Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Nov 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 malabsorpsion 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
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Hassan Ahangar
Name of organization / entity
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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 scienece

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 malabsorbtion 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/µl 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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Approval date

2019-08-27, 1398/06/05

Ethics committee reference number

IR.ZUMS.REC.1398.278

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Name of ethics committee

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Approval date

2019-10-02, 1398/07/10

Ethics committee reference number

IR.ZUMS.REC.1398.289

4

Ethics committee

Name of ethics committee

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Approval date

2019-02-19, 1397/11/30

Ethics committee reference number

IR.ZUMS.REC.1397.347

5

Ethics committee

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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
Spectrophotometery

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
Spectrophotometery

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

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Zanjan

Postal code

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Phone

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Email

Ahanghar@zums.ac.ir

2

Recruitment center

Name of recruitment center

Mousavi Hospital (coronary angiography registery)

Full name of responsible person

Ahmad Jalilvand

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3

Recruitment center

Name of recruitment center
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Khalil Mahmoodi
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4

Recruitment center

Name of recruitment center
Valiasr Endocrinology clinic (Diabetes Mellitus registery)
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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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
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No 72, Abidi Blv, Lashkari Expressway
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Tehran
Province
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Phone
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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
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Person responsible for scientific inquiries

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Person responsible for updating data

Contact

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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 storaged 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.