

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 sonographer/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 Glucocorticoid 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

Country

Iran (Islamic Republic of)

Phone

+98 86 3276 7803

Email address

sorbsorbian@gmail.com

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 receive 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 receive 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" (Empagliflozin), letter "P" (Pioglitazone) and letter "D" (Dual). The randomized 6-letter blocks will be PDPEED,DPDPPEE , EDPDPE, EEDPDP, PEEDPD, PPDPEEE,EDPPED ,PDPEPDE ,PDPEDE , DPEEPD, PDEEPD,DPPEED , PDEPDE, PPDDEE,DPDEEP , DEPEPD , DPPEDE, EPPDPDE, EPDPEDP, 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

8

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

9

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

10

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

11

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

12

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

Dr. Hamidreza Norouzi

Street address

Amiralmomenin hospital, Sardasht, Arak

City

Arak

Province

Markazi

Postal code

3848176941

Phone

+98 86 3836 0000

Email

it-amiralmomenin@arakmu.ac.ir

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Arak University of Medical Sciences

Full name of responsible person

Dr Davoud Hekmat Pou

Street address

Arak University of Medical Sciences, Sardasht, Arak

City

Arak

Province

Markazi

Postal code

3848176341

Phone

+98 86 3417 3639

Email

research@arakmu.ac.ir

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

Full name of responsible person

Dr Erfan Rezaeisafa

Position

Resident

Latest degree

Medical doctor

Other areas of specialty/work

Internal Medicine

Street address

Arak University of Medical Sciences, Sardasht, Arak

City

Arak

Province

Markazi

Postal code

3848176341

Phone

+98 86 3417 3639

Email

Sorbsorbian@gmail.com

Person responsible for scientific inquiries

Contact

Name of organization / entity

Arak University of Medical Sciences

Full name of responsible person

Dr Erfan Rezaeisafa

Position

Resident

Latest degree

Medical doctor

Other areas of specialty/work

Internal Medicine

Street address

Arak University of Medical Sciences, Sardasht, Arak

City

Arak

Province

Markazi

Postal code

3848176341

Phone

+98 86 3417 3639

Email

Sorbsorbian@gmail.com

Arak University of Medical Sciences, Sardasht, Arak

City

Arak

Province

Markazi

Postal code

3848176341

Phone

+98 86 3417 3639

Email

Sorbsorbian@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

Person responsible for updating data**Contact****Name of organization / entity**

Arak University of Medical Sciences

Full name of responsible person

Dr Erfan Rezaeisafa

Position

Resident

Latest degree

Medical doctor

Other areas of specialty/work

Internal Medicine

Street address