomization through each subject's last visit, up to a maximum of 26 weeks per subject
Method of measurement
Question

15

Description
Measured Quality of Life
Timepoint
0_26 Week
Method of measurement
Filling Short Form-36،MLHF، NYHA

16

Description
Anthropometric findings
Timepoint
0_12_26 Week
Method of measurement
Scale and Meter

17

Description
Mean Diuretic dosage taking
Timepoint
0_12_26 Week
Method of measurement
Question

18

Description
Mean spirometry findings
Timepoint
0_26 Week
Method of measurement
اسپیرومتری

19

Description
Incidence of acute renal failure (AKI)
Timepoint
Randomization through each subject's last visit, up to a maximum of 26 weeks per subject
Method of measurement
Observe BUN & Cr during study

20

Description
Hypoglycemia
Timepoint
Randomization through each subject's last visit, up to a maximum of 26 weeks per subject
Method of measurement
Question and BS chart

21

Description
Hyperkalemia
Timepoint
0_12_26 week
Method of measurement
Lab test

22

Description
Changes in the albuminuria
Timepoint
0_12_26 week
Method of measurement
Lab test

23

Description
Urinary tract/genital infection
Timepoint
Randomization through each subject's last visit, up to a maximum of 26 weeks per subject
Method of measurement
Question

24

Description
Diabetes ketoacidosis
Timepoint
Randomization through each subject's last visit, up to a maximum of 26 weeks per subject
Method of measurement
See hospitalization records

25

Description
Foot ulcer/Amputation
Timepoint
Randomization through each subject's last visit, up to a maximum of 26 weeks per subject
Method of measurement
Question

26

Description
High sensitivity C reactive protein (mg/L), Interleukin1، troponin I، N terminal pro-BNP (pg/mL) levels
Timepoint
0 , 26 Week
Method of measurement
Lab test

Intervention groups

1

Description
Intervention group: Tablet Empagliflozin 10 milligram daily over 6 months produced by Dr. Abidi pharmacy
Category
Treatment - Drugs

2

Description
Control group: placebo, daily over 6 months produced by Dr. Abidi pharmacy
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Masih Daneshvari Hospital
Full name of responsible person
Babak Sharif Kashani
Street address
Darabad Avenue, Shahid Bahonar Avenue
City
Tehran
Province
Tehran
Postal code
1956944413
Phone
+98 21 2610 5050
Email
pr.nritld@sbmu.ac.ir
Web page address
https://nritld.sbmu.ac.ir

2

Recruitment center
Name of recruitment center
Institute of Endocrinology and Metabolism Research and Training Center Iran University Medical Scien
Full name of responsible person
Mohammad Ebrahim Khamseh
Street address
Firooze Alley, Vali-asr Sq,
City
Tehran
Province
Tehran
Postal code
1593748711
Phone
+98 21 8894 5171
Email
iem@iuma.ac.ir

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Abidi pharmacy
Full name of responsible person
Elham Andalib
Street address
Ahmed Qusayr Street (Bucharest), below the Argentine Square. Alley 13. No. 5
City
Tehran
Province
Tehran
Postal code
1513815811
Phone
+98 21 4452 2451
Email
e.andalib@cobeldarou.com
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Abidi pharmacy
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
Iran University of Medical Sciences
Full name of responsible person
Mohammad Ebrahim Khamseh
Position
Professor
Latest degree
Subspecialist
Other areas of specialty/work
Internal Medicine
Street address
Behafarin ST, KarimkhanAVE, Vali-asr Sq, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1593748711
Phone
+98 21 8894 5246
Fax
Email
khamseh.m@iums.ac.ir

Person responsible for scientific inquiries

Contact

Name of organization / entity
Iran University of Medical Sciences
Full name of responsible person
Mohammad Ebrahim Khamseh
Position
Professor
Latest degree
Subspecialist
Other areas of specialty/work
Endocrinology & Metabolism
Street address
Behafarin ST, Karimkhan AVE, Vali-asr Sq, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1593747811
Phone
+98 21 8894 5246
Email
khamseh.m@iums.ac.ir

Person responsible for updating data

Contact

Name of organization / entity
Iran University of Medical Sciences
Full name of responsible person
Zohreh Maghsoomi
Position
Fellowship
Latest degree
Specialist
Other areas of specialty/work
Endocrinology & Metabolism
Street address
Behafarin ST, Karimkhan AVE, Vali-asr Sq, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1593747811
Phone
+98 21 8894 5246
Email
zmaghsoomi@gmail.com

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