Clinical Trial Protocol
Iranian Registry of Clinical Trials

16 Sep 2026

Comparing the effect of Empagliflozin, Pioglitazone and their combination, on sonographic and biochemical features of non-alcoholic fatty liver disease in diabetic patients

Protocol summary

Study aim

Comparing the effects of Empagliflozin, Pioglitazone and their dual-therapy on the severity of non-alcoholic fatty liver disease, based on sonographic and biochemical findings.

Design

Randomized, phase 2-3 trial with three parallel groups on 120 patients. Permutation randomization block technique was used.

Settings and conduct

This study will be done in Amiralmomenin clinic, Arak, Iran. Sonographies and laboratory tests will be done with the same instrument/kit and by the same sonographist/technician. Initially, laboratory tests will be requested to rule out secondary causes of liver disease and to check liver enzymes, CBC, lipid profile and HbA1c. Treatment duration will be 6 months, physician visits every 3 months and phone calls to assess compliance, every month. After 6 months, sonography and lab tests (except those used for exclusion of other causes) will be repeated. In this study the patients will receive a random drug envelope from a non-researcher collaborator.

Participants/Inclusion and exclusion criteria

Inclusion criterion: Type-2 diabetes patients aged 20-65 years with fatty liver by sonography. Exclusion criteria: Other causes of chronic liver disease or secondary fatty liver End-stage disease of other organs(Heart, Kidney) Cirrhosis Current use of Empagliflozin or Pioglitazone BMI>40, HbA1c>9 or <7 Glococorticoid use for at least 2 weeks during the last 2 months Pregnancy and lactation Hypothyroidism

Intervention groups

1- Empagliflozin tablet 10 mg once daily 2- Pioglitazone tablet 15 mg once daily 3- Empagliflozin tablet 10 mg+ Pioglitazone tablet 15 mg once daily

Main outcome variables

Percentage of patients in each group who achieve meaningful decrease in fibrosis and steatosis after treatment (sonographic). Mean change in fatty liver grade in each group after treatment (sonographic). Mean change in APRI, FIB-4 index scores after treatment.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20230903059343N1**
Registration date: **2023-10-04, 1402/07/12**
Registration timing: **prospective**

Last update: **2023-10-04, 1402/07/12**
Update count: **0**

Registration date

2023-10-04, 1402/07/12

Registrant information

Name

Erfan Rezaeisafa

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

2023-10-16, 1402/07/24

Expected recruitment end date

2024-01-14, 1402/10/24

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Comparing the effect of Empagliflozin, Pioglitazone and their combination, on sonographic and biochemical features of non-alcoholic fatty liver disease in diabetic patients

Public title

Comparing the effect of Empagliflozin, Pioglitazone and their combination, on the course of non-alcoholic fatty liver disease in diabetic patients

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

All patients with type 2 diabetes phenotype and fatty liver disease

Exclusion criteria:

History of alcohol ingestion Cirrhosis Heart failure, NYHA class III or IV Chronic kidney disease with GFR<45 ml/min Other chronic liver diseases including viral or autoimmune hepatitis Current use of Empagliflozine or Pioglitazone Use of known causative drugs for fatty liver including NSAIDs, Tamoxifen, Amiodarone and Valproate Use of antioxidant agents during the past 3 months, including Vitamin C, Zinc or Selenium-containing supplements. HbA1c less than 7 or more than 9 percent Type 1 diabetes or diabetes due to a specific secondary cause Pregnancy or Lactation Active cancer during the last two years Cardiovascular events during the last 3 months History of hypothyroidism Wilson's disease BMI>40 kg/m2 History of biliary obstruction Glucocorticoid use for 2 weeks during the last 2 months

Age

From **20 years** old to **65 years** old

Gender

Both

Phase

2-3

Groups that have been masked

No information

Sample size

Target sample size: **120**

Randomization (investigator's opinion)

Randomized

Randomization description

The patients will not be aware of the pattern of drug allocation for other patients. The patients will be visited by the physician, then go to one of the collaborators of the study to recieve their drugs. The collaborator will have no role in the treatment of the patients or analysis of the data. Each patient is placed in one of the groups based on the "permutation randomization block" method and recieve the corresponding drug box. In this study, the "permutation randomization block" method will be used for randomization with 6-ply blocks. In each block, each of the the following letters will be written on three cards: letter "E" (Empagloflozin), letter "P" (Pioglitazone) and letter "D" (Dual). The randomized 6-letter blocks will be PDPEED،DPDPEE ، EDPDPE، EEDPDP، PEEDPD، PPDPDEE،EDPPED ،PDPEPDE ،PDPEDE ، DPEEPD، PDEEPD،DPPEED ، PDEPDE، PPDDEE،DPEDEP ، DEPEPD ، DPPEDE، EPPDPDE، EPDPEPD، DEPDPEP. For example, the random allocation in the PDPEED block will be: The first patient allocated to D, the second to E, the third to E, the fourth to P, the fifth to D, and the sixth patient allocated to P.

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research ethics committee of Arak University of Medical Sciences

Street address

Arak University of Medical Sciences, Arak

City

Arak

Province

Markazi

Postal code

3848176341

Approval date

2023-07-04, 1402/04/13

Ethics committee reference number

IR.ARAKMU.REC.1402.112

Health conditions studied

1

Description of health condition studied

Non-alcoholic fatty liver disease

ICD-10 code

K76.0

ICD-10 code description

Fatty (change of) liver, not elsewhere classified

Primary outcomes

1

Description

The proportion of patients in Empagliflozin treatment group who achieve meaningful (at least one grade)

decrease in sonographic grade of their fatty liver disease.

Timepoint

At the start of the study, then 6 months later

Method of measurement

Sonography equipment

2

Description

The proportion of patients in Pioglitazone treatment group who achieve meaningful (at least one grade) decrease in sonographic grade of their fatty liver disease.

Timepoint

At the start of the study, then 6 months later

Method of measurement

Sonography equipment

3

Description

The proportion of patients in Empagliflozin plus Pioglitazone treatment group who achieve meaningful (at least one grade) decrease in sonographic grade of their fatty liver disease.

Timepoint

At the start of the study, then 6 months later

Method of measurement

Sonography equipment

4

Description

The mean change in sonographic grade in Empagliflozin group

Timepoint

At the start of the study, then 6 months later

Method of measurement

Sonography equipment

5

Description

The mean change in sonographic grade in Pioglitazone group

Timepoint

At the start of the study, then 6 months later

Method of measurement

Sonography equipment

6

Description

The mean change in sonographic grade in Empagliflozin plus Pioglitazone group

Timepoint

At the start of the study, then 6 months later

Method of measurement

Sonography equipment

7

Description

The mean change of APRI (AST to Platelet Ratio Index) score in Empagliflozin group

Timepoint

At the start of the study, then 6 months later

Method of measurement

Specific laboratory kit for Aspartate aminotransferase and Platelets, then using APRI formula

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Description

The mean change of APRI (AST to Platelet Ratio Index) score in Pioglitazone group

Timepoint

At the start of the study, then 6 months later

Method of measurement

Specific laboratory kit for Aspartate aminotransferase and Platelets, then using APRI formula

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Description

The mean change of APRI (AST to Platelet Ratio Index) score in Empagliflozin plus Pioglitazone group

Timepoint

At the start of the study, then 6 months later

Method of measurement

Specific laboratory kit for Aspartate aminotransferase and Platelets, then using APRI formula

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Description

The mean change in FIB-4 score in Empagliflozin group

Timepoint

At the start of the study, then 6 months later

Method of measurement

Specific laboratory kit for Aspartate aminotransferase and Platelets, then using FIB-4 formula

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Description

The mean change of FIB-4 score in Pioglitazone group

Timepoint

At the start of the study, then 6 months later

Method of measurement

Specific laboratory kit for Aspartate aminotransferase and Platelets, then using FIB-4 formula

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Description

The mean change of FIB-4 score in Empagliflozin plus Pioglitazone group

Timepoint

At the start of the study, then 6 months later

Method of measurement

Specific laboratory kit for Aspartate aminotransferase and Platelets, then using FIB-4 formula

Secondary outcomes

empty

Intervention groups

1

Description
Intervention group: Recipients of Empagliflozin 10mg daily for 6 months.
Category
Treatment - Drugs

2

Description
Intervention group: Recipients of Pioglitazone 15 mg daily for 6 months.
Category
Treatment - Drugs

3

Description
Intervention group: Recipients of Empagliflozin 10 mg+ Pioglitazone 15 mg daily for 6 months.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Amiralmomenin clinic
Full name of responsible person
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Sponsors / Funding sources

1

Sponsor
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Full name of responsible person
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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
Arak University of Medical Sciences
Proportion provided by this source
100
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

Person responsible for general inquiries

Contact
Name of organization / entity
Arak University of Medical Sciences
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Position
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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