

Clinical Trial Protocol

Iranian Registry of Clinical Trials

01 Aug 2026

The assessment of Empagliflozin Effects in diabetic patients with coronary artery disease: The EMPA-CARD Randomized Clinical Trial

Protocol summary

Study aim

The Effects of Empagliflozin in diabetic patients with coronary artery disease

Design

A Parallel Drug-Placebo, triple blind, stratified Randomized trial of 100 patients (50 patients each group) with the follow up period of 6 months.

Settings and conduct

This will be a Triple blind (outcome assessor and care provider, patients and Data Supervision Committee and Data Analyzer) trial in Zanjan,Iran. patients will be divided into 2 groups and will receive empagliflozin tablet 10 mg or placebo daily for 6 months. Blood sampling, ECG, echocardiogram will be obtained at the beginning of the study and the end of 6 months.

Participants/Inclusion and exclusion criteria

The study population included patients with type 2 diabetes with coronary artery disease. All of patients are treated with Aspirin 80mg/Daily and anti diabetic drugs for at least 3 month prior to the beginning of study and will have acceptable hemodynamic function. exclusion criteria: Pregnancy,heart failure or arrhythmia,moderate to severe liver,kidney,hematologic or malabsorption disease,psychological and electrolyte imbalance,use of alcohol,anti-inflammatory or antioxidant drugs,history of infection during last 1 month and major cardiac or cerebral accidents during 1 year or cardio-pulmonary surgeries and history of usage or allergy to SGLT2 inhibitors drugs.

Intervention groups

Population will be comprised of patients with type 2 diabetes with known coronary artery disease that will be divided into 2 groups of 50 patients. 1- Drug group: will be treated with empagliflozin tablet (10 mg/Daily). 2- Control group: will be treated with placebo tablets.

Main outcome variables

1) Changes in plasma Interleukin 6

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20190412043247N2**

Registration date: **2020-06-13, 1399/03/24**

Registration timing: **prospective**

Last update: **2020-06-13, 1399/03/24**

Update count: **0**

Registration date

2020-06-13, 1399/03/24

Registrant information

Name

Hassan Ahangar

Name of organization / entity

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-06-29, 1399/04/09

Expected recruitment end date

2020-09-30, 1399/07/09

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The assessment of Empagliflozin Effects in diabetic patients with coronary artery disease: The EMPA-CARD Randomized Clinical Trial

Public title

Assessment of Empagliflozin effects in coronary artery disease

Purpose

Basic science

Inclusion/Exclusion criteria

Inclusion criteria:

Age between 40-75 year-old HbA1c between 6.5 to 9 Diabetes mellitus type 2 Under fix continues anti-diabetic treatment for at least 3 month BMI less than 40 Fixed Diet and physical activity Resting heart rate between 60 to 100 b/min Use of Aspirin 80 mg/Daily for at least 3 month prior to the beginning of study Glomerular filtration rate (GFR)>45 Documented known Coronary Artery Disease

Exclusion criteria:

Pregnancy Heart Failure (NYHA class 3-4), Ejection Fraction <40% History of allergic reaction to SGLT2 inhibitors Drugs History of SGLT2 inhibitor Drugs usage Gastrointestinal malabsorption disease History of CABG, ACS, TIA, CVA or PCI during past 3 month History or presence of malignancy Severe HTN Anemia (Hb<10 g/dl) History of heart or lung transplant Major psychiatric disorders History of DKA Elevated liver enzymes >3 times upper normal limit Use of drugs prolonging QT interval Presence of Arrhythmia Electrolyte disorders Patients with Pace Maker Use of anti-coagulant or anti-platelet drugs for at least 3 months prior to the sampling Consumption of alcohol, Anti inflammatory drugs (except Aspirin) or Anti oxidant supplement Platelet count <100000/ μ l History of infection during 1 one month before sampling

Age

From **40 years** old to **75 years** old

Gender

Both

Phase

4

Groups that have been masked

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

Sample size

Target sample size: **100**

Randomization (investigator's opinion)

Randomized

Randomization description

Stratified randomization and the randomization unit is also individual. the strata of randomization in this study are Gender, HbA1c and age. Randomization sequence will be created using Winpepi analysis software using 3 strata based on treatment group A or B for 100 patients.

Blinding (investigator's opinion)

Triple blinded

Blinding description

1- Empagliflozin and placebo tablets have the same color, shape and package with the different code combination numbers (generated by random number table) for the 2 groups of A and B. 2- After enrollment , one code is assigned to each patient , which will be recognized by this code until the end of this study. 3- Patients, Researchers who receive information from patients, assess the outcomes and analyze the data of the study, Physicians and health care providers, The Data Supervision and Implementation Committee, which comprised of Zanjan University of Medical Sciences and Dr. Abidi Pharmaceutical Company will not aware that patients are receiving empagliflozin or placebo In such a way that all of the patients will be evaluated under the unique assigned code and the treatment group of A or B. The mentioned individuals will not know which code is empagliflozin or placebo. The only individual who knows about the patients assigned code and treatment group of A and B will be a consultant that has no communication to patients or the executive team members.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Zanjan University of Medical Sciences

Street address

Gavazang blv, Karmandan Quarter, Mousavi Hospital

City

Zanjan

Province

Zanjan

Postal code

4515613191

Approval date

2019-09-01, 1398/06/10

Ethics committee reference number

IR.ZUMS.REC.1398.279

2

Ethics committee

Name of ethics committee

Ethics committee of Zanjan University of Medical Sciences

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 4515613191
Approval date
 2019-08-27, 1398/06/05
Ethics committee reference number
 IR.ZUMS.REC.1398.278

3

Ethics committee
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 2019-10-02, 1398/07/10
Ethics committee reference number
 IR.ZUMS.REC.1398.289

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Ethics committee
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 2019-02-19, 1397/11/30
Ethics committee reference number
 IR.ZUMS.REC.1397.347

5

Ethics committee
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 Gavazang blv, Karmandan Quarter, Mousavi Hospital
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Approval date
 2020-02-05, 1398/11/16
Ethics committee reference number

IR.ZUMS.REC.1398.444

Health conditions studied

1

Description of health condition studied

Diabetes Mellitus type 2

ICD-10 code

E11

ICD-10 code description

Type 2 diabetes mellitus

2

Description of health condition studied

Coronary artery disease

ICD-10 code

I125.1

ICD-10 code description

Atherosclerotic heart disease of native coronary artery

Primary outcomes

1

Description

Changes in Plasma Interleukin 6

Timepoint

At the beginning of the study and the end of week 26

Method of measurement

Plasma IL-6 Elisa Kits

Secondary outcomes

1

Description

Changes in oxidative stress (Changes in lymphocytic reactive oxygen species level)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Flow cytometry

2

Description

Changes in oxidative stress (Changes in plasma levels of Malondialdehyde)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

colorimetric assay

3

Description

Changes in oxidative stress (Changes in plasma carbonyl level)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

colorimetric assay

4**Description**

Changes in oxidative stress (Changes in total plasma antioxidant capacity)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

FRAP assay

5**Description**

Changes in oxidative stress (Changes in plasma reduced glutathione level)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

colorimetric assay

6**Description**

Changes in oxidative stress (Changes in plasma catalase enzyme activity)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Spectrophotometry

7**Description**

Changes in oxidative stress (Changes in plasma superoxide dismutase enzyme activity)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Spectrophotometry

8**Description**

Changes in plasma interleukin 1b

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Interleukin 1b Elisa kit

9**Description**

Changes in platelet function

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Flow cytometric measurement (CD62-P expression on platelet surface)

10**Description**

Changes in serum total protein level

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Spectrophotometry

11**Description**

Changes in Hematopoietic status (Changes in hemoglobin)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Complete blood count test

12**Description**

Changes in glycemic status (Homeostatic Model Assessment of Insulin Resistance)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

HOMA-IR= fasting insulin (mU/mL) x fasting glucose (mg/dL)/405

13**Description**

Changes in glycemic status (Changes in serum basal insulin level)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Chemiluminescence assay

14**Description**

Changes in glycemic status (Changes in HbA1c)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Enzymatic assay

15**Description**

Changes in glycemic status (Changes in blood fasting blood sugar)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Enzymatic assay

16**Description**

Changes in serum high sensitive C-reactive protein

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Turbidimetric assay

17

Description

Changes in high sensitivity-Troponin I level

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Chemiluminescence assay

18

Description

Changes in serum Pro-BNP level

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Chemiluminescence assay

19

Description

Changes in serum BNP level

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Chemiluminescence assay

20

Description

Changes in echocardiographic parameters (Left ventricular function)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Echocardiographic measurement

21

Description

Changes in echocardiographic parameters (Right ventricular function)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Echocardiographic measurement

22

Description

Changes in hematopoietic status (Changes in serum erythropoietin)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Serum Erythropoietin Elisa kit

23

Description

Changes in hematopoietic status (Changes in Blood hematocrit)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Complete blood count test

24

Description

Changes in renal function (Changes in urine albumin to creatinine ratio)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Photometry/ Enzymatic assays

25

Description

Changes in renal function (Changes in urine micro albuminuria level)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Photometry assay

26

Description

Changes in lipid profile (Changes in serum total cholesterol level)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Enzymatic assay

27

Description

Changes in lipid profile (Changes in serum LDL cholesterol level)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Enzymatic assay

28

Description

Changes in lipid profile (Changes in serum HDL cholesterol level)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Enzymatic assay

29

Description

Changes in lipid profile (Changes in serum triglyceride

level)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Enzymatic assay

30

Description

Changes in electrocardiographic parameters (QT interval)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Electrocardiography

31

Description

Changes in electrocardiographic parameters (ST segment deviation)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Electrocardiography

32

Description

Changes in electrocardiographic parameters (T wave alternans)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Electrocardiography

33

Description

Changes in electrocardiographic parameters (PR interval duration)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Electrocardiography

34

Description

Changes in electrocardiographic parameters (QRS wave duration)

Timepoint

At the beginning of study and the end of week 26

Method of measurement

Electrocardiography

Intervention groups

1

Description

Intervention group: The 50 patients in the intervention group will be treated with Empagliflozine 10 mg daily for

6 months (made by Abidi Pharmaceutical Company).

Patients will continue the routine medical cares as before the study such as periodic medical visits and laboratory tests.

Category

Treatment - Drugs

2

Description

Control group: The 50 patients will be placed in the second group, the Control group, and will be treated with Placebo for 6 months. Patients will continue the routine medical cares as before the study such as periodic medical visits and laboratory tests.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Dr Hassan Ahangar's office

Full name of responsible person

Hassan Ahangar

Street address

7 th Tir Ave, Saadi St

City

Zanjan

Province

Zanjan

Postal code

5655124582

Phone

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Email

Ahanghar@zums.ac.ir

2

Recruitment center

Name of recruitment center

Mousavi Hospital (coronary angiography registry)

Full name of responsible person

Ahmad Jalilvand

Street address

Prof Sobuti Blvd, Karmandan quarter

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Email

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3

Recruitment center

Name of recruitment center

Dr Khalil Mahmoodi's Office

Full name of responsible person

Khalil Mahmoodi

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No 5, Zartosht building, Sadi Blvd

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4

Recruitment center

Name of recruitment center

Valiasr Endocrinology clinic (Diabetes Mellitus registry)

Full name of responsible person

Hossein Chiti

Street address

Sheykh Fazlolah Noori Expressway, Valiasr Square

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Zanjan University of Medical Sciences

Full name of responsible person

Mr Mohammad Ganji

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Email

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Web page address**Grant name**

1% share of university

Grant code / Reference number

1602001000

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

Zanjan University of Medical Sciences

Proportion provided by this source

50

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

2

Sponsor

Name of organization / entity

Dr. Abidi Pharmaceutical Company

Full name of responsible person

Seyed Amir Razavian

Street address

No 72, Abidi Blv, Lashkari Expressway

City

Tehran

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Tehran

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13897-76363

Phone

+98 21 4452 2451

Fax

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Email

info@doctor-abidi.com

Web page address**Grant name****Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

Dr. Abidi Pharmaceutical Company

Proportion provided by this source

50

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

Zanjan University of Medical Sciences

Full name of responsible person

Hassan Ahangar

Position

Assistant Proffessor

Latest degree

Subspecialist

Other areas of specialty/work

Cardiology

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Person responsible for scientific inquiries

Contact

Name of organization / entity

Zanjan University of Medical Sciences

Full name of responsible person

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Position

Assistant Proffessor

Latest degree

Subspecialist

Other areas of specialty/work

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Person responsible for updating data

Contact

Name of organization / entity

Zanjan University of Medical Sciences

Full name of responsible person

Sepehr Gohari

Position

Medical student

Latest degree

A Level or less

Other areas of specialty/work

General Practitioner

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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

Undecided - It is not yet known if there will be a plan to make this available

Title and more details about the data/document

Patient's raw data will be stored at online data repositories at the time study report. Study protocol will be reported in the form of a manuscript.

When the data will become available and for how long

After completing the study

To whom data/document is available

All individuals, legal, academic and non-academic

Under which criteria data/document could be used

will be made available to others without limitation by providing rational reason.

From where data/document is obtainable

By email to the corresponding

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

By email or letter to the corresponding

Comments

this study has substudies regarding some secondary outcomes including the echocardiographic findings, hematopoietic status, renal function, electrocardiographic findings and safety study.